



# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Shanghai, China

May 12-16, 2013

## Final Program





## Welcome from the chair

Welcome to the **2013 International Society for Therapeutic Ultrasound Symposium** at the Regal International East Asia Hotel in Shanghai, China on May 12-15, 2013.

A broad range of topics will be covered at ISTU 2013 including Modeling and Physics, Bioeffects of ultrasound and thermal therapy, Standards and Safety, Animal Models & Systems, Transducers and Devices, Treatment Planning and Control, Non-Invasive Monitoring and Assessment, Nanotechnology & microbubbles, Therapy System Development, Drug and Biotherapeutics Delivery(BBB), Neuromodulation/Ablation of Brain, Sonothrombolysis, Ultrasound Thermal Therapies, Ultrasound Non-thermal Therapies, Novel Therapeutic Systems and Strategies, Clinical Studies ect.

Esteemed experts from around the world have accepted our invitation to lecture on some of the most exciting developments taking place in therapeutic ultrasound. Oral sessions will be organized into two parallel tracks along with special plenary sessions for all participants.

We look forward to greeting you at the Monday reception and hope that everyone will join us for a Chinese Dinner at the Regal International East Asia Hotel.

We sincerely thank our sponsors and exhibitors without which conference would not be possible. See you soon in Shanghai!



Yazhu Chen

### Conference Chair

Prof. Yazhu Chen  
Biomedical Instrument Institute  
School of Biomedical Engineering  
Shanghai Jiao Tong University  
Room 123, No.3 Teaching Building(Med-X Institute),  
No.1954 Huashan Road, Xuhui District, Shanghai, China 200030.

### Cochair

Prof. Zhibiao Wang

### Executive Chair

Prof. Lisa Xuemin Xu



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# Program Committee

## Chair

**Brian Fowlkes**

## Cochair

**Guofeng Shen**

## Members

**Alfred Yu**

**Arik Hanenel**

**Beat Werner**

**Brian Fowlkes**

**Chris Diederich**

**Chrit Moonen**

**Cyril Lafon**

**Dennis Parker**

**Emad Ebbini**

**Feng Wu**

**Guofeng Shen**

**Jean Francois Aubrey**

**Joo Ha Hwang**

**Kim Butts Pauly**

**Nathan McDannold**

**Shunmugavelu Sokka**

**Stephen Meairs**

**Vera Khoklova**

**Wen-Shiang Chen**

**Yoichiro Matsumoto**

**Yufeng Zhou**

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## Local Committee

### Conference Chair

Yazhu Chen

### Conference Cochair

Zhibiao Wang

### Conference Executive Chair

Lisa Xuemin Xu

### Members

Guofeng Shen

Xunbin Wei

Yufeng Zhou

Weihai Yin

Siping Chen

Jianguo Li

Zhigang Wang

Xiaomeng Ma

Mingxi Wan

Bing Hu

Hairong Zheng

Weijun Peng

Zhimin Shao

Wei Guo

Xiaozhou Liu

Zheng Liu

jingfeng Bai

Bailin Gu

Guoxin Ren

Su Zhang

Gang Pan

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## Invited Speakers

**Yazhu Chen, Guofeng Shen** **13th May 09:00**

**Keynote:Therapeutic Ultrasound Development in China**

**Alfred C.H. Yu** **13th May 10:00**

**Invited Talk1:Sonoporation**

**Jongbum Seo** **13th May 14:12**

**Invited Talk2:Ultrasound-mediated drug delivery**

**Hao-Li Liu** **13th May 15:40**

**Invited Talk3:Ultrasound drug delivery through brain blood barrier**

**Yufeng Zhou** **13th May 16:21**

**Invited Talk4: Variation of bubble cavitation and temperature**

**Joo Ha Hwang** **14th May 08:30**

**Invited Talk5:Animal models for pre-clinical HIFU research**

**Arik Hananel** **14th May 10:30**

**Invited Talk6:Advances in MRg Brain Therapies**

**Young-Sun Kim** **14th May 13:00**

**Invited Talk7:HIFU in clinical application**

**Mathieu Pernot** **14th May 14:00**

**Invited Talk8:Monitoring of ultrasonic cardiac therapy using ultrafast imaging**

**Dennis Parker** **15th May 08:15**

**Invited Talk9:HAS (Hybrid Angular Spectral modeling) for transcranial beamforming**

**Cyril Lafon** **15th May 10:30**

**Invited Talk10: New devices and recent technology advances elevation during acculysis**

**Lawrence A. Crum** **15th May 13:50**

**Invited Talk11:Does twinkling result from stabilized microbubbles**

**Gail ter Haar** **15th May 15:10**

**Fry Lecture**



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## Committees

### **Fry Award**

Gail ter Haar, K. Hynynen, S. Umemura

### **Nominations/Election**

Chris Diederich, Brian Fowlkes, Kim Butts Pauly

### **Publications**

Guofeng Shen, Emad Ebbini, Jean-Francois Aubry

### **Sponsors/Exhibits**

Guofeng Shen, Yufeng Zhou, Jooha Hwang, Jean-Francois Aubry

### **Standards**

Mike Sekins, Vera Khokhlova, Gail ter Haar

### **Student Awards**

Jean-Francois Aubry, Yufeng Zhou, Kim Butts Pauly, Gail ter Haar

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## Program Overview





## Sunday, May 12

8:15-22:15 Registration

18:30-20:00 Welcome Cocktail Party

## Monday, May 13

Auditorium

Parallel sessions

08:30 Welcome Address

09:00 Key Note

09:40 Coffee Break

10:00 Invited Talk1 (**session 1A**)

10:24 Modeling and Physics  
(**Session 1A**)

12:00 Buffet Lunch

12:00 Buffet Lunch

13:00 Modeling and Physics  
(**Session 1B**)

13:00 Treatment Planning  
and Control (**Session 4A**)

13:24 Therapy Systems Developments  
(**Session 2**)

14:12 Invited Talk2 (**Session 2**)

14:30 Novel Systems and Devices  
(**Session 4B**)

14:36 Drug and Biotherapeutics  
Delivery (**Session 3**)

15:24 Coffee Break

15:30 Coffee Break

15:40 Invited Talk3 (**Session 3**)

15:45 Novel Systems and Devices  
(**Session 4B**)

16:04 Drug and Biotherapeutics  
Delivery (**Session 3**)

16:21 Invited Talk 4 (**Session 4B**)

18:30 RECEPTION

18:30 RECEPTION





## Tuesday, May 14

Auditorium	Parallel sessions
08:30 Invited Talk 5 ( <b>Session 5</b> )	8:30 Brain and Clinical Studies ( <b>Session 7</b> )
08:54 Fundamentals of Ultrasound Therapy ( <b>Session 5</b> )	
10:00 Coffee Break	10:00 Coffee Break
10:30 Fundamentals of Ultrasound Therapy ( <b>Session 5</b> )	10:30 Invited Talk6 ( <b>Session 7</b> )
	10:54 Brain and Clinical Studies ( <b>Session 7</b> )
12:00 Lunch Buffet	12:00 Lunch Buffet
13:00 Invited Talk 7 (Session 6)	<b>13:00</b> Non-Invasive Monitoring and Assessment ( <b>Session 8</b> )
13:24 Ultrasound Thermal Therapies ( <b>Session 6</b> )	
	14:00 Invited Talk8 ( <b>Session 8</b> )
14:30 Coffee Break	14:30 Coffee Break
15:00 Poster Session	15:00 Poster Session



## Wednesday, May 15

Auditorium	Parallel sessions
08:15 Invited Talk9 ( <b>Session 9</b> )	08:15 Ultrasound Thermal Therapies ( <b>Session 11</b> )
08:39 Non-Invasive Monitoring and Assessment ( <b>Session 9</b> )	
10:00 Coffee Break	10:00 Coffee Break
10:30 Non-Invasive Monitoring and Assessment ( <b>Session 9</b> )	10:30 Invited Talk10 ( <b>Session 12A</b> )
	10:54 Nanotechnology & Microbubbles ( <b>Session 12A</b> )
12:00 Lunch Buffet	12:00 Lunch Buffet
13:00 Nanotechnology & Microbubbles ( <b>Session 12B</b> )	
13:50 Invited Talk11 ( <b>Session 10</b> )	
14:14 Ultrasound Non-Thermal Therapies ( <b>Session 10</b> )	
14:50 Coffee Break	
15:10 Closing Session	
15:10 Fry lecture	
16:00 Award	
16:30 Tours	
18:30 Closing Cocktail Party	



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**Thursday, May 16**

**Visit ZhouZhuang**

<b>Time</b>	<b>Schedule</b>
<b>9:00 ~11:00</b>	<b>Set out</b>
<b>11:00~12:00</b>	<b>Visiting time</b>
<b>12:00~13:00</b>	<b>Lunch</b>
<b>13:00~15:00</b>	<b>Visiting time</b>
<b>15:00~17:00</b>	<b>Get back</b>

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## Oral presentations





# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Monday – May 13, 2013

<b>Modeling and Physics</b>		<b>Session 1A</b>
<b>Emad Emad Ebbini, Brian Fowlkes</b>		<b>Room1</b>
<b>9:00</b>	<b>Key Note</b>	
<b>9:40</b>	<b>Coffee Break</b>	
<b>10:00</b>	<b>Invited Talk 1</b>	
<b>10:24</b>	<b>Models of microbubble dynamics in acoustic droplet vaporization</b> J.L. Bull <sup>1</sup> , A. Qamar <sup>1</sup> , Z.Z. Wong <sup>1</sup> , D. Li <sup>1</sup> , Ann Arbor <sup>2</sup> , MI J.B. Fowlkes <sup>2</sup> , Ann Arbor <sup>3</sup> , MI A. Qamar <sup>3</sup> , R. Samtaney <sup>3</sup> (1) Biomedical Engineering, University of Michigan, (2) Radiology, University of Michigan,(3) Division of Physical Sciences, KAUST, Thuwal, SAUDI ARABIA	
<b>10:36</b>	<b>Image-based numerical modeling of hifu-induced lesions</b> M.K. Almekkawy <sup>1</sup> , I.A. Shehata <sup>1</sup> , A. Haritonova <sup>1</sup> , J.R. Ballard <sup>1</sup> , A.J. Casper <sup>1</sup> , E.S. Ebbini <sup>1</sup> , I.A. Shehata <sup>2</sup> (1)Electrical Engineering, University of Minnesota, Minneapolis MN,(2) Medical School, Cairo University , Cairo, EGYPT	
<b>10:48</b>	<b>High intensity focused ultrasound in liver tumor therapy: image based computational model</b> M.A. Solovchuk <sup>1</sup> , T.W. Sheu <sup>1</sup> , M.A. Solovchuk <sup>2</sup> , T.W. Sheu <sup>2</sup> , Thiriet <sup>3</sup> , LJLL <sup>3</sup> (1)Center for Advanced Study in Theoretical Sciences, National Taiwan University, Taipei, TAIWAN, (2) Engineering Science and Ocean Engineering, National Taiwan University, Taipei, TAIWAN M,(3) University of Paris N 6, Paris, FRANCE	
<b>11:00</b>	<b>High-intensity focused ultrasound ablation is an effective and safe treatment for cirrhotic hypersplenism: A prospective case series of 28 patients</b> J. Zhu Chongqing Medical University, Chongqing 400016, China., Chongqing Medical University, Chongqing 400016, China., Chongqing Medical University, Chongqing , chongqing, CHINA	



<b>11:12</b>	<p><b>Full acoustic and thermal characterization of hifu field in the present of a ribcage model</b></p> <p><b>R. Cao<sup>1</sup>, N.M. Le<sup>1</sup>, Z. Huang<sup>1</sup>, G.Nabi<sup>2</sup></b></p> <p>(1)School of Engineering, Physics and Mathematics, University of Dundee, Dundee, UNITED KINGDOM, (2) Department of Urology, Ninewells hospital, Dundee, UNITED KINGDOM</p>
<b>11:24</b>	<p><b>A hybrid simulation tool for the simulation of volumetric acoustic fields</b></p> <p><b>M. de Greef<sup>1</sup>, L.W. Bartels<sup>1</sup>, C. Moonen<sup>1</sup>, M. Ries<sup>1</sup>, J. Koskela<sup>2</sup></b></p> <p>(1)Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS,(2) Philips Healthcare, Vantaa, FINLAND</p>
<b>11:36</b>	<p><b>Evaluation of an improved wave-vector-frequency-domain method for nonlinear wave modeling</b></p> <p><b>Y. Jing<sup>1</sup>, J. Cannata<sup>2</sup>, HistoSonics<sup>2</sup></b></p> <p>(1)Mechanical and Aerospace Engineering, North Carolina State University, Raleigh, NC ,(2) Ann Arbor, MI</p>
<b>11:48</b>	<p><b>Full wave acoustic and thermal modeling of transcranial focused ultrasound surgery in a detailed anatomical head model</b></p> <p><b>A.Kyriakou<sup>1</sup>, E. Neufeld<sup>1</sup>, N. Kuster<sup>1</sup>, A. Kyriakou<sup>2</sup>, N. Kuster<sup>2</sup>, B. Werner<sup>3</sup></b></p> <p>(1)IT'IS Foundation, Zurich, SWITZERLAND,(2)ETHZ, Zurich, SWITZERLAND, (3) MR-Research, Kinderspital, Zurich, SWITZERLAND</p>

<b>Modeling and Physics</b>		<b>Session 1B</b>
<b>Alfred C. H. Yu, Jongbum Seo</b>		<b>Room1</b>
<b>13:00</b>	<p><b>Phase-amplitude optimized intercostal firing: a method of reference for intercostal techniques</b></p> <p><b>M. de Greef, L.W. Bartels, C. Moonen, M. Ries</b></p> <p>Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS</p>	
<b>13:12</b>	<p><b>Hifu scattering by the ribs: constrained optimization with a complex surface impedance boundary condition</b></p> <p><b>P. Gelat<sup>1</sup>, P. Gelat<sup>2</sup>, N. Saffari<sup>2</sup>, G. ter Haar<sup>3</sup></b></p> <p>(1) Acoustics and Ionising Radiation Division, National Physical Laboratory, Teddington, UNITED KINGDOM,(2) Department of Mechanical Engineering, University College London, London, UNITED KINGDOM,(3) Joint Physics Department, Institute of Cancer Research, Sutton, UNITED KINGDOM</p>	



<b>Therapy System Development</b>		<b>Session 2</b>
<b>Jongbum Seo, Alfred C. H. Yu</b>		<b>Room1</b>
<b>13:24</b>	<p><b>Hardware-independent pre-interventional planning, simulation, and application of focused ultrasound therapy</b></p> <p><b>D. Demedts<sup>1</sup>, C. Schumann<sup>1</sup>, J. Georgii<sup>1</sup>, C. von Dresky<sup>1</sup>, T. Preusser<sup>1</sup>, T. Preusser<sup>2</sup></b></p> <p>(1) Institute for Medical Image Computing, Fraunhofer MEVIS, Bremen, Bremen, GERMANY, (2) School of Engineering and Science, Jacobs University, Bremen, Bremen, GERMANY</p>	
<b>13:36</b>	<p><b>FUS-compatible MR imaging coil for clinical brain applications</b></p> <p><b>M. Eames<sup>1</sup>, J.W. Snell<sup>1</sup>, A. Hananel<sup>1</sup>, M. Jones<sup>2</sup>, High Filed LLC<sup>2</sup>, E. Minalga<sup>3</sup>, R. Hadley<sup>3</sup>, J.W. Snell<sup>4</sup>, A. Hananel<sup>4</sup></b></p> <p>(1) Focused Ultrasound Foundation, CHARLOTTESVILLE, VA, (2) St. Paul, MN, (3) University of Utah, Salt Lake City, UT, (4) University of Virginia, CHARLOTTESVILLE, VA</p>	
<b>13:48</b>	<p><b>Compact Modular MR-Guided HIFU System for Treatment of Liver Cancer</b></p> <p><b>K.M. Sekins<sup>1</sup>, S. Brunke<sup>1</sup>, X. Zeng<sup>1</sup>, S. Barnes<sup>1</sup>, J. Hopple<sup>1</sup>, D. Liu<sup>1</sup>, S. Hsu<sup>1</sup>, C. Lee<sup>1</sup>, C. Maleke<sup>1</sup>, J. Nam<sup>1</sup>, J. Eaton<sup>1</sup>, K. Wong<sup>1</sup>, L. Petrusca<sup>2</sup>, M. Viallon<sup>2</sup>, S. Terraz<sup>2</sup>, C. Becker<sup>2</sup>, R. Salomir<sup>2</sup>, C. Lorenz<sup>3</sup>, K.J. Kirchberg<sup>4</sup>, S.M. Shea<sup>4</sup>, S. Patil<sup>4</sup>, J. Barbot<sup>4</sup>, T. Meng<sup>4</sup>, E. Rothgang<sup>5</sup>, J. Roland<sup>5</sup></b></p> <p>(1) Ultrasound Division, Siemens Medical Solutions USA, Issaquah, WA, (2) Service de Radiologie, Hôpitaux Universitaires de Genève, Geneva, SWITZERLAND, (3) Siemens Medical Solutions USA, Malvern, PA, (4) Imaging &amp; Computer Vision, Siemens Corporate Research, Princeton, NJ, (5) MRI Division, Siemens AG, Erlangen, GERMANY</p>	
<b>14:00</b>	<p><b>Modular 2D Therapeutic Arrays for a Compact MR-Guided HIFU System</b></p> <p><b>S. Barnes<sup>1</sup>, J. Hopple<sup>1</sup>, D. Liu<sup>1</sup>, P. Lyons<sup>1</sup>, J. Eaton<sup>1</sup>, K. Wong<sup>1</sup>, X. Zeng<sup>1</sup>, S. Brunke<sup>1</sup>, S. Hsu<sup>1</sup>, C. Lee<sup>1</sup>, C. Maleke<sup>1</sup>, M.K. Sekins<sup>1</sup>, T. Clary<sup>2</sup></b></p> <p>(1) Ultrasound Division, Siemens Medical Solutions USA, Issaquah, WA, (2) The Inception Group, Sammamish, WA</p>	
<b>14:12</b>	<b>Invited Talk 2</b>	



<b>Drug and Biotherapeutics Delivery</b>		<b>Session 3</b>
<b>Hao-Li Liu, Yufeng Zhou, Yun Jing</b>		<b>Room 1</b>
<b>14:36</b>	<p><b>Intra-cerebral diffusion of irinotecan and temozolomide after unfocused ultrasound-induced opening of the bbb in rabbits</b></p> <p>K. Beccaria<sup>1</sup>, M. Canney<sup>1</sup>, CarThera<sup>1</sup>, K. Beccaria<sup>2</sup>, A. Carpentier<sup>2</sup>, L. Goldwirt<sup>3</sup>, C. Fernandez<sup>3</sup>, J. Piquet<sup>4</sup>, A. Carpentier<sup>5</sup>, C. Lafon<sup>6</sup>, J. Chapelon<sup>6</sup>, C. Lafon<sup>7</sup>, J. Chapelon<sup>7</sup></p> <p>(1)Paris, FRANCE, (2)Neurosurgery Department, Pitie-Salpetriere Hospital, Paris, FRANCE,(3) Pharmacology Department, Pitie-Salpetriere Hospital, Paris, FRANCE, (4) Laboratory of Biosurgical Research, Universit� Paris Descartes, Sorbonne Paris Cite, Paris, FRANCE, (5) Sorbonne University, Paris 6 School of Medicine, Paris, FRANCE, (6) Inserm, U1032, LabTau, Lyon, FRANCE, (7) Lyon 1 University, Lyon, FRANCE</p>	
<b>14:48</b>	<p><b>A preclinical toxicological study of repeated bbb opening using an implantable ultrasound transducer in primates</b></p> <p>C. Horodyckid<sup>1</sup>, M. Canney<sup>1</sup>, A. Vignot<sup>1</sup>, CarThera<sup>1</sup>, C. Horodyckid<sup>2</sup>, A. Carpentier<sup>2</sup>, A. Uzcategui Pedroza<sup>3</sup>, C. Lafon<sup>3</sup>, J. Chapelon<sup>3</sup>, P. Merlet<sup>4</sup>, A. Carpentier<sup>4</sup>, C. Lafon<sup>5</sup>, J. Chapelon<sup>5</sup></p> <p>(1)Paris, FRANCE, (2) Neurosurgery Department, Pitie-Salpetriere Hospital, Paris, FRANCE, (3) Inserm, U1032, LabTau, Lyon, FRANCE, (4) CEA, IR4M, SHFJ, Orsay, FRANCE, (5) Universit� Paris 6, UPMC, Paris, FRANCE, (5) University 1 Lyon, Lyon, FRANCE</p>	
<b>15:00</b>	<p><b>Focused ultrasound induced blood-brain barrier opening in macromolecule delivery</b></p> <p>S. Wang<sup>1</sup>, O.O. Olumolade<sup>1</sup>, E.E. Konofagou<sup>1</sup>, S. Osting<sup>2</sup>, C. Burger<sup>2</sup></p> <p>(1) Biomedical Engineering, Columbia University, New York, NY, (2) Neurology, University of Wisconsin Madison, Madison, WI</p>	
<b>15:12</b>	<p><b>Targeted drug delivery with focused ultrasound-induced blood-brain barrier opening using acoustically-activated nanodroplets</b></p> <p>C.C. Chen<sup>1</sup>, S. Wu<sup>1</sup>, O.O. Olumolade<sup>1</sup>, E.E. Konofagou<sup>1</sup>, E.E. Konofagou<sup>2</sup>, P.S. Sheeran<sup>3</sup>, P.A. Dayton<sup>3</sup></p> <p>(1) Biomedical Engineering, Columbia University, New York, NY, (2) Radiology, Columbia University, New York, NY, (3) Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University, Chapel Hill, NC</p>	
<b>15:24</b>	<b>Coffee Break</b>	
<b>15:40</b>	<b>Invited Talk 3</b>	
<b>16:04</b>	<p><b>Delivery of molecules of various sizes through blood brain barrier opening induced by long and short ultrasound pulses</b></p> <p>H. Chen<sup>1</sup>, A. Srivastava<sup>1</sup>, T. Sun<sup>1</sup>, E. Konofagou<sup>1</sup>, E. Konofagou<sup>2</sup></p> <p>(1) Department of Biomedical Engineering, Columbia University, New York, NY,(2) Department of Radiology, Columbia University, New York, NY</p>	





<b>16:16</b>	<p><b>Ultrasound-mediated gene therapy in swine livers using single element, multi-lensed high intensity ultrasound transducers</b></p> <p><b>M.L. Noble<sup>1</sup>, S. Song<sup>1</sup>, R.R. Sun<sup>1</sup>, L. Fan<sup>1</sup>, C.H. Miao<sup>1</sup>, K.P. Morrison<sup>2</sup>, G.W. Keilman<sup>2</sup>, M. Paun<sup>3</sup>, K.R. Loeb<sup>4</sup>, C.H. Miao<sup>5</sup></b></p> <p>(1) Seattle Children's Research Institute, Seattle, WA, (2) Sonic Concepts Inc., Bothell, WA, (3) Applied Physics Laboratory, University of Washington, Seattle, WA, (4) Fred Hutchinson Cancer Research Center, Seattle, WA, (5) Dept. of Pediatrics, University of Washington, Seattle, WA</p>
<b>16:28</b>	<p><b>MR-guided focused ultrasound induced hyperthermia for enhancing drug delivery in a pancreatic cancer mouse model</b></p> <p><b>N. Farr<sup>1</sup>, J. Hwang<sup>1</sup>, Y. Wang<sup>2</sup>, F. Starr<sup>2</sup>, S. D'Andrea<sup>3</sup>, J. Hwang<sup>3</sup>, D. Lee<sup>4</sup></b></p> <p>(1) Bioengineering, University of Washington, Seattle, WA, (2) Applied Physics Laboratory, University of Washington, Seattle, WA, (3) Department of Medicine, University of Washington, Seattle, WA, (4) Department of Radiology, University of Washington, Seattle, WA</p>
<b>16:40</b>	<p><b>Low intensity continuous ultrasound enhances drug delivery of zoledronic acid in a breast cancer bone metastases mouse model</b></p> <p><b>S. Tardoski<sup>1</sup>, J. Ngo<sup>1</sup>, D. Melodelima<sup>1</sup>, S. Tardoski<sup>2</sup>, P. Clazardin<sup>2</sup></b></p> <p>(1) LabTau, INSERM U1032, Lyon, 69003, FRANCE, (2) Lyos, INSERM U1033, Lyon, 69008, FRANCE</p>
<b>16:52</b>	<p><b>Low intensity focused ultrasound triggered local drug delivery from liposome-loaded microbubbles</b></p> <p><b>Y. Zong<sup>1</sup>, N. Zheng<sup>1</sup>, S. Xu<sup>1</sup>, M. Wan<sup>1</sup>, H. Su<sup>2</sup>, J. Hu<sup>2</sup></b></p> <p>(1)Department of Biomedical Engineering, Xian Jiaotong Universtiy, Xian, Shaan Xi, CHINA,(2) Department of Ultrasound, Xijing Hospital, Fourth Military Medical University, Xian, Shaan Xi, CHINA</p>
<b>17:04</b>	<p><b>In vivo rna interference using unseeded inertial cavitation and passive liposomal targeting</b></p> <p><b>R.A. Fowler<sup>1</sup>, J. Mestas<sup>1</sup>, C. Lafon<sup>1</sup>, K. Chettab<sup>2</sup>, D. Poloni<sup>2</sup>, C. Dumontet<sup>2</sup>, D. Tobin<sup>3</sup>, E. Nilssen<sup>3</sup></b></p> <p>(1) Inserm U1032 LabTAU, University of Lyon, Lyon, FRANCE, (2) Inserm U1052, CRCL, University of Lyon, Lyon, FRANCE, (3) Epitarget AS, Oslo, NORWAY</p>
<b>17:16</b>	<p><b>Potentiating the antitumor effects of taxanes with the antivasular effects of ultrasound stimulated microbubbles</b></p> <p><b>M. Todorova<sup>1</sup>, K. Hynynen<sup>1</sup>, D. Goertz<sup>1</sup>, M. Todorova<sup>2</sup>, V. Agache<sup>2</sup>, B. Chen<sup>2</sup>, T. Ibrahimli<sup>2</sup>, K. Hynynen<sup>2</sup>, D. Goertz<sup>2</sup>, R. Karshafian<sup>3</sup></b></p> <p>(1) Medical Biophysics, University of Toronto, Toronto, Ontario, CANADA,(2) Sunnybrook Research Institute, Toronto, Ontario, CANADA,(3) Ryerson University, Toronto, Ontario, CANADA</p>



<b>Treatment Planning and Control</b>		<b>Session 4A</b>
<b>Vera Khokhlova, Emad Ebbini</b>		<b>Room2</b>
<b>13:00</b>	<p><b>Robust detection and control of bubble activity with a single element, dual-mode transducer</b></p> <p><b>A.J. Casper<sup>1</sup>, E.S. Ebbini<sup>2</sup></b></p> <p>(1) Biomedical Engineering, University of Minnesota, Minneapolis, MN, (2) Electrical Engineering, University of Minnesota, Minneapolis, MN</p>	
<b>13:12</b>	<p><b>Patient specific modelling &amp; simulation of fus in moving organs: the vph project fusimo</b></p> <p><b>T. Preusser<sup>1</sup>, M. Guenther<sup>1</sup>, T. Preusser<sup>2</sup>, M. Bezzi<sup>3</sup>, J. Dankelman<sup>4</sup>, J. Jenne<sup>5</sup>, T. LangÃ,<sup>6</sup>, Y. Levy<sup>7</sup>, M. Mueller<sup>8</sup>, IG. Sat<sup>9</sup>, C. Tanner<sup>10</sup>, C. Tiu<sup>11</sup>, A. Melzer<sup>12</sup></b></p> <p>(1) Fraunhofer MEVIS, Bremen, GERMANY, (2) Jacobs University, Bremen, GERMANY, (3) Universita Degli Studi Di Roma La Sapienza, Rome, ITALY, (4) Technische Universiteit Delft, Delft, NETHERLANDS, (5) mediri GmbH Heidelberg, GERMANY, (6) Stiftelsen SINTEF, Trondheim, NORWAY, (7) InSightec Ltd, Tirat Carmel, ISRAEL, (8) BSmm spol s.r.o., Brno, CZECH REPUBLIC, (9) GE Medical Systems, Haifa, ISRAEL,(10) Swiss Federal Institute of Technology Zurich, Zurich, SWITZERLAND, (11) SMIT-Medis Foundation, Campina, ROMANIA, (12) IMSaT University Dundee, Dundee, UNITED KINGDOM</p>	
<b>13:24</b>	<p><b>Numerical estimation of hifu focal error to breast cancer treatment</b></p> <p><b>R. Narumi<sup>1</sup>, T. Azuma<sup>1</sup>, A. Sasaki<sup>1</sup>, S. Takagi<sup>1</sup>, Y. Matsumoto<sup>1</sup>, K. Okita<sup>2</sup>, K. Yoshinaka<sup>3</sup>, K. Okita<sup>4</sup>, S. Takagi<sup>4</sup>, J. Shidooka<sup>5</sup>, H. Furusawa<sup>5</sup></b></p> <p>(1)Department of Bioengineering, The University of Tokyo, Tokyo, JAPAN,(2) College of Industrial Technology, The Nihon University, Tokyo, JAPAN,(3) Human Technology Research Institute, Advanced Industrial Science and Technology, Tsukuba, JAPAN,(4) Organ and Body Scale Team, RIKEN, Wako, JAPAN,(5) Brestopia Namba Hospital, Miyazaki, JAPAN</p>	



<b>Treatment Planning and Control</b>		<b>Session 4A</b>
<b>Vera Khokhlova, Emad Ebbini</b>		<b>Room2</b>
<b>13:36</b>	<p><b>A realistic 2d model for ultrasound guided focused ultrasound surgery of kidney tumor</b></p> <p>X. Xiao<sup>1</sup>, T. Jiang<sup>1</sup>, Z. Huang<sup>1</sup>, G. Corner<sup>2</sup>, A. Melzer<sup>3</sup>,</p> <p>(1) School of Engineering, University of Dundee, Dundee, UNITED KINGDOM,(2) Medical Physics, Ninewells Hospital and Medical School, Dundee, UNITED KINGDOM,(3) Institute of Medical and Technology, University of Dundee, Dundee, UNITED KINGDOM</p>	
<b>13:48</b>	<p><b>Hifu beam localization using harmonic motion imaging</b></p> <p>Y. Han<sup>1</sup>, G.Y. Hou<sup>1</sup>, S. Wang<sup>1</sup>, E. Konofagou<sup>1</sup>, E. Konofagou<sup>2</sup></p> <p>(1) Biomedical Engineering, Columbia University, NewYork, NY, (2) Radiology, Columbia University, NewYork, NY</p>	
<b>14:00</b>	<p><b>A dosing planning method for renal denervation using high intensity focused ultrasound</b></p> <p>M. Gertner<sup>1</sup>, F.P. Curra<sup>1</sup>, S. Jing<sup>1</sup>, A. Sabet<sup>1</sup>, D. Perozek<sup>1</sup>, J. Zhang<sup>1</sup>, F.P. Curra<sup>2</sup></p> <p>(1) Kona Medical, Inc., Bellevue, WA, (2) Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA</p>	
<b>14:12</b>	<p><b>Feasibility of large volume tumor ablation using multiple-mode strategy with fast scanning method: a numerical study</b></p> <p>S. Qiao, G. Shen, Y. Yu, Z. Su, X. Ji, H. Wu, Y. Chen</p> <p>Biomedical Instrument Institue, Shanghai Jiao Tong University, Shanghai, CHINA</p>	

<b>Novel Therapeutic Systems and Strategies</b>		<b>Session 4B</b>
<b>Emad Ebbini, Vera Khoklova</b>		<b>Room2</b>
<b>14:30</b>	<p><b>Passive microlesion detection and mapping for treatment of hypertrophic cardiomyopathy</b></p> <p>Y.I. Zhu, D.L. Miller, C. Dou, O.D. Kripfgans</p> <p>Department of Radiology, University of Michigan, Ann Arbor, MI</p>	
<b>14:42</b>	<p><b>A unique pressure field using a high intensity ultrasound transducer with a multi-lens structure as a faceplate</b></p> <p>K.P. Morrison<sup>1</sup>, G.W. Keilman<sup>1</sup>, M.L. Noble<sup>2</sup>, C.H. Miao<sup>2</sup></p> <p>(1) Sonic Concepts, Inc., Bothell, WA,(2)Seattle Children's Research Institute, Seattle, WA</p>	
<b>14:54</b>	<p><b>Extracorporeal high intensity focused ultrasound system for renal denervation</b></p> <p>M. Gertner, D. Perozek</p> <p>J. Zhang, Kona Medical, Inc., Bellevue, WA</p>	



<b>15:06</b>	<p><b>Stimulated release of nucleic acid cancer biomarkers by hifu: a study in a rat prostate cancer model</b></p> <p><b>T. Khokhlova<sup>1</sup>, J.R. Chevillet<sup>2</sup>, M. Tewari<sup>2</sup>, T. Khokhlova<sup>3</sup>, Y. Wang<sup>3</sup>, J. Hwang<sup>3</sup></b></p> <p>(1)J. Hwang, Medicine, University of Washington, Seattle, WA,(2) Human Biology, Fred Hutchinson Cancer Research Center, Seattle, WA,(3) Applied Physics Laboratory, University of Washington, Seattle, WA</p>
<b>15:30</b>	<b>Coffee Break</b>
<b>15:45</b>	<p><b>Evaluation of Pulsed Focused Ultrasound Mediated Nanodroplet -Encapsulated Chemo-therapeutic Agent for Treatment of Prostate Cancer</b></p> <p><b>L. Chen<sup>1</sup>, X. Chen<sup>1</sup>, R. Gupta<sup>1</sup>, D. Cvetkovic<sup>1</sup>, B. Wang<sup>1</sup>, N. Rapoport<sup>1</sup>, C. Ma<sup>1</sup>, N. Rapoport<sup>2</sup></b></p> <p>(1) Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA, (2) Department of Bioengineering, University of Utah, Utah, UT</p>
<b>15:57</b>	<p><b>In-vivo tissue emulsification using boiling histotripsy hifu exposures</b></p> <p><b>V.A. Khokhlova<sup>1</sup>, J.C. Simon<sup>1</sup>, T.D. Khokhlova<sup>1</sup>, Y. Wang<sup>1</sup>, M. Paun<sup>1</sup>, F.L. Starr<sup>1</sup>, O. Sapozhnikov<sup>1</sup>, L.A. Crum<sup>1</sup>, M. Bailey<sup>1</sup>, T.D. Khokhlova<sup>2</sup>, V.A. Khokhlova<sup>3</sup>, O. Sapozhnikov<sup>3</sup></b></p> <p>(1) Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA,(2) Department of Gastroenterology, University of Washington, Seattle, WA,(3) Department of Acoustics, Physics Faculty, Moscow State University, Moscow, RUSSIAN FEDERATION</p>

<b>Transducers and Devices</b>		<b>Session 4B</b>
<b>Yufeng Zhou, Guofeng Shen, P. Zhong</b>		<b>Room2</b>
<b>16:09</b>	<p><b>Compact power driving device for high intensity focused ultrasound</b></p> <p><b>S. Jun, T. Kim, K. Kang, K. Son</b></p> <p>Alpinion Medical Systems, Alpinion Medical Systems, Seoul, KOREA, REPUBLIC OF</p>	
<b>16:21</b>	<b>Invited Talk 4</b>	
<b>16:45</b>	<p><b>Production and Performance Evaluation of a Semi-Concave Multi-Channel HIFU Transducer</b></p> <p><b>M. Kim, D. Kim, K. Kang, K. Son</b></p> <p>ALPINION MEDICAL SYSTEMS, Seoul, KOREA, REPUBLIC OF</p>	



**16:57 The comparison of acoustic field characterizations between spherical phased arrays with spiral and random layouts for focused ultrasound surgery: a simulation study**

**X. Ji<sup>1</sup>, Y. Yu<sup>1</sup>, G. Shen<sup>1</sup>, S. Qiao<sup>1</sup>, J. Bai<sup>1</sup>, H. Wu<sup>1</sup>, Z. Su<sup>1</sup>, Y. Chen<sup>1</sup>, Y. Yu<sup>2</sup>**

(1)School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA,(2) School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA

**17:09 A new FPGA-driven P-HIFU system with harmonic cancellation technique**

**H. Wu, G. Shen, Y. Yu, S. Qiao, Z. Su, X. Ji, Y. Chen**

School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA

**17:21 A heuristic model of stone comminution in shock wave lithotripsy**

**N. Smith, P. Zhong**

Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC



# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Tuesday – May 14, 2013

<b>Animal Models &amp; Systems</b>		<b>Session 5</b>
<b>Joo Ha Hwang, J.B. Fowlkes</b>		<b>Room1</b>
<b>8:30</b>	<b>Invited Talk 5</b>	
<b>8:54</b>	<b>Non-thermal High-intensity Focused Ultrasound for Breast Cancer Therapy</b> C. Ma, X. Chen, D. Cvetkovic, L. Chen Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA	
<b>9:06</b>	<b>Sonographic features of transplantable VX2 bone tumor model in rabbit</b> L. Chen, L. Jiang, B. Hu Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, Shanghai, CHINA	

<b>Bioeffects of therapeutic ultrasound</b>		<b>Session 5</b>
<b>Joo Ha Hwang, J.B. Fowlkes</b>		<b>Room1</b>
<b>9:18</b>	<b>The bioeffects of focused ultrasound on proliferation of endothelial cells for the treatment of lichen sclerosus</b> Y. Liu, L. Chen, Z. Wang, The College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA	
<b>9:30</b>	<b>Real-time imaging of cellular dynamics during low-intensity pulsed ultrasound exposure</b> Y. Hu <sup>1</sup> , A.C. Yu <sup>1</sup> , J.M. Wan <sup>2</sup> (1) Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG, (2) School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG	
<b>9:42</b>	<b>Assessment of high-intensity focused ultrasound (hifu) lesion using combined method of sonoelastography and numerical bio-heat transfer modelling</b> N.M. Le <sup>1</sup> , R. Cao <sup>1</sup> , Z. Huang <sup>1</sup> , G. Nabi <sup>2</sup> (1)Mechanical Engineering, University of Dundee, DUNDEE, Angus, UNITED KINGDOM, (2) Ninewells Medical School, University of Dundee, DUNDEE, Angus, UNITED KINGDOM	
<b>10:00</b>	<b>Coffee Break</b>	



<b>10:30</b>	<p><b>Low intensity ultrasound induces apoptosis via v<sub>dac</sub> channel on mitochondrial membrane: target for regulating cancer therapy or not?</b></p> <p><b>Y. Feng, M. Wan</b></p> <p>Department of Biomedical Engineering, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, CHINA</p>
<b>10:42</b>	<p><b>Acoustic Droplet Vaporization Enhanced High Intensity Focused Ultrasound Treatment of Tumor</b></p> <p><b>M. Zhu<sup>1</sup>, A. Zhang<sup>1</sup>, L. Xu<sup>1</sup>, L. Jiang<sup>2</sup>, M.L. Fabiilli<sup>3</sup>, J.B. Fowlkes<sup>3</sup></b></p> <p>(1) Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA, (2) Ultrasound in Medicine, Sixth Hospital, Shanghai Jiao Tong University, Shanghai, CHINA,(3) Radiology, University of Michigan Health System, MI</p>
<b>10:54</b>	<p><b>The different doses of SonoVue enhances in vivo goat liver ablation induced by high intensity focused ultrasound with different acoustic intensity:The shift of the location of coagulative necrosis</b></p> <p><b>L. Faqi, Y. Liangbo, Z. Ting, W. Qi, L. Chongyan, W. Yan, W. Zhibiao</b></p> <p>College of Biomedical Engineering,Chongqing medical university, State Key Laboratory of Ultrasound Engineering in Medicine Co-founded by Chongqing and MOST, Chongqing, Chongqing, CHINA</p>

<b>Standards and safety</b>		<b>Session 5</b>
<b>Joo Ha Hwang, J.B. Fowlkes</b>		<b>Room1</b>
<b>11:06</b>	<p><b>Quantitative measurement of highly focused ultrasound pressure field by optical phase contrast</b></p> <p><b>R. Miyasaka<sup>1</sup>, M. Syahid<sup>1</sup>, S. Yoshizawa<sup>1</sup>, S. Umemura<sup>1</sup>, S. Umemura<sup>2</sup></b></p> <p>(1) Electrical and Communication Engineering, Tohoku University, Sendai, JAPAN,(2) Biomedical Engineering, Tohoku University, Sendai, JAPAN</p>	
<b>11:18</b>	<p><b>Derivation of continuous wave mode output power values from burst mode measurements in high-intensity ultrasound applications</b></p> <p><b>J. Haller, V. Wilkens</b></p> <p>Physikalisch-Technische Bundesanstalt, Braunschweig, GERMANY</p>	
<b>11:30</b>	<p><b>An inverse method for estimation of the acoustic intensity in the focused ultrasound field</b></p> <p><b>Y. Yu<sup>1</sup>, G. Shen<sup>1</sup>, X. Ji<sup>1</sup>, S. Qiao<sup>1</sup>, H. Wu<sup>1</sup>, Z. Su<sup>1</sup>, Y. Chen<sup>1</sup>, Y. Yu<sup>2</sup></b></p> <p>(1)School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA, (2) School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA</p>	



<b>Ultrasound Thermal Therapies</b>		<b>Session 6</b>
<b>Young-Sun Kim, Yufeng Zhou, Guofeng Shen</b>		<b>Room1</b>
<b>13:00</b>	<b>Invited Talk 7</b>	
<b>13:24</b>	<p><b>High intensity focused ultrasound combined with neoadjuvant chemotherapy for breast cancer: A therapeutic effect study</b></p> <p>J. Liu, L. Gu</p> <p>Gynecology(ultrasound section), Shanghai Ninth People's Hospital Affiliated to Shanghai Jiaotong University, School of Medicine, Shanghai, Shanghai, CHINA</p>	
<b>13:36</b>	<p><b>Efficient generation of cavitation cloud in optically-transparent gel phantom by ultrasound exposure with negative-followed by positive-peak-pressure emphasized waves</b></p> <p>J. Yasuda<sup>1</sup>, A. Asai<sup>1</sup>, S. Yoshizawa<sup>1</sup>, S. Umemura<sup>2</sup></p> <p>(1) Department of Communication Engineering, Tohoku Univ., Sendai, Miyagi pref., JAPAN, (2) Department of Biomedical Engineering, Tohoku Univ., Sendai, Miyagi pref., JAPAN</p>	
<b>13:48</b>	<p><b>Multi-depth fractionated aesthetic ultrasound surgery</b></p> <p>M.H. Slayton<sup>1</sup>, S.M. Lyke<sup>1</sup>, P.G. Barthe<sup>1</sup>, P.G. Barthe<sup>2</sup></p> <p>(1)Guided Therapy Systems, LLC, Mesa, AZ, (2)Ardent Sound, Inc, Mesa, AZ</p>	
<b>14:00</b>	<p><b>Analysis of localized heat deposition and acoustic scattering of acoustic cavitation bubbles in tissue mimicking gel</b></p> <p>S. Yoshizawa<sup>1</sup>, A. Asai<sup>1</sup>, H. Okano<sup>1</sup>, T. Miyashita<sup>1</sup>, S. Umemura<sup>2</sup></p> <p>(1)Department of Communication Engineering, Tohoku University, Sendai, JAPAN,(2) Department of Biomedical Engineering, Tohoku University, Sendai, JAPAN</p>	
<b>14:30</b>	<b>Coffee Break</b>	
<b>15:00</b>	<b>Poster Session</b>	





<b>Brain</b>		<b>Session 7</b>
<b>Kim Butts Pauly, Arik Hananel</b>		<b>Room2</b>
<b>8:30</b>	<p><b>A cadaveric/phantom investigation of the transcranial treatment envelope for an mr-guided focused ultrasound system operating at 650 khz</b></p> <p>M. Khaled<sup>1</sup>, J. Snell<sup>1</sup>, J. Aubry<sup>1</sup>, A. Hananel<sup>1</sup>, W.J. Elias<sup>1</sup>, M. Eames<sup>2</sup>, J. Snell<sup>2</sup>, A. Hananel<sup>2</sup>, J. Aubry<sup>3</sup></p> <p>(1) Neurosurgery, University of Virginia, Charlottesville, VA, (2) Focused Ultrasound Foundation, Charlottesville, VA, (3) Institut Langevin, CNRS, Paris, FRANCE</p>	
<b>8:42</b>	<p><b>A magnetic resonance imaging, histological and dose modeling comparison of focused ultrasound, radiofrequency, and gamma knife radiosurgery lesions in swine thalamus</b></p> <p>J. Aubry<sup>1</sup>, J. Aubry<sup>2</sup>, M. Khaled<sup>3</sup>, J. Hilliard<sup>3</sup>, R.C. Frysinger<sup>3</sup>, J.P. Sheehan<sup>3</sup>, W.J. Elias<sup>3</sup>, M. Eames<sup>4</sup>, M. Wintermark<sup>5</sup>, B. Lopes<sup>6</sup>,</p> <p>(1)Department of Radiation Oncology, University of Virginia, Charlottesville, VA, (2) Institut Langevin, CNRS, Paris, FRANCE, (3) Department of Neurosurgery, University of Virginia, Charlottesville, VA,(4) Focused Ultrasound Foundation, Charlottesville, VA, (5) Department of Neuroradiology, University of Virginia, Charlottesville, VA, (6) Department of Neuropathology, University of Virginia, Charlottesville, VA</p>	
<b>8:54</b>	<p><b>The effect of 3d ute brain imaging-derived tissue types on focal intensity and location for transcranial mr-guided focused ultrasound surgery</b></p> <p>U. Vyas<sup>1</sup>, K. Butts Pauly<sup>1</sup>, E.M. Johnson<sup>2</sup>, M. Marx<sup>2</sup>, J.M. Pauly<sup>2</sup></p> <p>(1) Radiology, Stanford University, Stanford, CA, (2) Electrical Engineering, Stanford University, Stanford, CA</p>	
<b>9:06</b>	<p><b>Frequency dependence of ultrasound neuromodulation</b></p> <p>P. Ye<sup>1</sup>, R. King<sup>1</sup>, K. Butts Pauly<sup>1</sup>, J. Brown<sup>2</sup>, W. Newsome<sup>2</sup>, W. Newsome<sup>3</sup>, K. Butts Pauly<sup>4</sup></p> <p>(1)Bioengineering, Stanford University, Stanford, CA,(2) Howard Hughes Medical Institute, Stanford, CA,(3) Neurobiology, Stanford University, Stanford, CA,(4) Radiology, Stanford University, Stanford, CA</p>	
<b>9:18</b>	<p><b>Ultrasonic neuromodulation in awake monkey: modulation of saccade control</b></p> <p>Y. Younan<sup>1</sup>, T. Deffieux<sup>1</sup>, M. Tanter<sup>1</sup>, J. Aubry<sup>1</sup>, N. Wattiez<sup>2</sup>, P. Pouget<sup>2</sup>,</p> <p>(1)Institut Langevin, CNRS, Paris, FRANCE, (2) Institute of Brain and Spinal Cord, INSERM, Paris, FRANCE</p>	
<b>9:30</b>	<p><b>Intramembrane cavitation and brain stimulation using ultrasound</b></p> <p>E. Kimmel<sup>1</sup>, S. Shoham<sup>1</sup>, M. Plaksin<sup>2</sup></p> <p>(1)Biomedical Engineering Department, Technion, Haifa, ISRAEL, (2) Russel-Berrie Nanoscience Institute, Technion, Haifa, ISRAEL</p>	



<b>Clinical Studies</b>		<b>Session 7</b>
<b>Arik Hananel, Kim Butts Pauly</b>		<b>Room2</b>
<b>9:42</b>	<p><b>High intensity focused ultrasound tumor ablation: State of the art</b>  <b>L. Zhang<sup>1</sup>, L. Zhang<sup>2</sup>, Z. Wang<sup>2</sup>, Z. Wang<sup>3</sup></b></p> <p>(1) Clinical Center for Tumor Therapy, 2nd Hospital of Chongqing University of Medical Sciences, Chongqing, Sichuan, CHINA,(2) State Key Laboratory, Department of Biomedical Engineering, Chongqing University of Medical Sciences, Chongqing, Sichuan, CHINA,(3) National Engineering and Research Center for Ultrasound Medicine, Chongqing, Sichuan, CHINA</p>	
<b>10:00</b>	<b>Coffee Break</b>	
<b>10:30</b>	<b>Invited Talk 6</b>	
<b>10:54</b>	<p><b>Clinical evaluation of a toroidal hifu transducer designed for the treatment of liver metastases during an open procedure</b>  <b>D. Melodelima<sup>1</sup>, J. Vincenot<sup>1</sup>, J. Chapelon<sup>1</sup>, D. Melodelima<sup>2</sup>, A. Dupre<sup>2</sup>, Y. Chen<sup>2</sup>, M. Rivoire<sup>2</sup></b></p> <p>(1)LabTAU, INSERM, Lyon, FRANCE,(2) Department of surgery, CLB, Lyon, FRANCE</p>	
<b>11:06</b>	<p><b>A multicenter clinical trial of hifu ablation of uterine fibroid in china: safety &amp; effecacy</b>  <b>C. Chin<sup>1</sup>, D. He<sup>1</sup>, S. Chen<sup>1</sup>, T. Wang<sup>1</sup>, C. Chin<sup>2</sup>, D. He<sup>2</sup>, S. Chen<sup>2</sup>, T. Wang<sup>2</sup>, Y. Chen<sup>3</sup>, Y. Chen<sup>3</sup>, X. Ding<sup>4</sup></b></p> <p>(1)Biomedical Engineering, Shenzhen University, Shenzhen, Guangdong, CHINA,(2) Guangdong Key Laboratory for Biomedical Measurements and Ultrasound Imaging, National-Regional Key Technology Engineering Laboratory for Medical Ultrasound, Shenzhen, Guangdong, CHINA,(3) The Second Affiliated Hospital, Shantou University, Shantou, Guangdong, CHINA,(4) Shenzhen Promethe Medical Science and Technology Co., Ltd, Shenzhen, Guangdong, CHINA</p>	
<b>11:18</b>	<p><b>HIFU and Antitumor Immune Response</b>  <b>F. Wu</b></p> <p>Institute of Ultrasonic Engineering in Medicine, Chongqing Medical University, Chongqing, Chongqing, CHINA</p>	
<b>11:30</b>	<p><b>Temperature decay rates after sonication predict therapeutic responses of magnetic resonance imaging-guided high-intensity focused ultrasound ablation of uterine fibroids: analyses of intra-procedural thermal parameters</b>  <b>Y. Kim<sup>1</sup>, M. Park<sup>1</sup>, H. Rhim<sup>1</sup>, H. Lim<sup>1</sup>, B. Keserci<sup>2</sup>, K. Nurmilaukas<sup>3</sup>, M. KÄÄhler<sup>3</sup>,</b></p> <p>(1) Radiology, Samsung Medical Center, Sungkyunkwan University, Seoul, KOREA, REPUBLIC OF, (2) Philips Healthcare, Seoul, KOREA, REPUBLIC OF, (3) Philips Healthcare, Vantaa, FINLAND</p>	



<b>Non-Invasive Monitoring and Assessment</b>		<b>Session 8</b>
<b>Mathieu Pernot, Dennis Parker</b>		<b>Room2</b>
<b>13:00</b>	<b>MRI temperature map reconstruction from highly undersampled data</b> <b>P. Gaur<sup>1</sup>, W.A. Grissom<sup>2</sup></b> (1) Chemical and Physical Biology, Vanderbilt University, Nashville, TN, (2) Biomedical Engineering, Vanderbilt University, Nashville, TN	
<b>13:12</b>	<b>Implications of magnetic susceptibility differences between water and fat for absolute and fat referenced MR thermometry</b> <b>P. Baron, M. de Greef, R. Deckers, C.J. Bakker, J.G. Bouwman, L.W. Bartels</b> Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS	
<b>13:24</b>	<b>The use of hybrid MRI temperature and relaxation rate measurements to detect tissue changes in focused ultrasound procedures</b> <b>N. Todd, A. Payne, M. Diakite, D.L. Parker</b> Radiology/UCAIR, University of Utah, Salt Lake City, UT	
<b>13:36</b>	<b>Ultrasonography based motion tracking for mrgfus</b> <b>J.W. Jenne<sup>1</sup>, J. Schwaab<sup>1</sup>, C. Sarti<sup>1</sup>, A. Bongers<sup>1</sup>, M. GÄ¼nther<sup>1</sup>, J.W. Jenne<sup>2</sup>, M. GÄ¼nther<sup>2</sup>, S.H. Tretbar</b> (1) mediri GmbH, Heidelberg, GERMANY, (2) Fraunhofer MEVIS, Bremen, GERMANY, (3) Fraunhofer IBMT, St. Ingbert, GERMANY	
<b>13:48</b>	<b>Multifunctional organic-inorganic hybrid nanovesicles for MRI-guided High intensity focused ultrasound ablation</b> <b>Y. Li, D. Niu</b> School of materials science and engineering, Shanghai,CHINA	
<b>14:00</b>	<b>Invited Talk 8</b>	
<b>14:30</b>	<b>Coffee Break</b>	
<b>15:00</b>	<b>Poater Session</b>	



# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Wednesday – May 15, 2013

<b>Non-Invasive Monitoring and Assessment</b>		<b>Session 9</b>
<b>Dennis Parker, Mathieu Pernot, Joo Ha Hwang</b>		<b>Room1</b>
<b>8:15</b>	<b>Invited Talk 9</b>	
<b>8:39</b>	<b>Ultrasound tomography to monitor for breast cancer treatment using high intensity focused ultrasound therapy</b> T. Kanagawa <sup>1</sup> , H. Nakamura <sup>1</sup> , R. Aoyagi <sup>1</sup> , T. Azuma <sup>1</sup> , A. Sasaki <sup>1</sup> , S. Takagi <sup>1</sup> , K. Yoshinaka <sup>2</sup> (1)Y. Matsumoto, Department of Mechanical Engineering, The University of Tokyo, Tokyo, Tokyo, JAPAN,(2) Surgical Assist Technology Group, National Institute of Advanced Industrial Science and Technology, Tsukuba, Ibaraki, JAPAN	
<b>8:51</b>	<b>Evaluation of lesion-to-bubble ratio with polymer- and lipid-shelled microbubbles among ultrasonic imaging methods for monitoring high-intensity focused ultrasound</b> S. Zhang, C. Li, F. Zhou, S. Wang, M. Wan Department of Biomedical Engineering, Xi'an Jiaotong University, Xi'an, Shaanxi, CHINA	
<b>9:03</b>	<b>An integrated and real-time monitoring imaging technique of tissue damage, cavitation and blood perfusion for high intensity focused ultrasound (hifu) therapy</b> H. Zhong, G. Ding, Y. She, M. Wan Biomedical Engineering, Xi'an Jiaotong University, Xi'an, Shanxi, CHINA	
<b>9:15</b>	<b>Biplane ultrasound monitoring of high-intensity focused ultrasound lesion formation</b> S. Sasaki <sup>1</sup> , K. Matsuura <sup>1</sup> , S. Umemura <sup>1</sup> , S. Yoshizawa <sup>2</sup> , S. Umemura <sup>2</sup> (1)Biomedical Engineering, Tohoku University, Sendai, JAPAN,(2) Engineering, Tohoku University, Sendai, JAPAN	
<b>9:27</b>	<b>Development of coagulation monitoring system based on acoustic radiation force</b> N. Hirofumi <sup>1</sup> , A. Ryosuke <sup>1</sup> , A. Takashi <sup>1</sup> , S. Akira <sup>1</sup> , T. Shu <sup>1</sup> , M. Yoichiro <sup>1</sup> , Y. Kiyoshi <sup>2</sup> , F. Keisuke <sup>3</sup> , T. Hideki <sup>3</sup> , I. Kazunori <sup>3</sup> (1)Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN,(2) Department of Human Life Technology, Advanced Industrial Science and Technology, Tsukuba, JAPAN,(3) Hitachi-Aloka Medical, Tokyo, JAPAN	
<b>10:00</b>	<b>Coffee Break</b>	



10:30	<p><b>Feasibility of hifu cardiac therapy and monitoring using shear-wave imaging with dual mode intracardiac catheter</b></p> <p>W. Kwiecinski, J. Provost, M. Fink, M. Tanter, M. Pernot</p> <p>Institut Langevin, ESPCI, Paris, FRANCE</p>
10:42	<p><b>Real time shear waves imaging of hifu thermal ablation: in vivo evaluation in pig livers</b></p> <p>W. Kwiecinski<sup>1</sup>, M. Pernot<sup>1</sup>, M. Fink<sup>1</sup>, M. Tanter<sup>1</sup>, A. Mariani<sup>2</sup>, C. Cuenod<sup>2</sup>, F. Zinzindohoue<sup>2</sup>, A. Mariani<sup>3</sup>, C. Cuenod<sup>3</sup>, F. Zinzindohoue<sup>3</sup></p> <p>(1) Institut Langevin, ESPCI, Paris, FRANCE, (2) Department of Digestive &amp; General Surgery, Hopital Europ��en Georges Pompidou, Paris, FRANCE, (3) Paris Cardiovascular Research Center , Inserm, Paris, FRANCE</p>
10:54	<p><b>Passive cavitation detection during pulsed high-intensity focused ultrasound exposures of ex vivo tissues and in vivo mouse model of pancreatic tumors</b></p> <p>T. Li, H. Chen, T. Khokhlova, Y. Wang, J.H. Hwang</p> <p>Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA</p>
11:06	<p><b>The use of twinkling artifact of doppler imaging to monitor cavitation in tissue during hifu therapy</b></p> <p>O. Sapozhnikov<sup>1</sup>, O. Sapozhnikov<sup>2</sup>, T. Li<sup>2</sup>, T. Khokhlova<sup>3</sup>, J. Hwang<sup>3</sup>,</p> <p>(1)Faculty of Physics, Moscow State University, Moscow, RUSSIAN FEDERATION,(2) Applied Physics Laboratory, University of Washington, Seattle, WA,(3) Medicine, University of Washington, Seattle, WA</p>
11:18	<p><b>Monitoring FUS-induced BBB opening in non-human primates using transcranial cavitation detection in vivo</b></p> <p>S. Wu<sup>1</sup>, F. Marquet<sup>1</sup>, Y. Tung<sup>1</sup>, M. Downs<sup>1</sup>, C.C. Chen<sup>1</sup>, E. Konofagou<sup>1</sup>, T. Teichert<sup>2</sup>, M. Downs<sup>2</sup>, V. Ferrera<sup>2</sup></p> <p>(1)Biomedical Engineering, Columbia University, New York, NY(2) Neuroscience, Columbia University, New York, NY</p>
11:30	<p><b>Temperature imaging with ultrasonic transmission tomography for treatment control</b></p> <p>P.L. Carson<sup>1</sup>, M.L. Scarpelli<sup>1</sup>, S.Z. Pinter<sup>1</sup>, O.D. Kripfgans<sup>1</sup>, J. Yuan<sup>1</sup>, J.B. Fowlkes<sup>1</sup>, N. Duric<sup>2</sup></p> <p>(1)Radiology University of Michigan Health System, Ann Arbor, MI,(2) Karmanos Cancer Institute, Detroit, MI</p>
11:42	<p><b>Monitoring during slow denaturation and boiling using harmonic motion imaging for focused ultrasound (hmifu) ex vivo</b></p> <p>G.Y. Hou<sup>1</sup>, F. Marquet<sup>1</sup>, S. Wang<sup>1</sup>, E.E. Konofagou<sup>1</sup>, E.E. Konofagou<sup>2</sup></p> <p>(1)Biomedical Engineering, Columbia University, New York, NY, (2) Radiology, Columbia University, New York, NY</p>



<b>Nanotechnology &amp; Microbubbles</b>		<b>Session 12B</b>
<b>Lawrence A. Crum, Vera Khokhlova</b>		<b>Room1</b>
<b>13:00</b>	<b>Mesoporous Silica-based Smart System fo Improving Ultrasound Diagnosis Resolution and Treatment Efficacy</b> <b>K. Zhang, H. Chen, J. Shi</b> State Key Laboratory of High Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Shanghai, Shanghai, CHINA	
<b>13:12</b>	<b>Research for Evaluating the Efficacy of HIFU Treatment in Transplantable VX2 Bone Tumor with Contrast-Enhanced Ultrasound</b> <b>L. Chen, L. Jiang, B. Hu</b> Shanghai Jiaotong University Affiliated Sixth People’s Hospital, Shanghai, Shanghai, CHINA	
<b>13:24</b>	<b>A study of the interaction between ultrasound stimulated microbubbles and fibrin clots</b> <b>C. Acconcia<sup>1</sup>, K. Hynynen<sup>1</sup>, D. Goertz<sup>1</sup>, C. Acconcia<sup>2</sup>, K. Hynynen<sup>2</sup>, D. Goertz<sup>2</sup>, D</b> (1)Sunnybrook Research Institute, Toronto, Ontario, CANADA, (2) epartment of Medical Biophysics, University of Toronto, Toronto, Ontario, CANADA	

<b>Sonothrombolysis</b>		<b>Session 12B</b>
<b>Lawrence A. Crum, Vera Khokhlova</b>		<b>Room1</b>
<b>13:36</b>	<b>A rabbit carotid artery model for destroying clots using focused ultrasound and rtpa under mra monitoring.</b> <b>C. Damianou<sup>1</sup>, V. HadjiSavvas<sup>1</sup>, N. Mylonas<sup>2</sup>, C. Damianou<sup>3</sup>, K. Ioannides<sup>4</sup>, Radiology</b> (1) R&D, MEDSONIC LTD, Limassol, Limmassol, CYPRUS,(2) Computer Science, FREDERICK UNIVERSITY CYPRUS, Limassol, Limmassol, CYPRUS, (3) Electrical engineering department, Cyprus University of Technology, Limassol, Limmassol, CYPRUS,(4) Polikliniki Igia, Limassol, Limassol, CYPRUS	

<b>Ultrasound Non-Thermal Therapies</b>		<b>Session 10</b>
<b>Lawrence A. Crum, Vera Khokhlova</b>		<b>Room1</b>
<b>13:50</b>	<b>Invited Talk 11</b>	
<b>14:14</b>	<b>A boiling histotripsy system for deep tissue ablation</b> <b>A. Maxwell<sup>1</sup>, M. Bailey<sup>1</sup>, A. Maxwell<sup>2</sup>, W. Kreider<sup>2</sup>, T. Khokhlova<sup>2</sup>, O. Sapozhnikov<sup>2</sup>, M. Bailey<sup>2</sup>, V. Khokhlova<sup>2</sup>, P. Yuldashev<sup>3</sup>, O. Sapozhnikov<sup>3</sup>, V. Khokhlova<sup>3</sup></b> (1)Urology, University of Washington Medical Center, Seattle, WA,(2) Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA,(3) Department of Acoustics, Physics Faculty, Moscow State University, Moscow, RUSSIAN FEDERATION	



<b>14:26</b>	<b>Angiotripsy: a potential therapeutic technology of microbubble-enhanced acoustic cavitation</b> Z. Liu, P. Li, S. Gao, Y. Zhong, X. Zhao Department of Ultrasound, Xinqiao Hospital, The Third Military Medical University, Chongqing, CHINA
<b>14:38</b>	<b>Disruption of prostate microvasculature by combining microbubble-enhanced ultrasound and prothrombin</b> J. Zhang <sup>1</sup> , S. Wu <sup>1</sup> , Z. Liu <sup>1</sup> , Y. Liu <sup>2</sup> (1)Department of Ultrasound, xinqiao Hospital, The Third Military Medical University, Chongqing, Chongqing, CHINA, (2) Department of Urology, Xinqiao Hospital, The Third Military Medical University, Chongqing, Chongqing, CHINA
<b>14:50</b>	<b>Coffee Break</b>
<b>15:10</b>	<b>Fry Lecture</b> Gail Ter Haar
<b>16:00</b>	<b>Award</b>
<b>16:30</b>	<b>Tours</b>

<b>Ultrasound Thermal Therapies</b>		<b>Session 11</b>
<b>Yufeng Zhou, Guofeng Shen</b>		<b>Room2</b>
<b>8:15</b>	<b>Non-invasive toroidal hifu transducer for increasing the coagulated volume</b> D. Melodelima, J. Vincenot, A. Kocot, F. Chavier, J. Chapelon LabTAU, INSERM, Lyon, FRANCE	
<b>8:27</b>	<b>Thermal near-field management for volumetric magnetic resonance-guided high-intensity focused ultrasound (mr-hifu) ablation</b> J. Wijlemans <sup>1</sup> , M. van den Bosch <sup>1</sup> , M. de Greef <sup>2</sup> , L. Bartels <sup>2</sup> , C. Moonen <sup>2</sup> , M. Ries <sup>2</sup> , G. Schubert <sup>3</sup> , M. KÄ¶hler <sup>3</sup> , M. Ylihautala <sup>3</sup> (1) Department of Radiology, University Medical Center Utrecht, Utrecht, NETHERLANDS, (2) Image Sciences Institute, University Medical Center Utrecht, Utrecht, NETHERLANDS, (3) Philips Healthcare, Vantaa, FINLAND	
<b>8:39</b>	<b>In-vivo evaluation of volumetric magnetic resonance-guided high-intensity focused ultrasound (mr-hifu) ablation in porcine liver</b> J. Wijlemans <sup>1</sup> , M. van den Bosch <sup>1</sup> , M. de Greef <sup>2</sup> , L. Bartels <sup>2</sup> , C. Moonen <sup>2</sup> , M. Ries <sup>2</sup> , G. Schubert <sup>3</sup> , M. KÄ¶hler <sup>3</sup> , M. Ylihautala <sup>3</sup> (1)Department of Radiology, University Medical Center Utrecht, Utrecht, NETHERLANDS, (2) Image Sciences Institute, University Medical Center Utrecht, Utrecht, NETHERLANDS, (3) Philips Healthcare, Vantaa, FINLAND	



<b>8:51</b>	<p><b>Optimally enhanced heating for focused ultrasound surgery with split foci, dual-frequency or multi foci modes</b></p> <p><b>M. Lu, Y. Guan, M. Wan</b></p> <p>The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Xi'an Jiaotong University, Xi'an, Shanxi, CHINA</p>
<b>9:03</b>	<p><b>Effect of blood flow on hifu-induced heating and histopathological ablation in a clinically-relevant isolated, perfused porcine liver model</b></p> <p><b>D.J. Holroyd<sup>1</sup>, E. Mylonopoulou<sup>1</sup>, C. Jensen<sup>1</sup>, D. Chung<sup>1</sup>, J.J. Choi<sup>1</sup>, C.C. Coussios<sup>1</sup>, D.J. Holroyd<sup>2</sup>, R. Ravikumar<sup>2</sup>, P.J. Friend<sup>2</sup></b></p> <p>(1) Institute of Biomedical Engineering, University of Oxford, Oxford, UNITED KINGDOM, (2) Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UNITED KINGDOM</p>
<b>9:15</b>	<p><b>Large-volume coagulation by cavitation-enhanced heating with multiple hifu focal spots.</b></p> <p><b>H. Sasaki<sup>1</sup>, K. Nakamura<sup>1</sup>, K. Goto<sup>1</sup>, T. Miyashita<sup>1</sup>, S. Yoshizawa<sup>1</sup>, S. Umemura<sup>2</sup></b></p> <p>(1)Department of Communication Engineering, Tohoku University, Sendai, Miyagi, JAPAN,(2) Department of Biomedical Engineering Tohoku University, Sendai, Miyagi, JAPAN</p>
<b>9:27</b>	<p><b>Effect of perfusion on Heating in Liver Exposed to Pulsed High Intensity Focused Ultrasound</b></p> <p><b>X. Zhang</b></p> <p>College of Biomedical Engineering, Chongqing Medical University, Chongqing Medical University, Chongqing, Chongqing, CHINA</p>
<b>9:39</b>	<p><b>Ultrasound-guided transesophageal hifu exposures for atrial fibrillation treatment: first ex vivo experiments</b></p> <p><b>E. Constancier<sup>1</sup>, W. N'Djin<sup>1</sup>, J. Chapelon<sup>1</sup>, C. Lafon<sup>1</sup>, E. Constancier<sup>2</sup>, W. N'Djin<sup>2</sup>, J. Chapelon<sup>2</sup>, C. Lafon<sup>2</sup>, F. Bessi�re<sup>3</sup>, D. Grinberg<sup>3</sup>, P. Chevalier<sup>3</sup>, M. Pioche<sup>4</sup></b></p> <p>(1) LabTAU INSERM U1032, INSERM, Lyon, FRANCE, (2) Universit� Claude Bernard Lyon 1, Universit� de Lyon, Lyon, FRANCE, (3) H�pital Cardiologique Louis Pradel, Hospices Civils de Lyon, Lyon, FRANCE, (4) H�pital Edouard Herriot, Hospices Civils de Lyon, Lyon, FRANCE</p>
<b>10:00</b>	<p><b>Coffee Break</b></p>





<b>Nanotechnology &amp; Microbubbles</b>		<b>Session 12A</b>
<b>Yufeng Zhou, Cyril Lafon, Y. Matsumoto</b>		<b>Room2</b>
<b>10:30</b>	<b>Invited Talk 10</b>	
<b>10:54</b>	<b>Enhanced cavitation and heating of flowing polymer- and lipid-shelled microbubbles and phase-shift nanodroplets during focused ultrasound exposures</b> <b>S. Zhang, C. Li, F. Zhou, Y. Zong, S. Wang, M. Wan</b> Department of Biomedical Engineering, Xi'an Jiaotong University, Xi'an, Shaanxi, CHINA	
<b>11:06</b>	<b>Time lapse observation of phase change nano droplet after vaporization stimulated by ultrasound</b> <b>K. Takehara<sup>1</sup>, T. Azuma<sup>1</sup>, Y. Matsumoto<sup>1</sup>, S. Takagi<sup>2</sup>, S. Yamaguchi<sup>3</sup>, T. Nagamune<sup>3</sup>, I. Sakuma<sup>4</sup>, M. Maezawa<sup>5</sup>, K. Yoshinaka<sup>6</sup></b> (1)Bioengineering, the University of Tokyo, Tokyo, JAPAN,(2) Mechanical engineering, the University of Tokyo, Tokyo, JAPAN,(3) Chemistry and Biotechnology, the University of Tokyo, Tokyo, JAPAN,(4) Precision Engineering, the University of Tokyo, Tokyo, JAPAN,(5) Olympus Corporation, Tokyo, JAPAN, (6) National Institute of Advanced Industrial Science and Technology, Ibaraki, JAPAN	
<b>11:18</b>	<b>Dynamics of stembells in an ultrasound field</b> <b>T. Kokhuis<sup>1</sup>, A. van der Steen<sup>1</sup>, N. de Jong<sup>1</sup>, T. Kokhuis<sup>2</sup>, B. Naaijken<sup>2</sup>, L. Juffermans<sup>2</sup>, O. Kamp<sup>2</sup>, A. van der Steen<sup>2</sup>, N. de Jong<sup>2</sup>, B. Naaijken<sup>3</sup>, L. Juffermans<sup>4</sup>, O. Kamp<sup>5</sup>, M. Versluis<sup>6</sup>, M. Versluis<sup>7</sup>,</b> (1)Biomedical Engineering, Erasmus Medical Center, Rotterdam, NETHERLANDS, (2) ICIN, Netherlands Heart Institute, Utrecht, NETHERLANDS, (3) Pathology, VU Medical Center, Amsterdam, NETHERLANDS, (4) Physiology, VU Medical Center, Amsterdam, NETHERLANDS, (5) Cardiology, VU Medical Center, Amsterdam, NETHERLANDS,(6) Physics of Fluids Group, University of Twente, Enschede, NETHERLANDS, (7) MIRA Institute of Biomedical Technology and Technical Medicine, University of Twente, Enschede, NETHERLANDS	
<b>11:30</b>	<b>Microbubble manipulation using ultrasound standing wave generated in square column transducer</b> <b>K. Inoue<sup>1</sup>, H. Kaji<sup>1</sup>, R. Masuda<sup>1</sup>, H. Ushijima<sup>1</sup>, T. Azuma<sup>1</sup>, S. Takagi<sup>1</sup>, Y. Matsumoto<sup>1</sup>, K. Yoshinaka<sup>2</sup></b> (1)Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN,(2) National Institute of Advanced Industrial Industrial Science and Technology, Tsukuba, Ibaraki, JAPAN	



# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Shanghai, China

May 12-16, 2013

**Posters**

**Tuesday, 15:00-18:00**





**NO.1**

**How sonoporation disrupts cellular structural integrity: morphological and cytoskeletal observations**

**X. Chen[1], Y. Hu[1], R. Leow[1], A.C. Yu[1], J.M. Wan[2]**

[1]Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG [2] School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG

**NO.2**

**Developmental delays and subcellular stress as downstream effects of sonoporation**

**X. Chen[1], W. Zhong[1], A.C. Yu[1], J.M. Wan[2]**

[1]Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG [2] School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG

**NO.3**

**Real-time monitoring of the temperature during hifu treatment by acoustic radiation force impulse imaging**

**P. Yang, C. Wang, C. Zeng, R. Qiu, S. Lin, M. Qian, H. Zheng, J. Wang, Paul C.Lauterbur**

Research Center for Biomedical Imaging, Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guang, CHINA

**NO.4**

**A study on the change in plasma membrane potential during sonoporation**

**P. Qin[1], P. Cai[1], L. Du[2], L. Jin[2], A. Yu[3]**

[1],Department of Instrumentation Science and Engineering, Shanghai Jiaotong University, Shanghai, CHINA,[2] Department of Ultrasound, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, CHINA,[3] Medical Engineering Program, The University of Hong Kong, Hong Kong, CHINA

**NO.5**

**Comparative effectiveness of different frequencies ultrasound on Inflammatory pain release**

**C. She, H. Qiao, J. Bai, Z. Wang,**

College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA

**NO.6**

**Effect of low intensity ultrasound on ER and cyclinE Expression in Rats'uterine after Abortion Induced by Medication**

**W. Dan, L. Fang, Z. Wang**

College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA

**NO.7**

**Hifu therapy for local recurrence of prostate cancer after external beam radiotherapy and radical prostatectomy – 5,5 years experience**

**V. Solovov, Y. Matyash, D. Fesenko, R. Khametov**

Interventional Radiology, Samara Oncology Center, Samara, RUSSIAN FEDERATION



**NO.8**

**Dynamic contrast-enhanced MR imaging: predictor for treatment effect of ultrasound-guided high intensity focused ultrasound ablating uterine fibroids with hyperintense on T2-weighted MR imaging**

**W. Zhao, W. Zhao**

College of Biomedical Engineering, Chongqing Medical University, Chongqing, CHINA

**NO.9**

**Enhancement of focused ultrasound with micorbubbles on the delivery and treatments of anticancer nanodrug in different stages of brain tumors**

**H. Hung[1], Y. Hsu[1], S. Wu[1], W. Lin[1], T. Lin[2]**

[1] Institute of Biomedical Engineering, National Taiwan

University, Taipei, TAIWAN, [2] Institute of Pharmacology, National Taiwan University, Taipei, TAIWAN

**NO.10**

**Focused ultrasound induced blood-brain barrier opening to enhance temozolomide delivery for glioma treatment in rat**

**H. Liu[1], P. Chu[1], P. Lee[1], C. Huang[2], P. Chen[2], K. Wei[2], H.J. Wang[3]**

[1] Department of Electrical Engineering, Chang-Gung University,

Taoyuan, TAIWAN, [2] Department of Neurosurgery, Chang-Gung University and Memorial Hospital, Taoyuan, TAIWAN, [3] Department of Biological Sciences, National Sun Yat-sen University, Kaohsiung, TAIWAN

**NO.11**

**Targeted drug delivery against beta-amyloidosis in alzheimer's disease mouse models by using focused ultrasound technology**

**L.L. Strobel[1], R.M. Nitsch[1], B. Werner[2], E. Martin-Fiori[2]**

[1] Division of Psychiatry Research, University of Zurich, Zurich, SWITZERLAND, [2] MR-Center, University Children's Hospital, Zurich, SWITZERLAND

**NO.12**

**Effects of multiple ultrasound exposures on cisplatin delivery in in vitro opticell setup**

**N. Sasaki, C. Bos, R. Deckers, B. Lammertink, C. Moonen**

Division Imaging, UMC Utrecht, Utrecht, NETHERLANDS

**NO.13**

**Conformal drug delivery and instantaneous monitoring based on an inverse synthesis method at a diagnostic ultrasound platform**

**S. Xu, Z. Xu, H. Jiang, M. Lu, M. Wan**

Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Xi'an, Shaanxi, CHINA



#### **NO.14**

##### **Investigation on cavitation contribution in scleral permeability enhancement**

**A. Razavi[1], A. Birer[1], F. Chavier[1], J. Mestas[1], J. Chapelon[1], C. Lafon[1], A. Razavi[2], D. Clement[2], F. Romano[2], A. Begle[2]**

[1] LabTAU - Thérapie et Applications des Ultrasons, INSERM, Lyon, Rhone alpes, FRANCE,[2] EYETECHCARE, Rillieux la pape, Rhone alpes, FRANCE

#### **NO.15**

##### **Ultrasound targeted microbubble destruction stimulates cellular endocytosis in enhancing adeno-associated virus delivery**

**L. Jin[1], F. Li[1], L. Du[1], H. Wang[2], F. Wei[2], P. Qin[3]**

[1] Department of Ultrasound, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, Shanghai, CHINA,[2] Experimental Research Center, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, Shanghai, CHINA [3] Department of Instrumentation Science and Engineering, Shanghai Jiaotong University, Shanghai, Shanghai, CHINA

#### **NO.16**

##### **Permeability improvement and acoustic characterization for pla foams by ultrasound**

**G. Guo[1], D. Zhang[1], Q. Ma[2]**

[1] Key Laboratory of Modern Acoustics, Institute of Acoustics, Nanjing University, Nanjing, Jiangsu Province, CHINA, [2] Key Laboratory of Optoelectronics of Jiangsu Province, School of Physics and Technology, Nanjing Normal University, Nanjing, Jiangsu Province, CHINA

#### **NO.17**

##### **Refined ultrasound-mediated gene delivery using customized microbubbles**

**R.R. Sun, M.L. Noble, S. Min, S.S. Sun, C.H. Miao**

Immunity & Immunotherapies, Seattle Children's Research Institute, Seattle, WA

#### **NO.18**

##### **Effect of ultrasound intensity for bubble enhanced hifu with heating location control method**

**K. Yoshinaka[1], H. Utashiro[2], T. Azuma[2], A. Sasaki[2], S. Takagi[2], Y. Matsumoto[2]**

[1] Human technology Research Institute, AIST, Tsukuba, JAPAN, [2] The University of Tokyo, Tokyo, JAPAN

#### **NO.19**

##### **The development of magnetic resonance surface coil for hifu ablation in a mini-pig model**

**S.C. Hwang[1], P.H. He[1], H. Chang[1], I.Y. Kuo[1], C. Yao[1], T.H. Fang[1], L.Y. Shyu[2]**

[1] Division of Medical Engineering Research, National Health Research Institutes, Zhunan, Miaoli, TAIWAN, [2] Biomedical Engineering, Chung-Yuan Christian University, Chung Li, Taoyuan, TAIWAN



**NO.20**

**Investigation on the acoustic signal characteristics of boiling bubble produced in ex vivo bovine liver during hifu irradiation**

Y. Li, F. Li, H. Ai, M. Zhong, W. Qi

College of Biomedical Engineering, Chongqing Medical University, Chongqing, CHINA

**NO.21**

**Dual CCD high-precision positioning method of focused ultrasound body sculpting system**

D. Li

Research, Company, Shanghai, Shanghai, CHINA

**NO.22**

**Robotic assistance in the evaluation of the position of a hifu lesion during image guided fus**

A. Melzer[1], X. Xiao[2], Z. Huang[2]

[1] Institute for Medical Science and Technology, University of Dundee, Dundee, UNITED KINGDOM [2] School of Engineering, University of Dundee, Dundee, UNITED KINGDOM

**NO.23**

**What are the best methods of assessing advancement in the field of focused ultrasound?**

D. Tyshlek[1], A. Hananel[1], N. Kassell[1], H. Huff-Simonin[1], N. Kassell[2]

[1] Focused Ultrasound Foundation, Charlottesville, VA,[2] Department of Neurosurgery, University of Virginia, Charlottesville, VA

**NO.24**

**Magnetic resonance is promising in contributing to find an ultrasound dose definition**

J. Kramme[1], M. Günther[1], J. Jenne[1], M. Günther[2], J. Haller[3], J. Jenne[4]

[1] Fraunhofer MEVIS - Institute for Medical Image Computing, Bremen, GERMANY, [2] Faculty of Physics and Electronics, University of Bremen, Bremen, GERMANY, [3] Physikalisch-Technische Bundesanstalt, Braunschweig, GERMANY, [4] Mediri GmbH, Heidelberg, GERMANY

**NO.25**

**Electromagnetic hydrophone for high intensity focused ultrasound measurement**

P. Grasland-Mongrain[1], J. Mari[1], B. Gilles[1], C. Lafon[1], P.Grasland-Mongrain[2], J. Mari[2], B. Gilles[2], C. Lafon[2]

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**NO.26**

**The research on image denoising in sound field measurement based on infrared imaging**

Z. Su[1], G. Shen[1], Y. Yu[1], S. Qiao[1], X. Ji[1], H. Wu[1], M. Zhu[1], Y. Yu[2]

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#### **NO.27**

##### **Development of ultrasound guided high intensity focused ultrasound system with robot manipulator for treatment of early breast cancer**

**K. Fujiwara[1], H. Takeuchi[1], K. Itani[1], N. Abe[2], K. Yoshinaka[3], T. Yonetsuji[4], T. Azuma[4], A. Sasaki[4], S. Takagi[4], I. Sakuma[4], Y. Matsumoto[4]**

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#### **NO.28**

##### **Assessment and correction of phase aberrations in the breast for mrgfus**

**A. Farrer[1], D.A. Christensen[1], A. Farrer[2], S. Almquist[2], D.L. Parker[2], A. Payne[2], S. Almquist[3], D.L. Parker[4], A.Payne[4], D.A. Christensen[5]**

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#### **NO.29**

##### **Dedicated 8 channel head receive array for transcranial mr guided focused ultrasound surgery**

**B. Werner[1], E. Martin[1], F. Resmer[2], T. Lanz[2]**

[1] Center for MR-Research, University Children's Hospital, Zurich, ZH, SWITZERLAND [2] Rapid Biomedical GmbH, Rimpar, GERMANY

#### **NO.30**

##### **Fus-compatible mr imaging coil for large animal brain applications**

**M.D. Eames[1], J.W. Snell[1], M. Jones[2]**

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#### **NO.31**

##### **Wireless energy transmission using ultrasound for implantable devices**

**Z. Yang, H. Wang, D. Zeng, Z. Wang**

College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA



**NO.32**

**Radiation Force Calculation of Cylindrical Focusing Transducer and Array on Ray Acoustics Model**

**S. Duan[1], W. Shou[2], B. Hu[2], Z. Zhan[3], W. Shou[4], B. Hu[4]**

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**NO.33**

**Characterization of 1-3 single crystal/epoxy composite ultrasonic transducer for elevated temperature application**

**Z. Wu, X. Kui, S. Li**

Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, CHINA

**NO.34**

**An improved mri guided ultrasound system for superficial tumor hyperthermia**

**S. Chen, G. Shen, Z. Su, M. Zhu, S. Qiao, Y. Bo, Y. Chen**

Biomedical Instrument Institute, Shanghai Jiao Tong University, Shanghai, CHINA

**NO.35**

**Finite element simulation of acoustic wave propagation and energy deposition in bone during extracorporeal shock wave treatment**

**X. Wang, D. Zhang, J. Tu**

School of Physics, Nanjing University, Key Laboratory of Modern Acoustics, Nanjing, Jiangsu, CHINA

**NO.36**

**Dose-effect Study of Pancreatic Cancer Cell Apoptosis Induced by Focused Ultrasound in Vitro**

**Q. Guo[1], L. Jiang[1], B. Hu[1], Q. Guo[2], L. Jiang[2], B. Hu[2]**

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**NO.37**

**Sonoluminescence and sonochemiluminescence study of cavitation field in a 1.2mhz focused ultrasound**

**H. Yin, Y. Qiao, H. Cao, M. Wan**

The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, Shanxi, CHINA





#### **NO.38**

##### **High-speed imaging of ultrasound-mediated bacterial biofilm removal**

**B. Goh[1], M. Conneely[1], P. Cambell[1], B. Goh[2], H. Kneuper[3], T. Palmer[3], E. Klaseboer[4], B. Khoo[5]**

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#### **NO.39**

##### **Study of thermal dose behind ribs caused by focused ultrasound**

**X. Liu, F.Zhang, X. Gong**

Institute of Acoustics, Nanjing, CHINA

#### **NO.40**

##### **Numerical simulation of temperature distribution during transcranial tumor therapy of high intensity focused ultrasound**

**Q. Zhang, Y. Wang, W. Zhou, F. Xue, J. Zhang, X. Jian**

Biomedical Engineering, Tianjin Medical University, Tianjin, CHINA

#### **NO.41**

##### **Evaluation of hifu-induced lesion region using temperature threshold and equivalent thermal dose methods**

**S. Chang, F. Xue, W. Zhou, J. Zhang, X. Jian**

School of Biomedical Engineering, Tianjin Medical University, Tianjin, Tianjin, CHINA

#### **NO.42**

##### **Research on the lesion segmentation of breast tumor mr images based on fcm-ds theory**

**Z. Liangbin[1], M. Wenjun[1], S. Xing[1], Z. Su[1], L. Yuehua[2], Z. Yuemin[3], C. Li[4]**

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#### **NO.43**

##### **Heating simulations of pulsed high-intensity focused ultrasound in the presence of heterogeneous tissue**

**Hao ZHOU, Yin-fei ZHENG, Hui-long DUAN**

Key laboratory of Biomedical Engineering of Ministry of Education, Zhejiang University, Hangzhou, Zhejiang, CHINA



**NO.44**

**Dedicated 8 channel head receive array for transcranial mr guided focused ultrasound surgery**

**B. Werner[1], E. Martin[1], F. Resmer[2], T. Lanz[2],**

[1]Center for MR-Research, University Children's Hospital, Zurich, ZH, SWITZERLAND,[2]Rapid Biomedical GmbH, Rimpar, GERMANY

**NO.45**

**Study of mechanism of sonoporation using lipid bilayer and surface-modified microbubble**

**K. Hirose[1], T. Azuma[1], A. Sasaki[1], S. Takagi[1], Y. Matsumoto[1], K. Yoshinaka[2],**

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**NO.46**

**Temperature measurement of hifu using a thin-film thermocouple array**

**K. Matsuki[1], R. Narumi[1], T. Azuma[1], A. Sasaki[1], T. Kanagawa[1], S. Takagi[1], Y. Matsumoto[1], K. Yoshinaka[2], K. Okita[3]**

[1]Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN,[2] National Institute of Advanced Industrial Science and Technology, Tsukuba, JAPAN,[3] Mechanical Engineering, Nihon University, Tokyo, JAPAN

**NO.47**

**Low field home-built permanent mr guided focused ultrasound integration system**

**G. Li[1], D. Li[1], J. Dong[1], D. Li[2], J. Dong[2]**

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# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Shanghai, China

May 12-16, 2013

**Oral Presentation  
(Abstract)**





**Oral session 1A**

**2013/5/13 10:24:00**

**CONTROL ID:** 1681308

**TITLE:** MODELS OF MICROBUBBLE DYNAMICS IN ACOUSTIC DROPLET VAPORIZATION

**AUTHORS/INSTITUTIONS:** J.L. Bull, A. Qamar, Z.Z. Wong, D. Li, Biomedical Engineering, University of Michigan, Ann Arbor, MI|J.B. Fowlkes, Radiology, University of Michigan, Ann Arbor, MI|A. Qamar, R. Samtaney, Division of Physical Sciences, KAUST, Thuwal, SAUDI ARABIA|

**ABSTRACT BODY:**

**OBJECTIVES:** This work is motivated by a developmental gas embolotherapy technique that involves injecting superheated liquid droplets that are small enough to pass through capillaries and subsequently vaporizing the droplets with ultrasound to selectively form vascular microbubbles. The vaporization of a superheated perfluoropentane (C5F12) droplet is a rapid process and results in a gas bubble that is approximately 125 to 150 times the volume of the liquid droplet from which it originated. Our objective is to model bubble evolution in acoustic droplet vaporization within a confined tube, representing a blood vessel.

**METHODS:** The vaporization process is modeled theoretically, and using a combined theoretical and computational model. The theoretical model is also used to describe the evolution of bubbles that are small compared to the tube diameter. With modifications, the theoretical model is used to model acoustic-driven oscillation of a microbubble. For larger bubbles, relative to the tube diameter, a full computational model is used to describe the bubble evolution and is coupled to the initial vaporization model.

**RESULTS:** The model results are compared to results from our ultra-high-speed camera experiments, and close agreement between the experimental bubble evolution and the prediction of the model is noted. It is demonstrated that the tube affects both the bubble evolution and the resulting flow and stress fields. Additionally, it is demonstrated that the bubbles can be non-spherical during the growth phase, even in the case of bubbles that are small compared to the tube diameter. The microbubble oscillation predictions agree closely with experimental data, including the dependence on acoustic parameters and tube parameters.

**CONCLUSIONS:** The effects of confinement in a tube of either an acoustically vaporized droplet or an acoustically oscillated bubble can be significant even when the bubble or droplet is much smaller than the tube diameter.

This work is supported by NIH grant R01EB006476.



**Oral session 1A**

**2013/5/13 10:36:00**

**CONTROL ID:** 1671649

**TITLE:** IMAGE-BASED NUMERICAL MODELING OF HIFU-INDUCED LESIONS

**AUTHORS/INSTITUTIONS:** M.K. Almekkawy, I.A. Shehata, A. Haritonova, J.R. Ballard, A.J. Casper, E.S. Ebbini, Electrical Engineering, University of Minnesota, Minneapolis, MN | I.A. Shehata, Medical School, Cairo University, Cairo, EGYPT |

**ABSTRACT BODY:**

**OBJECTIVE:** Simulate the results of a lesion formation experiment based on actual in vivo treatments. The case was to target atherosclerotic plaque within the posterior wall of the external femoral artery of large (100 – 140 Kg) FH swine partially obscured by another artery on the high intensity focused ultrasound (HIFU) path. The targeting was conducted in the form of seven adjacent HIFU shots that were placed across the circumference of the posterior wall of the artery, with 1 mm spacing circumferentially. Steering the beam from the geometric focus was achieved using “electronic steering”.

**METHODS:** We present a finite difference time domain (FDTD) simulation modeling of the wave propagation in heterogeneous medium from the surface of a 3.5 MHz array prototype with 32-elements. The array has a lateral and elevation focus at 40 mm with fenestration in its center through which a 7.5 MHz diagnostic transducer can be placed. After segmentation of the ultrasound image obtained for the treatment region in-vivo, we integrated this anatomical information into our simulation to account for different parameters that may be caused by these multi-layer anatomical complexities. The proposed simulation model considered the effect of wall thickness of large arteries & the heat sink effect of flowing blood. To maintain the stability of this model, the grid spacing is  $(\lambda/9)$  and the temporal step follows the Courant condition.

**RESULTS:** The area of induced HIFU thermal damage was defined as the tissue area that reached a thermal dose equivalent to 43 °C for 240 minutes. The simulation program showed that HIFU was able to induce damage in the prefocal region instead of the target area. The HIFU lesions, as predicted by our simulation, greatly correlated with the actual damage detected in histology.

**CONCLUSIONS:** The results provide an early validation for the feasibility of using image-based modeling of the acoustic and thermal field in heterogeneous tissues. Image-based modeling could play a critical role in treatment planning when HIFU is used in precision lesion formation noninvasively. The model shows the formation of lesion in the prefocal plan instead of the target area. This is attributed to the great heat sink area within the HIFU path, the accumulation of heating process of seven shots in a small area and the highly attenuated region of connective tissue surrounds the artery that absorb high amount of the exposed power.



**Oral session 1A**

**2013/5/13 10:48:00**

**CONTROL ID:** 1671751

**TITLE:** HIGH INTENSITY FOCUSED ULTRASOUND IN LIVER TUMOR THERAPY: IMAGE BASED COMPUTATIONAL MODEL

**AUTHORS/INSTITUTIONS:** M.A. Solovchuk, T.W. Sheu, Center for Advanced Study in Theoretical Sciences, National Taiwan University, Taipei, TAIWAN|M.A. Solovchuk, T.W. Sheu, Engineering Science and Ocean Engineering, National Taiwan University, Taipei, TAIWAN|M. Thiriet, LJLL, University of Paris N 6, Paris, FRANCE|

**ABSTRACT BODY:**

**OBJECTIVES:** Focused ultrasound treatment of liver tumor is problematic, because large blood vessels act as a heat sink. Convective cooling can reduce the necrosed volume and liver can regenerate. To avoid the damage of large blood vessels and regeneration of the tumor, basic understanding of the factors that affect the tumor ablation is necessary for the planning and optimization of the treatment. Importance of nonlinear propagation effects, blood flow cooling and acoustic streaming effects is investigated during focused ultrasound therapy. A computational model that can be used in a patient specific liver geometry is constructed.

**METHODS:** The developed computational model is based on the nonlinear Westervelt equation with relaxation effects taken into account, bioheat equations for the perfused tissue and blood flow domains. The nonlinear Navier-Stokes equations are employed to describe the flow in the large blood vessels. The effect of acoustic streaming is also taken into account. Three dimensional meshes for the hepatic artery, hepatic vein, vena cava and liver were reconstructed on the basis of the MRI image. The present numerical experiments are carried out in a patient specific liver model.

**RESULTS:** From this three-dimensional field-coupling study it was found that in large blood vessel both the convective cooling and acoustic streaming can significantly change the temperature field and thermal lesion near blood vessels. If destruction of all tumour cells near the blood vessel boundary is necessary, a shorter sonication time with higher power deposition is suggested.

**CONCLUSIONS:** The proposed three dimensional physical model for HIFU study was conducted in an image-based liver geometry. The theoretical feasibility to necrotize the tumors close to major veins was shown. Owing to nonlinear effect the temperature in the focal region can be significantly increased compared with the linear case. Nonlinear effects can help to ablate tumors close to blood vessel wall. These results can be further used to construct a surgical planning platform for the non-invasive HIFU tumor ablating therapy in real liver geometry on the basis of MRI image.



**Oral session 1A**

**2013/5/13 11:00:00**

**CONTROL ID:** 1678272

**TITLE:** High-intensity focused ultrasound ablation is an effective and safe treatment for cirrhotic hypersplenism: A prospective case series of 28 patients

**AUTHORS/INSTITUTIONS:** J. Zhu, Chongqing Medical University, Chongqing 400016, China., Chongqing Medical University, Chongqing 400016, China., Chongqing Medical University, Chongqing , chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** To assess the safety, efficacy and clinical prospects of high-intensity focused ultrasound (HIFU) in treatment of cirrhotic hypersplenism.

**METHODS:** A total of 28 patients who suffered the disease were treated with HIFU ablation. All patients underwent HIFU ablation were closely followed-up over a year. MRI scan was performed and the spleens were observed. Blood counts and liver function tests were also determined.

**RESULTS:** In the follow-up process, the levels of white blood cell, Platelets and liver function in the blood after HIFU were significantly higher than those of levels before HIFU. The MRI in the days of 14 after HIFU treatment showed the ablation area turned into non-perfused volume in the spleen. The percentage of damaged part of the spleen from HIFU is  $(27.20\% \pm 6.07\%)$  (range 16.90%~42.34%). In addition, the symptoms (eg, epistaxis and gingival bleeding) were ameliorated significantly or even disappeared and the quality of life was improved.

**CONCLUSIONS:** Splenic HIFU ablation is a safe, effective and noninvasive approach for cirrhotic hypersplenism and it has a potential good prospect in clinical application.



**Oral session 1B**

**2013/5/13 11:12:00**

**CONTROL ID:** 1671797

**TITLE:** FULL ACOUSTIC AND THERMAL CHARACTERIZATION OF HIFU FIELD IN THE PRESENT OF A RIBCAGE MODEL

**AUTHORS/INSTITUTIONS:** R. Cao, N.M. Le, Z. Huang, School of Engineering, Physics and Mathematics, University of Dundee, Dundee, UNITED KINGDOM|G. Nabi, Department of Urology, Ninewells hospital, Dundee, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVE:** In the treatment of abdominal organs using high intensity focused ultrasound (HIFU), the patient's ribs are in the pathway of the HIFU beams which could result in acoustic distortion, occasional skin burns and insufficient energy delivered to the target organs. Characterization of acoustic field based on a 3D reconstructed model of the ribcage is required for helping select the accurate dose of HIFU energy in treatment planning. The aim of this study was to provide the full characterization of HIFU field with the effect of ribcage model.

**METHODS:** In this study, the ribcage phantom reconstructed from a patient's CT images was created by tissue mimicking materials and its effect on acoustic field was characterized. The effect of the ribcage on acoustic field has been provided in acoustic pressure distribution, acoustic power and temperature diffusion. And the relation between acoustic power, acoustic pressure and temperature was estimated. The input voltage and current of the HIFU transducer were monitored to investigate the relation between acoustic power and input of HIFU transducer. MATLAB was applied to find the coefficients of an exponential function polynomial that can fit the data, input peak-peak voltage to acoustic power.

**RESULTS:** The HIFU acoustic field was characterized with human ribcage phantom in the ultrasound beam path. Measurement result shows focus splitting with one main focus and two secondary intensity maxima. With the presence of ribcage phantom, the acoustic pressure was reduced by 48.3% and another two peak values were observed near the main focus, reduced by 65.0% and 71.7% respectively. The acoustic power was decreased by 47.5% to 54.3%. The exponential relation between input and acoustic power has been established.

**CONCLUSIONS:** The 3D reconstructed model and phantoms were used to investigate the impact of ribcage on the delivery of HIFU energy. With the characterization result, the form of the focus, the acoustic power, acoustic pressure and temperature rise are provided before the HIFU treatment, which are significant to determine the HIFU delivery dose. In conclusion, this ribcage model and characterization technique will be useful for the further study in the abdominal HIFU treatment.





**Oral session 1B**

**2013/5/13 11:24:00**

**CONTROL ID:** 1669242

**TITLE:** A HYBRID SIMULATION TOOL FOR THE SIMULATION OF VOLUMETRIC ACOUSTIC FIELDS

**AUTHORS/INSTITUTIONS:** M. de Greef, L.W. Bartels, C. Moonen, M. Ries, Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS|J. Koskela, Philips Healthcare, Vantaa, FINLAND|

**ABSTRACT BODY:**

**OBJECTIVE:** Numerical simulation is an important tool in the development and implementation of new high intensity focused ultrasound applications and devices. A commonly used simulation method is Fourier-based field continuation which is computationally efficient but has potentially a large memory footprint and its performance for non-planar structures has not thoroughly been studied so far. An alternative simulation method recently developed is the stochastic acoustic ray tracing method which can handle arbitrarily shaped tissue interfaces. The method registers the complex pressure contribution by every transmit element at meshed surfaces. A hybrid method was developed that combines both methods in order to be able to compute volumetric acoustic pressure fields in a target region while at the same time incident intensity on obstructing structures is obtained.

**METHODS:** For a planar stack of media including ribs intersecting the beam cone, the pressure field was calculated by stochastic ray tracing in a planar detector perpendicular to the beam axis, positioned behind the ribs. To calculate the volumetric pressure field, the per-element complex pressure contributions were summed, weighing each contribution by the channel's complex amplitude (for the purpose of beam steering). Subsequently, the total pressure field was propagated in the spectral domain and transformed back to the spatial domain slice-by-slice. The algorithm was implemented using CUDA and calculations were performed on a Tesla C2075 graphics card. During stochastic ray tracing, complex pressures were recorded in a second planar detector placed behind the first detector. Pressure distributions according to the stochastic ray tracer and the hybrid method were compared in this plane.

**RESULTS:** The total pressure field was calculated after ray tracing for a volume of 513x513x513 voxels in 1.9s, excluding 2.2s initialization. Good correspondence was found between the pressure field computed with the hybrid method and computed by ray tracing alone at the location of the second detector.

**CONCLUSIONS:** The hybrid solver provides fast and memory efficient calculation of volumetric pressure fields behind complex heterogeneous geometries while providing incident intensities on obstructing structures. By summation of per-element pressure contributions, the pressure fields during volumetric ablations can be computed in 2-4s per focal point position.



**Oral session 1B**

**2013/5/13 11:36:00**

**CONTROL ID:** 1670846

**TITLE:** EVALUATION OF AN IMPROVED WAVE-VECTOR-FREQUENCY-DOMAIN METHOD FOR NONLINEAR WAVE MODELING

**AUTHORS/INSTITUTIONS:** Y. Jing, Mechanical and Aerospace Engineering, North Carolina State University, Raleigh, NC|J. Cannata, HistoSonics, Ann Arbor, MI| **ABSTRACT BODY:**

**OBJECTIVE:** In this paper, a recently developed wave-vector-frequency-domain method for nonlinear wave modeling is improved and verified by systematical numerical studies and underwater experiments.

**METHODS:** A better numeric scheme based on the Trapezoidal integration is proposed that significantly increases the modeling accuracy, thereby allowing for a larger step-size and shorter computation time. Plane waves are first discussed to validate the improved algorithm. Experimental verifications are also conducted. A highly focused transducer is used to generate short high intensity pulses. 2D scans are conducted at a pre-focal plane, which are later used as the input to the numerical model to predict the acoustic field at other planes including focal and post-focal planes.

**RESULTS:** For the plane wave problems, the original and present algorithms are compared to the analytical solution. It is found that the present algorithm can improve the accuracy of the previous version by an order of magnitude. Good agreement is also found between the numerical predictions using the present algorithm with experimental results. Less than 10% discrepancy is observed, and the error could be partly due to the noise in the measurement and the spatial averaging effect of the hydrophone.

**CONCLUSIONS:** An improved wave-vector-frequency-domain nonlinear wave propagation model is studied in this paper. Compared with a previous study, an improved numerical scheme which utilizes the trapezoidal integration is proposed and it yields a significantly higher accuracy. Experimental studies for a therapeutic transducer are carried out which successfully validate the numerical model. Good agreement is found on both pre-focal plane and focal plane.



**Oral session 1B**

**2013/5/13 11:48:00**

**CONTROL ID:** 1671798

**TITLE:** FULL WAVE ACOUSTIC AND THERMAL MODELING OF TRANSCRANIAL FOCUSED ULTRASOUND SURGERY IN A DETAILED ANATOMICAL HEAD MODEL

**AUTHORS/INSTITUTIONS:** A. Kyriakou, E. Neufeld, N. Kuster, IT'IS Foundation, Zurich, SWITZERLAND|A. Kyriakou , N. Kuster, ETHZ, Zurich, SWITZERLAND|B. Werner, MR-Research, Kinderspital, Zurich, SWITZERLAND|

**ABSTRACT BODY:**

**OBJECTIVE:** Focused ultrasound (FUS) allows for deep brain interventions that are minimally invasive and cause negligible collateral damage. Patient-specific treatment planning is of high interest for treatment optimization, outcome prediction, and risk assessment, and can also be used for applicator development. However, the modeling of acoustic propagation in complex anatomies (with effects such as standing waves, reflections, absorption) and that of applicators with no principal wave propagation direction, such as the semi-spherical transducer used in the clinical ExAblate4000 Neuro System, requires computationally expensive full wave simulations. Thermal modeling in turn requires physiological aspects such as perfusion and thermoregulation to be considered.

**METHODS:** A detailed anatomical head model (45 tissues) was segmented from MR data and a CAD model of the ExAblate (1024 elements) generated. The efficient parallelized full wave acoustic FDTD-based solver that was implemented is capable of handling complex geometries, inhomogeneous tissue distributions, and non-linear behavior, and was used to determine the acoustic pressure distribution. The induced heating was determined using a thermal solver (based on Pennes Bioheat Equation), which allows thermoregulation and coagulation-induced vascular shutdown to be accounted for. To validate the acoustic simulations, 3D measurements of the acoustic interference pattern generated by a single-element transducer in the wake of manufactured obstacles were performed using a robot-controlled hydrophone in a water-tank.

**RESULTS:** Full wave acoustic simulations of this setup were performed (<1hr simulation time). The impact of tissue inhomogeneity on the energy deposition was apparent and focused corrections were achieved by obtaining phase-corrections for every element through reverse wave propagation from a point source at the target location. Additional simulations assessed the impact of non-linearity. Comparison between simulations and measurements using the Gamma method showed good agreement.

**CONCLUSIONS:** High resolution full-wave acoustic and thermal simulations of FUS induced transcranial heating were performed and the impact of selected parameters studied. Experimental validation of the acoustic solver in generic setups was successful and enhanced validation including in vivo MR thermometry will soon be performed.



**Oral session 1B**

**2013/5/13 13:00:00**

**CONTROL ID:** 1671830

**TITLE:** PHASE-AMPLITUDE OPTIMIZED INTERCOSTAL FIRING: A METHOD OF REFERENCE FOR INTERCOSTAL TECHNIQUES

**AUTHORS/INSTITUTIONS:** M. de Greef, L.W. Bartels, C. Moonen, M. Ries, Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS |

**ABSTRACT BODY:**

**OBJECTIVE:** Obstruction by the thoracic cage of acoustic wave propagation is a major problem in high intensity focused ultrasound interventions in the abdomen. Several methods have been proposed to reduce exposure of the ribs to acoustic intensity. By projecting the ribs onto the transducer and switching off those elements that are, in terms of surface area, for more than 50% in the projection, it has been shown that rib heating can be substantially reduced. Alternative switch-off methods based on an exposure metric obtained from acoustic measurements have been demonstrated to be feasible. In this study we present a phase-amplitude optimization method that maximizes the ratio of the intensity exposure of the target and the intensity exposure of obstructing structures. This method provides a theoretical upper-bound for the performance of switch-off strategies and hence provides a best case intercostal sonication scenario. In addition, it provides a reference in the analysis of other intercostal firing strategies.

**METHODS:** For a heterogeneous tissue stack including obstructing ribs, the per-element pressure contribution to the focus and to the ribs was calculated using stochastic ray tracing. Based on these contributions, an intensity kernel matrix  $Q$  was constructed for every surface element (pixel or triangle) so that  $I = v^*Qv$ , with  $I$  the acoustic intensity and  $v$  the excitation vector of the phased-array transducer ( $*$  denotes the complex-conjugate). Based on a region-of-interest defined for both the target as well as the ribs, the matrices were averaged and the ratio of the focal point intensity and rib intensity poses a generalized eigenvalue problem that was solved to obtain a set of complex channel amplitudes.

**RESULTS:** Phase-amplitude optimization showed that constructive interference patterns on the ribs could be successfully mitigated, leading to reduced rib heating at the same focal point intensity. Element switch-off based on projection of the ribs showed an increase in total rib incident intensity up to a factor of two compared to phase-amplitude optimization.

**CONCLUSIONS:** We presented a phase-amplitude optimization method that, based on a linear exposure metric, successfully reduces rib heating. Optimization of both phases and amplitudes showed to be essential.



**Oral session 1B**

**2013/5/13 13:12:00**

**CONTROL ID:** 1676647

**TITLE:** HIFU SCATTERING BY THE RIBS: CONSTRAINED OPTIMIZATION WITH A COMPLEX SURFACE IMPEDANCE BOUNDARY CONDITION

**AUTHORS/INSTITUTIONS:** P. Gelat, Acoustics and Ionising Radiation Division, National Physical Laboratory, Teddington, UNITED KINGDOM|P. Gelat, N. Saffari, Department of Mechanical Engineering, University College London, London, UNITED KINGDOM|G. ter Haar, Joint Physics Department, Institute of Cancer Research, Sutton, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVES:** One of the challenges of trans-rib high-intensity focused ultrasound (HIFU) treatment is the need to transmit sufficient energy through the ribcage to ablate tissue whilst minimising the formation of side lobes, and sparing healthy tissue. Ribs strongly absorb and reflect ultrasound. This may result in overheating of bone and overlying tissue during treatment, leading to skin burns. Successful treatment of a patient with tumours in the upper abdomen therefore requires a thorough understanding of the way acoustic and thermal energy is deposited.

**METHODS:** A boundary element approach was developed to predict the field of a multi-element HIFU array scattered by human ribs in 3D, the topology of which was obtained from CT scan data<sup>[1]</sup>. This has been reformulated as a constrained least squares minimization problem in which the velocity of each individual element on the array is an optimization variable<sup>[2]</sup>. Dissipative mechanisms inside the propagating medium have been accounted for, together with a complex impedance condition at the surface of the ribs.

**RESULTS:** The methodology has been tested at an excitation frequency of 1 MHz on a spherical multi-element array in the presence of ribs. A 46% reduction in the maximum acoustic pressure magnitude on the surface of the ribs has been achieved, with only a 3% reduction in the peak focal pressure compared to the spherical focusing case. The results have been compared against other focusing and rib-sparing methods.

**CONCLUSIONS:** The use of a constrained minimization approach based on a boundary element formulation has enabled the acoustic field produced by a multi-element HIFU array in the presence of anatomical ribs to be optimized such that the pressure magnitude on the surface of the ribs did not exceed a specified damage threshold, whilst ensuring pressures above the ablation threshold at the focus. The flexibility of the constrained minimization approach was demonstrated against other methods.

[1] Gélat P, ter Haar G and Saffari N 2011 Modelling of the acoustic field of a multi-element HIFU array scattered by human ribs *Phys. Med. Biol.* 56 5553-5581.

[2] Gélat P, ter Haar G and Saffari N 2012 The optimization of acoustic fields for ablative therapies of tumours in the upper abdomen *Phys. Med. Biol.* 57 8471-8497.



## Oral session 2

2013/5/13 13:24:00

**CONTROL ID:** 1672007

**TITLE:** HARDWARE-INDEPENDENT PRE-INTERVENTIONAL PLANNING, SIMULATION, AND APPLICATION OF FOCUSED ULTRASOUND THERAPY

**AUTHORS/INSTITUTIONS:** D. Demedts, C. Schumann, J. Georgii, C. von Dresky, T. Preusser, Institute for Medical Image Computing, Fraunhofer MEVIS, Bremen, Bremen, GERMANY|T. Preusser, School of Engineering and Science, Jacobs University, Bremen, Bremen, GERMANY|

### **ABSTRACT BODY:**

**OBJECTIVES:** We present a software prototype combining pre-interventional planning and simulation of focused ultrasound therapy with plan execution on arbitrary transducer devices. It consists of a four-step workflow for data management, therapy planning, simulation, and plan execution.

**METHODS:** The software implements parts of the DICOM protocol which allows for seamless integration into clinical environments. MRI data are automatically obtained from configured scanners and serve as planning source for sonications to be applied. An automatic sonication positioning algorithm can be used to generate an initial therapy plan for a defined target region. Tools for removal, creation and adaption of focal spots help to adjust the generated planning result. An efficient GPU simulation of single focal spots and entire planning results consisting of multiple sonications can be performed. The simulation result is used for both plan quality evaluation in terms of lesion coverage and sparing of risk structures as well as for phase shift and amplitude optimization of the transducer's elements. A segmentation of structures located inside the sound path may be created during planning in order to let the system deactivate specific transducer elements and to take different tissue densities into account while computing the phase shift values. Plan execution is performed via a hardware abstraction layer separating the generic plan data structure from implementation details of the specific FUS ablation system. Each sonication's properties such as phase values, amplitude, start time, and duration are mapped to acoustic irradiation commands for the specific transducer hardware.

**RESULTS:** The prototype has been tested with a spherical shaped transducer system consisting of 256 elements provided by Image Guided Therapy. In order to support other transducer devices, the software can easily be extended by plugins providing communication abstraction for the specific hardware manufacturer.

**CONCLUSIONS:** A hardware-independent, integrated software assistant for FUS therapy has been described allowing for seamless integration into clinical environments. Future work includes the integration of numerical methods

to compute optimal therapy plans with respect to transducer geometry and user defined criteria.



**Oral session 2**

**2013/5/13 13:36:00**

**CONTROL ID:** 1684303

**TITLE:** FUS-compatible MR imaging coil for clinical brain applications

**AUTHORS/INSTITUTIONS:** M. Eames, J.W. Snell, A. Hananel, Focused Ultrasound Foundation, CHARLOTTESVILLE, VA|M. Jones, High Filed LLC, St. Paul, MN|E. Minalga, R. Hadley, University of Utah, Salt Lake City, UT|J.W. Snell, A. Hananel, University of Virginia, CHARLOTTESVILLE, VA|

**ABSTRACT BODY:**

**OBJECTIVES:** With the recent CE mark approval of trans-cranial MR-guided focused ultrasound (tcMRg-FUS), the treatment of neurological disorders with non-invasive focused ultrasound is on its way to becoming an accepted clinical treatment. In order to gain wider acceptance among clinicians, it is critical to address the marginal MR image quality for this image-guided procedure. We demonstrate an updated, clinically viable, water-resistant MR coil solution to be used in conjunction with tcMRg-FUS.

**METHODS:** An ex-vivo human skull with custom-fitted tissue-mimicking MRg-FUS brain phantom (ATS Laboratories, Inc., Bridgeport, CT) was used to assess imaging quality. The skull was degassed before placing in the water bath of an InSightec (Tirat Carmel, Haifa, Israel) ExAblate Neuro FUS transducer positioned such that the range axis of the transducer was directed vertically upwards. A pair of water-sealed 5"-diameter MR imaging coil loops (Highfield LLC, St. Paul, MN) were positioned on opposing lateral sides of the skull in the water bath. Both gradient-echo and spin-echo MR sequences were used to assess SNR with respect to body coil imaging in a single mid-coronal image bisecting the custom coil loops. A low-power, proof of concept FUS sonication was performed to assess quality of MR thermometry in terms of noise standard deviation away from FUS thermal spot.

**RESULTS:** Using a GRE imaging sequence with TR=500ms, TE=12ms, flip-angle=90, we recorded a factor of 3.1 improvement in SNR. Imaging with the T2 FSE imaging sequence used in clinical FUS cases with TR=500ms and TE=100ms, we recorded a factor of 3.2 improvement in SNR. With the T2-weighted sequence, a factor of 4.1

improvement in SNR was calculated using the NEMA single-channel method for multi-channel coils. In MR thermometry images, noise standard deviation in a 2 square-centimeter area was calculated to be 0.8 when using the body coil and 0.2 when using the FUS-compatible coil, further corroborating the 3-4 fold improvement in SNR.

**CONCLUSIONS:** Significant qualitative and quantitative SNR improvement was realized using this custom, FUS-compatible MR imaging coil. We plan to demonstrate improvements in diagnostic and thermal imaging with the FUS transducer in clinical orientation (in which the range axis of the transducer is directed horizontally) prior to the ISTU meeting. Work is underway to help manufacturers incorporate the design in products for clinical use.



**Oral session 2**

**2013/5/13 13:48:00**

**CONTROL ID:** 1699836

**TITLE:** Compact Modular MR-Guided HIFU System for Treatment of Liver Cancer

**AUTHORS/INSTITUTIONS:** K.M. Sekins, S. Brunke, X. Zeng, S. Barnes, J. Hopple, D. Liu, S. Hsu, C. Lee, C. Maleke, J. Nam, J. Eaton, K. Wong, Ultrasound Division, Siemens Medical Solutions USA, Issaquah, WA|L. Petrusca, M. Viallon, S. Terraz, C. Becker, R. Salomir, Service de Radiologie , H.pitaux Universitaires de Genève, Geneva , SWITZERLAND|C. Lorenz, Siemens Medical Solutions USA, Malvern, PA|K.J. Kirchberg, S.M. Shea, S. Patil, J. Barbot, T. Meng, Imaging & Computer Vision, Siemens Corporate Research, Princeton, NJ|E. Rothgang, J. Roland, MRI Division, Siemens AG, Erlangen, GERMANY|

**ABSTRACT BODY:**

**OBJECTIVES:** A prototype MR-guided HIFU system is developed for treatment of human liver tumors. The system is compact and portable, allowing the patient support/applicator module to be easily installed on and removed from a MR Table.

**METHODS:** The HIFU system was used with a Siemens Magnetom Trio a Tim System™ 3T scanner, with software (SW) exploiting and extending the utility of the Interactive Front End™ and TMAP™ (MR thermometry) SW prototype packages. The applicator has a high power (>2 KWac), high element count (>18,000) HIFU array capable of significant electronic steering. The beamforming electronics are embedded in the array, enabling the low profile patient support platform. A base module has power and control electronics, and a fluid system delivering pressure-and flow-controlled degassed water to the applicator. The SW allows dosing strategies (focal scanning patterns, dose power and time) to either be selected from those recommended by the system, or manually input. Targeting is confirmed via low energy shots and thermometry, or by MR ARFI images. HIFU is delivered through a subcostal acoustic window with the patient prone, tilted toward the left lateral decubitus position. As part of treatment planning, the operator designates an "acoustic tunnel" within which the energy is confined to avoid critical structures. Temperatures are monitored via multi-planar PRFS MR thermometry (interleaved with HIFU transmission and synchronized with breathing), and dose histories and peak tissue temperatures are stored, guiding treatment assessment and subsequent dosing.

**RESULTS:** System attributes, treatment planning, control and workflow are discussed. Data is presented on ablation in ex vivo liver phantoms including respiratory motion demonstrator, and on MR compatibility (passive and active). Significant HIFU steering flexibility is confirmed. Magnetic susceptibility imaging artifacts are minimal, enabling mm-accuracy in spatial registration of the device in the MR coordinate frames based on 3D high resolution imaging. Therapeutic beamforming integrity is maintained in spite of the array electronics being in the magnet bore.

**CONCLUSIONS:** The hardware and software components for a newly developed compact MR-guided HIFU system is described. Phantom experiments demonstrated satisfying system performance, clinical workflow and MR compatibility.





## Oral session 2

2013/5/13 14:00:00

**CONTROL ID:** 1700675

**TITLE:** Modular 2D Therapeutic Arrays for a Compact MR-Guided HIFU System

**AUTHORS/INSTITUTIONS:** S. Barnes, J. Hopple, D. Liu, P. Lyons, J. Eaton, K. Wong, X. Zeng, S. Brunke, S. Hsu, C. Lee, C. Maleke, M.K. Sekins, Ultrasound Division, Siemens Medical Solutions USA, Issaquah, WA | T. Clary, The Inception Group, Sammamish, WA |

### **ABSTRACT BODY:**

**OBJECTIVES:** A high-power fine pitch 2D array module was developed as the basic acoustic building block for configurable and size variable HIFU system transducers (super arrays of the module). In one embodiment, an MR compatible HIFU system for treatment of human liver tumors was developed. Electronic steering of the resulting super array allows control of the therapeutic treatment region without mechanical movement of the transducer. Needing no means for mechanical position control, use of the compact design did not require modification of the MR system table.

**METHODS:** The 2D array module unit (center frequency  $\approx 1\text{MHz}$ ) has 1,152 elements (96-[azimuth] by 12 [elevation] elements ) and includes an embedded beamformer having on off control of each individual 2D element. The beamformer can be programmed via a serial interface while transmitting, and can produce rapid focus scanning patterns producing large thermal ablation volumes. The array can produce an average surface power density  $>12\text{W/cm}^2$  over long periods, with peak surface power density  $> 25 \text{ W/cm}^2$ .

**RESULTS:** The prototype liver HIFU system transducer description and acoustic performance are discussed. Data includes that from water tank testing and MR thermometry imaging of tissue-mimicking phantoms during HIFU insonation. The prototype system used sixteen of the 2D-array acoustic modules, to produce a 2 x 8 super-array of modules having 18,432 individual elements in the applicator, with a 13cm x 11cm rectangular acoustic aperture. An integral coupling fluid bolus within a flexible membrane conforms to the patient. The fine-pitch of the array enables therapeutic beams (f-number = 0.9), to be steered to angles exceeding  $55^\circ$  in azimuth and  $45^\circ$  in elevation. Measurements of the acoustic beams produced by the system had a -3dB beam-width  $\leq 2 \text{ mm}$  in both azimuth and elevation, which closely matches simulated predictions. Rapidly scanned beam patterns produced single dose thermal ablation volumes  $>1\text{cm}^3$ . Careful attention was paid to magnetic susceptibility of the array components producing an applicator with virtually no MR image distortion or shadowing.

**CONCLUSIONS:** A configurable HIFU array module was realized with significant power and HIFU steering capability. Array beam forming was stable, with the array beamforming electronics in the magnet bore, and susceptibility imaging artifacts from the applicator were negligible.



### Oral session 3

2013/5/13 14:36:00

**CONTROL ID:** 1671794

**TITLE:** INTRA-CEREBRAL DIFFUSION OF IRINOTECAN AND TEMOZOLOMIDE AFTER UNFOCUSED ULTRASOUND-INDUCED OPENING OF THE BBB IN RABBITS

**AUTHORS/INSTITUTIONS:** K. Beccaria, M. Canney, CarThera, Paris, FRANCE|K. Beccaria, A. Carpentier, Neurosurgery Department, Pitie-Salpetriere Hospital, Paris, FRANCE|L. Goldwirt, C. Fernandez, Pharmacology Department, Pitie-Salpetriere Hospital, Paris, FRANCE|J. Piquet, Laboratory of Biosurgical Research, Université Paris

Descartes, Sorbonne Paris Cite, Paris, FRANCE|A. Carpentier, Sorbonne University, Paris 6 School of Medicine, Paris, FRANCE|C. Lafon, J. Chapelon, Inserm, U1032, LabTau, Lyon, FRANCE|C. Lafon, J. Chapelon, Lyon 1 University, Lyon, FRANCE|

#### **ABSTRACT BODY:**

**OBJECTIVE:** The blood-brain barrier (BBB) is a major impediment to the intra-cerebral diffusion of drugs in the treatment of primitive brain tumors. In this work, the effect of US-induced BBB opening on the intra-cerebral diffusion of Irinotecan (CPT11) and Temozolomide (TMZ) was assessed.

**METHODS:** Seventeen rabbits were sonicated on a region of the right hemisphere after craniotomy and in the presence of SonoVue while seventeen others served as controls and had only right craniotomy, without sonication and without SonoVue injection. US-induced BBB opening of sonicated rabbits was performed by pulsing a 1 MHz planar ultrasound transducer with a duty cycle of 2.5% and an in situ acoustic pressure level of 0.6 MPa. Two different timings of drug injection were assessed. In the first protocol ("H0.5", n=16), the drug was injected at T-5min, blood was harvested at T+25min and the animals were sacrificed at T+30min. In the second protocol ("H0.75", n=18), the drug was injected at T+15min, blood was harvested at T+40min and the animals were sacrificed at T+45min. The blood and intra-cerebral concentrations of Irinotecan and Temozolomide were measured by ultra-performance liquid chromatography.

**RESULTS:** Intra-cerebral concentrations of both TMZ and CPT11 were enhanced in regions where the BBB was opened in comparison to the contralateral hemisphere in both protocols ( $p < 0.01$  and  $p < 0.0001$  for CPT11, and  $p = 0.02$  and  $p = 0.03$  for TMZ, at H0.5 and H0.75 respectively). The same significant difference was observed when the

concentration of drug in the rabbits with BBB opening was compared against the group without opening ( $p < 0.001$  and  $p < 0.0001$  for CPT11, and  $p < 0.01$  and  $p = 0.02$  for TMZ, at H0.5 and H0.75 respectively). Intra-cerebral diffusion of drugs in control hemispheres, considered as spontaneous diffusion, was on average 2.5% for CPT11 and 34% for TMZ. After opening of the BBB, these values were increased by +159% for CPT11 and by +23% for TMZ. Intra-cerebral diffusion of both CPT11 and TMZ was systematically significantly improved in the cortex ( $p < 0.05$ ), but diffusion in the deep brain was more heterogeneous. No significant difference was observed when the non-sonicated hemispheres of treated and control rabbits was compared.

**CONCLUSIONS:** US-induced opening of the BBB allows for enhanced intra-cerebral diffusion of both Irinotecan and Temozolomide. Work supported by CarThera SAS.



### Oral session 3

2013/5/13 14:48:00

**CONTROL ID:** 1671813

**TITLE:** A PRECLINICAL TOXICOLOGICAL STUDY OF REPEATED BBB OPENING USING AN IMPLANTABLE ULTRASOUND TRANSDUCER IN PRIMATES

**AUTHORS/INSTITUTIONS:** C. Horodyckid, M. Canney, A. Vignot, CarThera, Paris, FRANCE|C. Horodyckid, A. Carpentier, Neurosurgery Department, Pitie-Salpetriere Hospital, Paris, FRANCE|A. Uzcatogui Pedroza, C. Lafon, J. Chapelon, Inserm, U1032, LabTau, Lyon, FRANCE|P. Merlet, CEA, IR4M, SHFJ, Orsay, FRANCE|A. Carpentier, Université Paris 6, UPMC, Paris, FRANCE|C. Lafon, J. Chapelon, University 1 Lyon, Lyon, FRANCE|

#### **ABSTRACT BODY:**

**OBJECTIVE:** Brain tumor prognosis is presently poor due to the low response of patients to chemotherapy treatments after surgery. The main limitation to the efficacy of chemotherapy in the brain is the blood-brain barrier (BBB). It has been shown that delivery of pulsed ultrasound (US) in combination with echogenic microbubbles can temporarily disrupt the BBB to deliver drugs that normally can not reach interstitial brain tissue. In this work, an implantable US device was developed and used to assess the toxicity of repeated US-induced opening of the BBB.

**METHODS:** A 10-mm diameter, 1 MHz unfocused ultrasound transducer was fixed to the skull bone in a burr hole in three primates and left implanted for 3 months. BBB opening was performed every 15 days by connecting the transducer to an external generator using a transdermal needle connection. The transducer was operated in pulse mode with a duty cycle of 2.5% with acoustic pressure levels of 0.6 MPa to 0.8 MPa and intravenous injection of Sonovue (0.1 cc/kg, Bracco Imaging, Geneva, Switzerland) for 120 seconds at each sonication to induce BBB opening. MRI imaging was performed after sonications to verify BBB opening. PET imaging and electrophysiological analysis were also used to assess the safety of repeated BBB opening and to monitor for adverse effects.

**RESULTS:** MRI images acquired after sonication showed a T1-contrast enhancement area in front of the transducer that corresponded well with the acoustic field and that did not display evidence of hemorrhagic or ischemic processes. A small oedematous spot, without mass effect, was observed on FLAIR images, and resolved by day 2. At day 15, MRI control showed strictly normal brain in all primates, with a totally closed BBB. PET scans images with [18F]FDG and [18F]DPA-714 did not show any change in cerebral metabolism of glucose or any signs of inflammation. No epileptic-signs or non-pathologic conduction were observed in EEG. The behavior of all of the primates appeared to be normal. In histological analysis, no haemorrhagic processes and only a few red cell extravasations were observed.

**CONCLUSIONS:** We confirmed that unfocused ultrasound can be used to repeatedly and temporarily open the BBB at an acoustic pressure of 0.8 MPa (1 MHz) without any adverse effects. Work supported by CarThéra SAS.



**Oral session 3**

**2013/5/13 15:00:00**

**CONTROL ID:** 1672328

**TITLE:** FOCUSED ULTRASOUND INDUCED BLOOD-BRAIN BARRIER OPENING IN MACROMOLECULE DELIVERY

**AUTHORS/INSTITUTIONS:** S. Wang, O.O. Olumolade, E.E. Konofagou, Biomedical Engineering, Columbia University, New York, NY|S. Osting, C. Burger, Neurology, University of Wisconsin Madison, Madison, WI|

**ABSTRACT BODY:**

**OBJECTIVE:** Recombinant Adeno-Associated Virus (rAAV) is a promising gene therapy vector and used in clinical trials (by direct injection) for the treatment of Parkinson's Disease (PD). Focused Ultrasound (FUS) in combination with microbubbles (MB) has been shown capable of inducing reversible blood-brain barrier (BBB) opening. This study aimed at investigating the feasibility of using FUS to non-invasively deliver macromolecules (such as rAAVs) through the opened BBB in mice in vivo.

**METHODS:** BBB openings were induced in the caudate putamen (CPu) with a single-element FUS transducer (center frequency 1.5 MHz) and in-house manufactured MB. Two types of macromolecules were used: 2-MDa fluorescently labeled Dextran and rAAV serotype 1 (rAAV1). Five mice were co-injected with MB and 100  $\mu$ l Dextran solution (15 g/ml) via the tail vein, followed by FUS sonication (pulse length 6.7 ms, pulse repetition frequency 5 Hz, peak rarefactional pressures 0.45 MPa). For rAAV1 delivery, sonications were performed (at 1.5 MPa) after co-injecting MB and 100  $\mu$ l rAAV1 particles ( $5.9 \times 10^{12}$  GC/ml). Animals were allowed to survive for one month. Brain samples were stained for green fluorescent protein (GFP) using the ABC-DAB method. In addition, neurons and astrocytes were stained using anti-NeuN and anti-GFAP antibodies.

**RESULTS:** It was concluded from the Dextran experiments that the 2-MDa Dextran molecules were able to cross the BBB using the aforementioned acoustic parameters. The diffusion of the 2-MDa Dextran covered the entire CPu area. Although the accumulation of 2MDa Dextran in the proximity of the blood vessels was identified, enhanced fluorescence was also detected in the extracellular space. The whole sonicated hemisphere (the CPu and cortex) showed significant rAAV1 transduction, detected via the DAB staining of GFP. Nonetheless, the transduction was less uniform compared to the diffusion of 2-MDa Dextran. Co-localization of GFP positive and NeuN positive cells revealed rAAV1 transduced neurons in the sonicated hemisphere. It was also observed that some astrocytes were transduced by rAAV1 as indicated by co-localizations of GFP and GFAP signals.

**CONCLUSIONS:** FUS in combination with MB provide a non-invasive and targeted approach for gene delivery to the brain. This study demonstrated the feasibility of delivering rAAV1 and very large molecules (up to 2-MDa) to the murine brain parenchyma in vivo.



### Oral session 3

2013/5/13 15:12:00

**CONTROL ID:** 1672405

**TITLE:** TARGETED DRUG DELIVERY WITH FOCUSED ULTRASOUND-INDUCED BLOOD-BRAIN BARRIER OPENING USING ACOUSTICALLY-ACTIVATED NANODROPLETS

**AUTHORS/INSTITUTIONS:** C.C. Chen, S. Wu, O.O. Olumolade, E.E. Konofagou, Biomedical Engineering, Columbia University, New York, NY|E.E. Konofagou, Radiology, Columbia University, New York, NY|P.S. Sheeran, P.A. Dayton, Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University, Chapel Hill, NC|

#### **ABSTRACT BODY:**

**OBJECTIVE:** Focused ultrasound (FUS) in the presence of microbubbles has been shown to increase the permeability of the blood-brain barrier (BBB), thus allowing targeted delivery of therapeutic agents for the treatment of central nervous system diseases. Microbubbles currently are the only agents that are used to facilitate FUS-induced BBB opening. However, they are constrained within the intravascular space due to their micronscale size, limiting the delivery effect at or near the microvessels. In this study, we tested the feasibility to utilize a new class of contrast agents, phase-shift nanodroplets, to mediate FUS-induced BBB opening for targeted drug delivery in the brain.

**METHODS:** 3-kDa dextran was used as the model drug to signify BBB opening after FUS was applied to target the left hippocampus of C57/BL mice in the presence of either nanodroplets or conventional microbubbles. The acoustic pressure was varied between 0.15 and 0.60 MPa to be clinically relevant. The fluorescence enhancement was quantified to compare the delivery efficiency. Passive cavitation detection was used in the attempt to establish a correlation between the amount of dextran delivered and the acoustic emission recorded during sonication.

**RESULTS:** The BBB opening was consistently achieved using nanodroplets at pressures higher or equal to 0.45 MPa, while the pressure threshold decreased to 0.30 MPa for microbubbles. The stable cavitation threshold for nanodroplets was found to be significantly lower than that of microbubbles. For each acoustic pressure, microbubbles produced greater fluorescence enhancement compared to nanodroplets. The dextran delivery achieved using nanodroplets was found to be more homogenous within the targeted region, and no inertial cavitation was induced even at the highest pressure. Histological evaluation revealed minor damage for sonications at 0.60 MPa using microbubbles, corresponding to the onset of inertial cavitation.

**CONCLUSIONS:** The present study demonstrated for the first time the feasibility of nanodroplet-mediated FUS-induced BBB opening. Our results highlighted the possibility to develop this technology for potential extravascular targeted drug delivery, extending the delivery region beyond the cerebral vasculature. Future studies are needed to optimize the droplet composition in order to decrease the activation pressure and to achieve higher delivery efficiency.



### Oral session 3

2013/5/13 16:04:00

**CONTROL ID:** 1672464

**TITLE:** DELIVERY OF MOLECULES OF VARIOUS SIZES THROUGH BLOOD BRAIN BARRIER OPENING INDUCED BY LONG AND SHORT ULTRASOUND PULSES

**AUTHORS/INSTITUTIONS:** H. Chen, A. Srivastava, T. Sun, E. Konofagou, Department of Biomedical Engineering, Columbia University, New York, NY|E. Konofagou, Department of Radiology, Columbia University, New York, NY|

#### **ABSTRACT BODY:**

**OBJECTIVE:** Focused ultrasound (FUS) with either long (~10 ms) or short (2.3  $\mu$ s) pulses has been used in the delivery of molecules of various sizes through the blood brain barrier (BBB). One major challenge for the clinical application of this technique is to control the BBB opening size. In this study, the size of BBB opening induced by long and short ultrasound pulses was estimated using fluorescent dextrans of various molecular weights.

**METHODS:** After intravenously injection of microbubbles (MBs), mice were sonicated on one side of the hippocampus using pulsed ultrasound (1.5 MHz frequency, 0.2 s pulse repetition period, 11 minute duration) with a peak negative pressure of 0.3, 0.5, or 0.8 MPa. For short pulse cases, the targeted regions were sonicated every 0.2 s by 1000 pulses with a pulse length of 2.3  $\mu$ s (3 cycles) and a pulse repetition frequency of 100 kHz. For long pulse cases, a single pulse was emitted every 0.2 s, and the pulse length was selected to keep the exposure (ultrasound intensity  $\times$  total number of cycles) the same for both cases. Dextran of a molecular weight of 3, 70, 150 or 2000 kDa was mixed with the MBs before injection. Dextran delivery was quantified using fluorescence imaging of sectioned brain slides. A 7.5 MHz transducer was used as a passive cavitation detector for cavitation monitoring.

**RESULTS:** First, at 0.3 MPa, only 3 kDa dextran was delivered through the BBB; at 0.5 MPa, 3, 70 and 150 kDa dextrans were delivered trans-BBB; at 0.8 MPa, all four dextrans including the 2000 kDa one were delivered through the opened BBB. Second, the afore mentioned pressure dependence of BBB opening size was observed for both short and long ultrasound pulses. Third, compared with the long pulse ones, short pulse cases showed increase in the area of fluorescence and a more homogeneous distribution of the dextrans. Fourth, stable cavitation was detected at all pressure levels; however, only at 0.8 MPa, inertial cavitation was observed at 100% probability.

**CONCLUSIONS:** The study results suggest that stable cavitation is always associated with BBB opening and inertial cavitation is required for the delivery of larger molecules. These results indicate that BBB opening size is pressure dependent, which can be used to control the delivery of therapeutic agents of different sizes across the BBB.

(Supported in part by the NIH grant R01AG038961)



**Oral session 3**

**2013/5/13 16:16:00**

**CONTROL ID:** 1659152

**TITLE:** ULTRASOUND-MEDIATED GENE THERAPY IN SWINE LIVERS USING SINGLE ELEMENT, MULTILENSED HIGH INTENSITY ULTRASOUND TRANSDUCERS

**AUTHORS/INSTITUTIONS:** M.L. Noble, S. Song, R.R. Sun, L. Fan, C.H. Miao, Seattle Children's Research Institute, Seattle, WA|K.P. Morrison, G.W. Keilman, Sonic Concepts Inc., Bothell, WA|M. Paun, Applied Physics Laboratory, University of Washington, Seattle, WA|K.R. Loeb, Fred Hutchinson Cancer Research Center, Seattle, WA|C.H. Miao, Dept. of Pediatrics, University of Washington, Seattle, WA|

**ABSTRACT BODY:**

**OBJECTIVE:** We have successfully demonstrated ultrasound (US)-mediated transfection of a reporter gene into pig livers. Using a 1.1 MHz large diameter, unfocused (H105) US transducer at 2.7 MPa peak negative pressure (8400 W), we obtained a 64-fold enhancement in luciferase expression compared to sham-control, with minimal tissue damage. This transducer allowed us to deliver uniform high pressures to large tissue volume in a short amount of time, which is crucial before microbubbles (MBs) and plasmids evacuates the treatment site. However, its planar design significantly limits the electrical energy input. New transducers were developed by utilizing spherical (H185A) and cylindrical (H185B) concave lenses to focus the acoustic signal and reduce the electrical power requirement, which allowed us to investigate gene transfection at high pressures.

**METHODS:** All three transducers have a central frequency of 1.1 MHz: (1) H105 is an apodized, dual element transducer with a 52-mm effective diameter; (2) H185A is a mono-element transducer, which contains 19 individual 10-mm plano-concave lenses with a 20-mm focus; (3) H185B is also a mono-element transducer, which has 5 planoconcave lenses with a cylindrical focus of 20-mm. The pGL4/MB solution was injected via a segmental portal vein branch with occlusion of the inferior vena cava while US was applied on the liver surface for 4 mins (20 cycle pulses, 50 Hz PRF). After 24 hrs, pigs were sacrificed, and the treated and control lobes were sectioned and processed to evaluate luciferase expression.

**RESULTS:** At 2.7 MPa, luciferase expression in pig livers using H185A are improved, up to 5-fold better than studies with H105 or up to 313-fold higher compared to sham-control. Studies using H185B also enhanced gene transfection, up to 2-fold better than H105 and up to 122-fold higher compared to sham-control. Preliminary results from studies using H185A and H185B at 3.3 MPa also showed considerable enhancement from H105 and sham pigs with minimal liver tissue damage.

**CONCLUSIONS:** The use of new lenses has enabled us to improve high intensity US transducer design with reduced electrical power input and improved robustness. This will allow us to continue our exploration of US-mediated gene transfection in large animals at higher pressures to further enhance gene transfection efficiency.



### Oral session 3

2013/5/13 16:28:00

**CONTROL ID:** 1669760

**TITLE:** MR-GUIDED FOCUSED ULTRASOUND INDUCED HYPERTHERMIA FOR ENHANCING DRUG DELIVERY IN A PANCREATIC CANCER MOUSE MODEL

**AUTHORS/INSTITUTIONS:** N. Farr, J. Hwang, Bioengineering, University of Washington, Seattle, WA|Y. Wang, F. Starr, Applied Physics Laboratory, University of Washington, Seattle, WA|S. D'Andrea, J. Hwang, Department of Medicine, University of Washington, Seattle, WA|D. Lee, Department of Radiology, University of Washington, Seattle, WA|

#### **ABSTRACT BODY:**

**OBJECTIVE:** Pancreatic cancer has one of the lowest survival rates because current therapies are ineffective. Dense stromal tissue and poor vascular perfusion limits drug penetration and uptake into the tumor tissue. Growing evidence suggests that hyperthermia in combination with temperature sensitive liposomal (TSL) drug delivery can lead to increased organ perfusion and drug extravasation resulting in high local drug concentration. Enhanced drug delivery may be achieved using Magnetic Resonance-guided High Intensity Focused Ultrasound (MR-HIFU) in conjunction with a heat triggered drug delivery system. MR-guided heating methods enable accurate and precise spatial and temporal control of heating.

**METHODS:** An orthotopic model of the KPC pancreas cancer mouse model was used for the studies. An animal positioning system with an integrated 4-channel small animal Magnetic Resonance Imaging (MRI) coil (Philips Medical Systems, Helsinki, Finland) was used on the MRgFUS system (Sonalleve., Philips Healthcare) to hold, image and treat the mice assigned in experimental group. Mice were treated by targeting sonications (1.2 MHz frequency, 7W acoustic power) in 5-10 minute increments with a total time of 30 minutes after injection of TSLs loaded with doxorubicin (ThermoDox., Celcion Corporation). Temperature elevations during sonications were monitored by a gradient echo based echo planar imaging (EPI) sequence with EPI factor 5, TE/TR: 16/25 ms, flip angle 20 degree, dynamic scan time 1.8s. A small gel phantom placed beside the mouse was used to monitor the magnetic drift for temperature correction. Mice were sacrificed immediately after treatment and tumor, spleen, liver and kidney were collected. All samples were evaluated for drug concentration. Survival mice were sacrificed after three days.

**RESULTS:** Preliminary fluorescence evaluation of the samples revealed increased focal nuclear uptake of doxorubicin in tumors treated with MR-HIFU hyperthermia with systemically administered doxorubicin loaded TSLs.

**CONCLUSIONS:** Hyperthermia therapy in a small animal was successful using a clinically available MR-HIFU system for acute and survival studies.





### Oral session 3

2013/5/13 16:40:00

**CONTROL ID:** 1671097

**TITLE:** LOW INTENSITY CONTINUOUS ULTRASOUND ENHANCES DRUG DELIVERY OF ZOLEDRONIC ACID IN A BREAST CANCER BONE METASTASES MOUSE MODEL

**AUTHORS/INSTITUTIONS:** S. Tardoski, J. Ngo, D. Melodelima, LabTau, INSERM U1032, Lyon, 69003, FRANCE | S. Tardoski, P. Clézardin, Lyos, INSERM U1033, Lyon, 69008, FRANCE |

#### **ABSTRACT BODY:**

**OBJECTIVE:** As a treatment of bone metastases, zoledronate (ZOL) acts as an inhibitor of osteoclasts-mediated bone resorption. Antitumoral effects of ZOL have been described in vitro at high doses, incompatible with a clinical use. Here we report the feasibility of using low intensity continuous ultrasound to enhance the delivery of ZOL in tumor cells.

**METHODS:** First, in vitro experiments were performed in order to measure the penetration of ZOL into tumor cells. In vivo, 69 mice bearing breast cancer bone metastases were randomized into 5 groups. A single dose of ZOL was combined with a daily application of low intensity continuous ultrasound (US). This dose of ZOL was calculated equivalent to the 4-mg clinical dose. A transducer working at a frequency of 2.9 MHz was used. The free field acoustic power was 7 watts applied for 30 minutes to produce thermal effects (temperature rise of 5°C) in bone tumors. US treatments were performed each day for 15 days. Efficacy of treatments was measured by radiography (area of the osteolytic lesions in mm<sup>2</sup>), histomorphometry (Tumor Burden/Soft Tissue Volume: TB/STV) and immunohistochemistry.

**RESULTS:** In vitro, US-generated hyperthermia enhances the penetration of ZOL 3 times compared with no US. In vivo, it was found that US alone did not have any inhibitory effect on bone destruction when compared to vehicle-treated animals. A statistically significant decrease of bone destruction and skeletal tumor burden was found in mice that received a daily treatment of continuous US with ZOL (1.3±0.4 mm<sup>2</sup>, TB/STV=11%) compared with vehicle (6.6±1.6, TB/STV=62%) and, more importantly, with ZOL alone (TB/STV=46%). Tumor cells proliferation was decreased by 70% in animal who received ZOL and a daily application of US. In this group angiogenesis was reduced by 75% compared to ZOL alone, supporting the observed decrease of tumor burden. US exposure conditions have not created cavitation. No lesions were observed in surrounding tissues.

**CONCLUSIONS:** Daily application of low intensity continuous US in combination with a single dose of ZOL allows a synergistic effect leading to a decrease of bone destruction as well as a reduced skeletal tumor burden. US enhances membrane cell permeability as well as the bioavailability of ZOL for tumor cells. Clinical doses of ZOL and US were used, suggesting that clinical application of such therapy is possible.



**Oral session 3**

**2013/5/13 16:52:00**

**CONTROL ID:** 1671160

**TITLE:** LOW INTENSITY FOCUSED ULTRASOUND TRIGGERED LOCAL DRUG DELIVERY FROM LIPOSOMELOADED MICROBUBBLES

**AUTHORS/INSTITUTIONS:** Y. Zong, N. Zheng, S. Xu, M. Wan, Department of Biomedical Engineering, Xian Jiaotong Universtiy, Xian, Shaan Xi, CHINA|H. Su, J. Hu, Department of Ultrasound, Xijing Hospital, Fourth Military Medical University, Xian, Shaan Xi, CHINA|

**ABSTRACT BODY:**

**OBJECTIVE:** In this paper, we focus on the preparation of liposome-loaded microbubble with high drug encapsulation efficiency and the method of its localized drug delivery at desirable site under ultrasound monitor imaging, that can be achieved by locally application of focused ultrasound leading to microbubble disruption.

**METHODS:** We prepared the liposome with high encapsulation efficiency of weakly alkaline drug (>80%) by transmembrane ammonium sulfate gradients method, and loaded the liposome on lipid-shelled microbubbles via biotin-avidin bridge to carry a high load of bioactive agent (fluorescent model drug or anticancer drug sunitinib malate). The liposome-loaded microbubbles are triggered to disrupt under an synthesized and optimized sequence of lower intensity focused ultrasound (LIFU) pulses from a 128-element diagnostic linear array with transmit frequency of 5MHz and release drug in a focal region on a clinical ultrasound system. That is, synthesized LIFU pulse was used as a “controlling” field for drug delivery and disruption monitoring of liposome-loaded microbubbles. The in vitro flowing phantom, cell and in vivo kidney cancer model in mice experiments were used to demonstrate localized drug delivery under LIFU pulses with Ultrasonix Sonix Touch ultrasound system.

**RESULTS:** In the in vitro flowing phantom experiment, the impact of the power and pulse repeat frequency of transmitted focused ultrasound pulses, concentration of microbubbles and flowing rate on drug release efficiency under flowing condition was studied to determine the optical parameters for drug delivery. Then we used GRC-1 kidney cell monolayer to demonstrate that drug transfer can be limited to cells that are in the region of ultrasonic focus. The flow cytometry and cell viability test results indicate the mechanism of drug delivery might be that free drug was released from liposome under ultrasound exposure and enter the cell through sonoporation effect, not that liposomes fused with cellular membrane releaseing their contents into the cell. Additionally, the animal experiment results show that the drug carriers can be controllable released within the blood circulation by synthesized LIFU pulse.

**CONCLUSIONS:** Liposome-loaded microbubbles combined with LIFU may offer a highly promising combination of ultrasound therapeutic and monitoring imaging on commercial ultrasound scanner.



### Oral session 3

2013/5/13 17:04:00

**CONTROL ID:** 1683997

**TITLE:** IN VIVO RNA INTERFERENCE USING UNSEEDED INERTIAL CAVITATION AND PASSIVE LIPOSOMAL TARGETING

**AUTHORS/INSTITUTIONS:** R.A. Fowler, J. Mestas, C. Lafon, Inserm U1032 LabTAU, University of Lyon, Lyon, FRANCE|K. Chettab, D. Poloni, C. Dumontet, Inserm U1052, CRCL, University of Lyon, Lyon, FRANCE|D. Tobin, E. Nilssen, EpiTarget AS, Oslo, NORWAY|

#### **ABSTRACT BODY:**

**OBJECTIVES:** RNA interference-mediated gene silencing (RNAi) is a promising avenue for treating many pathological conditions. RNAi consists of transfecting small interfering RNA (siRNA) into the cell for target inhibition of disease relevant gene transcripts. To date, the majority of RNAi studies using acoustic cavitation have used microbubbles as cavitation seeds. Unseeded cavitation presents the advantage of creating cavitation within the tumoral extracellular space; unreachable by microbubbles. The aim of this study was to evaluate the use of acoustic cavitation without microbubbles for in vivo delivery of siRNA-loaded liposomes for gene suppression.

**METHODS:** The study was performed in xenograft tumours (MDA-231) grown in SCID mice. Modified SSB siRNA (Sjogren syndrome antigen B) was encapsulated in un-charged, sonosensitive liposomes (EpiTarget AS, Oslo, Norway). Ultrasound (US) was applied 2 hours after systemic injection (100 $\mu$ L, 166 $\mu$ g siRNA) with two 1.1MHz transducers placed confocally, beams crossed at 110°, and peak negative pressure reaching 15.6MPa. Tumors were localized with a Terason 12MHz imaging probe, and were swept through the focus at 1mm/s. Cavitation was confirmed in situ by backscattered broad band noise, and by hyperechogenic regions observed by the imaging probe. US safety was assessed by visual inspection, and analysis of annexin V and PI expression (apoptosis and cell viability indicators) using fluorescence-activated cell sorting (FACS). Gene expression was measured by rtPCR of SSB (housekeeping gene PPIB) 48 hours after treatment (time of sacrifice).

**RESULTS:** Mild irritation was observed on the tumors of sonicated mice. No significant difference in cell viability or apoptosis was seen between groups. Liposomal siRNA combined with US resulted in 35 $\pm$ 7% inhibition of SSB expression compared to untreated tissue, and 48 $\pm$ 6% compared to sonicated tissue.

**CONCLUSIONS:** This initial study demonstrates the use of a confocal ultrasound set-up for unseeded cavitation delivery of an siRNA loaded liposome. In vivo inhibition of gene expression was achieved with a neutrally-charged siRNA loaded liposome without significant toxicity. Additional studies will be performed to optimize the US settings for efficacy, toxicity and repeatability.



### Oral session 3

2013/5/13 17:16:00

**CONTROL ID:** 1700482

**TITLE:** POTENTIATING THE ANTITUMOR EFFECTS OF TAXANES WITH THE ANTIVASCULAR EFFECTS OF ULTRASOUND STIMULATED MICROBUBBLES

**AUTHORS/INSTITUTIONS:** M. Todorova, K. Hynynen, D. Goertz, Medical Biophysics, University of Toronto, Toronto, Ontario, CANADA|M. Todorova, V. Agache, B. Chen, T. Ibrahimli, K. Hynynen, D. Goertz, Sunnybrook Research Institute, Toronto, Ontario, CANADA|R. Karshafian, Ryerson University, Toronto, Ontario, CANADA|

#### **ABSTRACT BODY:**

**OBJECTIVE:** Ultrasound stimulated microbubbles (USMBs) are being investigated to improve the uptake of anticancer agents into tumor tissue. However, in many circumstances the uptake of anticancer agents is not limited by their inability to extravasate, which motivates the examination of other methods by which USMBs may enhance their effects. It has been shown recently that USMBs can shut down blood flow within tumors. We have reported that the antitumor effects of taxanes (docetaxel - DTX and paclitaxel - PTX) are enhanced when followed with 'antivascular' USMB treatments. Here we examine the influence of the relative timing of taxane and USMB treatments, and employ a histologic approach to assess the role of drug uptake changes in achieving these effects.

**METHODS:** EMT6 tumors were initiated subcutaneously in BalbC mice. Growth experiments were conducted with control, drug only, USMB-only, and two combined USMB+drug groups. In one combined group, drugs were administered 10mins prior to USMB treatments, and in the second this order was reversed. Both DTX (5mg/kg) and PTX (6mg/kg) drug groups were examined (8 groups, n=6-8/group). Additional acute experiments (n=4-5/group) were conducted, with tissue harvested 30mins post-treatment. The distribution of  $\gamma$ H2aX, a marker of DNA damage used as a surrogate indicator for the presence of DTX, was quantified as a function of distance from microvessels.

**RESULTS:** The USMB treatments resulted in a pronounced vascular shutdown within the tumor centers. The combined USMB+drug groups produced significant ( $p < 0.001-0.05$ ) growth inhibition relative to the control, drug only and USMB-only groups. This occurred independent of the relative order of drug/USMB scheduling. The histology results indicated higher levels of  $\gamma$ H2aX for the DTX and USMB+DTX groups relative to controls, but there was not a difference between the DTX and USMB+DTX groups, indicating that the uptake of DTX was not promoted by the USMB treatments.

**CONCLUSIONS:** These data provide further evidence that antivascular USMB treatments can potentiate the effects of taxane drugs. The occurrence of these effects when drugs are administered after a vascular shutdown, coupled with the histologic data suggest that drug uptake is not the primary mechanism of therapy enhancement. These results have direct parallels to those achieved when small molecule vascular disrupting agents are coupled with taxanes.



**Oral session 4A**

**2013/5/13 13:00:00**

**CONTROL ID:** 1671675

**TITLE:** ROBUST DETECTION AND CONTROL OF BUBBLE ACTIVITY WITH A SINGLE ELEMENT, DUAL-MODE TRANSDUCER

**AUTHORS/INSTITUTIONS:** A.J. Casper, Biomedical Engineering, University of Minnesota, Minneapolis, MN | E.S. Ebbini, Electrical Engineering, University of Minnesota, Minneapolis, MN |

**ABSTRACT BODY:**

**OBJECTIVE:** A real-time system for monitoring and controlling bubble activity during ultrasound therapies is presented. A single element transducer was used in a dual-mode fashion to both deliver high-intensity focused ultrasound (HIFU) and monitor the focus for bubble activity with pulse echo imaging.

**METHODS:** An FPGA was used to coordinate imaging and HIFU excitation by temporally interleaving both at 1000 FPS. The pulse-echo data was analyzed in real-time on-board the FPGA and used to control the HIFU therapy with microsecond latency. The dual-mode nature of the transducer inherently aligned the imaging focus with the therapy focus. This inherent alignment ensured the pulse-echo imaging was sensitive to events in the HIFU focus.

**RESULTS:** This system was used to collect in-vitro results demonstrating bubble detection and control using an integrated-backscatter bubble detection algorithm across a range of intensities, transducers, and tissues. A 2.5 MHz and a 3.5 MHz transducer were used at intensities between 2-5 kW/cm<sup>2</sup> and 10-17 kW/cm<sup>2</sup>, respectively, in porcine liver and bovine heart tissue. These results demonstrate robust detection of bubble activity and control the HIFU intensity so as to prevent

overexposure in individual lesions using a single element transducer. Additional results are presented which extend the single lesion control scheme to volumetric ablations where the bubble detection feedback is used to adaptively adjust the in-situ HIFU intensity to minimize the risk of both over and under treatment.

**CONCLUSIONS:** Real-time monitoring of backscattered signals from a dual-mode ultrasound transducer allow for robust detection and control of bubble activity.



**Oral session 4A**

**2013/5/13 13:12:00**

**CONTROL ID:** 1671754

**TITLE:** PATIENT SPECIFIC MODELLING & SIMULATION OF FUS IN MOVING ORGANS: THE VPH PROJECT FUSIMO

**AUTHORS/INSTITUTIONS:** T. Preusser, M. Guenther, Fraunhofer MEVIS, Bremen, GERMANY|T. Preusser, Jacobs University, Bremen, GERMANY|M. Bezzi, Universita Degli Studi Di Roma La Sapienza, Rome, ITALY|J. Dankelman, Technische Universiteit Delft, Delft, NETHERLANDS|J. Jenne, mediri GmbH, Heidelberg, GERMANY|T. Lang., Stiftelsen SINTEF, Trondheim, NORWAY|Y. Levy, InSightec Ltd, Tirat Carmel, ISRAEL|M. Mueller, IBSmm spol s.r.o., Brno, CZECH REPUBLIC|G. Sat, GE Medical Systems, Haifa, ISRAEL|C. Tanner, Swiss Federal Institute of Technology Zurich, Zurich, SWITZERLAND|C. Tiu, SMIT-Medis Foundation, Campina, ROMANIA|A. Melzer, IMSaT University Dundee, Dundee, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVES:** High intensity focused ultrasound (FUS) for the treatment of lesions in the liver is challenged by the movement of the organs under breathing. Often the target is additionally shielded by the rib cage. It is hypothesized that the full potential of FUS for abdominal organs can be unleashed only with sophisticated software for planning, execution and monitoring combined with advanced hardware. The EU project FUSIMO develops a software demonstrator for the patient specific planning of MR guided FUS in the liver. The goal is to base the therapy planning on a predictive outcome simulation taking organ motion into account.

**METHODS:** The FUSIMO system integrates three patient specific models: (i) an organ motion model for the deformation of the relevant anatomical structures during breathing; (ii) a tissue model for the ultrasound propagation, the energy distribution as well as the tissue heating and cooling; (iii) an organ/tumour model for the tissue's response to the therapy. The software demonstrator coordinates the models and combines them with data from patient specific imaging with MR or Ultrasound.

**RESULTS:** The models are combined with a workflow-oriented user interface. The model for organ motion is derived from imaging data of a cohort of volunteers and parameterized for each individual patient. The prediction of ultrasound propagation and tissue damage are based on the state of the art hybrid angular spectrum method and well-established perfusion and damage models. The FUSIMO system is being evaluated on Thiel embalmed cadavers.

**CONCLUSIONS:** The FUSIMO demonstrator shall support the assessment of the feasibility of MRgFUS intervention in the liver by predicting the outcome, detecting risks and avoiding them, monitoring the progress and tracking deviations from the planned procedure. The project shows that organ specific modelling and simulation of MRgFUS in moving organs is feasible. We expect our system to allow the safe application of MRgFUS on moving abdominal organs such as the liver.



**Oral session 4A**

**2013/5/13 13:24:00**

**CONTROL ID:** 1672103

**TITLE:** NUMERICAL ESTIMATION OF HIFU FOCAL ERROR TO BREAST CANCER TREATMENT

**AUTHORS/INSTITUTIONS:** R. Narumi, T. Azuma, A. Sasaki, S. Takagi, Y. Matsumoto, Department of Bioengineering, The University of Tokyo, Tokyo, JAPAN|K. Okita, College of Industrial Technology, The Nihon University, Tokyo, JAPAN|K. Yoshinaka, Human Technology Research Institute, Advanced Industrial Science and Technology, Tsukuba, JAPAN|K. Okita, S. Takagi, Organ and Body Scale Team, RIKEN, Wako, JAPAN|J. Shidooka, H. Furusawa, Brestopia Namba Hospital, Miyazaki, JAPAN |

**ABSTRACT BODY:**

**OBJECTIVE:** Acoustic inhomogeneity in the propagation media of HIFU (High Intensity Focused Ultrasound) has a potential risk to cause a focal error. Many research groups reported that the focal error of HIFU beam was critical when propagating media included bones. On the other hand, the focal error due to weakly heterogeneous such as breast tissue was not sufficiently studied. A numerical estimation of focal error after the propagation through breast tissue was described.

**METHODS:** Breast model was constructed from a 3D MRI breast data. All pixel intensity in the volume image was assigned to 4 kinds of typical material; water, connective tissue, fat and glandula mammaria. The respective sound speed of latter three materials were 1465, 1547, and 1615m/s. HIFU simulator based on a finite-time-domain-method developed in Riken was employed. The simulation grid size was 0.1mm, and was generated through an interpolation from 0.625 mm pitch MRI image data. A 56-channel HIFU transducer with both aperture width and focal length were 100 mm and with a center frequency of 2 MHz was used.

**RESULTS:** Three separated peaks were observed after propagation of breast tissue. The focal shift amount was a few millimeter in both lateral and propagation directions. To confirm the relation between the acoustical inhomogeneous and the focal error, time reversal method in this simulation was employed. A virtual sound source was fixed at the original focal point and a distribution of propagation time on the surface of HIFU transducer was calculated. Based on this value, HIFU beam was transmitted. In this case, focal error was successfully suppressed. This result showed that focal error in breast tissue was caused by acoustic inhomogeneous. Finally, to evaluate an effect of skin and that of mixed structure of fat and glandula mammaria independently, two following models were built; the former included a skin and water and the latter included water, fat and glandula mammaria. In these results, focal error was observed only in the model including water, fat and glandula mammaria. This results showed that acoustic inhomogeneity inside of breast was more essential than that of the breast surface.

**CONCLUSIONS:** It was found that the focal error was caused by the acoustic inhomogeneous in breast tissue, based on numerical simulation using MRI data. This effect was caused by the internal structure of the breast. This error could be suppressed by the time reversal method.



**Oral session 4B**

**2013/5/13 13:36:00**

**CONTROL ID:** 1672135

**TITLE:** A REALISTIC 2D MODEL FOR ULTRASOUND GUIDED FOCUSED ULTRASOUND SURGERY OF KIDNEY TUMOR

**AUTHORS/INSTITUTIONS:** X. Xiao, T. Jiang, Z. Huang, School of Engineering, University of Dundee, Dundee, UNITED KINGDOM|G. Corner, Medical Physics, Ninewells Hospital and Medical School, Dundee, UNITED KINGDOM|A. Melzer, Institute of Medical and Technology, University of Dundee, Dundee, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVE:** High-intensity focused ultrasound (HIFU) is an expanding non-invasive medical intervention for thermal ablation of tumors. However, one main limitation in HIFU treatment is the abdominal movement in liver and kidney caused by respiration. The study has set up a tracking model which mainly comprises of a target carrying box and a motion driving balloon. In this paper, it is developed to investigate the main issues of HIFU on moving targets which includes motion tracking method and HIFU ablation estimation.

**METHODS:** A real-time B-mode ultrasound guidance method suitable for tracking of the abdominal organ motion in 2D was established and tested. For the setup, the phantoms mimicking moving organs are carefully prepared with agar surrounding round-shaped egg-white as the target of focused ultrasound ablation. Physiological phantoms and animal tissues are driven moving reciprocally along the main axial direction of the ultrasound image probe with slightly motion perpendicular to the axial direction. The moving speed and range could be adjusted by controlling the inflation and deflation speed and amount of the balloon driven by a medical ventilator. A 6-DOF robotic arm was used to position the focused ultrasound transducer. The overall system was trying to estimate to simulate the actual movement caused by human respiration. HIFU ablation experiments using phantoms and animal organs were conducted to test the tracking effect. Ultrasound strain elastography was used to post estimate the efficiency of the tracking algorithms and system.

**RESULTS:** The tracking error on the motion detection was estimated by comparing the size of the lesions caused by the FUS between when the target is moving and not moving. In moving state, the axial size of the lesion (perpendicular to the movement direction) are averagely 4mm, which is one third larger than the lesion got when the target was not moving. The main error comes from the mechanical control of the robotic arm.

**CONCLUSIONS:** The tracking model was proven to be helpful for solving main issues for motion tracking problems in HIFU experiments. This presents the possibility of developing a low-cost real-time method of tracking organ motion during HIFU treatment in liver or kidney.





**Oral session 4B**

**2013/5/13 13:48:00**

**CONTROL ID:** 1672460

**TITLE:** HIFU BEAM LOCALIZATION USING HARMONIC MOTION IMAGING

**AUTHORS/INSTITUTIONS:** Y. Han, G.Y. Hou, S. Wang, E. Konofagou, Biomedical Engineering, Columbia University, NewYork, NY|E. Konofagou, Radiology, Columbia University, NewYork, NY|

**ABSTRACT BODY:**

**OBJECTIVE:** Several ultrasound-based imaging modalities have been proposed for image guidance and monitoring of High-Intensity Focused Ultrasound (HIFU) surgery. However, accurate localization and characterization of the effective region of treatment (thermal lesion) remain the obstacles in the clinical implementation of HIFU ablation. Harmonic motion imaging for focused ultrasound (HMIFU) is a novel HIFU therapy monitoring method based on radiation-force-induced localized displacement. The capability of relative stiffness mapping has been validated in previous studies. In this study, the induced displacement was utilized to localize the HIFU focal spot inside the tissue prior to treatment.

**METHODS:** The HMIFU setup consists of a 4.75-MHz HIFU transducer using an amplitude-modulated HIFU beam for tissue probing, and a confocal 7.5-MHz single-element, pulse-echo transducer used for simultaneous RF acquisition. The phantom experiments were conducted on four tissue-mimicking gelatin phantoms and three measurements on each with a Young's modulus at 10 kPa and 15 kPa. A focal zone was defined according to the increases of displacement at the focus in axial direction predicting the lesion area. Under the same input parameters, in vitro

experiments were performed on two canine liver specimens to validate the lesion region with a defined focal zone. For ablation, the in situ acoustic intensity was equal to 4200 W/cm<sup>2</sup> and the duration was equal to 120 s to cause the lesion.

**RESULTS:** The focal zone defined by -1.5-dB of the peak HMI displacement was measured to be 12.58 mm in the 10 kPa phantom and 15.15mm in the 15 kPa one. The focal zones were trackable inside the phantom when moving the transducer in the axial direction. The in vitro measurements showed good agreement between the HMI predicted focal zone and the induced HIFU lesion. A 92.7% overlap was shown between the three predicted focal zones and three lesions induced.

**CONCLUSIONS:** HMI for focused ultrasound (HMIFU) has been experimentally shown to be capable of predicting and tracking the focal region in both phantoms and tissues in vitro. The accuracy of beam localization was verified by HMI of the post-ablated tissue. The beam localization method could be fully integrated into a 2D HMIFU system in future in vivo studies.



**Oral session 4B**

**2013/5/13 14:00:00**

**CONTROL ID:** 1672481

**TITLE:** A DOSING PLANNING METHOD FOR RENAL DENERVATION USING HIGH INTENSITY FOCUSED ULTRASOUND

**AUTHORS/INSTITUTIONS:** M. Gertner, F.P. Curra, S. Jing, A. Sabet, D. Perozek, J. Zhang, Kona Medical, Inc., Bellevue, WA|F.P. Curra, Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA|

**ABSTRACT BODY:**

**OBJECTIVE:** Accurate and practical treatment planning is vital for achieving safe and effective high-intensity focused ultrasound (HIFU) treatments. In this paper, a systematic dose planning strategy for optimizing noninvasive HIFU treatments in human subjects is presented.

**METHODS:** The approach combined the usage of a computationally efficient, intensity-time product and an acoustic-thermal simulation method based on models constructed from 3D CT or magnetic resonance tomography datasets from human subjects. The intensity-time product, which incorporates the acoustic characteristics of the therapy field from the simulation, provide the linkage between the thermal dose and the therapy system controlling parameters, such as, treatment time, output acoustic energy, pulse duty cycles, etc.

**RESULTS:** Numerical, bench top and animal experiment results were used to validate the method prior to clinical work. Subsequently, clinical work demonstrated evidence of external acoustic denervation of the renal nerves targeted from the posterior direction.

**CONCLUSIONS:** The methods and tools described may be employed for dose planning for an arbitrary HIFU transducer configuration, therapy application and anatomical region.



**Oral session 4B**

**2013/5/13 14:12:00**

**CONTROL ID:** 1680068

**TITLE:** Feasibility of large volume tumor ablation using multiple-mode strategy with fast scanning method: a numerical study

**AUTHORS/INSTITUTIONS:** S. Qiao, G. Shen, Y. Yu, Z. Su, X. Ji, H. Wu, Y. Chen, Biomedical Instrument Institute, Shanghai Jiao Tong University, Shanghai, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** When using HIFU to ablate a tumor with large volume, numerous sonications are necessary to cover the whole treatment area in the traditional scanning method with single focus, because the focal size of ultrasound is relatively small compared with that of tumor. In the consideration of safety and efficiency, the treatment parameters including foci arrangement, sonication sequence, duration of each sonication, the intersonication cooling time, need to be effectively determined, which leads to a complex problem of planning. The present paper proposed a multiple-mode strategy to ease the complexity for the HIFU treatment of large tumor, in which fast scanning method was used to generate the basic element of treatment.

**METHODS:** In the fast scanning method, a single focus was moved rapidly along the predetermined scanning paths with 10 Hz of switching focus frequency, indicating that each sonication on one location was conducted for 0.1 s before the ultrasound focus was immediately steered to the next focus location. The effect of scanning path to the size of lesion and treatment time was negligible, making it suitable for generating treatment element instead of single focus. Three different focus pattern was applied in the fast scanning method and regarded as basic element to respectively ablate target area with the size of 16, 36 and 64 mm<sup>2</sup> in the focal plane. The treatments using multiple modes were investigated by calculating the bio-heat transfer equation, and compared to those using traditional scanning method.

**RESULTS:** The target areas were all fully ablated by using multiple-mode strategy, and the total treatment time were respective 154, 262 and 431 s. Compared to the results of traditional method, the treatment time was significantly reduced. Because the size of basic element formed by fast scanning method in the new strategy was larger than the single focus, the number of required elements for ablation was less. Hence total cooling time between consecutive treatment elements was shorter in the multiple-mode strategy.

**CONCLUSIONS:** Based on the simulation results, multiple-mode strategy with fast scanning method is able to fully ablate large tumor, and more efficient than the single focus scanning method. Using different focus patterns in fast scanning method can result in different size of treatment element, which provides more flexibility in applying this new strategy.



**Oral session 4B**

**2013/5/13 14:30:00**

**CONTROL ID:** 1659483

**TITLE:** PASSIVE MICROLESION DETECTION AND MAPPING FOR TREATMENT OF HYPERTROPHIC CARDIOMYOPATHY

**AUTHORS/INSTITUTIONS:** Y.I. Zhu, D.L. Miller, C. Dou, O.D. Kripfgans, Department of Radiology, University of Michigan, Ann Arbor, MI|

**ABSTRACT BODY:**

**OBJECTIVE:** Transcutaneous High Amplitude Myocardial Contrast Echocardiography (HAMCE) with microbubbles can produce diffuse cell loss from cavitation microlesions. The objective was to exploit this bioeffect in a novel therapeutic system for treatment of hypertrophic cardiomyopathy. A key factor is the creation of a multi-parameter prediction function of microbubble and biological responses.

**METHODS:** An preclinical imaging system with HIFU synchronization and receive-only imaging has been implemented on a research platform (Verasonics Inc., Redmond, WA). A cavitation mapping technique was employed to spatially locate and depict microbubble activity during treatment and to monitor microlesioning in real-time. Ultrasound contrast agent (USCA), Definity (Lantheus Med. Imag., Billerica, MA), was diluted into phosphor buffered saline (PBS, pH=5.0) and pumped at 4 cm/s in a dialysis tubing setup (1.5 cm dia). Polystyrene spheres (Duke Scientific, Palo Alto, CA) were employed as linear scatterers (LS) (0.15 g/1100 mL, in a water and glycerol suspension). Spectral data from LS was compared to USCA for system transfer function equalization. Single element HIFU transducers (A314S and A381S, Panametrics, MA) were driven in burst mode (10 cycles, 5.5 MPa pp) acoustic pressure at the focus and a duty cycle of 22 Hz. Passive cavitation detection was implemented using a linear array (L7-4, ATL, Seattle, WA). The acoustic emissions and scattered signal from the volume of interest was beam-formed by a delay-and-sum algorithm followed by signal integration.

**RESULTS:** Mapped cavitation signals were observed laterally within 1.5 mm of the HIFU transducer focus and axially within the pulse length. Acoustic emissions from USCA reached from fundamental to 8th harmonic for a 1 MHz excitation and were accessible in the bandwidth of the L7-4 for all tested dilutions (25  $\mu$ L, 50  $\mu$ L, 100  $\mu$ L, 200  $\mu$ L stock per liter saline). Ratios of higher harmonic to fundamental frequency increased with drive pressure and exceeded 5 dB.

**CONCLUSIONS:** This unified therapy and monitoring system adequately delineates the spatial location of triggered microbubble dynamics. Future implementations will combine premature electrocardiogram complexes with cavitation activity mapping to predict microlesioning during the ablation procedure in heart tissue. The presented analysis can be implemented in real-time for therapy progression feedback, allowing for rapid translation to a clinical setting.



**Oral session 4B**

**2013/5/13 14:42:00**

**CONTROL ID:** 1671641

**TITLE:** A UNIQUE PRESSURE FIELD USING A HIGH INTENSITY ULTRASOUND TRANSDUCER WITH A MULTILENS STRUCTURE AS A FACEPLATE

**AUTHORS/INSTITUTIONS:** K.P. Morrison, G.W. Keilman, Sonic Concepts, Inc., Bothell, WA | M.L. Noble, C.H. Miao, Seattle Children's Research Institute, Seattle, WA |

**ABSTRACT BODY:**

**OBJECTIVE:** The delivery of uniform high intensity ultrasound (HIU) over a large aperture area has proven to enhance gene transfection in large tissue volumes using planar transducers. One must consider a transducer's geometry, frequency and sound speed of the tissue medium to determine its near field distance and the lateral focal full-width half maximum (FWHM). The underlying H-185 transducer uses unique geometric concepts to increase gene transfection rates compared with planar transducers.

**METHODS:** Mechanical constraints allowed for a flat 1.1 MHz transducer with a .50 mm aperture. The desired acoustic parameters were written to:

- a) Disrupt the diffraction field within 1 cm from the transducer to eliminate near field effects
- b) Develop a pressure focal gain of 2 within 1 cm from the transducer's surface
- c) Sustain 2 to 2.8 focal gain throughout the treatment volume up to 5 cm from the transducer
- d) Sustain constant pressure throughout the treatment volume
- e) Sustain >65% conversion efficiency from 0.9 to 1.3 MHz
- f) Achieve a peak negative pressure of 3.3 MPa at the radiating surface

The natural focus for a .50 mm planar device is estimated to reach its peak pressure gain of 2 at 46 cm from the transducer's surface. Standard multi-channel electronics and array transducers would require equipment outside the budget of this project. Therefore, point spread function simulations were used to assist in developing a design by superimposing multiple slightly focused elements using one channel.

**RESULTS:** The H-185 configuration has been designed to meet all of the criteria outlined above and uses one RF channel, one piezoceramic element and a faceplate comprised of multiple plano-concave lenses. The faceplate material uses a proprietary conductive composition to acoustically match between the piezoceramic and tissue, and to yield a maximum allowable efficiency over a large operating band. Two different faceplate geometries were developed:

- 1) H-185A uses multiple spherical lenses to achieve slight focusing along the focal axis
- 2) H-185B uses multiple cylindrical lenses to achieve slight focusing along the focal plane

The concave lenses were designed specific to the faceplate material in both cases.

**CONCLUSIONS:** Experimental measurements of the H-185 validated the acoustic parameters outlined above and has proven to increase gene transfection compared to a planar transducer in large animals.



**Oral session 4B**

**2013/5/13 14:54:00**

**CONTROL ID:** 1672475

**TITLE:** EXTRACORPOREAL HIGH INTENSITY FOCUSED ULTRASOUND SYSTEM FOR RENAL DENERVATION

**AUTHORS/INSTITUTIONS:** M. Gertner, D. Perozek, J. Zhang, Kona Medical, Inc., Bellevue, WA|

**ABSTRACT BODY:**

**OBJECTIVE:** Hypertension is a leading attributable cause of death worldwide. It is a significant, growing global healthcare problem affecting over one billion people and is associated with an increased risk of heart attack, stroke, heart failure, kidney disease and death. An innovative invasive and non-invasive therapy system for treatment of hypertension using focused ultrasound is under development at Kona Medical.

**METHODS:** The current version of the Kona system utilizes a target catheter which delivers an ultrasound signal with acoustic time of flight (ATOF) to provide targeting and 3D target motion tracking of the renal artery. A therapeutic system with a phased array has been developed to provide focused acoustic energy from outside a patient to ablate or inhibit nerves leading to and from the kidney. Unlike other renal denervation methods which rely on a catheter emitting therapeutic energy through the wall of the renal artery to affect the renal nerves, the therapeutic energy Kona

system delivers originates entirely from outside the patient and can be delivered to renal artery with smaller diameters.

**RESULTS:** The system, which incorporates the ATOF, 3D motion for the array as well as electronic phasing in depth direction tracks motion of the renal artery deliver therapeutic energy to a well-defined region around the renal artery. The system has been developed and validated in bench top tests and animal experiments prior to clinical human feasibility trials.

**CONCLUSIONS:** The initial human feasibility trials demonstrate that external acoustic denervation of the renal nerves from outside the patient is achievable. The company is developing a fully non-invasive system which will ultimately expand the eligible patient population and offer a potentially safer and less expensive treatment for hypertension than catheter based systems.



**Oral session 4B**

**2013/5/13 15:06:00**

**CONTROL ID:** 1678830

**TITLE:** STIMULATED RELEASE OF NUCLEIC ACID CANCER BIOMARKERS BY HIFU: A STUDY IN A RAT PROSTATE CANCER MODEL

**AUTHORS/INSTITUTIONS:** T. Khokhlova, J. Hwang, Medicine, University of Washington, Seattle, WA|J.R. Chevillet, M. Tewari, Human Biology, Fred Hutchinson Cancer Research Center, Seattle, WA|T. Khokhlova, Y. Wang, J. Hwang, Applied Physics Laboratory, University of Washington, Seattle, WA|

**ABSTRACT BODY:**

**OBJECTIVES:** The ability of ultrasound to stimulate the release of cancer-specific protein biomarkers into the circulation was recently reported, however, physical and biological mechanisms behind it are unclear. Here, the release of a recently established class of nucleic acid-based cancer biomarkers – microRNAs (miRNAs) – by high intensity focused ultrasound (HIFU) was investigated in a rat prostate cancer model. The benefits of two different HIFU treatment protocols causing localized tissue lysis or mild hyperthermia in stimulation of miRNA release were compared.

**METHODS:** Copenhagen rats were implanted subcutaneously on the hind limb with syngeneic MatLyLu prostate cancer cell line. HIFU exposures at 1.1 MHz, optimized for either partial lysis of the tumor tissue or sublethal heating thereof (ISPPA=120 W/cm<sup>2</sup>, 50% duty cycle, 1-minute exposure) were performed in two groups of animals (n=8) after the tumor reached 12 mm in diameter. The control group received sham exposure. Lysis of the tumor tissue was performed using boiling-histotripsy, in which boiling is induced in several milliseconds at the transducer focus by a high amplitude nonlinear HIFU pulse, and the interaction of the boiling bubble with HIFU field leads to tissue emulsification. Blood withdrawals were performed before and immediately after each exposure, and at several post treatment points: 30 minutes, 1, 3 and 24 hours. The blood samples were processed into plasma and profiled for the relative abundance of 375 miRNAs by qRT-PCR arrays. Prospective biomarkers were identified based on graft cell line profiling and low background expression in rat plasma.

**RESULTS:** The number of copies of tumor-specific miRNAs (miR-34c, miR-9, miR-129-5p, miR-100, miR-196a) were substantially increased (2-34-fold) within 15 minutes after HIFU-induced tumor lysis, but not HIFU-induced mild hyperthermia. This increase returned to baseline within 1-3 hours. The concentration of a broadly expressed miR-16 was used as a negative control and did not change significantly.

**CONCLUSIONS:** This study indicates that HIFU-induced localized tissue lysis may be used to enhance the diagnostic yield of the tumor-specific nucleic acid biomarkers, and thus serve as a “non-invasive biopsy” of undiagnosed tissue masses. Work supported by NIH (1K01EB015745, R01CA154451), American Cancer Society/Canary Foundation (to J.R.C.) and Damon Runyon-Rachleff Innovation Award (to M.T.).



## Oral session 4B

2013/5/13 15:45:00

**CONTROL ID:** 1683078

**TITLE:** Evaluation of Pulsed Focused Ultrasound Mediated Nanodroplet-Encapsulated Chemo-therapeutic Agent for Treatment of Prostate Cancer

**AUTHORS/INSTITUTIONS:** L. Chen, X. Chen, R. Gupta, D. Cvetkovic, B. Wang, N. Rapoport, C. Ma, Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA|N. Rapoport, Department of Bioengineering, University of Utah, Utah, UT|

### **ABSTRACT BODY:**

**OBJECTIVES:** We developed techniques for the formulation of docetaxel-encapsulated nanodroplets, which respond to ultrasound. This study aims to investigate the improvement of prostate cancer treatment by a novel drug delivery technique combining pulsed high-intensity focused ultrasound (pHIFU) exposures and docetaxel-encapsulated nanodroplets under MR image guidance using prostate cancers grown orthotopically in nude mice.

**METHODS:** Human prostate cancer (LNCaP) cells were implanted orthotopically. Tumor growth was monitored using MRI. When the tumors reached a designated volume of  $91 \pm 21$  mm<sup>3</sup>, tumor-bearing mice were randomly divided into 5 groups (n=5). Group 1 animals were treated with an IV injection of docetaxel-encapsulated nanodroplets (DTX-ND) + pFUS. Animals in Group 2 were treated with pFUS alone. Animals in Group 3 were injected (IV) with docetaxel-encapsulated nanodroplets (DTX-ND) alone, Group 4 received free docetaxel and Group 5 was used as control. The mean diameter of the drug-loaded nanodroplets was  $220 \pm 30$  nm. Ultrasound treatment parameters were 1MHz, 25W acoustic power, 10% duty cycle and 60 seconds for each sonication. After treatment, animals were allowed to survive for 4 weeks. Tumor volumes were measured on MRI.

**RESULTS:** Compared with the control group, significant tumor growth delay was observed in Group 1 with  $p=0.039$  at 4 weeks after treatment. There was no significant tumor growth delay observed for Group 2 ( $p=0.477$ ), Group 3 ( $p=0.209$ ) and Group 4 ( $p=0.476$ ).

**CONCLUSIONS:** Our preliminary results showed a great potential for prostate cancer therapy using targeted docetaxel + nanodroplets, which could be activated by pHIFU. More animal studies are warranted to confirm the results and to further optimize the docetaxel + nanodroplets delivery and pHIFU parameters.





**Oral session 4B**

**2013/5/13 15:57:00**

**CONTROL ID:** 1683965

**TITLE:** IN-VIVO TISSUE EMULSIFICATION USING BOILING HISTOTRIPSY HIFU EXPOSURES

**AUTHORS/INSTITUTIONS:** V.A. Khokhlova, J.C. Simon, T.D. Khokhlova, Y. Wang, M. Paun, F.L. Starr , O. Sapozhnikov, L.A. Crum, M. Bailey, Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA|T.D. Khokhlova, Department of Gastroenterology, University of Washington, Seattle, WA|V.A. Khokhlova, O. Sapozhnikov, Department of Acoustics, Physics Faculty, Moscow State University, Moscow, RUSSIAN FEDERATION|

**ABSTRACT BODY:**

**OBJECTIVES:** Shock-wave heating and millisecond boiling in HIFU fields have been shown to result in mechanical emulsification of ex-vivo tissue with or without thermal denaturation. This approach has been named boiling histotripsy. Acoustic atomization within the HIFU-induced boiling bubble has been tested in ex-vivo tissues as a mechanism for boiling histotripsy. The goal of this work was to extend the approach to in-vivo exposures in porcine liver and to compare tissue atomization and treatment outcomes to the ex-vivo case.

**METHODS:** Sonications were performed using a 2 MHz 8-element annular array using a water-filled coupling cone. The lesions were produced in the exposed liver of the anesthetized animal at depths of 6 - 18 mm using a pulsing protocol (1-500 ms pulse durations and 0.01-0.1 duty factor). The corresponding in-situ shock amplitude was derived from water measurements and estimated as 93 - 100 MPa. All exposures were monitored using B-mode ultrasound. Immediately post-exposure, the liver was excised and boiling-histotripsy lesions were produced in ex-vivo setting in a separate lobe using the same exposure parameters. The mechanical and thermal tissue damage in the lesions was then evaluated histologically. In a separate experiment, a 2 MHz, single element transducer was positioned underneath a liver lobe, so that the focus was located at the liver surface without the capsule to create an acoustic fountain and atomization in-vivo. The estimated in situ shock amplitude was 66 MPa. Atomization was filmed using a high-speed camera; after the exposures, the liver surface was examined for evidence of erosion. While the flat liver surface did not entirely mimic the boiling bubble created in bulk boiling histotripsy, it allowed visualization of the atomization process in detail.

**RESULTS:** It was shown that the size and the shape of the emulsified lesions obtained in-vivo agreed well with those obtained in ex-vivo tissue samples with the same exposure parameters. The in-vivo lesions contained more red blood cells, both lysed and intact, and the thermal effects were less pronounced than in the ex-vivo exposures. The efficiency of tissue atomization was shown to be similar if not higher in-vivo as compared to ex-vivo.

**CONCLUSIONS:** These results demonstrated the feasibility of using boiling histotripsy for tissue emulsification as a promising clinical approach in HIFU. Work supported by NIH 1K01EB015745 and 2R01EB007643-05.



Oral session 4B

2013/5/13 16:09:00

CONTROL ID: 1675069

TITLE: COMPACT POWER DRIVING DEVICE FOR HIGH INTENSITY FOCUSED ULTRASOUND

AUTHORS/INSTITUTIONS: S. Jun, T. Kim, K. Kang, K. Son, Alpinion Medical Systems, Alpinion Medical Systems, Seoul, KOREA, REPUBLIC OF |

**ABSTRACT BODY:**

**OBJECTIVES:** Power driving device generates electrical power to treatment transducer. The transducer transforms electrical power into acoustic output power that is very intense and strongly focused. It is core for High intensity focused ultrasound (HIFU) system, which treats certain cancers and other conditions by the noninvasive thermal ablation of the affected tissue. HIFU surgery has to allow energy to be focused deep in the body inducing noninvasive local temperature elevation. In additional, it is possible to therapy the targeted tissue. A lot of HIFU Systems are with multi-element phased array transducer and offers simultaneous multiple focusing for large volume tissue treatment and short total treatment times. In addition, the phased arrays can provide sub-array modalities to effectively avoid the ultrasound propagation obstacles such as the human rib cage in focused ultrasound surgery. Recently, researchers are continuously trying to improve system performance and effort to reduce system size and cost by relying on system integration.

**METHODS:** The electrical output power and transmit waveform of the power driving device was measured according to change of amplitude, frequency, phase, delay each channels independently. The measured data were analyzed in order to evaluate the performance of the power driving device which was developed. Also, real time condition of device was recorded during transmit.

**RESULTS:** The result of maximum electrical output power was 6W/Ch and total power when 512 Channels transmit was about 3KW. As a program in RTC variable amplitude of output is from 0Vpp to 300Vpp and frequency range was from 0.5MHz to 10MHz. The phase and delay by channels were possible to control resolution at 6.25ns. The resolution of phase is 2.25degree, if the frequency of transmit is 1MHz.

**CONCLUSIONS:** In this work, the power driving device can be used HIFU systems with phased array transducer with less or 512elements that could be confirmed though experimental results. In addition, it will be able to offer a variety of treatment methods because each channel is controlled independently. In the present work, we have developed the power driving device that is more correctly treatment to the desired location without affecting intervening tissue and side effects.



**Oral session 4B**

**2013/5/13 16:45:00**

**CONTROL ID:** 1678968

**TITLE:** Production and Performance Evaluation of a Semi-Concave Multi-Channel HIFU Transducer

**AUTHORS/INSTITUTIONS:** M. Kim, D. Kim, K. Kang, K. Son, ALPINION MEDICAL SYSTEMS, Seoul, KOREA, REPUBLIC OF |

**ABSTRACT BODY:**

**OBJECTIVES:** HIFU (High Intensity Focused Ultrasound) transducer are generally concave in shape in order to get high intensity gain using converged ultrasound beam to their geometrical focus. For USg(Ultrasound guide) HIFU systems, an ultrasound imaging device is used to monitor the procedure of HIFU treatment, in which the image probe is generally positioned at the center of apex of the concave surface of the HIFU transducer. However, the location of the probe yields poor image quality since the distance from the probe to the treatment area is far unlike the conventional ultrasound imaging where the image probe is contact directly with human body.

**METHODS:** As a strategy to overcome this problem, the semi-concave HIFU transducer for enhancement in image quality was suggested in this study. The center frequency of the transducer was chosen to be 1 MHz, and its focus should be steered electrically within  $\pm 1$  cm in radial direction and 7 ~ 11 cm in axial direction for the volumetric treatment. The general criterion for the maximum intensity in grating lobes is at least -10 dB of the intensity in the main lobe for safe delivery of HIFU.

**RESULTS:** In order to evaluate the transducer performance, we measured acoustic power and sound field in a water tank. And temperature profiles outside the focal region as well as at the focus were measured in an agar-phantom.

**CONCLUSIONS:** As a result, the feasibility of the application of this transducer to HIFU treatment was confirmed.



**Oral session 4B**

**2013/5/13 16:57:00**

**CONTROL ID:** 1681428

**TITLE:** THE COMPARISON OF ACOUSTIC FIELD CHARACTERIZATIONS BETWEEN SPHERICAL PHASED ARRAYS WITH SPIRAL AND RANDOM LAYOUTS FOR FOCUSED ULTRASOUND SURGERY: A SIMULATION STUDY

**AUTHORS/INSTITUTIONS:** X. Ji, Y. Yu, G. Shen, S. Qiao, J. Bai, H. Wu, Z. Su, Y. Chen, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA | Y. Yu, School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** Steering the focus over a large field with low grating lobes is of importance for phased arrays in focused ultrasound surgery. To steer ultrasound beams along or off axis without grating lobes, theoretically the inter-element spacing should be not greater than half wavelength. However, in practice this spacing requirement could hardly be satisfied if higher frequencies used. Besides, it also needs a large number of elements within the current apertures, which would significantly increase the cost and complexity associated with ultrasound driving circuits of individual transducers. Therefore, to reduce grating lobes with the inter-element spacing limit relaxed, random sparse phased arrays has been studied and constructed previously. But random arrays still have the issue of over-heated near field.

**METHODS:** This simulation study compared the acoustic field characterizations between phased arrays with spiral and random element distributions for focused ultrasound surgery, given steering ranges and grating lobes. Two element layouts were based on the design of spherical phased arrays, both of which had 128 circular elements (6 mm diameter) resonated at the frequency of 1.05 MHz. These elements were mounted onto the same spherical shell, which had a 130-mm radius of curvature and a 100-mm aperture. The acoustic fields of steering the focus in the lateral and axial directions were simulated for the characterizations of two layouts.

**RESULTS:** Simulation results demonstrated that the spiral layout had the lower ratio of grating lobes to main lobe than the random one with the same position focused.

**CONCLUSIONS:** The spherical phased array with spiral layout could produce the acoustic field with grating lobes extended over the wider region at reduced level.



**Oral session 4B**

**2013/5/13 17:09:00**

**CONTROL ID:** 1681608

**TITLE:** A new FPGA-driven P-HIFU system with harmonic cancellation technique

**AUTHORS/INSTITUTIONS:** H. Wu, G. Shen, Y. Yu, S. Qiao, Z. Su, X. Ji, Y. Chen, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** An ultrasound transducer excited by a waveform with harmonic cancellation can produce a sound field with low grating lobes and has high electroacoustic efficiency. This study introduces a FPGA-driven ultrasound amplifier system with low harmonic distortion, which needs no additional filtering circuitry at the amplifier output. Without additional filtering circuitry, the amplifier can work in a wide bandwidth. And an FPGA phase signal generator can generate square waveform with high frequency and high phase precision, especially for large number of element.

**METHODS:** Two channels of square waveform signal from FPGA phase signal generator drive one amplifier, which have a phase difference of  $\pi/3$ . Each channel is divided into two channels, passing through an inverter and a compensator respectively. All the four channels are added together in two centre-tapped transformers. A voltage-changeable DC power supply is added to the transformers. The secondary voltage of the transformer is the amplified signal, driving the ultrasound transducer after an electronic matching circuit. So, when we need a phased array with 65 elements, an FPGA chip is chosen which has more than 130 general outputs and meet the requirement of timing constrain.

**RESULTS:** The output waveform of the amplifier with harmonic cancellation had fewer harmonic components and higher electroacoustic efficiency than the amplifier without harmonic cancellation.

**CONCLUSIONS:** The study demonstrates that the amplifier driven by an FPGA signal generator meets the requirements of high frequency and high phase precision.



**Oral session 4B**

**2013/5/13 17:21:00**

**CONTROL ID:** 1671617

**TITLE:** A HEURISTIC MODEL OF STONE COMMINUTION IN SHOCK WAVE LITHOTRIPSY

**AUTHORS/INSTITUTIONS:** N. Smith, P. Zhong, Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC |

**ABSTRACT BODY:**

**OBJECTIVE:** A heuristic model is developed to describe the progression of stone comminution in shock wave lithotripsy (SWL).

**METHODS:** The 4-coefficient heuristic model is an adaptation of the Weibull theory for brittle fracture to stone comminution in SWL, which incorporates threshold values for dose and the average peak pressure,  $P+(avg)$ , incident on a stone that are required to initiate fragmentation. The model is validated against in vitro stone comminution data from two stone types (hard and soft BegoStone) obtained at various positions in lithotripter fields produced by two different electromagnetic (EM) shock wave sources in both water and 1,3-butanediol (a cavitation-suppressing fluid).

The model is subsequently used to assess the performance of a newly developed acoustic lens for EM lithotripters, which produces a broad beam width and modified pulse profile in comparison with the original lens.

**RESULTS:** Static stone comminution results reveal dose- and holder fluid-independent  $P+(avg)$  thresholds to initiate fragmentation of soft (4.5~6.0 MPa) and hard (6.9~8.2 MPa) BegoStones, whereas the shock number to initiate fragmentation depends critically on holder fluid (i.e., cavitation) and  $P+(avg)$ . Using experimentally determined fragmentation thresholds, the heuristic model correlates well to stone comminution results for a given stone type and holder fluid ( $R^2 \geq 0.91$ ). Contours of the heuristic model indicate that there are comminution lines resembling asymptotes for both  $P+(avg)$  and dose along which one should not expect to dramatically increase efficacy. The predictive capabilities of the model are assessed using simulated respiratory motion, where in 8 of 12 simulations, the results of the heuristic model were statistically similar ( $p > 0.07$ ) to experimental stone comminution results. Furthermore, the model accurately predicts a statistical improvement ( $p < 0.01$ ) in stone comminution using the new lens in 4 of 5 simulations.

**CONCLUSIONS:** Static and simulated respiratory motion results have demonstrated the value of this heuristic model in elucidating the physical basis for improved performance of the new lens. The model also provides a rationale for the selection of SWL treatment protocols to achieve effective stone comminution without elevating the risk of tissue injury.



**Oral session 5**

**2013/5/14 8:54:00**

**CONTROL ID:** 1684054

**TITLE:** Non-thermal High-intensity Focused Ultrasound for Breast Cancer Therapy

**AUTHORS/INSTITUTIONS:** C. Ma, X. Chen, D. Cvetkovic, L. Chen, Radiation Oncology, Fox Chase Cancer Center, Philadelphia, PA|

**ABSTRACT BODY:**

**OBJECTIVES:** High intensity focused ultrasound (HIFU) has been investigated for ablative therapy and drug enhancement for gene therapy and chemotherapy. The aim of this work is to explore the feasibility of pulsed high-intensity focused ultrasound (pHIFU) for non thermal cancer therapy using an in vivo animal model.

**METHODS:** An InSightec ExAblate 2000 with a 1.5T GE MR scanner was used in this study. Suitable ultrasound parameters were investigated to perform non-thermal sonications. Breast tumor cells (107), MCF-7 line were injected subcutaneously in the flanks of the female mice (n = 12). When tumors reached the volume of  $78 \pm 28$  mm<sup>3</sup> as measured on MRI, the tumor-bearing mice (n = 6) were treated with pHIFU (1 MHz frequency; 25 W acoustic power; 0.1 duty cycle; 60 sec duration). A total of 4 to 6 sonications were used to cover the entire tumor volume under MR image guidance. The animals were allowed to survive for 4 weeks after the treatment. The tumor volume was measured on MRI weekly post treatment and was compared with that of the control group (n = 6).

**RESULTS:** Significant tumor growth delay was observed in the tumor-bearing mice treated with pHIFU. The mean tumor volume for the pHIFU treated mice grew 3%, 17%, 11% at 1 week, 3 weeks and 4 weeks after the treatment, respectively, while the mean tumor volume of the control mice grew 25%, 41% and 48%, respectively, over the same time periods. Statistical analyses yielded p values P=0.034, P=0.005 and P=0.017 at 1 week, 3 weeks and 4 weeks post-treatment respectively.

**CONCLUSIONS:** Our results demonstrated that non-thermal pHIFU has a great potential for cancer therapy. Further experiments are needed to understand the cell killing mechanisms of pHIFU and to derive optimal ultrasound parameters and fractionation schemes to maximize the therapeutic effect of pHIFU.



**Oral session 5**

**2013/5/14 9:06:00**

**CONTROL ID:** 1699717

**TITLE:** Sonographic features of transplantable VX2 bone tumor model in rabbit

**AUTHORS/INSTITUTIONS:** L. Chen, L. Jiang, B. Hu, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** Establish experimental rabbit model with VX2 malignant bone tumor as an ideal experimental animal model for high intensity focused ultrasound(HIFU) treatment in bone tumor. To study the Sonographic features of transplantable VX2 bone tumor model in rabbit.

**METHODS:** Twenty New Zealand white rabbits were inoculated with VX2 tumor in cavitas medullaris of right tibia and taken sequential ultrasound and magnetic resonance imaging(MRI) examination to observe growth characteristics in different periods, and make sure of the best time for bone tumor treatment with HIFU in the subsequent research. New Zealand white rabbits were inoculated with VX2 tumor in cavitas medullaris of right tibia and taken sequential ultrasound and magnetic resonance imaging(MRI) examination to observe growth characteristics in different periods, and make sure of the best time for bone tumor treatment with HIFU in the subsequent research.

**RESULTS:** 20 rabbits were all successfully inoculated with VX2 tumor in cavitas medullaris of right tibia. Tumor grew in the local cavitas medullaris of tibia and periosteal reaction could be observed on sonography in 1-2nd week, cortical bone of tibia were destroyed, soft tissues outside of bone were invaded on sonography image in 2-3th week. Necrosis and liquification in the center of the tumor could be seen on sonography, and metastasis also could be found in other part of the body in 3-4th week.

**CONCLUSIONS:** Ultrasonic energy could pass through the destroyed cortical bone of tibia and accumulate in the VX2 tumor area. Combined with sonography characteristics of the VX2 tumor in cavitas medullaris of right tibia, it is clear that 3 weeks after tumor transplantation is the best time for VX2 bone tumor model treatment of HIFU.





## Oral session 5

2013/5/14 9:18:00

**CONTROL ID:** 1658181

**TITLE:** THE BIOEFFECTS OF FOCUSED ULTRASOUND ON PROLIFERATION OF ENDOTHELIAL CELLS FOR THE TREATMENT OF LICHEN SCLEROSUS

**AUTHORS/INSTITUTIONS:** C. Li, Y. Liu, L. Chen, Z. Wang, The College of Biomedical Engineering, Chongqing

Medical University, Chongqing, Chongqing, CHINA|

### **ABSTRACT BODY:**

**OBJECTIVE:** To study the bioeffects of FU near field with commonly used exposure parameters on the endothelial cells.

**METHODS:** FU near field of different frequency (10.1MHz and 11.2MHz) and power (4.3W and 5W) was performed to stimulate in vitro human umbilical vein endothelial cells ( ECV304 ) cell lines for 5, 10, 15, 20, 25, and 30 s; and the cell proliferation was measured by MTT assay after 24 h. One-dimensional SDS-PAGE was performed to separate proteins from irradiated and normal endothelial cells. Different proteins (pre- and post- irradiation) were identified by LC-ESI-IT MS/MS.

**RESULTS:** The relative survival ratio of ECV304 measured by MTT assay showed a high value and statistically significant increase when focused ultrasound was applied at 11.2 MHz and 4.3 W for 10 s. The frequency and irradiation duration, but not the power, had significant influence on cell relative survival. Protein difference banding,

decolorizing, and enzyme solution processing after LC-ESI-IT MS/MS and data retrieval in the SWISSPROT protein database successfully identified seven different proteins: AP - 2 complex subunit  $\beta - 1$  (AP-2Compound), zinc finger protein 649 (ZNF649) cells, ubiquitin-like modifier activating enzyme 1 (UBA1), transitional endoplasmic reticulum ATPase (TER ATPase),  $\alpha$ -actinin - 1 (Actn1), actin, and proenkephalin A precursor. 43% participated in cell signal transduction, 29% were cytoskeletal protein, and 28% participated in cell motility.

**CONCLUSIONS:** FU can stimulate the proliferation of endothelial cells by induced cell skeleton system and activated related signal path. Further studies are recommended to understand and confirm the involvement of various mechanisms in cellular signaling and proliferation.



## Oral session 5

2013/5/14 9:30:00

**CONTROL ID:** 1671584

**TITLE:** REAL-TIME IMAGING OF CELLULAR DYNAMICS DURING LOW-INTENSITY PULSED ULTRASOUND EXPOSURE

**AUTHORS/INSTITUTIONS:** Y. Hu, A.C. Yu, Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG|J.M. Wan, School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG |

### **ABSTRACT BODY:**

**OBJECTIVE:** Although the therapeutic potential of low-intensity pulsed ultrasound is unquestionable, the wave-matter interactions involved in the process remain to be vaguely characterized. Here we seek to undertake a series of in-situ cellular imaging studies that aim to analyze the mechanical impact of low-intensity pulsed ultrasound on attached fibroblasts from three different aspects: membrane, cytoskeleton, and nucleus.

**METHODS:** Our experimental platform comprised an in-house ultrasound exposure hardware that was coupled to a confocal microscopy system. The waveguided ultrasound beam was geometrically aligned to the microscope's field-of-view that corresponds to the center of a polystyrene dish containing fibroblasts. Short ultrasound pulses (5 cycles; 2 kHz PRF) with 0.8 MPa peak acoustic pressure (0.21 W/cm<sup>2</sup> SPTA intensity) were delivered over a 10 min period. Live imaging was performed on both membrane (CellMask) and cytoskeleton (actin-GFP, tubulin-RFP) over the entire observation period (up to 30 min after end of exposure). Also, pre- and post-exposure fixed-cell imaging was conducted on the nucleus (Hoechst 33342) and two cytoskeleton components related to stress fibers: F-actin

(phalloidin-FITC) and vincullin (Alexa Fluor 647 conjugated). To study whether mechanotransduction was responsible in mediating ultrasound-cell interactions, some experiments were conducted with the addition of gadolinium that blocks stretch-sensitive ion channels.

**RESULTS:** Cell shrinkage was evident over the course of low-intensity pulsed ultrasound exposure. This was accompanied with contraction of actin and tubulin. Also, an increase in central stress fibers was observed at the end of exposure, while the nucleus was found to have decreased in size. Interestingly, after the exposure, a significant rebound in cell volume was observed over a 30 min. period. These effects were not observed in cases with gadolinium blockage of mechanosensitive ion channels.

**CONCLUSIONS:** Our results suggest that low-intensity pulsed ultrasound would transiently induce remodeling of a cell's membrane and cytoskeleton, and it will lead to repression of nucleus. This indicates that ultrasound after all represents a mechanical stress on cellular membrane. The post-exposure outgrowth phenomenon is also of practical relevance as it may be linked to the stimulatory effects that have been already observed in low-intensity pulsed ultrasound treatments.



**Oral session 5**

**2013/5/14 9:42:00**

**CONTROL ID:** 1671757

**TITLE:** ASSESSMENT OF HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) LESION USING COMBINED METHOD OF SONOELASTOGRAPHY AND NUMERICAL BIO-HEAT TRANSFER MODELLING

**AUTHORS/INSTITUTIONS:** N.M. Le, R. Cao, Z. Huang, Mechanical Engineering, University of Dundee, DUNDEE, Angus, UNITED KINGDOM|G. Nabi, Ninewells Medical School, University of Dundee, DUNDEE, Angus, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVES:** The aims of this paper are to 1) quantify the HIFU lesion along the beam-axis plane using sonoelastography, 2) simulate the experiment using Bio-Heat transfer equation, 3) correlate the sonoelastographic lesion with the temperature distribution from the model and 4) validate the findings on ex-vivo sheep liver

**METHODS:** HIFU-induced lesions in fresh ex-vivo sheep liver were produced at various acoustic power (38 W and 27 W, or the equivalent temporal-averaged focal intensity of 380 Wcm<sup>-2</sup> and 540 Wcm<sup>-2</sup>) and in two sets of sonication duration (30 s and 40 s). The elastograms of the lesion were then captured (UltrasonixTABLET system) and segmented using Seeded-region growing algorithm. The numerical model of the temperature distribution was also built and compared with the elastogram of the coagulated tissue (lower strain rate). The ultrasonic power deposition rate at the HIFU focus, which acts as a heat source, was calculated from the pressure measurement using needle hydrophone (D=0.5 mm, PA Ltd.). The temperature distribution based on Bio-Heat Transfer equation was simulated in the same condition as created in ex-vivo sheep liver.

**RESULTS:** The sizes of the lesions under sonoelastography are significantly different in the 10 seconds time step (constant focal intensity at 500 Wcm<sup>-2</sup>, N=3), and at 160 Wcm<sup>-2</sup> difference (constant 40 seconds duration, N=3). The temperature distribution correlates well with the segmented elastogram of the HIFU-induced lesion (both form concentric ellipsoid).

**CONCLUSIONS:** Sonoelastography is capable of indirectly quantifying the temperature distribution produced by HIFU in biological tissue. Further work is needed to simulate the necrosis tissue as determined by the temperature distribution for a more accurate correlation.



## Oral session 5

2013/5/14 10:30:00

**CONTROL ID:** 1671786

**TITLE:** LOW INTENSITY ULTRASOUND INDUCES APOPTOSIS VIA VDAC CHANNEL ON MITOCHONDRIAL MEMBRANE: TARGET FOR REGULATING CANCER THERAPY OR NOT?

**AUTHORS/INSTITUTIONS:** Y. Feng, M. Wan, Department of Biomedical Engineering, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, CHINA |

### **ABSTRACT BODY:**

**OBJECTIVES:** Low intensity ultrasound induced apoptosis of several carcinoma cells has been regarded as potential assistant cancer therapeutic regimen. It has been proved mitochondrion was involved in it. However, detailed mechanism has not been elucidated. Understanding it would give us a chance to regulate the curative effects of cancer treatment.

**METHODS:** Human hepatocarcinoma HepG2 cells were irradiated by low intensity US at different ultrasound intensity (ISPTA, from 0.1W/cm<sup>2</sup> to 0.3W/cm<sup>2</sup>) for the irradiation time from 30 seconds to 5 minutes. And then the cells were cultured for 12 h before the collection. The control and irradiated cells were examined by light and fluorescent microscopy respectively to get the morphological alteration of irradiated cells. Cells viability and apoptosis were examined by trypan blue staining and flow cytometry with double staining of FITC-labelled Annexin-V/PI. Key proteins responded to irradiation were screened out by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDSPAGE) and shotgun proteomic methods with Agilent 1100 HPLC-Chip-MS technology.

**RESULTS:** Morphological characteristics of apoptotic cells, such as condensation of nucleus, chromatin margination and formation of apoptotic bodies, were found in US irradiated cells, however few in control cells. The percentage of apoptotic cells increased more than 15% after US irradiation. Several proteins, such as HSPs, programmed cell death proteins, p53-inducible protein, and especially VDAC and its chaperone protein BID and BAX, were differently expressed in irradiated cells and identified successfully by shotgun proteomics. The proteins responded to US irradiation are always the key ones on the mitochondrial permeability transition (MPT) channel or caspase cascade. Moreover, it revealed the VDAC channel was closely related to the release of cytochrome C and cell apoptosis.

**CONCLUSIONS:** Low intensity ultrasound induced apoptosis in the study. The functional analysis of key proteins revealed US-induced apoptosis was mitochondria-dependent and caspases-dependent, where VDAC channel is significantly important. Regulating VDAC channel could act as the target for the cancer therapy.



## Oral session 5

2013/5/14 10:42:00

**CONTROL ID:** 1679024

**TITLE:** Acoustic Droplet Vaporization Enhanced High Intensity Focused Ultrasound Treatment of Tumor

**AUTHORS/INSTITUTIONS:** M. Zhu, A. Zhang, L. Xu, Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, CHINA|L. Jiang, Ultrasound in Medicine, Sixth Hospital, Shanghai Jiao Tong University, Shanghai, CHINA|M.L. Fabiilli, J.B. Fowlkes, Radiology, University of Michigan Health System, University of Michigan Health System, MI|

### **ABSTRACT BODY:**

**OBJECTIVES:** High intensity focused ultrasound (HIFU) is a popular tumor treatment technique with minimal side effect. However, since the focal zone of the HIFU beam is very small, the therapy is time-consuming. Some clinical trials have shown treatment times of several hours to completely ablate a large tumor Acoustic droplet vaporization (ADV) is a promising technique enhancing the therapeutic outcome of the treatment.

**METHODS:** Fifteen days after subcutaneous 4T1 tumor inoculation, mice were assigned to three groups., HIFU treatment was started after the droplet/saline injection using a HY2900 (Wuxi Haiying Techonology, China). A focal intensity and exposure duration of 2344W/cm<sup>2</sup> and 150ms, respectively, was used. The total exposure locations numbered 25, 5×5 array (2.4 mm center-to-center spacing), which formed a 1.2cm square plane with depth of 0.8cm. Group 3 received no droplet injection or treatment. The tumor was imaged using B-mode and contrast enhanced

ultrasound (CEUS) immediately after HIFU exposure. Mice were euthanatized 24 h later and tumors harvested and sectioned for TTC and H&E staining

**RESULTS:** No difference in echogenicity in B-mode image of tumor in group with saline injection was observed after treatment. A hypoechoic region appeared only in the center of the tumor in CEUS image. Significant changes in echogenicity were observed for mice in the group with droplets injection. About 70% of the tumor area was found to be hypoechoic as shown in the CEUS image, indicating necrosis formation. TTC results showed tumors from group 3 appeared red indicating metabolic activity with limited areas of white. In group 2, the tumor core was necrotic while the periphery was still metabolically active. In group 1 the entire tumor volume was metabolically inactive, suggesting complete necrosis. According to analysis in Image J, the mean necrotic area in group 1 was 3-fold greater than group 2 ( $p < 0.01$ ). H&E stained sections of tumor further proved the differences in degree of necrosis in various groups. the cells were totally destroyed in group 1 and nuclei were missing or shrunk in the group with saline injection, the tumor core was necrotic while the periphery was still metabolically active.

**CONCLUSIONS:** The preliminary results presented in this manuscript confirm the therapeutic advantage of combined HIFU and ADV.



**Oral session 5**

**2013/5/14 10:54:00**

**CONTROL ID:** 1681773

**TITLE:** The different doses of SonoVue enhances in vivo goat liver ablation induced by high intensity focused ultrasound with different acoustic intensity: The shift of the location of coagulative necrosis

**AUTHORS/INSTITUTIONS:** L. Faqi, Y. Liangbo, Z. Ting, W. Qi, L. Chongyan, W. Yan, W. Zhibiao, College of Biomedical Engineering, Chongqing medical university, State Key Laboratory of Ultrasound Engineering in Medicine Co-founded by Chongqing and MOST, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Explore the shift of necrosis location when the different dose of ultrasound contrast agents (SonoVue) enhance high-intensity focused ultrasound (HIFU) treatment .

**METHODS:** Forty-five Nanjiang goats were adopted. The control group was administered HIFU exposure only, the experiment group was administered HIFU combined with SonoVue, the concentration of SonoVue is 0.01ml/kg, 0.03ml/kg, 0.05ml/kg in respectively. The tissue in goat liver was ablated by on single exposure of HIFU with 150W, 250W, 350W acoustic power respectively and 15s exposure time at 30mm focal depth. Before HIFU we used US image to measure the distance between focus center and liver envelope vertically in the HIFU pathway. Animals were sacrificed and dissected 1W later, and the sizes of necrosis and the distance from necrosis location to the liver envelope in the HIFU pathway were measured.

**RESULTS:** It was obvious that the volume of the coagulation necrosis was bigger than the control group ( $P < 0.05$ ) when the exposure conditions of the experiment group was not at 150W-0.01ml/kg. When using 0.05ml/kg SonoVue and 350W and 250W acoustic power, more than 50% of the shift were unacceptable (more than half of the necrosis length); however an optimal result was obtained when using 0.03ml/kg sonovue and 250W acoustic power, which produced a lesion about 7 times larger than the control group and an acceptable shift (less than half of the lesion length).

**CONCLUSIONS:** SonoVue can substantially enhance the HIFU ablation, but the shift of necrosis location was produced by larger acoustic power and higher dose of SonoVue. The accuracy of necrosis location and the maximum enhancement could be guaranteed under the conditions with 250 W acoustic power and 0.03 ml/kg SonoVue dose.



## Oral session 5

2013/5/14 11:06:00

**CONTROL ID:** 1671559

**TITLE:** QUANTITATIVE MEASUREMENT OF HIGHLY FOCUSED ULTRASOUND PRESSURE FIELD BY OPTICAL PHASE CONTRAST

**AUTHORS/INSTITUTIONS:** R. Miyasaka, M. Syahid, S. Yoshizawa, S. Umemura, Electrical and Communication Engineering, Tohoku University, Sendai, JAPAN|S. Umemura, Biomedical Engineering, Tohoku University, Sendai, JAPAN|

### **ABSTRACT BODY:**

**OBJECTIVE:** Accurate measurement of ultrasound field is important to ensure and improve the safety and efficacy of the medical use of ultrasound. Optical measurement can have an advantage over hydrophone measurement in that it can obtain the pressure field in a short time. The optical phase contrast method works by inserting a phase plate into the focal plane of a Schlieren lens of the Schlieren optical measurement setup. In this study, this method is tested to capture the projection acoustic fields, from which the pressure field is reconstructed by CT (Computed Tomography) algorithm.

**METHODS:** This phase contrast method utilizes the property of the lens, which forms the spatial Fourier spectrum of objects on the focal plane. The position of the column must be set corresponding to the DC component of the spectrum on the focal plane of the Schlieren lens and its depth is such that the DC component is advanced by  $\pi/2$

relative to other components. A pulsed-laser beam was expanded by a beam expander and collimated by the first Schlieren lens. The collimated laser passed into the ultrasound field in the water tank, and then converged by the second Schlieren lens. The projections of the ultrasonic pressure field were obtained with a charge coupled device (CCD) camera. The light source and the transducer were synchronized every 1 ms, at a shutter speed of the CCD camera of 1 ms. First, 15 images with and without ultrasound were acquired and averaged. This was repeated 90 times when the transducer was rotated every  $2^\circ$  until  $180^\circ$ . These images were used to reconstruct a 3D image of the ultrasonic pressure field applying a CT algorithm. The same highly focused ultrasound field was also measured with a hydrophone.

**RESULTS:** Overall agreement between the ultrasound pressure fields from the optical and hydrophone measurement were observed. Furthermore, the absolute negative and positive main peaks of the ultrasound pressure accorded well.

**CONCLUSIONS:** We successfully reconstructed a highly focused ultrasound pressure field from the optical images applying a phase contrast method at a relatively low pressure level. Further study is needed to reconstruct a highly focused ultrasound field with an intensity level close to the actual HIFU treatment.



**Oral session 5**

**2013/5/14 11:18:00**

**CONTROL ID:** 1671714

**TITLE:** DERIVATION OF CONTINUOUS WAVE MODE OUTPUT POWER VALUES FROM BURST MODE MEASUREMENTS IN HIGH-INTENSITY ULTRASOUND APPLICATIONS

**AUTHORS/INSTITUTIONS:** J. Haller, V. Wilkens, Physikalisch-Technische Bundesanstalt, Braunschweig, GERMANY |

**ABSTRACT BODY:**

**OBJECTIVE:** In several therapeutic applications, high-intensity ultrasound is used in (quasi) continuous wave (cw) mode, i.e. sonications lasting for a few seconds. However, characterization of the output power of transducers in this mode with a radiation force balance with an absorbing target is a challenging task due to heating effects within and possible thermal destruction of the target. One way of overcoming these problems is to measure in burst mode while applying the same amplitude of input voltage and to derive measurement results to cw case. However, transient effects at the beginning and the end of each burst require the knowledge of an 'effective duty factor',  $D_{\text{Reff}}$ , to correctly extrapolate to cw case. One existing method to determine  $D_{\text{Reff}}$  is to measure it at a low input voltage as the ratio of output power in burst mode to output power in cw mode.

**METHODS:** In this work an alternative method for determining  $D_{\text{Reff}}$  is presented, which allows the measurement at any input voltage amplitude:  $D_{\text{Reff}}$  can be calculated as the ratio of the temporal integral over the squared input voltage rf signal in burst mode to the temporal integral over the squared transient voltage signal in cw mode. The latter one can be obtained from steady-state waveforms that are extracted from the burst mode signals as well. Thus, with this method, it is not necessary to apply cw signals at all. To evaluate the relevance of this electrically determined  $D_{\text{Reff}}$  for the acoustical output parameters, they are compared to acoustically determined ones, i.e. the ratio of the pulse-pressure-squared integral ppsi to a respective cw value, which can be calculated from hydrophone measurements.

**RESULTS:** The measurement results clearly show that there is a dependence of  $D_{\text{Reff}}$  on the input voltage amplitude. Additionally, the comparison of the electrically determined  $D_{\text{Reff}}$  with acoustically determined ones shows that the former are well suited for extrapolating output power measurements performed in burst mode to cw case.

**CONCLUSIONS:** The presented method is well suited for the derivation of continuous wave mode output power values for high-intensity ultrasound applications from measurements that are performed with radiation force balances with absorbing targets in burst mode while reducing problems that arise from the significant heating of the target.





**Oral session 5**

**2013/5/14 11:30:00**

**CONTROL ID:** 1681448

**TITLE:** AN INVERSE METHOD FOR ESTIMATION OF THE ACOUSTIC INTENSITY IN THE FOCUSED ULTRASOUND FIELD

**AUTHORS/INSTITUTIONS:** Y. Yu, G. Shen, X. Ji, S. Qiao, H. Wu, Z. Su, Y. Chen, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA|Y. Yu, School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Recently, a new method which based on infrared (IR) imaging was introduced. Authors (A. Shaw, et al and M. R. Myers, et al) have established the relationship between absorber surface temperature and incident intensity during the absorber was irradiated by the transducer. Theoretically, the shorter irradiating time makes estimation more in line with the actual results. But due to the influence of noise and performance constrains of the IR camera, it is hard to identify the difference in temperature with short heating time.

**METHODS:** An inverse technique is developed to reconstruct the incident intensity distribution using the surface temperature with shorter irradiating time. The algorithm is validated using surface temperature data generated numerically from three-layer model which was developed to calculate the acoustic field in the absorber, the absorbed acoustic energy during the irradiation, and the consequent temperature elevation.

**RESULTS:** To assess the effect of noisy data on the reconstructed intensity profile, in the simulations, the different noise levels with zero mean were superposed on the exact data.

**CONCLUSIONS:** Simulation results demonstrate that the inversion technique can provide fairly reliable intensity estimation with satisfactory accuracy.



**Oral session 6**

**2013/5/14 13:24:00**

**CONTROL ID:** 1681513

**TITLE:** High intensity focused ultrasound combined with neoadjuvant chemotherapy for breast cancer: A therapeutic effect study

**AUTHORS/INSTITUTIONS:** J. Liu, L. Gu, Gynecology(ultrasound section), Shanghai Ninth People's Hospital Affiliated to Shanghai Jiaotong University, School of Medicine, Shanghai, Shanghai, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** To investigate the safety and therapeutic efficacy of breast cancer treated with low power high intensity focused ultrasound (HIFU) in combination with neoadjuvant chemotherapy preoperatively.

**METHODS:** 50 operable female patients with pathologically confirmed breast cancer were divided into HIFU group and control group randomly, with 25 patients in each group. Preoperatively, patients in HIFU group were treated with HIFU in combination with adjuvant chemotherapy, and patients in control group were treated with only adjuvant chemotherapy. Both groups were accepted with improved radical surgery. Before and after treatment, all patients were accepted with examinations such as blood routine, liver function, renal function and ultrasonography respectively. And medicamentous adverse reaction was observed during whole procedure

**RESULTS:** After treatment, the size of primary tumor in HIFU group decreased more obviously than that of control group. The differences were significant( $P < 0.05$ ). The blood flow of primary tumor was decreased obviously and the clinical stages of most patients were cut down obviously. There was no significance of medicamentous adverse reaction between HIFU group and control group( $P > 0.05$ ).

**CONCLUSIONS:** HIFU in combination with neoadjuvant chemotherapy is a safe and effective method for the treatment of breast cancer. No serious complications occur for any cases. Therefore it is necessary for effects of the therapy to be further studied.



## Oral session 6

2013/5/14 13:36:00

**CONTROL ID:** 1671092

**TITLE:** EFFICIENT GENERATION OF CAVITATION CLOUD IN OPTICALLY-TRANSPARENT GEL PHANTOM BY ULTRASOUND EXPOSURE WITH NEGATIVE-FOLLOWED BY POSITIVE-PEAK-PRESSURE EMPHASIZED WAVES

**AUTHORS/INSTITUTIONS:** J. Yasuda, A. Asai, S. Yoshizawa, Department of Communication Engineering, Tohoku Univ., Sendai, Miyagi pref., JAPAN|S. Umemura, Department of Biomedical Engineering, Tohoku Univ., Sendai, Miyagi pref., JAPAN|

### **ABSTRACT BODY:**

**OBJECTIVE:** Cavitation microbubbles can be generated by highly negative pressure of ultrasound. To utilize them effectively as well as safely for therapeutic purposes, highly efficient as well as controlled generation of them is important. However, producing negative pressure over the cavitation threshold by focused ultrasound is difficult because of the nonlinear propagation combined with the focal phase shift. Furthermore, controlling them is also difficult once they are generated. To solve these problems, we are proposing the “Dual Frequency Ultrasound Exposure” method. This method makes it possible to synthesize waveforms emphasizing either the positive-peak pressure (P waves) or the negative-peak pressure (N waves) by superimposing the second harmonic onto the fundamental.

**METHODS:** In this study, two experiments were performed. First, an optically transparent gel was exposed to four different types of dual-frequency ultrasound exposure sequences, and the behavior and amount of the generated cavitation bubbles were compared under a high-speed camera. The fundamental frequency was 0.8 MHz. In the PP and NN sequences, the P and N waves were continued for 125  $\mu$ s, respectively. In the NP sequence, the N and P waves were used in the earlier and later 62.5  $\mu$ s, respectively, and they were exchanged in the PN sequence. Next, the acoustic fields of the P and N waves under the highly nonlinear propagation were measured by an optic hydrophone.

**RESULTS:** The amount of bubbles generated by the NP sequence was significantly more than other three sequences, suggesting it is the most efficient sequence to generate a large focal cavitation bubble cloud. It is thought that the small amount of cavitation bubbles, generated by the N waves in the earlier duration, are thought to have provided a pressure-release surface converting the P to highly N waves which further generated cavitation bubbles in the later duration. Furthermore, the measured negative and positive pressure distributions of the N and P wave fields, respectively, agreed well with the optically observed distributions of cavitation inception and cavitation cloud growth.

**CONCLUSIONS:** These suggest that the dual frequency ultrasound exposure method can generate bubble cloud at high efficiency and control it temporally because it was not formed until the P waves were exposed.



Oral session 6

2013/5/14 13:48:00

**CONTROL ID:** 1672257

**TITLE:** MULTI-DEPTH FRACTIONATED AESTHETIC ULTRASOUND SURGERY

**AUTHORS/INSTITUTIONS:** M.H. Slayton, S.M. Lyke, P.G. Barthe, Guided Therapy Systems, LLC, Mesa, AZ|P.G. Barthe, Ardent Sound, Inc, Mesa, AZ|

**ABSTRACT BODY:**

**OBJECTIVE:** Aesthetic ultrasound surgery provides the ability to treat at precise, clinically relevant depths with varied lesion size. This represents a major advantage compared to cosmetic laser and RF based energy sources. We present results of pre-clinical and clinical research aimed at establishing the feasibility of three-dimensional fractional deposition of focused ultrasound energy in the first 3 mm of skin. Conformal thermal lesions were created in ex-vivo porcine muscle and live human skin in a variety of depths and geometries. Gross pathology demonstrating a three-dimensional pattern of non-intersecting lesions was micro-photographed and characterized in porcine tissue, and followed up to thirty days post treatment in human tissue.

**METHODS:** Image/treat transducers from 7.5 to 10 MHz, focal depths of 1 to 3 mm, and energies of 160 to 300 mJ were used to lay down a three-dimensional pattern of non-intersecting thermal lesions in freshly excised porcine muscle tissue. Human skin was treated in vivo at 120 to 360 mJ per lesion. Results were photographed immediately post-treatment and followed up to 30 days.

**RESULTS:** Porcine tissue lesion geometry was measured. Average lesion dimensions approximated by a sphere ranged from 360 micron ( $\pm 19\%$ ) to 520 micron ( $\pm 23\%$ ) varying with the energy settings. Measured depth and distance between the thermal lesions were within  $\pm 13\%$  of the focal depth and lesion spacing. In human skin all lesions for all energy settings were completely resolved during the follow-up period. At lower energy settings of 120 mJ and 160 mJ lesions were completely resolved by day 2. Mild erythema and localized swelling were the only transient side effects and resolved within 48 hours or less.

**CONCLUSIONS:** In conclusion, skin may be successfully treated in a three-dimensional fractionated manner with predictable and precise deposition of thermal damage. In vivo results demonstrate tolerability and fast resolution with minimal side effects. ultrasound; surgery; skin; aesthetics



## Oral session 6

2013/5/14 14:00:00

**CONTROL ID:** 1667307

**TITLE:** ANALYSIS OF LOCALIZED HEAT DEPOSITION AND ACOUSTIC SCATTERING OF ACOUSTIC CAVITATION BUBBLES IN TISSUE MIMICKING GEL

**AUTHORS/INSTITUTIONS:** S. Yoshizawa, A. Asai, H. Okano, T. Miyashita, Department of Communication Engineering, Tohoku University, Sendai, JAPAN|S. Umemura, Department of Biomedical Engineering, Tohoku University, Sendai, JAPAN|

### **ABSTRACT BODY:**

**OBJECTIVE:** When cavitation bubbles are generated by HIFU in its focal region, the thermal and viscous dissipation of the oscillating bubbles increase localized heat deposition in the vicinity of the focal region. The bubbles also have an effect on the temperature distribution in the region around the focus through their scattering of the ultrasound waves. The objective of this study is to investigate the ultrasonic absorption in the focal region and the effect of the scattered ultrasound by analyzing experimental results.

**METHODS:** A transducer and a tissue mimicking gel were placed in a water tank. The focal length and diameter of the transducer was 100 mm. The driving frequency was 1.2 MHz. Cavitation bubbles were induced and forced to oscillate in a tissue mimicking gel by high-intensity ultrasound burst followed by relatively low-intensity continuous wave at an intensity of 42 and 0.6 kW/cm<sup>2</sup>, respectively. The total exposure time was 5 s. The cavitation bubbles were observed with a high-speed camera. The temperature change was measured with a thermocouple at 2.7 mm away from the focal point in a lateral direction. The change of the ultrasonic absorption owing to the cavitation bubbles was investigated by dividing the absorption into that in the focal region and in the other region. The analysis was achieved by curve fitting of the simulated temperature rise in which either of the absorption in the focal region or the other region was considered.

**RESULTS:** The simulation results considering the absorption of the two regions well fit the measured temperature changes. The generated heat in the focal region with cavitation bubbles were about the twice of that without bubbles. Furthermore, the heat generated outside the focal region was about three times of that without bubbles. The results indicate that the cavitation bubbles had a great influence on the heat generation in the region outside of the focal region as well as in the focal region, which may be caused by the ultrasound scattering from the bubbles.

**CONCLUSIONS:** The effect of the heating enhancement by cavitation bubbles was divided into that in the focal region and in the other region. The results show that the effect of the acoustic scattering from the bubbles is important to be considered for the temperature distribution in the bubble-enhanced heating as well as the localized heat deposition.



**Oral session 7**

**2013/5/14 8:30:00**

**CONTROL ID:** 1672062

**TITLE:** A CADAVERIC/PHANTOM INVESTIGATION OF THE TRANSCRANIAL TREATMENT ENVELOPE FOR AN MR-GUIDED FOCUSED ULTRASOUND SYSTEM OPERATING AT 650 KHZ

**AUTHORS/INSTITUTIONS:** M. Khaled, J. Snell, J. Aubry, A. Hananel, W.J. Elias, Neurosurgery, University of Virginia, Charlottesville, VA|M. Eames, J. Snell, A. Hananel, Focused Ultrasound Foundation, Charlottesville, VA|J. Aubry, Institut Langevin, CNRS, Paris, FRANCE|

**ABSTRACT BODY:**

**OBJECTIVE:** The purpose of this study is to assess the feasibility of treating clinically relevant targets with a mid-frequency transcranial MRgFUS system.

**METHODS:** The focused ultrasound equipment used for this work is the InSightec ExAblate Neuro system (Tirat Camel, Israel) operating at 650 kHz. This system is designed to be operated with patient cranial CT volume to permit skull phase aberration correction and with treatment-day MR images for planning and real-time thermometry. To satisfy these technical requirements with an ex-vivo human skull, two cadaveric datasets comprising volumetric cranial MR and CT datasets were used in conjunction with the previously recovered skulls from the respective cadavers. The pre-treatment planning feature of the InSightec planning software permitted the coregistration of treatment day MR, cadaveric CT, and cadaveric MR, permitting the FUS targeting to be performed on full MR brain volumes for the skull in use. The clinical indications being evaluated in this study were epilepsy (targeting the amygdala/ hippocampus and anterior 2/3 of corpus callosum), OCD (targeting area Cg25 -subgenual cingulate gyrus), major depressive disorder (targeting anterior capsule), addiction (targeting nucleus accumbens), dystonia and PD (targeting GPi) and hypothalamic hamartomas. The Vim was also targeted as a reference for comparison to the other targets. A standard, clinically relevant sonication of 1100W lasting 12 seconds was applied throughout the volume of each target site.

**RESULTS:** All targets were determined to be within the technical treatment envelop in these experimental models including cadavers with a CRW frame. However, projected treatment time for the largest target (in the treatment of epilepsy) was around 4 hours for the hippocampus and 2 hours for the anterior 2/3 of corpus callosum when sonication and requisite cooling times were considered.

**CONCLUSIONS:** Technical feasibility was confirmed for the targets in question, but there exists a need to accelerate the treatment for large volumetric target volumes.



**Oral session 7**

**2013/5/14 8:42:00**

**CONTROL ID:** 1672402

**TITLE:** A MAGNETIC RESONANCE IMAGING, HISTOLOGICAL AND DOSE MODELING COMPARISON OF FOCUSED ULTRASOUND, RADIOFREQUENCY, AND GAMMA KNIFE RADIOSURGERY LESIONS IN SWINE THALAMUS

**AUTHORS/INSTITUTIONS:** J. Aubry, Department of Radiation Oncology, University of Virginia, Charlottesville, VA|J. Aubry, Institut Langevin, CNRS, Paris, FRANCE|M. Khaled , J. Hilliard , R.C. Fry singer, J.P. Sheehan, W.J. Elias, Department of Neurosurgery, University of Virginia, Charlottesville, VA|M. Eames, Focused Ultrasound Foundation, Charlottesville, VA|M. Wintermark, Department of Neuroradiology, University of Virginia, Charlottesville, VA|B. Lopes , Department of Neuropathology, University of Virginia, Charlottesville, VA|

**ABSTRACT BODY:**

**OBJECTIVE:** The purpose of this study was to compare stereotactic lesioning modalities in a large brain model of thalamotomy.

**METHODS:** A unilateral thalamotomy was performed in piglets using focused ultrasound (FUS), radiofrequency (RF), and gamma knife radiosurgery (RS). Standard clinical lesioning parameters were used for each treatment: FUS energy was adjusted under MR control to achieve maximal voxel temperature of 55-60°C with the ExAblate Neuro system (InSightec) operating at 710kHz; RF lesions were made at 72°C for 60s with a 1.1mm diameter lesioning electrode; to cover the clinical range used for RS thalamotomy, two animals were treated with a maximal dose of 160 Gray, and two animals with 130 Gray, with a Gamma Knife Perfexion unit. The same parameters were used as input in numerical models to compute dose profiles. Thermal dose was computed with an in-house bioheat equation solver: ultrasonic energy deposition was based on acoustic beam characteristics and RF energy deposition was modeled with an electromagnetic field solver (open EMS, University of Duisburg-Essen, Germany). Radiation dose profile was calculated by using an idealized top-hat beam profile of each collimated beam. Clinical, MRI, and histological assessments were made at early (<72 hours), subacute (1 week), and late (1-3 months) time intervals.

**RESULTS:** FUS and RF lesions developed similarly by MRI and histology (mean 2mm radius for 72 hours histology). T2 MRI revealed three concentric lesional zones at 48 hours with resolution of perilesional edema by 1 week. Acute ischemic infarction with macrophage infiltration was most prominent at 72 hours with subsequent resolution of the inflammatory reaction and coalescence of the necrotic zone. There was no apparent difference in ischemic penumbra or 'sharpness' between FUS or RF lesions. Gamma Knife RS lesions presented differently with latent effects, less circumscribed lesions at 3 months, and apparent histologic changes seen in white matter beyond the thalamic target. Simulations showed a 90% dose diminution at a distance of 2mm for FUS, 2.7mm for RF and 9mm for RS.

**CONCLUSIONS:** In swine thalamus, FUS and RS lesions evolve similarly by MRI, histology, and theoretical modeling. Gamma knife RS produced more delayed lesions and resulted in white matter changes beyond the thalamic target.



**Oral session 7**

**2013/5/14 8:54:00**

**CONTROL ID:** 1672468

**TITLE:** THE EFFECT OF 3D UTE BRAIN IMAGING-DERIVED TISSUE TYPES ON FOCAL INTENSITY AND LOCATION FOR TRANSCRANIAL MR-GUIDED FOCUSED ULTRASOUND SURGERY

**AUTHORS/INSTITUTIONS:** U. Vyas, K. Butts Pauly, Radiology, Stanford University, Stanford, CA|E.M. Johnson, M. Marx, J.M. Pauly, Electrical Engineering, Stanford University, Stanford, CA|

**ABSTRACT BODY:**

**OBJECTIVE:** For transcranial MR-guided focused ultrasound surgery (tcMRgFUS) in the brain, Computed Tomography (CT) imaging is used currently for correcting for distortions in the location and shape of the beam's focus due to heterogeneities of the cranium.<sup>1</sup> Due to minimal soft tissue contrast in CT imaging and slow speed of simulations using a fully 3D patient head model<sup>1</sup> only the effect of the calvarium has been included when correcting for phase aberrations clinically.<sup>2</sup> In this work we use high resolution UTE images and rapid 3D ultrasound beam simulations to demonstrate the effect of additional anatomical features of the head (derived from MR imaging) on the location and intensity of the focal zone. This work will provide a framework to a) assess the effect of additional anatomical structures at the focus, and b) determine patient-specific tissue acoustic properties using UTE images.

**METHODS:** A 3D UTE pulse sequence acquired three echoes at 0.068ms, 1.788ms, and 3.348ms, imaging parameters 1.5T GE scanner, 23.6cm FOV, 1mm<sup>3</sup> resolution, 10° FA, 125kHz BW, 8ms TR. A clustering algorithm using the intensity decay profiles of the voxels over the echo times was used to create a segmented model with tissue

types: water, skin, subcutaneous fat, marrow, cortical bone, galea aponeurotica and white/grey matter. The hybrid angular spectrum<sup>3</sup> beam propagation technique simulated the clinical tcMRgFUS InSightec ExAbalate 4000 hemispherical transducer (1024-elements, 650 kHz) with the 3D head model; calculation time was 2sec. Tissue

properties assumed<sup>4</sup>  $c$  in m/s and  $\alpha$  in Np/cm/Mhz: skin-1505,0.26, fat/marrow-1450,0.03,galea-1529,0.05,white/grey matter-1560, 0.04, homogeneous- 1500, 0.4.

**RESULTS:** The effect of the tissue specificity is seen when comparing homogenous paths to that using all the segmented tissues (excluding the skull). The results show a 2mm change in the on-axis focal location and a 20% decrease in the focal intensity compared to the homogenous tissue focus when considering only additional MR-derived tissue types.

**CONCLUSIONS:** Using 3D UTE images of the head, we demonstrate using simulations, the effect of additional MR imaging-derived tissue types on focal location and intensity in a clinical tcMRgFUS transducer.





## Oral session 7

2013/5/14 9:06:00

**CONTROL ID:** 1671720

**TITLE:** FREQUENCY DEPENDENCE OF ULTRASOUND NEUROMODULATION

**AUTHORS/INSTITUTIONS:** P. Ye, R. King, K. Butts Pauly, Bioengineering, Stanford University, Stanford, CA|J. Brown, W. Newsome, Howard Hughes Medical Institute, Stanford, CA|W. Newsome, Neurobiology, Stanford University, Stanford, CA|K. Butts Pauly, Radiology, Stanford University, Stanford, CA|

### **ABSTRACT BODY:**

**OBJECTIVE:** Ultrasound neuromodulation is an increasingly studied method for safely and effectively achieving physiologic effects in animal models and humans. While many parameters affecting ultrasound neuromodulation have been investigated in vivo, the effect of ultrasound frequency has been less thoroughly quantified. Understanding the frequency dependence of ultrasound neuromodulation will be critical for optimizing future treatment protocols. In this study, we quantify the frequency dependence of ultrasound neuromodulation in the mouse model.

**METHODS:** Three single-element focused transducers were used to stimulate mice at low, intermediate, and high frequencies ranging from 300kHz to 2.9MHz at intensities from 0.30 mW/cm<sup>2</sup> to 8.3 W/cm<sup>2</sup> (spatial peak pulsed average) for 80ms single pulses. CBL-7 mice were anesthetized throughout stimulus with isoflurane between 0.335% and 0.7% delivered with 1 L/min of O<sub>2</sub>, depending on individual mouse waking and stimulus thresholds. Motor output was recorded through forelimb electromyography signals and analyzed to calculate success rate and contraction latency. Ultrasound intensities incident on motor cortex were estimated by scaling hydrophone-measured transducer beam profiles in water with mouse skull attenuation (through-transmission substitution technique).

**RESULTS:** Our results show that given a constant duration of ultrasound stimulus, higher frequencies require increasing amount of spatial peak pulse average intensity to maintain the same success rate of eliciting motor response. The intensity required increases by more than an order of magnitude between 300 and 600 kHz, while at higher frequencies the rate of increase becomes more moderate. Ultrasound frequency also affects contraction latency; increased frequencies lead to longer latencies between stimulus and contraction, ranging from 52 ms at 300 kHz to 130 ms at 2.3 MHz (linear fit R<sup>2</sup> = 0.53).

**CONCLUSIONS:** Our observed frequency trend in the mouse model demonstrates that lower ultrasound frequencies are substantially more effective in eliciting ultrasound neuromodulation at lower intensities. Ultrasound frequency also affects the latency of the contraction, pointing to another form of frequency dependence. As future studies aim to increase spatial resolution by using higher ultrasound frequencies, an improved, quantitative understanding of the neuromodulatory frequency response will be important in attempting to optimize this inevitable tradeoff.



**Oral session 7**

**2013/5/14 9:18:00**

**CONTROL ID:** 1672427

**TITLE:** ULTRASONIC NEUROMODULATION IN AWAKE MONKEY: MODULATION OF SACCADE CONTROL

**AUTHORS/INSTITUTIONS:** Y. Younan, T. Deffieux, M. Tanter, J. Aubry, Institut Langevin, CNRS, Paris, FRANCE | N. Wattiez, P. Pouget, Institute of Brain and Spinal Cord, INSERM, Paris, FRANCE |

**ABSTRACT BODY:**

**OBJECTIVE:** Neuromodulation of the rat and mouse brain under mild anesthesia have been recently reported by various groups, using low-intensity low frequency pulsed ultrasound. In this work, antisaccade latencies have been modulated with non-invasive low intensity focused ultrasound (FUS) in the brain of two awake Macaca Mulatta monkeys (Monkey Y and Monkey L).

**METHODS:** Animals were specifically trained in an antisaccade (AS) paradigm, in which they were required to initially keep fixation on a maroon central stimulus. After fixation onset, this stimulus disappeared and a peripheral red target appeared, right or left. Monkeys were trained not to look at this peripheral target but instead initiate as soon as possible a saccade towards the opposite direction. Eye movements were recorded with an infra-red eye tracker (Eyelink 1k, SR-Research, Ontario, Canada), and eye position was digitized and stored for off-line analyses. In a series of 23 independent experiments, animals performed 3 blocks of AS training per session: a baseline 100 trials block (50 left/50 right) of AS; a 400 trials block (360 trials without FUS (180 for each side) and 40 trials with FUS (20 for each side); a last block of 100 trials, as post-test. FUS consisted in continuous 100ms sonication with a 320KHz transducer (H115, Sonic Concept, Bothell, WA, USA) focused at the Frontal Eye Field (identified according to stereotaxic coordinates). The estimated derated pressure in the brain was  $0.35 \pm 0.05$  MPa (ISPTA  $13.46 \pm 3.78$  mW/cm<sup>2</sup>).

**RESULTS:** Ipsilateral mean AS latencies with ultrasound stimulation were significantly (t-test ; monkey Y:  $p=.0345$ , monkey L:  $p= .0311$ ) increased compared to the non-stimulation condition (monkey Y: +14ms; monkey L: +15 ms). Post sonication clinical examination and MR imaging did not show any neurological change.

**CONCLUSIONS:** The study demonstrates the feasibility of using FUS to causally modulate behaviour in awake nonhuman primate brain and supports the use of this approach to study brain function and its non-invasive neuromodulation for exploratory and therapeutic purposes.



**Oral session 7**

**2013/5/14 9:30:00**

**CONTROL ID:** 1701048

**TITLE:** INTRAMEMBRANE CAVITATION AND BRAIN STIMULATION USING ULTRASOUND

**AUTHORS/INSTITUTIONS:** E. Kimmel, S. Shoham, Biomedical Engineering Department, Technion, Haifa, ISRAEL | M. Plaksin, Russel-Berrie Nanoscience Institute, Technion, Haifa, ISRAEL |

**ABSTRACT BODY:**

**OBJECTIVE:** Ultrasound is capable of non-invasively and non-destructively stimulating neurons. While diverse applications for this effect are emerging, the mechanism is still unknown. A unified sub-cellular-level model (termed "bilayer sonophore" or BLS) was developed two years ago to explain the mechanisms of interaction of ultrasound and biological tissue. The BLS model is extended here in an attempt to investigate the mechanisms that underline the interaction between ultrasound and any excitable tissue in general and the neuron in particular.

**METHODS:** A mechano-electric model for manipulation of neurons by ultrasound is developed here by combining two models: (i) the mechanistic BLS model combines the physics of bubble dynamics with cell biomechanics to determine the dynamics of the vibrating two lipid leaflets of the bilayer membrane; and the oscillations of the gas pockets that form between the two leaflets, i.e. intramembrane cavitation; and (ii) the bioelectric Hodgkin and Huxley model: that includes varying membrane capacitance and electric potential, and trans-membrane voltage gated channels.

**RESULTS:** Simulation results reveal the conditions needed to generate action potential spikes in a neuron using ultrasound stimulus, and ultrasound intensity and pulse duration are predicted to increase the number of action potential spikes. The effect of the ultrasound frequency below 1MHz on the number of action potential spikes is much smaller.

**CONCLUSIONS:** Close agreement is found after calibration between the predicted number of action potential spikes and the measured success rates in inducing EMG in mice. The mice were subjected to ultrasound stimulation to the motor cortex, a recent study done in Stanford University and published on January 2013. Note that this agreement between theory and experiment required no change in the assumptions and only a minor adjustment in one parameter out of more than 30 independent parameters. As such, the neuron-BLS model and the original BLS models are more trusted now as a base for new applications where ultrasound stimulates neurons and other cells, respectively.



**Oral session 7**

**2013/5/14 9:42:00**

**CONTROL ID:** 1681553

**TITLE:** High intensity focused ultrasound tumor ablation: State of the art

**AUTHORS/INSTITUTIONS:** L. Zhang, Clinical Center for Tumor Therapy, 2nd Hospital of Chongqing University of Medical Sciences,, Chongqing, Sichuan, CHINA|L. Zhang, Z. Wang, State Key Laboratory, Department of Biomedical Engineering, Chongqing University of Medical Sciences, Chongqing, Sichuan, CHINA|Z. Wang, National Engineering and Research Center for Ultrasound Medicine, Chongqing, Sichuan, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** High-intensity focused ultrasound (HIFU) is a technique to destroy tissue at depth within the body, selectively and without harming overlying and adjacent structures within the path of the beam because the ultrasonic intensity at the beam focus is much higher than that outside of the focus.

**METHODS:** Diagnostic ultrasound is the first imaging modality used for guiding HIFU ablation. In 1997, a patient with osteosarcoma was first successfully treated with ultrasound imaging-guided HIFU in Chongqing, China. Over the last decade, thousands of patients with uterine fibroids, liver cancer, breast cancer, pancreatic cancer, bone tumors, and renal cancer have been treated with ultrasound imaging-guided HIFU. This ultrasound imaging-guided HIFU system [Chongqing Haifu (HIFU) Tech Co., Ltd., Chongqing, China] first equipped in Asia, now in Europe.

**RESULTS:** Several research groups reported their results showing that HIFU ablation is safe, effective and feasible in treating human solid tumors. Recently, the group from Chongqing has reported that HIFU can achieve complete tumor necrosis even when the lesion is located adjacent to the major hepatic blood vessels. Indeed, there is no discernible damage to the major vessels, even though the adjacent tumor has been completely ablated. The group from Milan also reported that HIFU is effective and safe in treating solid tumors in difficult locations. Currently, several groups from Italy, Spain, and Russia have shown the encouraging results. The patients were deemed not candidate for surgery, nor suitable for local ablative techniques, have been successfully treated with HIFU.

**CONCLUSIONS:** Based on several research groups' reports, as well as our ten-year clinical experience, we conclude that HIFU is a promising technique, and it's safe and effective in treating human solid tumors. Most importantly, this technique offers another alternative when those patients have no other treatment available.



**Oral session 7**

**2013/5/14 10:54:00**

**CONTROL ID:** 1671263

**TITLE:** CLINICAL EVALUATION OF A TOROIDAL HIFU TRANSDUCER DESIGNED FOR THE TREATMENT OF LIVER METASTASES DURING AN OPEN PROCEDURE

**AUTHORS/INSTITUTIONS:** D. Melodelima, J. Vincenot, J. Chapelon, LabTAU, INSERM, Lyon, FRANCE | D. Melodelima, A. Dupre, Y. Chen, M. Rivoire, Department of surgery, CLB, Lyon, FRANCE |

**ABSTRACT BODY:**

**OBJECTIVE:** An ultrasound device that uses a toroidal HIFU transducer guided by ultrasound imaging was evaluated clinically for the treatment of colorectal liver metastases during an open procedure. Our long-term objective is to associate HIFU with hepatic resection. Here we report clinical results obtained on 18 patients. The principal objective was to validate the effectiveness, accuracy, tolerance and safety of the HIFU treatment. In addition, the response to HIFU was assessed using ultrasound imaging and compared with histological analysis.

**METHODS:** 18 patients with liver metastases and scheduled for elective surgical resection of their tumors were included. The transducer has a toroidal shape with a diameter of 70 mm and is divided into 256 emitters of 0.13 cm<sup>2</sup> each. The radius of curvature is 70 mm to enable treatment of the deepest regions of the liver. The operating frequency was 3 MHz. A 7.5 MHz ultrasound imaging probe was placed in the centre of the device to guide the treatment. The imaging plane was aligned with the HIFU focal zone. Two single thermal ablations were created in each patient after laparotomy and just before the planned liver resection.

**RESULTS:** 36 HIFU lesions were performed. Consistent with our previous experience, the demarcation between ablated and non-ablated tissue was apparent in ultrasound images as a hypoechoic boundary and a central hyperechoic zone. The dimensions measured on ultrasound imaging were correlated ( $r=0.92$ ) with dimensions measured during histological analysis. The average coagulated volume obtained from a 40 s total exposure in the liver was  $5.6 \pm 2.6$  cm<sup>3</sup> (1.9 – 11.4) with an average diameter of  $21.6 \pm 4.5$  mm (12.0 – 28.0) and an average depth of  $28.4 \pm 6.3$  mm (20.0 – 43.0). Patients have tolerated the treatment well. There was no hemodynamics and respiratory changes. No HIFU-related complications occurred during surgery and 30 days postoperatively. The HIFU device can enable the treatment of 94% of the liver volume.

**CONCLUSIONS:** This HIFU treatment using a toroidal transducer is feasible, safe and well tolerated. The treatment is characterized by its brevity (40 seconds for one single ablation of 5-6 cm<sup>3</sup>). This device is capable of achieving selective ablation of predefined liver regions. Ultrasound imaging evidence of complete ablation of the target region can be taken to infer histological success.



**Oral session 7**

**2013/5/14 11:06:00**

**CONTROL ID:** 1681686

**TITLE:** A MULTICENTER CLINICAL TRIAL OF HIFU ABLATION OF UTERINE FIBROID IN CHINA: SAFETY & EFFECACY

**AUTHORS/INSTITUTIONS:** C. Chin, D. He, S. Chen, T. Wang, Biomedical Engineering, Shenzhen University, Shenzhen, Guangdong, CHINA|C. Chin, D. He, S. Chen, T. Wang, Guangdong Key Laboratory for Biomedical Measurements and Ultrasound Imaging, National-Regional Key Technology Engineering Laboratory for Medical Ultrasound, Shenzhen, Guangdong, CHINA|Y. Chen, Y. Chen, The Second Affiliated Hospital, Shantou University, Shantou, Guangdong, CHINA|X. Ding, Shenzhen Promethe Medical Science and Technology Co., Ltd, Shenzhen, Guangdong, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** To determine the safety and efficacy of a new ultrasound-guided HIFU device and associated uterine fibroid (UF) treatment protocol, which does not involve real-time temperature monitoring, in a multicenter clinical trial.

**METHODS:** According to the guideline defined by SFDA, a clinical trial was run at the Xijing Hospital of Fourth Military University, Shantou University Second Affiliated Hospital and First Hospital of Jiling University. One hundred and twelve UF patients confirmed by both ultrasound and MRI (36 patients had multiple lesions) were recruited into the study. HIFU ablation was performed using a PRO2008 focused ultrasound treatment system (Shenzhen Promethe Medical Co.). Patient inclusion and exclusion criteria were pre-defined and the trial was regulated by the relevant ethics authorities. Medical data and contrast enhanced MRI were collected before, one month after and six months after the treatment. Non-perfused region and total tumor volume were measured from the MRI data sets. Pre-defined outcome criteria for efficacy were primarily percent reduction of total tumor volume and secondarily relief of clinical symptoms.

**RESULTS:** At the six month follow-up, 71% of the patients were found to achieve at least 10% tumor volume reduction, with 37% of all patients responded with more than 30% in tumor volume reduction. Prior to treatment, 20 patients suffered from excessive menstrual bleeding and 6 patients suffered from menstrual bloating. At the six months follow-up, these numbers fell to 8 and 2, respectively. Side effects during and following treatment were reported by 12.5% of all patients. Side effects were temporary, mild and varied, including skin inflammation and first degree skin burns, minor aches, virginal bleeding and discharge. Within a week, all side effects resolved without treatment. Further analysis revealed that reduction in perfused tumor volume was larger than reduction in total tumor volume. The data also suggest that success of treatment may be correlated to type and location of tumors.

**CONCLUSIONS:** The was the first clinical trial of HIFU ablation for UF treatment in China. The results show that HIFU treatment can be safe for UF treatment without real time temperature monitoring. A significant fraction of the patient responded positively to HIFU treatment as quantified by tumor volume reduction and symptom amelioration.



**Oral session 7**

**2013/5/14 11:18:00**

**CONTROL ID:** 1683956

**TITLE:** HIFU and Antitumor Immune Response

**AUTHORS/INSTITUTIONS:** F. Wu, Institute of Ultrasonic Engineering in Medicine, Chongqing Medical University, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** The ideal cancer therapy not only induces the death of all localized tumor cells without damage to surrounding normal tissue, but also activates a systemic antitumor immunity. High intensity focused ultrasound (HIFU) has the potential to be such a treatment, as it can non-invasively ablate a targeted tumor below the skin surface, and may subsequently augment host antitumor immunity.

**METHODS:** This presentation is to introduce our clinical and animal studies related to antitumor immune response to HIFU ablation, and to discuss the potential mechanisms involved in HIFU-enhanced host antitumor immunity.

**RESULTS:** Our findings are as follow: 1) Host immune suppression induced by tumor cells can be lessened or relieved after HIFU ablation as the tumor is completely ablated, leading to renewed host antitumor immunity. 2) HIFU ablation can modify tumor antigenicity, and upregulate expression of HSPs, which act as tumor vaccines to produce potent cellular immune responses. 3) Cytokines are secreted by immune cells at the inflammatory margin of the ablation-treated region, presenting a milieu for the development of mature CTLs. 4) Large amounts of cellular debris are gradually phagocytized by macrophages and other cells that can function as APCs.

**CONCLUSIONS:** HIFU-induced antitumor immune responses may play an important role in local recurrence and metastasis of cancer.



**Oral session 7**

**2013/5/14 11:30:00**

**CONTROL ID:** 1672878

**TITLE:** TEMPERATURE DECAY RATES AFTER SONICATION PREDICT THERAPEUTIC RESPONSES OF MAGNETIC RESONANCE IMAGING-GUIDED HIGH-INTENSITY FOCUSED ULTRASOUND ABLATION OF UTERINE FIBROIDS: ANALYSES OF INTRA-PROCEDURAL THERMAL PARAMETERS

**AUTHORS/INSTITUTIONS:** Y. Kim, M. Park, H. Rhim, H. Lim, Radiology, Samsung Medical Center, Sungkyunkwan University, Seoul, KOREA, REPUBLIC OF | B. Keserci, Philips Healthcare, Seoul, KOREA, REPUBLIC OF | K. Nurmilaukas, M. K.hler, Philips Healthcare, Vantaa, FINLAND |

**ABSTRACT BODY:**

**OBJECTIVES:** To evaluate whether or not the intra-procedural thermal parameters predict immediate or delayed therapeutic response of magnetic resonance imaging-guided high-intensity focused ultrasound (MR-HIFU) ablation of uterine fibroids.

**METHODS:** A total of 105 symptomatic uterine fibroids (mean 8.0 cm / 251.8 mL) in 71 women (mean 43.3 years) who were treated with volumetric MR-HIFU ablation were analyzed. The correlations between the tumor-averaged intra-procedural thermal parameters (peak temperature, thermal dose efficiency [volume of 240 equivalent minute at 43°C estimate/volume of treatment cells], temperature decay rate after sonication) and the immediate ablation efficiency (non-perfused volume [NPV] at immediate follow-up/treatment cell volume) or the ablation sustainability (NPV at 3-month follow-up/NPV at immediate follow-up) were assessed using linear regression test.

**RESULTS:** A total of 2818 therapy sonications were analyzed. At immediate follow-up MR (n=105), NPV to fibroid volume ratio and ablation efficiency were  $0.68 \pm 0.26$  and  $1.35 \pm 0.75$ , respectively. The greater thermal dose efficiency ( $B=1.839$ ,  $p<0.001$ ) and the slower temperature decay ( $B=1.561$ ,  $p=0.049$ ) were independently significant factors for the better immediate ablation efficiency. At 3-month follow-up (n=77), NPV decreased to  $41.2 \pm 22.2$  % of the original volume, and only the slower temperature decay turned out to be significantly associated with the better ablation sustainability ( $B=0.839$ ,  $p=0.039$ ).

**CONCLUSIONS:** The post-sonication temperature decay rate predicts both the immediate and the delayed therapeutic responses, whereas the thermal dose efficiency predicts the immediate therapeutic response of MR-HIFU ablation of uterine fibroids.





Oral session 8

2013/5/14 13:00:00

CONTROL ID: 1672242

TITLE: MRI TEMPERATURE MAP RECONSTRUCTION FROM HIGHLY UNDERSAMPLED DATA

AUTHORS/INSTITUTIONS: P. Gaur, Chemical and Physical Biology, Vanderbilt University, Nashville, TN|W.A. Grissom, Biomedical Engineering, Vanderbilt University, Nashville, TN|

ABSTRACT BODY:

**OBJECTIVE:** We propose and validate a method to reconstruct accurate temperature maps without aliasing artefacts or temporal smoothing, even at high acceleration.

**METHODS:** We use an iterative algorithm to fit a sparse phase shift directly to k-space data. We constrain the magnitude of the accelerated image to match that of a fully-sampled image, thereby eliminating the possibility of aliased temperature map solutions. Simulations and Experiments: 1) k-Space data were simulated for a golden angle radial (GA) trajectory. Phase change maps were reconstructed at 4x acceleration using Temporally Constrained Reconstruction (TCR) and the proposed method. 2) GA data of a heated gel phantom were acquired at 3T. Temperature maps were reconstructed using an image-domain hybrid method with 1x and 8x acceleration, and at 8x using the proposed method. 3) Brain images were collected without heat to validate the k-space signal model in vivo. Temperature maps were reconstructed using image-domain hybrid and the proposed method using 1x and 25x acceleration.

**RESULTS:** 1) The proposed method achieved finer temporal resolution and no visible aliasing artefacts (RMSE  $4.3e-3$  rad, max error 0.08 rad) compared to TCR (RMSE  $8.7e-3$  rad, max error 0.29 rad). Increased temporal regularization would decrease TCR aliasing artefacts, but this would further degrade temporal resolution. 2) Compared to the 1x image-domain reconstruction, the 8x image-domain map contained artefactual temperature rises across the phantom. The proposed method's map had no undersampling artefacts. A probe measured  $16.1^{\circ}\text{C}$  change in the tube. Mean/standard deviation in the maps are  $14.7\pm 2.7$  (image-domain 1x),  $13.7\pm 3.9$  (image-domain 8x), and  $15.6\pm 1.7^{\circ}\text{C}$  (proposed 8x). 3) At 1x acceleration, both image-domain and k-space-based temperature estimates produce low mean errors ( $<1^{\circ}\text{C}$ ) over the brain. At 25x the image-domain temperature maps contained large aliasing artefacts (RMSE  $8.1^{\circ}\text{C}$ ), but the k-space-based maps reflected a globally increased temperature uncertainty due to lower SNR, but no significant aliasing artefacts (RMSE  $1.2^{\circ}\text{C}$ ).

**CONCLUSIONS:** We introduced a constrained k-space-based temperature reconstruction method and demonstrated that it estimates temperature changes accurately at high acceleration factors without temporal blurring or aliasing artefacts. The method will readily extend to 3D, where it will enable accurate real-time volumetric thermometry at a high frame rate.



**Oral session 8**

**2013/5/14 13:12:00**

**CONTROL ID:** 1698692

**TITLE:** IMPLICATIONS OF MAGNETIC SUSCEPTIBILITY DIFFERENCES BETWEEN WATER AND FAT FOR ABSOLUTE AND FAT REFERENCED MR THERMOMETRY

**AUTHORS/INSTITUTIONS:** P. Baron, M. de Greef, R. Deckers, C.J. Bakker, J.G. Bouwman, L.W. Bartels, Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, NETHERLANDS|

**ABSTRACT BODY:**

**OBJECTIVES:** Fat referenced MR Thermometry has been suggested for temperature monitoring during MRgHIFU. Our objective was to research the implications of spatial water/fat (and thus susceptibility) distributions on both the measured absolute temperature and fat referenced temperature change.

**METHODS:** Simulation of absolute temperature measurements in heterogeneous tissue: A high resolution (0.63x0.63x0.63mm<sup>3</sup>) water suppressed T1-w 3D scan of the breast was segmented to create a realistic susceptibility distribution. Subsequently, multi-GE imaging was simulated for a down sampled (2.5x2.5x5mm<sup>3</sup>) resolution. The water/fat frequency differences obtained with a two peak fitting model were used to calculate apparent absolute temperature maps. Experiment of absolute temperature in homogeneous tissue: At 3T, a single voxel spectroscopy measurement was acquired in ex vivo duck liver, with the liver rotated at six different angles with respect to the B<sub>0</sub> field so as to vary the susceptibility induced field inhomogeneity. The temperature variation was calculated from the water/fat frequency difference obtained using jMRUI software. Simulation of referenced temperature change: The temperature evolution was simulated for a HIFU ablation of a tumor/fat boundary. The average true temperature change and fat-referenced temperature change were computed for two perpendicular B<sub>0</sub> orientations for an imaging voxel (1x1x1mm<sup>3</sup>) at the focus.

**RESULTS:** Simulation: Large variations in the apparent temperature were found throughout the breast ranging from 8°C to 73°C. Experiment: For the six liver orientations, a temperature standard deviation of 1.8°C was measured. Simulation: For the temperature change of 30°C, fat-referenced thermometry either overestimated (+6.6°C) or underestimated (-2°C) the temperature change depending on the B<sub>0</sub> orientation.

**CONCLUSIONS:** Differences in water/fat susceptibility may play an important role in fat-referenced MR Thermometry. For absolute thermometry, larger temperature variations were found in a heterogeneous water/fat distribution (breast) compared to a more homogeneous one (liver). Our results may partly explain the large temperature variations observed in the breast by McDannold et.al. (MRM 2007;58:1117). In further research we will examine the inter-subject variation of the water/fat frequency shift and the influence of multiple fat spectral peaks on the measurements.



**Oral session 8**

**2013/5/14 13:24:00**

**CONTROL ID:** 1701913

**TITLE:** The use of hybrid MRI temperature and relaxation rate measurements to detect tissue changes in focused ultrasound procedures

**AUTHORS/INSTITUTIONS:** N. Todd, A. Payne, M. Diakite, D.L. Parker, Radiology/UCAIR, University of Utah, Salt Lake City, UT|

**ABSTRACT BODY:**

**OBJECTIVES:** Focused ultrasound procedures would benefit from improved methods to measure temperature in lipids and to detect thermal damage in all tissues. The objective of this study is to use a hybrid PRF/T1/T2\* MRI pulse sequence for simultaneous measurement of proton resonance frequency (PRF) temperature, T1 relaxation time, and T2\* relaxation time in tissue, and analyze the behavior of T1 and T2\* as a function of both temperature and thermal dose. This information could help determine the onset of tissue thermal damage during MR-guided HIFU procedures.

**METHODS:** A 2-D gradient echo sequence with multiple echoes and alternating flip angles is used to measure image phase, T1, and T2\*. Continuous imaging was performed during both ex vivo and in vivo HIFU heating of muscle tissue, providing simultaneous PRF temperature, T1, and T2\* maps with 1.5 x 1.5 x 4.0 mm spatial resolution and 5.7 second temporal resolution. Ex vivo experiments were performed in pork muscle and in vivo experiments were performed in rabbit thigh muscle. Experiment sets consisted of two HIFU heatings: a low power sonication that induced temperature rises below the thermal damage threshold, and a high power sonication that created enough heating to cause thermal damage. The first run was used to calibrate T1 and T2\* changes with temperature, and the second run was used to analyze the behavior of T1 and T2\* as a function of thermal dose.

**RESULTS:** For sub-damage temperature rises, T1 and T2\* demonstrated linear and reversible changes with temperature (T1 increasing and T2\* decreasing) for both the ex vivo and in vivo cases. For the ex vivo case, T2\* demonstrated an irreversible decrease in value that correlated with thermal dose, however permanent changes in T1 values were not detected for the absolute temperatures achieved ( $\leq 62^\circ$  C). For the in vivo case, T2\* values decreased initially with temperature rise, but then increased as significant thermal dose accumulated. The correlation between this inflection point and thermal dose is still under investigation. T1 values for the in vivo case did not show immediate changes from linearity over the course of heating for the absolute temperatures achieved ( $\leq 65^\circ$  C).

**CONCLUSIONS:** Additional information gained from simultaneous measurement of T1 and T2\* may be useful for helping to determine the onset of thermal damage during HIFU ablation procedures.



**Oral session 8**

**2013/5/14 13:36:00**

**CONTROL ID:** 1671806

**TITLE:** ULTRASONOGRAPHY BASED MOTION TRACKING FOR MRgFUS

**AUTHORS/INSTITUTIONS:** J.W. Jenne, J. Schwaab, C. Sarti, A. Bongers, M. Günther, mediri GmbH, Heidelberg, GERMANY|J.W. Jenne, M. Günther, Fraunhofer MEVIS, Bremen, GERMANY|S.H. Tretbar, Fraunhofer IBMT, St. Ingbert, GERMANY|

**ABSTRACT BODY:**

**OBJECTIVE:** The non invasive treatment of moving organs like liver, pancreas or kidney with high intensity focused ultrasound (HIFU/FUS) is still a challenge. The highly precise ablation with HIFU requires real-time knowledge of tumor position with mm precision. Beside the use of MR tracking methods like NavEchoes, it was shown in vitro that the use of diagnostic ultrasound (ultrasonography) could be an adequate tracking method for MRgFUS [1]. The aim of this work is to build up an MR compatible tracking device using diagnostic ultrasound imaging for MRgFUS.

**METHODS:** The hardware of the developed US-tracking system is based on a Digital Phased Array System (DiPhAS) developed by Fraunhofer Institute for Biomedical Engineering IBMT, St Ingbert, Germany. It comprises the ultrasound beam former with a screen directly placed in front of the MR-magnet, a diagnostic ultrasound probe and a special ultrasound tracking probe (2x64 element phased array). The tracking probe spans up two perpendicularly oriented ultrasound image planes and was designed to enable a 3D tracking. The acquired US-data are sent to a workstation in the console room of the MRI scanner which controls the whole tracking unit. The tracking software (Sonoplan II) analyzes the ultrasound image stream (3-4 ms/slice) and calculates the position of pre-defined contours, i.e. structures such as the diaphragm, organ borders, vessels or the tumor as such. Beside the 2D-translation, the tracking algorithm analyzes the rotation as well as the 2D scaling of the contour (5DOF).

**RESULTS:** MR-compatibility of US-tracking system was tested in a 1.5 and a 3T MR-system. At 1.5T the noise level of the MR images was slightly increased, while at 3T no artifacts were seen. The robustness of the tracking algorithm [2] allowed tracking even in case of limited image quality such as poor contrast or high noise. The tracking frame rate was 25-40Hz with a delay of about 70ms.

**CONCLUSIONS:** The developed US-tracking device is MR compatible and allows quasi real-time tracking of organ structures. In the next step the tracking system will be combined with an MRgFUS unit and an automated MR slice correction based on the US-tracking should be integrated. [1] Aboiroux et.al. Phys Med Biol. 2012, 57:N159–N171 [2] Feinberg et.al. Magn Reson Med. 2010, 63(2):290-296



## Oral session 8

2013/5/14 13:48:00

**CONTROL ID:** 1681431

**TITLE:** Multifunctional organic-inorganic hybrid nanovesicles for MRI-guided High intensity focused ultrasound ablation

**AUTHORS/INSTITUTIONS:** Y. Li, D. Niu, School of materials science and engineering, Shanghai, --- Please Select --, CHINA |

### **ABSTRACT BODY:**

**OBJECTIVES:** As an alternative non-invasive approach for tumor therapy, high intensity focused ultrasound (HIFU) is proposed to aim at the deep tumor target extracorporeally but accurately, leading to irreversible cell death by rapid heat and mechanical energy accumulation, whereas leaving the penetrated skin and tissue safe. An ideal noninvasive therapy can be achieved if two prerequisites are fulfilled, which are the accurate imaging information acquisition and the precise energy delivery to the target.

**METHODS:** A facile self-assembly/sol-gel methodology has been developed to synthesize PEGylated magnetite/perfluorooctyl bromide-loaded organic-inorganic hybrid vesicles (designated as P-Fe<sub>3</sub>O<sub>4</sub>/PFOB@OIHVs), which show great potentials in dual-modality US/MR imaging and intensified imaging-guided HIFU liver cancer ablation.

**RESULTS:** The typical morphology, structure, and diameter of P-Fe<sub>3</sub>O<sub>4</sub>/PFOB@OIHVs were analyzed by various techniques including transmission electron microscopy (TEM), energy dispersive X-ray spectroscopic (EDS), dynamic light scattering (DLS) and so on. The results show that the nano-sized organic-inorganic hybrid vesicles displayed an average diameter of 175 nm, unique calotte-like morphology and satisfactory stability under physiological conditions. By the co-encapsulation of superparamagnetic magnetite nanoparticles and liquid perfluorocarbon PFOB, the multifunctional nanovesicles could not only be used as a dual-mode contrast agent for T<sub>2</sub>-weighted MR and contrast-enhanced US imagings for accurate cancer diagnosis and monitoring, but also be used as therapeutic agents for effective HIFU ablation. With the help of P-Fe<sub>3</sub>O<sub>4</sub>/PFOB@OIHVs, the focused ultrasound can be precisely located on the VX2 tumor tissue in the liver of rabbits under MR imaging guidance and a greatly enhanced HIFU therapeutic efficacy has been achieved.

**CONCLUSIONS:** It is concluded that the obtained multifunctional organic-inorganic hybrid nanovesicles with unique but uniform nanostructure and long-term stability in biological environment can be applied for the efficient diagnosis and treatment of cancers by integrating non-invasive US/MR imaging techniques and imaging-guided HIFU surgery.



## Oral session 9

2013/5/15 8:39:00

**CONTROL ID:** 1666128

**TITLE:** ULTRASOUND TOMOGRAPHY TO MONITOR FOR BREAST CANCER TREATMENT USING HIGH INTENSITY FOCUSED ULTRASOUND THERAPY

**AUTHORS/INSTITUTIONS:** T. Kanagawa, H. Nakamura, R. Aoyagi, T. Azuma, A. Sasaki, S. Takagi, Y. Matsumoto, Department of Mechanical Engineering, The University of Tokyo, Tokyo, Tokyo, JAPAN | K. Yoshinaka, Surgical Assist Technology Group, National Institute of Advanced Industrial Science and Technology, Tsukuba, Ibaraki, JAPAN |

### **ABSTRACT BODY:**

**OBJECTIVE:** USCT [US (Ultrasound)-Computed Tomography] for the breast cancer is a promising monitoring tool for HIFU (High Intensity Focused Ultrasound) therapy. Especially, the sound speed and attenuation profiles acquired by the USCT are suitable for a targeting and a monitoring for HIFU. A preliminary investigation of USCT for weakly heterogeneous tissues as a model of the breast is described. For simplicity, a US path was assumed to be straight. The attenuation, diffraction, and refraction effects, which are considerably smaller than those in hard tissues because

of weak heterogeneity of the breast model, were omitted. Our objective is to discuss the validity of this assumption from an image reconstructed.

**METHODS:** We considered a two-dimensional scale-downed breast model with a diameter of 35 mm including two circular tissues: fat and lesion with diameters of 7.5 and 10 mm. This breast model was covered by a 256-elements ring-array transducer with a diameter of 35 mm, and was in rectangular water of 40 mm. Each element radiated a single transmission US pulse with a center frequency of 2 MHz. The US propagation was computed by the commercial software PZFlex using a finite element method with a rectangular grid of 0.077 mm. We calculated arriving times of US at each element, and image reconstruction was carried out by two different methods: ART (Algebraic Reconstruction Technique) and SART (Simultaneous ART).

**RESULTS:** The reconstructed image of sound speed agreed with qualitatively the original one in both the cases of ART and SART. We therefore retrieved the weak heterogeneity of sound speed, especially the reconstructed speed in the normal tissue was close to original speed with an average error and a standard deviation of 4 and 79 m/s, respectively. However, respective errors of fat and lesion were 50 and 40 m/s. The noise and circular artifact were also detected, which implied a path variation due to refraction or diffraction of US. Utilizing SART then intensively decreased the noise.

**CONCLUSIONS:** We performed the image reconstruction of sound speed for the breast model under the assumption of straight US path, by using algebraic methods. As a result, the reconstructed images agreed qualitatively with original one, although the noise and artifact were detected. To improve reconstruction, various modifications such as diffraction and refraction effects will be reported in the conference.



**Oral session 9**

**2013/5/15 8:51:00**

**CONTROL ID:** 1670606

**TITLE:** EVALUATION OF LESION-TO-BUBBLE RATIO WITH POLYMER- AND LIPID-SHELLED MICROBUBBLES AMONG ULTRASONIC IMAGING METHODS FOR MONITORING HIGH-INTENSITY FOCUSED ULTRASOUND

**AUTHORS/INSTITUTIONS:** S. Zhang, C. Li, F. Zhou, S. Wang, M. Wan, Department of Biomedical Engineering, Xi'an Jiaotong University, Xi'an, Shaanxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVE:** The uses of high-intensity focused ultrasound (HIFU) for the treatment of tumors located in various tissues are being investigated due to the development of the medical imaging techniques for targeting and monitoring HIFU during recent years. US would present a number of advantages such as its portability, low-cost, real-time imaging capability, simple integration with the HIFU system and its extensive availability. During HIFU treatment, bubble activity may be the result of both cavitation and boiling. Recently, increased therapeutic effects have been shown that stabilized gas-filled microbubbles (MBs) have been potential to aid treatment during HIFU, creating interest in developing ultrasound therapy methods using MBs. The acoustic posterior shadowing of these bubbles during HIFU influences the accuracy for defining the location and range of ablated thermal lesion. In this work, we got inspired from contrast-to-tissue ratio for ultrasound contrast imaging and proposed the term "lesion-to-bubble ratio (LBR)" to discriminate between the thermal lesion and the surrounding bubbles.

**METHODS:** B-mode ultrasound images, differential integrated backscatter (DIBS) images and Nakagami images for monitoring were evaluated with LBR when polymer- and lipid-shelled microbubbles were used to aid treatment during HIFU application at different acoustic power levels in transparent tissue-mimicking phantoms. 2-D RF data backscattered from lesions were captured by a linear array imaging probe of a modified diagnostic US machine during HIFU and were processed to obtain various ultrasonic parameter images.

**RESULTS:** Compared with B-mode and DIBS images, the ultrasonic Nakagami images were not subject to the significant shadowing effects of bubbles and had higher values of LBR. The values of LBR in the ultrasonic monitoring images with MBs were lower than those pure controls measured at the same exposure parameters but without MBs.

**CONCLUSIONS:** Ultrasonic Nakagami images may provide a promising modality to visualize the thermal lesion when the shadowing effect of bubbles was strong while the lesion was small. This work was a preliminary study and further in vivo studies were necessary to investigate the feasibility of using the ultrasonic Nakagami image to visualize the ablated region from the shadowing effects of bubbles induced by HIFU.



**Oral session 9**

**2013/5/15 9:03:00**

**CONTROL ID:** 1671093

**TITLE:** AN INTEGRATED AND REAL-TIME MONITORING IMAGING TECHNIQUE OF TISSUE DAMAGE, CAVITATION AND BLOOD PERFUSION FOR HIGH INTENSITY FOCUSED ULTRASOUND (HIFU) THERAPY

**AUTHORS/INSTITUTIONS:** H. Zhong, G. Ding, Y. She, M. Wan, Biomedical Engineering, Xi' an Jiaotong University, Xi'an, Shannxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVE:** This paper proposed an integrated and real-time monitoring imaging technique to visualize the whole changes of treated area and cavitation bubble activity simultaneously during HIFU treatment, and obtain the blood perfusion images for evaluation of therapeutic effect after HIFU treatment by the choice of RF data frames on different data acquisition time.

**METHODS:** HIFU delivery is briefly interrupted with the HIFU completely off for RF data acquisition during HIFU treatment. Two consecutive RF data frames with different transmit waveforms are acquired before, between and after HIFU exposures. The transmit waveforms of one frame are positive pulses, and those of the other frame are negative pulses. This technique is similar to pulse-inversion technique, and we name it frame-pulse-inversion (FPI). An algorithm called sum-squared difference (SSD) is combined with the FPI technique to obtain the monitoring images for improving sensitivity, which was called FPISSD imaging method. The dynamic monitoring images reflecting whole changes of treated area including tissue damage and cavitation bubble activity could be obtained by choosing the two RF data frames with positive pulse transmission before and during HIFU treatment. The dynamic cavitation bubble images could be obtained by choosing the two consecutive RF data frames between HIFU exposures. By injecting contrast agent into blood vessels, the blood perfusion images could be obtained by choosing the two consecutive RF data frames after HIFU treatment.

**RESULTS:** The experiment results of porcine muscle in vitro and rabbit kidney in vivo verified the validity of the proposed monitoring imaging method. The FPISSD method was compared with the pulse-inversion harmonic (PIH) method, which was often used in conventional contrast-enhanced imaging. The results showed that the FPISSD algorithm had higher sensitivity than PIH method.

**CONCLUSIONS:** The proposed monitoring imaging method can provide integrated information of tissue damage, cavitation bubble activity and blood perfusion during and after HIFU treatment. The method just involved simple operations including addition, subtraction and multiplication, therefore it is easy to realize and need not large computational time. The proposed method has the potential to be realized in real-time on low-cost ultrasound platform.





**Oral session 9**

**2013/5/15 9:15:00**

**CONTROL ID:** 1671808

**TITLE:** BIPLANE ULTRASOUND MONITORING OF HIGH-INTENSITY FOCUSED ULTRASOUND LESION FORMATION

**AUTHORS/INSTITUTIONS:** S. Sasaki, K. Matsuura, S. Umemura, Biomedical Engineering, Tohoku University, Sendai, JAPAN|S. Yoshizawa, S. Umemura, Engineering, Tohoku University, Sendai, JAPAN|

**ABSTRACT BODY:**

**OBJECTIVE:** In order to enhance the safety and accuracy of high intensity focused ultrasound (HIFU) treatment, a noninvasive method to monitor lesion formation is as important as a HIFU technology itself. Either MRI or ultrasonic imaging is currently used for this purpose, and the latter is chosen in this study because of its lower expense and higher spatial resolution. Tissue coagulation induced by HIFU has been detected using the distribution of cross-correlation coefficient and the differential images between two motion-compensated RF images before and after the HIFU exposure. Biplane RF images are employed in this study because the motion cannot necessarily be compensated in a single plane.

**METHODS:** A freshly excised porcine liver was perfused with degassed saline and dissected to samples, and a sample was set in a tank containing degassed water at 34°C. The sample was exposed to HIFU at several hundred W/cm<sup>2</sup>, and ultrasonic RF data were acquired before and after the exposure. Tissue motion was calculated by block matching and compensated for each plane. Then, the tissue coagulation was estimated using the distribution of cross-correlation coefficient and the differential images.

**RESULTS:** In the distribution of cross-correlation coefficient, low correlation was observed in and around the focal spot of HIFU exposure in both planes. This indicates that low correlation was caused not by the translational tissue motion but by the change in texture induced by the tissue coagulation. The size of the region with low correlation was slightly larger than the size of actual coagulation region. In the differential B-mode images, decrease in brightness was observed in the HIFU focal spot, but the size of the region with lower brightness was slightly smaller than the size of actual coagulation region. Increase in brightness was observed in the area surrounding the region. The pathology showed slight contraction and changes in alignment of hepatic cells in the coagulation region, which may have decreased in the B-mode brightness. This contraction may have been accompanied by the expansion of the surrounding area, which may have decreased the correlation and increased the B-mode brightness in the surrounding area.

**CONCLUSIONS:** Decrease in both correlation and B-mode brightness was observed in the focal spot of HIFU exposure. Further study combining these changes may make the accurate estimation of the size of coagulation possible.



## Oral session 9

2013/5/15 9:27:00

**CONTROL ID:** 1671838

**TITLE:** DEVELOPMENT OF COAGULATION MONITORING SYSTEM BASED ON ACOUSTIC RADIATION FORCE

**AUTHORS/INSTITUTIONS:** N. Hirofumi, A. Ryosuke, A. Takashi, S. Akira, T. Shu, M. Yoichiro, Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN|Y. Kiyoshi, Department of Human Life Technology, Advanced Industrial Science and Technology, Tsukuba, JAPAN|F. Keisuke, T. Hideki, I. Kazunori, Hitachi-Aloka Medical, Tokyo, JAPAN|

### **ABSTRACT BODY:**

**OBJECTIVE:** Localized Motion Imaging (LMI) to detect stiffness change caused by High Intensity Focused Ultrasound (HIFU) is described. A focal tissue can be moved using acoustic radiation force due to HIFU intensity. In LMI, we used an amplitude-modulated (AM) HIFU to generate localized tissue oscillation at the focal point. By measuring the amplitude of tissue oscillation before and after HIFU surgery, we can detect the thermal coagulation area. In this study, detection of the thermal coagulated area using LMI is our objective.

**METHODS:** We investigated the amplitude change of tissue oscillation using LMI before and after heating by HIFU. The HIFU intensity for heating was 1000 W/cm<sup>2</sup>, and exposure time was 15 s. On the other hand, HIFU intensity for LMI was 500 W/cm<sup>2</sup>, and exposure time was 1 s. Temperature increase by this condition was estimated 13 K. In LMI process, an one-dimensional displacement distribution was estimated from a cross correlation between two consecutive echo signals in the time axis. To measure two-dimensional view of LMI, a lateral scan was performed. An interval time between each one-dimensional LMI measurement was over 1 minute to suppress a risk of thermal coagulation. The lateral scan pitch and the range of the scan area were 1 and 20 mm, respectively. We use porcine liver samples as tissue samples. HIFU frequency and beam width at focal point in lateral direction were 2.2 MHz and 1 mm. AM frequency of HIFU in LMI was 67 Hz.

**RESULTS:** Using LMI displacement maps before and after HIFU heating, we generated amplitude decrease area map. Since modules of rigidity increases with thermal coagulation, the amplitude decrease area means estimated coagulated area. The LMI image showed a conical shape coagulated area that is typical lesion shape caused by HIFU coagulation. This shape and size of estimated area roughly agreed with an actual cross-sectional image after sample cutting. In the deep part, LMI results showed over estimation in size. One possible reason of this effect was caused by decrease of the radiation force due to an attenuation increase at the coagulated area.

**CONCLUSIONS:** To evaluate LMI for detection of thermal coagulated area caused by HIFU surgery, we performed the experiment using porcine liver as tissue sample. As a result, the estimated coagulation area map indicated a closer agreement with actual coagulation area.



**Oral session 9**

**2013/5/15 10:30:00**

**CONTROL ID:** 1671995

**TITLE:** FEASIBILITY OF HIFU CARDIAC THERAPY AND MONITORING USING SHEAR-WAVE IMAGING WITH DUAL MODE INTRACARDIAC CATHETER

**AUTHORS/INSTITUTIONS:** W. Kwiecinski, J. Provost, M. Fink, M. Tanter, M. Pernot, Institut Langevin, ESPCI, Paris, FRANCE |

**ABSTRACT BODY:**

**OBJECTIVE:** Atrial fibrillation (AF) is the most common cardiac arrhythmia and is the cause of 15-20% of strokes. AF can be treated by creating continuous, transmural ablation lines in the heart chambers to isolate or eliminate electrically abnormal regions. However, clinically available systems based on radio-frequency ablation are associated with high recurrence rates in part because they cannot be used to create transmural lesions nor monitor their extent. In this work, we have developed and validated ex vivo a novel non-contact dual-mode ablation and imaging ultrasound catheter, which can perform both High-Intensity Focused Ultrasound (HIFU) and Shear-Wave Imaging (SWI) to create transmural lesions and monitor their extent in real-time.

**METHODS:** A 64-element intracardiac transducer (6 MHz, 0.2 mm pitch, Vermon, France) mounted on 9F catheter was designed and built for dual mode imaging/therapy. Shear waves were generated remotely in fresh porcine myocardial (n=10) and atrial (n=6) samples with the transducer and recorded (10000 frames/s) with an ultrafast scanner prototype (Supersonic Imagine, France) to map the shear modulus. This prototype can perform both transmit/receive imaging sequences and transmit HIFU sequences (4W/channel). HIFU lesions were then induced using the same probe by a focused transmit during 10s. Post-treatment SWI were then performed and the elasticity ratio between pre and post treatment was compared with the area of ablated tissue.

**RESULTS:** The acoustic output power was measured with an acoustic radiation force balance. A total acoustic power of 2.6 W corresponding to an acoustic intensity of 11W/cm<sup>2</sup> at the surface of the probe was measured during 10 s without any visible overheating effects. Thermal lesions were created after 10 seconds of emission. Thermal lesions of approximately 3x2 mm<sup>2</sup> were visible on the shear modulus maps. The stiffness was found to increase from 31kPa±12kPa to 82kPa±30kPa at the boundary of the ablated zone and up to 150±43kPa in the core of the lesion. Comparison with gross pathology shows that a stiffness ratio of 2.6±0.46 between pre and post treatment determined the lesions boundaries.

**CONCLUSIONS:** We have demonstrated the feasibility of both thermal ablation and monitoring using the same ultrasonic catheter in ex-vivo samples. This direct therapy/imaging association could lead to a precise and reliable atrial fibrillation treatment.



**Oral session 9**

**2013/5/15 10:42:00**

**CONTROL ID:** 1672052

**TITLE:** REAL TIME SHEAR WAVES IMAGING OF HIFU THERMAL ABLATION: IN VIVO EVALUATION IN PIG LIVERS

**AUTHORS/INSTITUTIONS:** W. Kwiecinski, M. Pernot, M. Fink, M. Tanter, Institut Langevin, ESPCI, Paris, FRANCE|A. Mariani, C. Cuenod, F. Zinzindohoue, Department of Digestive & General Surgery, Hopital Européen Georges Pompidou, Paris, FRANCE|A. Mariani, C. Cuenod, F. Zinzindohoue, Paris Cardiovascular Research Center , Inserm, Paris, FRANCE|

**ABSTRACT BODY:**

**OBJECTIVE:** High Intensity Focused Ultrasound is a promising technique for thermoablative surgery of the liver. It has the advantage of being non-invasive and inoffensive for tissue surrounding the treatment zone. Still, in many clinical applications it remains ineffective because of the lack of precise and easily implementable lesion monitoring. We have shown previously that local tissue elasticity estimation with Shear-Wave Imaging (SWI) can be used to map in real-time the formation of thermal lesions (Arnal et al., IEEE UFFC 2011). In this study we propose the use of shear wave imaging to monitor HIFU ablation in in vivo pig livers.

**METHODS:** A therapy-imaging confocal ultrasound system has been designed. Therapy was performed with a focused single element (2.25MHz, 38mm diameter, F/D 1, Imasonic, France) mechanically aligned with a conventional ultrasonic linear imaging probe (6MHz, 192 elements, 0.2mm pitch, Vermon, France). The system was installed on the liver with an open surgery approach. 3 pigs were used and a number of 10 lesions were created by a 2D motorized displacement of the single element. SWI was performed and recorded with an ultrafast scanner prototype (Supersonic

Imagine, France) before and after each ablation sequence. The 2D maps of elasticity ratio between pre and post treatment was compared with the area of ablated tissue in order to assess the efficiency of shear wave imaging to quantify the extent of the lesion.

**RESULTS:** By applying 35W of electrical power, the ablating probe was able to generate a peak pressure  $7.8\text{MPa} \pm 250\text{kPa}$  at the focal depth, during 20sec. With an imaging frame rate of 10000 frames/s and 3 shear wave generations per sample, we were able to image the lesion section (approximately 5mm diameter). After comparison of the tissue color change on the tissue slices, a stiffness ratio of  $3.1 \pm 0.51$  between pre and post treatment on the 2D elasticity maps was found to determine lesions frontiers. The liver stiffness was found to increase from  $6.4\text{kPa} \pm 0.3\text{kPa}$  to a mean of  $26.1\text{kPa} \pm 2.5\text{kPa}$  in the ablated zone.

**CONCLUSIONS:** We have demonstrated the feasibility of HIFU thermal ablation monitoring using SWI in in vivo liver samples. This technique could lead to a real time mapping of lesions and significantly improve the quality of thermal ablation in liver.



**Oral session 9**

**2013/5/15 10:54:00**

**CONTROL ID:** 1672398

**TITLE:** PASSIVE CAVITATION DETECTION DURING PULSED HIGH-INTENSITY FOCUSED ULTRASOUND EXPOSURES OF EX VIVO TISSUES AND IN VIVO MOUSE MODEL OF PANCREATIC TUMORS

**AUTHORS/INSTITUTIONS:** T. Li, H. Chen, T. Khokhlova, Y. Wang, J.H. Hwang, Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA|

**ABSTRACT BODY:**

**OBJECTIVE:** Pulsed high intensity focused ultrasound (HIFU) has been demonstrated to enhance drug penetration into tumor tissue through acoustic cavitation. To effectively deliver chemotherapeutic drugs into tumors, such as pancreatic tumors, it is important to monitor the site and extent of cavitation activity during HIFU treatment, and find the pressure level necessary to reliably induce that activity in a given tissue. The dependence of the probability of cavitation occurrence and the cavitation activity level on HIFU peak negative pressure was studied previously in ex-

vivo tissues and gel phantoms. However, the relevance of these measurements in in vivo exposures and whether they are tissue-dependent remain controversial. In this study, cavitation monitoring was performed during pulsed HIFU exposures in gel phantoms, ex vivo tissues and mouse pancreatic tumors in vivo. The probability of cavitation occurrence and the level of cavitation activity were compared between tissue types at varying HIFU peak negative pressure levels and correlated to the degree of chemotherapeutic drug (doxorubicin) delivery.

**METHODS:** A passive cavitation detector (PCD), aligned confocally with a 1.1MHz HIFU transducer, was used to monitor bubble activity. Pulsed HIFU exposures (peak negative pressures 1.6-12MPa), were applied to gel phantoms and ex vivo tissues: porcine kidney and fat, bovine liver and tongue. The signals collected by PCD were filtered by a combination of a band-pass (2-8MHz) and a notch shaped comb filter to obtain the broadband noise corresponding to inertial cavitation. The filtered PCD signal was used to identify the site of cavitation. In the in vivo exposures, a transgenic KPC mouse bearing a pancreatic tumor was injected with doxorubicin, and drug uptake was evaluated by fluorescence imaging.

**RESULTS:** The peak negative pressures sufficient to achieve 50% probability in cavitation occurrence in water-based tissues (kidney and liver) and gel phantoms were very similar (9-11MPa). For tissues with higher fat content (tongue and fat), the levels were much smaller (4-7MPa).

**CONCLUSIONS:** Both the cavitation noise level and the cavitation probability were found to be higher in vivo than ex vivo at the same peak negative pressures, and were correlated with the degree of drug uptake by the pancreatic tumors. Work is supported by the NIH grant R01CA154451.



**Oral session 9**

**2013/5/15 11:06:00**

**CONTROL ID:** 1672471

**TITLE:** THE USE OF TWINKLING ARTIFACT OF DOPPLER IMAGING TO MONITOR CAVITATION IN TISSUE DURING HIFU THERAPY

**AUTHORS/INSTITUTIONS:** O. Sapozhnikov, Faculty of Physics, Moscow State University, Moscow, RUSSIAN FEDERATION | O. Sapozhnikov, T. Li, Applied Physics Laboratory, University of Washington, Seattle, WA | T. Khokhlova, J. Hwang, Medicine, University of Washington, Seattle, WA |

**ABSTRACT BODY:**

**OBJECTIVE:** In high intensity focused ultrasound (HIFU) therapy, it is important to monitor the presence and activity of microbubbles in tissue during treatment. The current methods have several limitations. Passive cavitation detection (PCD) is reliable and sensitive in real-time cavitation monitoring but provides minimal spatial information. B-mode imaging can detect hyperecho formation, but has limited sensitivity, especially to small-size, non-violently-collapsing microbubbles. Here, a new method for microbubble detection is proposed, based on “twinkling” artifact (TA) of Doppler imaging. TA occurs when Color Doppler ultrasound is used to image hard objects in tissue (e.g., kidney stones), and is displayed as brightly colored spots. As demonstrated recently, TA can be explained by irregular scattering of the Doppler ensemble pulses from the fluctuating microbubbles trapped in crevices of the kidney stone. The goal of this study is to use TA to detect cavitation bubbles in tissue induced by pulsed HIFU exposures.

**METHODS:** Pulsed HIFU exposures of polyacrylamide gel phantoms and ex-vivo bovine liver were performed with 1.1 MHz transducer producing focal peak negative pressures of 1.5-11MPa. Ultrasound imaging of the HIFU exposures was performed using the Verasonics Ultrasound Engine with a clinical probe (ATL HDI L7-4). The imaging plane was aligned with the axis of the HIFU transducer and the imaging was performed in “flash” transmitting mode, when all the array elements were excited simultaneously to emit a quasi-plane wave. The imaging system was triggered by the

trailing edge of each HIFU pulse to acquire one Doppler image and one B mode image, to avoid saturation by the scattered HIFU waves. At each HIFU negative pressure level, the cavitation activity was monitored by TA and the broadband emissions were recorded by a focused PCD, aligned confocally with the HIFU transducer.

**RESULTS:** Over the course of the exposures, the intensity of the TA correlates well with the broadband noise level recorded by the PCD. The results at lower pressure level indicate that TA is more sensitive to the onset of cavitation than both PCD and conventional B-mode imaging.

**CONCLUSIONS:** The study has shown that TA has the advantages to both localize and quantify cavitation activity during HIFU exposure. Work supported by RFBR and NIH (EB007643, 1K01EB015745, R01CA154451).



## Oral session 9

2013/5/15 11:18:00

**CONTROL ID:** 1679697

**TITLE:** Monitoring FUS-induced BBB opening in non-human primates using transcranial cavitation detection in vivo

**AUTHORS/INSTITUTIONS:** S. Wu, F. Marquet, Y. Tung, M. Downs, C.C. Chen, E. Konofagou, Biomedical Engineering, Columbia University, New York, NY|T. Teichert, M. Downs, V. Ferrera, Neuroscience, Columbia University, New York, NY|

### **ABSTRACT BODY:**

**OBJECTIVES:** Focused ultrasound (FUS) with microbubbles (MB) has shown great promise in assisting brain drug delivery by noninvasively and locally opening the blood-brain barrier (BBB). Real-time monitoring with transcranial passive cavitation detection (PCD) is critical to achieve efficacy and safety without requiring on-line MRI. The objective is to investigate feasibility of a uniform focal spot at the pressures used in non-human primates (NHP) in vivo and guidance of opening using PCD through a human skull in vitro with the use of lipid-shelled, monodisperse MB (4-5  $\mu$  m).

**METHODS:** In the in vitro experiments, the MB were injected into a channel in the phantom below a degassed human skull to mimic a set of brain capillaries within FUS focal spot. During sonication (fc: 0.5 MHz, PNP: 50-450 kPa), a confocal hydrophone served as PCD. The harmonic, ultraharmonic, and broadband signal amplitudes within 1-5 MHz of the PCD signals with and without the skull in place were separated using comb filters for quantifying the stable/inertial cavitation dose (SCD/ICD). In the in vivo experiments, the MB were injected intravenously in two rhesus macaques at the beginning of sonication (200–275 kPa), with a total of 23 sonications in caudate/putamen while monitoring the SCD and ICD in real time. Both T1w and T2w MRI were performed after sonication to confirm the opening and lacking of edema, respectively.

**RESULTS:** In the in vitro experiments, the transcranial PCD attenuation was found to be 93% through the human skull. In the in vivo experiments, there was 96% (22/23) success in opening the BBB at 250-275 kPa, with a null ICD while the SCD reached a plateau at 20 dB in 10 s after the MB injection. The MR images showed highly repeatable opening patterns over multiple trials with a mean focal shift of 1 mm. No significant difference was observed in terms of PCD monitoring and BBB disruption between the caudate and putamen. No edema, behavioral or physiological changes were observed after treatment in any of the animals.

**CONCLUSIONS:** The SCD using harmonic signals and ICD were analyzed within 1-5 MHz through the human skull and used to monitor the bubble activity during BBB opening in NHP in vivo with real-time feedback. BBB opening in primates was achieved with null ICD and found to be 96% successful and reproducible within millimeters without MR targeting or guidance while maintaining the required safety.



**Oral session 9**

**2013/5/15 11:30:00**

**CONTROL ID:** 1684915

**TITLE:** TEMPERATURE IMAGING WITH ULTRASONIC TRANSMISSION TOMOGRAPHY FOR TREATMENT CONTROL

**AUTHORS/INSTITUTIONS:** P.L. Carson, M.L. Scarpelli, S.Z. Pinter, O.D. Kripfgans, J. Yuan, J.B. Fowlkes, Radiology, University of Michigan Health System, Ann Arbor, MI|N. Duric, Karmanos Cancer Institute, Detroit, MI|

**ABSTRACT BODY:**

**OBJECTIVES:** We aim to show ultrasound imaging of temperature for HIFU and hyperthermia control. Despite the strong temperature dependence of hyperthermic enhancement of chemo and radiation therapy, monitoring of temperature is done primarily with invasive probes. MRI is expensive for the long, daily hyperthermia treatments. The relatively simple relation of speed of sound to temperature makes ultrasound, and particularly ultrasonic transmission tomography (UTT) in accessible anatomy, a good prospect for imaging hyperthermia and thermal ablation and providing feedback to reduce deviations from desired temperature distributions. Transmission speed of sound plus reflection and attenuation imaging will help identify tissue types so temperature elevations above ambient can be tracked with the speed of sound and so US or microwave propagation and heating properties can be predicted.

**METHODS:** A prototype UTT breast imaging system (Delphinus Medical Technologies, Inc) providing high resolution SOS, reflection and attenuation images at one frame per second was used to image a test object in a warm water bath. The test object was a long annulus of 15% gelatin and water with a water tube along the axis. The temperature of the gelatin was elevated a few degrees. Imaging was performed with the water in the tube cooled and then with it warmed.

**RESULTS:** Low noise SOS images were obtained, despite a highly attenuating silicone tube outside the annulus for return of the water passing down the center of the annulus. Segmentation of the structures and application of the known curves of SOS(T) for gelatin and water provided accurate temperature images, but with strong edge discontinuities. These discontinuities were consistent with partial volume effects when applying different SOS(T) curves on either side of the discrete boundaries. Application of a linear combination SOS(T) curves for the two materials weighted by the system edge response function provided expected smooth temperature profiles ( $\sigma < 0.5^\circ\text{C}$  in the water).

**CONCLUSIONS:** Lipid, fiber, and water content of tissues at body temperature can be estimated from SOS, attenuation and reflection images, possibly supplemented by earlier MRI or CT. At some fat/water content ratio and temperature, the slope of SOS(T) will be zero. But this will not be the case at other temperatures achieved temporarily for clarification. Supported in part by DoD/BCRP award No. BC095397.





## Oral session 9

2013/5/15 11:42:00

**CONTROL ID:** 1672435

**TITLE:** MONITORING DURING SLOW DENATURATION AND BOILING USING HARMONIC MOTION IMAGING FOR FOCUSED ULTRASOUND (HMIFU) EX VIVO

**AUTHORS/INSTITUTIONS:** G.Y. Hou, F. Marquet, S. Wang, E.E. Konofagou, Biomedical Engineering, Columbia University, New York, NY | E.E. Konofagou, Radiology, Columbia University, New York, NY |

### **ABSTRACT BODY:**

**OBJECTIVE:** HMIFU is a recently developed high-intensity focused ultrasound (HIFU) treatment monitoring method with feasibilities demonstrated in vitro and in vivo. However, successful application of HMIFU requires capability of monitoring changes in the local tissue mechanical property, i.e., estimation of the HMI displacement under both thermal and acoustical effects (i.e., boiling, cavitation, nonlinearity effect). The present study aims at investigating the robustness of HMIFU for monitoring of HIFU treatment at low acoustic powers (2-5W) for 240 minutes (slow denaturation) or high acoustic powers (7-11W) for 30 seconds (boiling).

**METHODS:** A 4.755-MHz HIFU transducer was used in ex vivo canine livers (n=9). The carrier frequency was amplitude-modulated at 25 Hz to induce a 50 Hz oscillatory radiation force at the focus. The induced focal tissue motion is tracked by a confocally-aligned 7.5 MHz pulse-echo transducer. An analog band-pass filter ( $f_{c1}=5.84, f_{c2}=8.66$  MHz at -60dB) was used to filter out the HIFU harmonics prior to displacement estimation. By removing the filter and operating the pulse-echo transducer in passive mode, the same setup was used for passive cavitation detection (PCD). A bare-wire thermocouple (25 $\mu$ m diameter) was used to monitor focal temperature during HIFU treatment.

**RESULTS:** Displacement, cavitation activity, and temperatures were simultaneously monitored. Treatment at high power/short duration observed immediate focal boiling detected as high broadband noise on the PCD measurements. Despite the decorrelation due to boiling, HMI displacement monitoring was found to be feasible with an average of 33% decrease in the lesion-to-background HMI displacement ratio upon lesion formation. At moderate acoustic powers with longer exposure times the temperatures reached below 80°C and displacement monitoring showed progressive decrease (i.e., slow tissue denaturation) of 49% with robust estimations at higher correlation than at higher powers.

**CONCLUSIONS:** This study explored the capability of HMIFU monitoring of HIFU treatment with lesion formation under high powers with short exposure (boiling) and moderate power with long exposure time (slow denaturation). HMI displacement was capable of accurately depicting slow denaturation and boiling with the latter exhibiting noise levels that could be used to determine the presence of boiling. Supported by NIH R01EB014496.



**Oral session 12B**

**2013/5/15 13:00:00**

**CONTROL ID:** 1677865

**TITLE:** Mesoporous Silica-based Smart System fo Improving Ultrasound Diagnosis Resolution and Treatment Efficacy

**AUTHORS/INSTITUTIONS:** K. Zhang, H. Chen, J. Shi, State Key Laboratory of High Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Shanghai, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** Our objective is to improve the ultrasound diagnostic resolution and therapeutic efficacy, especially in HIFU theray, so as to drop the currently employed high diagnostic mechanical index and treatment power and to improve ultrasound diagnostic precision and therapeutic safety.

**METHODS:** We designed and synthesized novel ultrasound contrast agents (UCAs) and therapeutic enhancement ahents (TEAs) to achieve our aforementioned objectives. To this end, firstly we synthesized biocompatible mesoporous silica vectors, and then the as-prepared vectors were integrated with a rich variety of functional groups, mediums, tools or technological means, consequently coming into a composite system capable of further improving ultrasound diagnosis and therapy on basis of vectors.

**RESULTS:** A novel and general in situ hydrophobic shell-protected selective etching strategy has been developed to synchronously synthesize and modify hollow mesoporous silica nanoparticles (HMSNs) or rattle-type mesoporous silica nanoparticles (RMSNs) with well-defined morphology. As-prepared HMSNs and RMSNs via aforementioned strategy, could both achieve excellent in vitro ultrasound imaging, and meanwhile, RMSNs displayed a predominant structure preference over HMSN, when both were employed as ultrasound contrast agents (UCAs). Furthermore, after integrating with a mild solid-liquid-gas (SLG) tri-phase transition medium, whose properties are completely different from those conventional liquid-gas dual-phase transition mediums, a new multifunctional nanotheranostic system was constructed. Depending on its phase transition between solid phase and liquid phase, it facilitated co-entrapment of hydrophobic and hydrophilic drugs and their temperature-triggered release. Moreover, thanks to its another phase transition between liquid phase and gaseous phase, evaporable microbubbles enable the improvement of ultrasound imaging and HIFU therapy efficacy. As well, another two smart systems were also fabricated; one is CO<sub>2</sub>-release system sensitive to pH and temperature, and another is NO-release system sensitive to ultrasound, both of which performed well in treating cancer under secured ultrasound activation and irradiation in an on-demand manner.

**CONCLUSIONS:** Vectors, or its composite systems could all significantly improve ultrasound imaging contrast and ultrasound therapeutic efficacy.



**Oral session 12B**

**2013/5/15 13:12:00**

**CONTROL ID:** 1699731

**TITLE:** Research for Evaluating the Efficacy of HIFU Treatment in Transplantable VX2 Bone Tumor with Contrast-Enhanced Ultrasound

**AUTHORS/INSTITUTIONS:** L. Chen, L. Jiang, B. Hu, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** In this study, we first established an experimental rabbit model with VX2 malignant bone tumor as an ideal experimental animal model for high intensity focused ultrasound(HIFU) treatment in bone tumor. Then we observed the changes in Contrast-Enhanced ultrasonography before and after HIFU treatment, measured the treated area after received the certain therapeutic dose of HIFU, with the purpose to evaluate the efficacy of HIFU treatment in transplantable VX2 bone tumor.

**METHODS:** In aseptic condition, twenty New Zealand white rabbits were inoculated with VX2 tumors in cavitas medullaris of right tibia. HIFU treatment were carried on three weeks after VX2 bone tumors were transplanted. Ultrasonic microbubbles (Sonovue) were injected into ear marginal vein, to observe perfusion in the treated area and compare the changes in Contrast-Enhanced ultrasonography before and after HIFU treatment.

**RESULTS:** Contrast-Enhanced ultrasonography before HIFU treatment: after 20 bone tumor rabbit models microbubbles injected, the tumors in the cavitas medullaris of right tibia were rapidly and obviously perfused, with clear boundaries and irregular shape. Average size was measured: Vertical diameter was  $17.614 \pm 0.955$ mm; anteroposterior diameter was  $10.414 \pm 1.142$ mm. Contrast-Enhanced ultrasonography after HIFU treatment: treated region was out of perfusion, Average size was measured: Vertical diameter was  $8.010 \pm 0.584$ mm; anteroposterior diameter was  $7.540 \pm 0.499$ mm. While the untreated region still had microbubbles perfusion. Histopathological examination: lots of vigorously growth tumor cells were found in the untreated bone tumor tissue section, with disordered arrangement, large nucleus, significant atypia, but great necrosis was not observed. After HIFU treatment, there was no blue stained tumor cells and large flake coagulation necrosis found in the targeted region. While tumor cells with large nucleus and significant atypia were still found in the peripheral untreated region.

**CONCLUSIONS:** HIFU can cause coagulation necrosis in the target region, but do not destroy the tissues around and fixed position accurately. Contrast-Enhanced ultrasound examination can evaluate the efficacy of HIFU treatment in the early stage through the changes of the blood flow in the target region before and after HIFU treatment.



**Oral session 12B**

**2013/5/15 13:24:00**

**CONTROL ID:** 1700329

**TITLE:** A study of the interaction between ultrasound stimulated microbubbles and fibrin clots

**AUTHORS/INSTITUTIONS:** C. Acconcia, K. Hynynen, D. Goertz, Sunnybrook Research Institute, Toronto, Ontario, CANADA|C. Acconcia, K. Hynynen, D. Goertz, Department of Medical Biophysics, University of Toronto, Toronto, Ontario, CANADA|

**ABSTRACT BODY:**

**OBJECTIVES:** In this study, we examine the pressure dependence of the interaction between US stimulated MBs and human fibrin clots.

**METHODS:** Fibrin clots derived from human fibrinogen were formed with a 0.25mm channel to permit the introduction of contrast agent at a dilution ratio of 1:5000. Clots were situated under a microscope apparatus equipped with fluorescent and fast frame cameras(10kHz). 1 MHz pulsed US was applied in the form of 20 successive 1ms pulses at a 15% duty cycle. The transmit pressures applied were 0.2,0.4,0.8 and 1.6 MPa. 200nm fluorescent beads were used to delineate the fluid/clot boundary during and after exposure under widefield microscopy. Following exposures, 3D two-photon fluorescent microscopy was employed to assess damage to the fluorescently labelled fibrin network.

**RESULTS:** Within clots, MBs were frequently drawn together and coalesced under secondary radiation forces before continuing as a single, larger MB. In some cases, a primary MB shed smaller daughter MBs into the surroundingmatrix. MB velocities within the clots increased with transmit pressure, ranging from 0.011-0.09. 0.25-0.38 and 0.510.84m/s for the 0.4,0.8 and 1.6MPa exposures, respectively. MBs persisted, in place, between pulses and resumed penetration upon the arrival of subsequent pulses. In all cases >0.2MPa, a patent 'tunnel' remained in the fibrin network along the penetration path, and the extent of this network disruption was greatest for the 1.6MPa case. Thetransport of fluorescent beads was also observed that fluids may be drawn into the clots from the adjacent channel, a behavior that may have relevance to the potential uptake of lytic agents.

**CONCLUSIONS:** These results provide direct evidence that MBs can disrupt and penetrate fibrin networks, the primary structural component of thrombus. Complex MB behaviour is indicated, involving in part the interplay between primary and secondary radiation forces, and the oscillations of MBs within a confining matrix. An improved understanding of this process and its dependence on exposure conditions may provide insights that are relevant to the development of more effective thrombolysis exposure schemes.



**Oral session 12B**

**2013/5/15 13:36:00**

**CONTROL ID:** 1663471

**TITLE:** A RABBIT CAROTID ARTERY MODEL FOR DESTROYING CLOTS USING FOCUSED ULTRASOUND AND RTPA UNDER MRA MONITORING.

**AUTHORS/INSTITUTIONS:** C. Damianou, V. HadjiSavvas, R&D, MEDSONIC LTD, Limassol, Limmassol, CYPRUS|N. Mylonas, Computer Science, FREDERICK UNIVERSITY CYPRUS, Limassol, Limmassol, CYPRUS|C. Damianou, Electrical engineering department, Cyprus University of Technology, Limassol, Limmassol, CYPRUS|K. Ioannides, Radiology, Polikliniki Igia, Limassol, Limassol, CYPRUS|

**ABSTRACT BODY:**

**OBJECTIVE:** The potential of using focused ultrasound combined with the thrombolytic drug recombinant tissue plasminogen activator (rt-PA) under magnetic resonance angiography (MRA), to dissolve clots in the carotid of a New Zealand rabbit in vivo is evaluated.

**METHODS:** A spherically-focused transducers of 5 cm diameter; focusing at 10 cm and operating at 1 MHz was used. The transducer was placed inside a custom made plastic holder which is coupled to the carotid artery. A pulsed ultrasound protocol was used that maintains a tissue temperature increase of less than 1°C in the clot (called safe temperature). The temperature was acquired using a thermocouple which is placed near the clot.

**RESULTS:** Initially the artery was opened using rt-PA alone. With rt-PA alone 50 % of the artery was opened in about 120 mins. It was found that the time needed for opening 50 % of the artery using rt-PA and Focused ultrasound was decreased with acoustic intensity. With an intensity (20 W/cm<sup>2</sup> SATA) that is not causing artery heating (less than 1°C) the time needed to open 50% of the artery is 50 mins. The proposed protocol was monitored using Magnetic Resonance Angiography (MRA) every 1 min.

**CONCLUSIONS:** Focused ultrasound has the potentials to dissolve clots that are injected in the carotid of rabbits in vivo. The procedure is safe because with the protocols used the artery temperature was less than 1 °C. With focused ultrasound the time needed to open the artery is decreased. MRA clearly shows the opening of the artery. The acquisition of MRA is slow (1 min) but since the procedure takes close to 50 mins this is not causing any problem.



**Oral session 10**

**2013/5/15 14:14:00**

**CONTROL ID:** 1682852

**TITLE:** A BOILING HISTOTRIPSY SYSTEM FOR DEEP TISSUE ABLATION

**AUTHORS/INSTITUTIONS:** A. Maxwell, M. Bailey, Urology, University of Washington Medical Center, Seattle, WA|A. Maxwell, W. Kreider, T. Khokhlova, O. Sapozhnikov, M. Bailey, V. Khokhlova, Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, Seattle, WA|P. Yuldashev, O. Sapozhnikov, V.

Khokhlova, Department of Acoustics, Physics Faculty, Moscow State University, Moscow, RUSSIAN FEDERATION|

**ABSTRACT BODY:**

**OBJECTIVES:** Mechanical disintegration of soft tissues has been demonstrated with pulsed high-intensity focused ultrasound. This method utilizes shock wave exposures combined with HIFU-induced boiling or cavitation to break down the targeted tissue into homogeneous, liquefied debris with no indication of thermal damage. This work presents a system for generating histotripsy lesions in tissue through significant overlying tissue paths.

**METHODS:** A 1-MHz piezoelectric focused transducer with 14.7-cm diameter and 14-cm focal length was built as a confocal 7-element assembly. An RF amplifier was constructed to apply up to 30 kW electrical power to the transducer for pulse durations up to 10 ms. These parameters provided capability to operate the transducer in both boiling histotripsy and cavitation histotripsy modes. The transducer output was characterized by nonlinear modeling based on the Westervelt equation using measurements from acoustic holography to set a boundary condition. The transducer hologram was measured at low power in a 5.5-cm prefocal plane, and nonlinear simulations were performed at greater power levels. Simulated results were compared with direct measurement of the focal pressure using a fiber-optic hydrophone. Lesions were generated with the system in ex vivo bovine liver at depths up to 6 cm. A derating procedure developed for nonlinear highly-focused HIFU fields was used (with  $\alpha = 0.5$  dB/cm/MHz) to scale the output pressure to compensate for energy losses at different depths.

**RESULTS:** Focal waveforms could be measured with a hydrophone up to 30% maximum pressure output. Above this level, simulations provided acoustic parameters of the field, but cavitation prevented measurement. Lesions were formed in liver with shock waves above an in situ pressure threshold of  $p_+ = 77$  MPa and  $p_- = -14$  MPa for 10 ms pulse lengths. Initial measurements indicated that the thresholds for forming histotripsy lesions at different depths could be accurately estimated from derating within  $\sim 10\%$  of the amplitude. Experimentally, lesions were achieved at 6 cm depth at 26% of the maximum pressure amplitude of the array, leaving the possibility for deeper treatments.

**CONCLUSIONS:** The results suggest that current transducer technologies enable delivery of boiling histotripsy therapy at clinically-relevant depths, and a combined measurement and modeling approach can be used for treatment planning. Work supported by NIH 2T32DK00779-11A1 and 2R01EB007643-05.



**Oral session 10**

**2013/5/15 14:26:00**

**CONTROL ID:** 1673832

**TITLE:** ANGIOTRIPTY: A POTENTIAL THERAPEUTIC TECHNOLOGY OF MICROBUBBLE-ENHANCED ACOUSTIC CAVITATION

**AUTHORS/INSTITUTIONS:** Z. Liu, P. Li, S. Gao, Y. Zhong, X. Zhao, Department of Ultrasound, Xinqiao Hospital, The Third Military Medical University, Chongqing, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** Angiotripsy, a therapeutic technique using microbubble-enhanced ultrasound (MEUS) cavitation, has demonstrated the capability of disrupting pathological microvasculatures of many diseases. The study reviews many recent applications of angiotripsy in tumor therapy, prostate ablation, and liver hemostasis, etc.

**METHODS:** Therapeutic ultrasound (US) device: The transducer comprised of a slight-focused concave disc. It was operated with the frequency of 831 kHz, the peak negative pressure of 2.6-4.8MPa and the duty cycle of 0.18-0.5%. Microbubble: A lipid microbubble with a mean diameter of 2  $\mu\text{m}$  was used for microbubble-enhanced US (MEUS) treatment at 0.1 mL/kg. Animal models: This included subcutaneous Walker 256 tumor of rat, VX2 tumor of rabbit, prostate of canine and surgical exposed in vivo rabbit liver. Data analysis: Contrast-enhanced US (CEUS) was performed to assess the blood perfusion of tumor or liver. The specimens were finally harvested for gross and histological examinations.

**RESULTS:** In the experiment of Walker 256 tumor and VX2 tumor, MEUS of 4.3-4.8 MPa successfully disrupted the tumor vasculature and blocked off tumor microcirculation completely for 24 hours, confirmed by CEUS quantifications. The tumor microvasculature was found to be significantly disrupted with hemorrhage, hematoma with intercellular edema. In the experiment of prostate ablation, gross and histological examination found severe microvascular rupture with hemorrhage and thrombosis in the MEUS-treated prostates. Forty-eight hours after treatment, massive necrosis happened. In the experiment of liver hemostasis, the haemorrhage stopped immediately after 2 min MEUS treatment but bleeding continued in the controls treated by ultrasound or microbubble alone. The bleeding scores and the 10-min hemorrhagic volumes dropped significantly in the MEUS group compared with those of the controls ( $p < 0.01$ ). The hemorrhagic mechanism appears to be the extensive swelling of hepatocytes, which formed a joint compression on regional liver circulation. In the experiment of enhancing liver ethanol ablation, the mean necrotic volume of the livers treated by MEUS+ethanol (3.3  $\text{cm}^3$ ) was over 10 times larger than that of the ethanol only (0.3  $\text{cm}^3$ ).

**CONCLUSIONS:** Angiotripsy provides a novel therapeutic method for tumor angiogenesis disruption, prostate ablation and liver hemostasis, etc. It is clinical potential in treating many diseases.



**Oral session 10**

**2013/5/15 14:38:00**

**CONTROL ID:** 1675730

**TITLE:** DISRUPTION OF PROSTATE MICROVASCULATURE BY COMBINING MICROBUBBLE-ENHANCED ULTRASOUND AND PROTHROMBIN

**AUTHORS/INSTITUTIONS:** J. Zhang, S. Wu, Z. Liu, Department of Ultrasound, xinqiao Hospital, The Third Military Medical University, Chongqing, Chongqing, CHINA|Y. Liu, Department of Urology, Xinqiao Hospital, The Third Military Medical University, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** We tried to destruct the prostate vasculature using microbubble-enhanced ultrasound (MEUS) prothrombin on canine prostate.

**METHODS:** The prostates of 20 male mongrel canine were surgically exposed. Ten prostates were treated by combined MEUS and prothrombin (PMEUS). The other 10 prostates were treated by the therapeutic ultrasound with prothrombin (PTUS) or the prothrombin only served as the controls. Prothrombin was intravenously infused at 20 IU/kg. MEUS was induced by a therapeutic ultrasound device at a peak negative pressure of 4.47 MPa and microbubble injection. Contrast enhanced ultrasound (CEUS) was performed to assess the blood perfusion of the prostates. Then prostates were harvested at post 60 min and 48h respectively for pathological examination.

**RESULTS:** The CEUS peak value of the prostate significantly dropped from  $36.2 \pm 5.6$  to  $27.1 \pm 6.3$  after treatment in PMEUS group but it remained in the two control groups. Histological examination found severe microvascular rupture, hemorrhage and thrombosis only in the PMEUS treated prostates at post 60 min. Forty-eight hours after treatment, massive necrosis and infiltration of white blood cell happened.

**CONCLUSIONS:** This study demonstrated that PMEUS can disrupt the normal microvasculature of canine prostate and induce massive necrosis. It could potentially become a new noninvasive method for BPH treatment.





**Oral session 11**

**2013/5/15 8:15:00**

**CONTROL ID:** 1671105

**TITLE:** NON-INVASIVE TOROIDAL HIFU TRANSDUCER FOR INCREASING THE COAGULATED VOLUME

**AUTHORS/INSTITUTIONS:** D. Melodelima, J. Vincenot, A. Kocot, F. Chavrier, J. Chapelon, LabTAU, INSERM, Lyon, FRANCE |

**ABSTRACT BODY:**

**OBJECTIVE:** Earlier work showed that HIFU transducers based on a toroidal geometry generates simultaneously a ring-shaped focal zone as well as an overlap of ultrasound beams behind this first focus, which contributes to increase the size of ablations. Based on this principle, a device was developed for the treatment of liver metastases during surgery. This HIFU device allowed the creation of large ablations in the liver (6-8 cm<sup>3</sup>) in a short time (40 seconds). Here we report a new design for toroidal transducers that allows treating large volume of tissues in depth and in a short amount of time, without damaging intervening tissues.

**METHODS:** A spindle torus is generated by the rotation of a circle around an axis of revolution with a distance between the axis and the center of the circle lower than the radius of the circle. The obtained volume is composed of two envelopes that can be used to create a toroidal transducer. To date, our previous work on toroidal transducers used the outer envelope. In this work a transducer geometry, based on the interior part of a torus, has been developed. This produces a focus that is ring-shaped but the ultrasound beams intersect between this principal focal ring and the transducer surface to increase the coagulated volume. The operating frequency was 2.5 MHz. The radius of curvature was 70 mm with a diameter of 67 mm. An ultrasound imaging probe was placed in a central circular opening of 26 mm in diameter. The transducer was also divided into 32 rings of 78mm<sup>2</sup> each.

**RESULTS:** Twenty ablations were produced in vitro by using electronic beam steering. Each ablation was created in 55 seconds. The average depth of intervening tissues (skin-fat-muscle) was 11±1 mm and the average depth of liver tissues that have been spared by HIFU ablations was 21±4 mm. No significant temperature rise in intervening tissues was measured (maximal temperature: 41°C). The dimensions of the ablations were an average diameter of 20±2 mm and an average depth of 31±3 mm.

**CONCLUSIONS:** This device can be used to spare superficial tissues and to treat liver tissues in depth in a short time. The lesions have a very well-delimited geometry. Using a transducer based on a spherical geometry with similar characteristics (frequency, radius of curvature, diameter ...) a treatment time about twenty times longer would be necessary to reproduce the same coagulated volume.



## Oral session 11

2013/5/15 8:27:00

**CONTROL ID:** 1671164

**TITLE:** THERMAL NEAR-FIELD MANAGEMENT FOR VOLUMETRIC MAGNETIC RESONANCE-GUIDED HIGHINTENSITY FOCUSED ULTRASOUND (MR-HIFU) ABLATION

**AUTHORS/INSTITUTIONS:** J. Wijlemans, M. van den Bosch, Department of Radiology, University Medical Center Utrecht, Utrecht, NETHERLANDS|M. de Greef, L. Bartels, C. Moonen, M. Ries, Image Sciences Institute, University Medical Center Utrecht, Utrecht, NETHERLANDS|G. Schubert, M. K.hler, M. Ylihautala, Philips Healthcare, Vantaa, FINLAND|

### **ABSTRACT BODY:**

**OBJECTIVE:** MR-HIFU is currently under development for oncological applications, in particular thermal ablation of malignant tumors. For applications such as uterine fibroid ablation, temperature increase in the near field (i.e. the tissues between transducer and focus) does generally not lead to adverse effects. However, for ablation in highly perfused organs such as the liver, high acoustical powers are required to achieve sufficient temperature increase in the target. This increases the risk of undesired tissue damage in the near-field. Skin burn is therefore the most frequently reported complication after MR-HIFU ablation. Allowing cool-down between individual sonications is effective, but decreases the duty-cycle of the procedure. Here, we characterize in an in-vivo porcine liver model undesired energy deposition in the near-field and investigate the possibility to alleviate this effect by actively cooling the near field using an acoustically transparent, water-cooled cushion.

**METHODS:** A pig was placed on a clinical 1.5T MR-HIFU therapy system. Luxtron thermo-sensors were placed I) directly (1.2mm) under the skin, II) proximally (8mm from the skin) in the subcutaneous (SC) fat layer, i.e. on the interface between fat and muscle. In addition, core body temperature was measured. Sonications were performed with and without active near field tissue cooling.

**RESULTS:** In absence of cooling a temperature of 33.6°C was found subcutaneously and 37.4°C in the SC fat layer. Active cooling with 15°C water decreased the temperature to 19°C and 33.6°C respectively (gradient in the adipose layer 1.53°C/mm). Relative temperature increase (7°C for 3kJ/cm<sup>2</sup> and 13.4°C for 3.5 kJ/cm<sup>2</sup>) during sonication was found similar for both cases (cooled/non-cooled). Core body temperature was not affected by the active cooling.

**CONCLUSIONS:** These results demonstrate cooling of near field as an effective measure to prevent skin burns during MR-HIFU ablation. This is achieved by a decrease in baseline temperature and an effective contribution to heat extraction during the sonication for 1-7mm of tissue depth. As expected, the cooling effect diminishes with increasing tissue depth and thickness of the SC fat layer. Cooling allows to increase the ablation duty-cycle and shifts the risk of undesired tissue damage from the (sub-) cutaneous layers towards the diaphragmatic fascia and the abdominal muscle.



**Oral session 11**

**2013/5/15 8:39:00**

**CONTROL ID:** 1671176

**TITLE:** IN-VIVO EVALUATION OF VOLUMETRIC MAGNETIC RESONANCE-GUIDED HIGH-INTENSITY FOCUSED ULTRASOUND (MR-HIFU) ABLATION IN PORCINE LIVER

**AUTHORS/INSTITUTIONS:** J. Wijlemans, M. van den Bosch, Department of Radiology, University Medical Center Utrecht, Utrecht, NETHERLANDS|M. de Greef, L. Bartels, C. Moonen, M. Ries, Image Sciences Institute, University Medical Center Utrecht, Utrecht, NETHERLANDS|G. Schubert, M. Kehler, M. Ylihautala, Philips Healthcare, Vantaa, FINLAND|

**ABSTRACT BODY:**

**OBJECTIVE:** MR-HIFU is emerging as a potential treatment modality for liver cancer. However, both the ablation of hepatocellular carcinoma (HCC) and metastatic liver tumors require the ablation of substantial volumes. Recent studies have established a link between the energy density in the near field and the occurrence of undesired tissue damage in cutaneous and subcutaneous tissues. Clinical evidence from ultrasound-guided HIFU interventions reconfirmed this type of damage as the most frequent acute complication of this type of intervention. Consequently, larger ablation volumes have to be split in sub-volumes, which are sequentially sonicated after regular cool-down intervals. The presented in-vivo study investigates the feasibility of the creation of larger continuous ablation volumes in the healthy liver of a porcine model. Particular emphasis is placed on the investigation of cellular viability in the core ablation zone, the hemorrhagic rim and in the vicinity of larger vessels.

**METHODS:** Energy delivery in the middle liver lobe is achieved by a clinical Philips Sonalleve HIFU platform, which is integrated in a 1.5T MR-system. Respiratory induced motion is compensated by gating both the MR-Thermometry and HIFU (mechanically assisted respiration, resulting in a duty cycle of 66%). The endpoint for each sonication is a target temperature of 65°C in the 0.6ml sub-volumes ( with 450W acoustic power ~20s). The extent of the complete lesion is assessed by dynamic contrast-enhanced T1-weighted MRI and by a subsequent pathological examination including staining for cellular viability.

**RESULTS:** The deposition of a thermal energy of 9-11kJ results in a complete necrosis in the target area (i.e. no viable cells). However, similar to the findings of Jiang et al., the presence of larger vessels (>1.5mm) leads to an increased number of viable liver cells, which are clustered in the direct vicinity of the vessel walls.

**CONCLUSIONS:** First results indicate a close correspondence between the estimated thermal dose, the non-perfused volume and the pathological examination. Challenging remains the presence of peristaltic motion in the gastrointestinal tract during the lengthy intervention, which frequently leads to spatial mismatches between the planning and the energy deposition.



**Oral session 11**

**2013/5/15 8:51:00**

**CONTROL ID:** 1671580

**TITLE:** OPTIMALLY ENHANCED HEATING FOR FOCUSED ULTRASOUND SURGERY WITH SPLIT FOCI, DUALFREQUENCY OR MULTI FOCI MODES

**AUTHORS/INSTITUTIONS:** M. Lu, Y. Guan, M. Wan, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Xi' an Jiaotong University, Xi'an, Shanxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVE:** To substantially enhance heating in HIFU treatment, several methods such as split foci, multi foci and dual-frequency modes are used. The cavitation-enhanced heating protocols will be implemented experimentally using four-element split-focus array.

**METHODS:** We have the hypothesis that if arrange multi foci using a phased array in a style of a wavelength distance between neighboring foci in focal plane, the result will not only enlarge focal zone, but also temporally enhanced heating effect due to neighboring anti-direction-vibration in enhanced-heating absorption. We can confirm this hypothesis by comparison the experiment result of four split foci with 180-degree phase shift between neighbor elements with that of a single focus with 0-degree phase shift using a four-element split-focus array. Further, to enhance cavitation heating, the experiment was implemented in transparent-gel-phantom using the dual frequency of 1.2 MHz and 2.4 MHz and four split foci with split-focus array. Finally, an increase-PRF approach was formed by keeping other treatment parameters unchanged only increasing PRF from 1 to 10 Hz to make use of pulse-induced cavitation. The mechanisms were explored from high-speed video observations and PCD signal analysis.

**RESULTS:** When using same acoustic power dose while the peak intensity of split foci being only a half of that single focus, the lesion size of 4 split foci is 6 times more than that of single focus, and the initiating lesion of 4 split foci is only a half time less than that of single focus. The interferences from neighboring foci speed up heating rate. The lesion size with 10-Hz PRF is about 1.4 times of that with 1-Hz PRF.

**CONCLUSIONS:** For focused ultrasound surgery or thermal therapy, the optimal multi-focus arrangement is the neighboring foci keeping at a wavelength distance and split foci using 180-dgree phase shift driving. The experiment results demonstrate that the method of dual frequency of 1.2 MHz and 2.4 MHz combined with four split foci and increasing PRF protocol are effective in cavitation-enhanced heating effect.



## Oral session 11

2013/5/15 9:03:00

**CONTROL ID:** 1672077

**TITLE:** EFFECT OF BLOOD FLOW ON HIFU-INDUCED HEATING AND HISTOPATHOLOGICAL ABLATION IN A CLINICALLY-RELEVANT ISOLATED, PERFUSED PORCINE LIVER MODEL

**AUTHORS/INSTITUTIONS:** D.J. Holroyd, E. Mylonopoulou, C. Jensen, D. Chung, J.J. Choi, C.C. Coussios, Institute of Biomedical Engineering, University of Oxford, Oxford, UNITED KINGDOM | D.J. Holroyd, R. Ravikumar, P.J. Friend, Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UNITED KINGDOM |

### **ABSTRACT BODY:**

**OBJECTIVE:** A major limitation in thermal ablative therapies in current clinical practice is the "heat sink" effect from major vasculature, causing variability in heating, incomplete tissue ablation and treatment failure. The objective of this study was to assess the effects of blood flow on HIFU, which remain largely unknown, using a unique extracorporeal liver perfusion device, which can maintain a liver ex vivo in a physiological, functional state for up to 72 h.

**METHODS:** Porcine livers were perfused with whole blood at 37 C. A 1.067 MHz HIFU transducer was confocally aligned with a 128-element diagnostic array, allowing B-mode imaging and passive acoustic mapping during HIFU exposure. The liver was immersed in degassed isotonic colloid solution. Two tissue regions were targeted: i)

microperfused (MP) and ii) areas adjacent ( $\leq 2$ mm) to a large ( $\geq 5$  mm) vessel (LV). Real time thermometry data during 1 s 1.06 MHz CW HIFU exposures at peak rarefaction pressures (PRFP) of 1.85 to 5.81 MPa, were obtained from a 200  $\mu$ m thermocouple inserted into the HIFU focal volume under B-mode guidance. Thermometry was performed in each location both in the presence and absence of perfusion, with the perfusion device turned off. Temperature data were used to define HIFU parameters for subsequent studies, in which ablation of tissue surrounding  $\geq 5$ mm blood vessels and in MP areas were attempted. Treated tissue was subjected to histopathological analysis to assess tissue damage and cell death/viability.

**RESULTS:** Ablative temperature rises could be attained in both MP and LV regions at clinically relevant PRFPs ( $\geq 5.81$  MPa). There were no significant differences in peak temperature rise in MP regions compared to LV areas at any PRFP tested ( $p > 0.05$ ). Paired sample analysis failed to demonstrate any significant difference between peak temperature rise in the presence of perfusion and in zero flow conditions, for each location ( $p > 0.15$ ). Histopathological examination of HIFU lesions revealed that cell death, indicating complete tissue ablation, could be achieved up to 5 mm vessel wall.

**CONCLUSIONS:** HIFU therapy is minimally affected by the heat sink effect imparted by large blood vessels and complete ablation of hepatic tissue can be achieved up to a large vessel wall of  $\geq 5$  mm. Further clinical studies are required to confirm the potential of HIFU ablation in treating perivascular tumours.



**Oral session 11**

**2013/5/15 9:15:00**

**CONTROL ID:** 1672337

**TITLE:** LARGE-VOLUME COAGULATION BY CAVITATION-ENHANCED HEATING WITH MULTIPLE HIFU FOCAL SPOTS.

**AUTHORS/INSTITUTIONS:** H. Sasaki, K. Nakamura, K. Goto, T. Miyashita, S. Yoshizawa, Department of Communication Engineering, Tohoku University, Sendai, Miyagi, JAPAN | S. Umemura, Department of Biomedical Engineering, Tohoku University, Sendai, Miyagi, JAPAN |

**ABSTRACT BODY:**

**OBJECTIVE:** A drawback of HIFU (High-intensity Focused Ultrasound) treatment is the need of a long treatment time for a large tumor due to a small therapeutic volume by a single exposure. Enhancing the heating effect of ultrasound by cavitation bubbles may solve this problem. To maximize this possibility, we are developing a method to generate cavitation bubbles in multiple focal spots close to each other and use them to enhance ultrasonic heat efficiently.

**METHODS:** Chicken breast muscle meat was degassed and used to test the method we proposed and named as "Triggered HIFU". In this method, a high-intensity and short pulse, named as "Trigger Pulse", generate cavitation bubbles first, Then a low-intensity and long-duration burst, named as "Heating Waves", oscillate the cavitation bubbles to enhance its heating effect. Three different sequences were compared. In the first sequence, a relatively long Trigger Pulse was followed by a relatively long burst of Heating Waves. In the second sequence, a sequence of a Trigger Pulse followed by Heating Waves was repeated many times. In the third sequence, only Heating Waves was irradiated. An array transducer was used to move the focal point at each corner of a 6-mm square quickly within the life time of cavitation bubbles.

**RESULTS:** The coagulation volume with a Trigger Pulse or pulses was significantly larger than that by Heating Waves alone. However, the degree of enhancement did not simply increase as the Trigger Pulse intensity increased. The result seems to depend on the relation between the directions of the ultrasound propagation and the muscle fiber. Whether the repetition of Trigger Pulses increased the coagulation volume than a single Trigger Pulse also depended on the relation of the directions.

**CONCLUSIONS:** Triggered HIFU with multiple foci was proven to be effective to coagulate a large volume in a relatively short time. However, the results show that the intensity and repetition period of Trigger Pulses must be optimized depending on the acoustic characteristic of the tissue.



**Oral session 11**

**2013/5/15 9:27:00**

**CONTROL ID:** 1682034

**TITLE:** Effect of perfusion on Heating in Liver Exposed to Pulsed High Intensity Focused Ultrasound

**AUTHORS/INSTITUTIONS:** X. Zhang, College of Biomedical Engineering, Chongqing Medical University, Chongqing Medical University, Chongqing, Chongqing, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** To study the effect of perfusion on heating in vitro pork liver exposed to pulsed high intensity focused ultrasound

**METHODS:** A circulated and a non-circulated pork liver were exposed to pHIFU for 20 s at a 20 mm depth respectively. Pulsed HIFU was maintained at 80 W acoustic power, 100 Hz pulse repetition frequency. The duty cycles were 20%, 30% and 40%. After 10 repeated pHIFU irradiations under every parameter, all 60 exposures were performed with 30 in the circulated liver and the other 30 in the non-circulated liver. During pHIFU exposures, the temperatures in the focal region were detected using a thermocouple embedded into the livers. The B-mode images were also collected at the moment after irradiations and compared with those before HIFU. After all exposures, the two livers were sliced into 1~2 mm, and the maximum lesions were photographed. Then, the volumes of the pictured necrosis were computed with a software Jupiter.

**RESULTS:** During all pHIFU exposures, the heating rates and the mean peak temperatures in the circulated liver were significantly smaller ( $p < 0.05$ ). After the circulated liver exposed to pHIFU, the lesser hyperecho regions and lesions were observed ( $p < 0.05$ ). However, the values of increased echoes in the B-mode images were very nearly the same after the two liver irradiations.

**CONCLUSIONS:** The thermal deposition in the tissues around vessels were less because of circulation of blood flow.



**Oral session 11**

**2013/5/15 9:39:00**

**CONTROL ID:** 1683996

**TITLE:** ULTRASOUND-GUIDED TRANSESOPHAGEAL HIFU EXPOSURES FOR ATRIAL FIBRILLATION TREATMENT: FIRST EX VIVO EXPERIMENTS

**AUTHORS/INSTITUTIONS:** E. Constanciel, W. N'Djin, J. Chapelon, C. Lafon, LabTAU INSERM U1032, INSERM, Lyon, FRANCE|E. Constanciel, W. N'Djin, J. Chapelon, C. Lafon, Université Claude Bernard Lyon 1, Université de Lyon, Lyon, FRANCE|F. Bessi re, D. Grinberg, P. Chevalier, H.pital Cardiologique Louis Pradel, Hospices Civils de Lyon, Lyon, FRANCE|M. Pioche, H.pital Edouard Herriot, Hospices Civils de Lyon, Lyon, FRANCE|

**ABSTRACT BODY:**

**OBJECTIVES:** Atrial fibrillation (AF) is the most frequent cardiac arrhythmia. Endocardial ablation is currently performed to treat this disease. The main target of this procedure is to isolate the pulmonary veins by thermal ablation. However transmural lesions are difficult to obtain and this invasive technique is less helpful for patients with well-settled AF. High-Intensity Focused Ultrasound (HIFU) devices have been designed to improve the transmuralities of the lesions but they all require invasive interventions. Transesophageal HIFU probes are in development but none of them integrate imaging system to guide the procedure. Recently, an ultrasound-guided transesophageal HIFU device has been designed to perform a complex procedure, the HIFU "mini-Maze". It was made with a 3 MHz 8-ring HIFU transducer including in its center a 5 MHz 64-element imaging transducer. The HIFU transducer could focus the ultrasound beam over a broad range of depths from 17 to 55 mm to perform lesions in various areas, while preserving intervening tissues. The aim of this study was to demonstrate the ability of this probe to perform ex vivo transesophageal cardiac ablation under ultrasound guidance.

**METHODS:** A first experiment was performed on an explanted pig heart/lung/esophagus block. An artificial ventilator and an extracorporeal circulation system were used to mimic in-vivo conditions. Elementary lesions were performed transesophageally in myocardium. A second experiment was carried out ex vivo/in situ on a 40-kg pig. Transesophageal linear lesions were performed by juxtaposition of elementary lesions in interventricular septum. For each experiment, the on-board imaging transducer was used to target the exposure areas.

**RESULTS:** These preliminary experiments gave promising results. Indeed the first one showed that wide transmural lesions could be obtained in targeted areas while preserving the esophagus despite the proximity of air-filled lungs and the liquid flow at 37°C inside the heart. The second one showed that homogeneous linear lesions could be obtained in deep seated tissues under realistic anatomical conditions by scanning targeted areas with HIFU under ultrasound guidance.

**CONCLUSIONS:** In vivo trials are ongoing to confirm that ultrasound-guided transesophageal HIFU devices can contribute significantly to AF treatment. [Supported by ANR TecSan Grant No. ANR-11-TECS-004]





**Oral session 12A**

**2013/5/15 10:54:00**

**CONTROL ID:** 1670608

**TITLE:** ENHANCED CAVITATION AND HEATING OF FLOWING POLYMER- AND LIPID-SHELLED MICROBUBBLES AND PHASE-SHIFT NANODROPLETS DURING FOCUSED ULTRASOUND EXPOSURES

**AUTHORS/INSTITUTIONS:** S. Zhang, C. Li, F. Zhou, Y. Zong, S. Wang, M. Wan, Department of Biomedical Engineering, Xi'an Jiaotong University, Xi'an, Shaanxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVE:** Cavitation and/or heating are the primary mechanisms of numerous therapeutic applications of ultrasound. Various shelled microbubbles (MBs) and phase-shift nanodroplets (NDs) have been used to enhance local cavitation and/or heating, creating interests in developing ultrasound therapy using these shelled MBs and NDs, such as in thermal ablation of tumors, localized drug delivery, sonoporation, gene transfer, non-invasive sonothrombolysis, lithotripsy, histotripsy and so on. Comparison of cavitation and heating among various MBs and NDs is needed as a reference for various investigations and applications. Our previous work have demonstrated the potential use of flowing lipid-shelled MBs to minimize thermal losses from perfusion during focused ultrasound (FU) exposures and compared cavitation and heating between flowing polymer- and lipid-shelled MBs. The objective of the present work is to compare the efficiency of flowing polymer- and lipid-shelled MBs and phase-shift NDs in cavitation and heating during focused ultrasound exposures.

**METHODS:** Cavitation activity and temperature were investigated when the solution of polymer- and lipid-shelled MBs and NDs flowed through the vessel in a tissue-mimicking phantom with varying flow velocities when exposed by FU at various acoustic power levels.

**RESULTS:** The inertial cavitation dose (ICD) and temperature for the shelled MBs and NDs were higher than those for the saline. Temperature initially increased with increasing flow velocities of the shelled MBs, followed by a decrease of the temperature with increasing flow velocities when the velocity was much higher. Meanwhile, ICD showed a trend of increases with increasing flow velocity. For the phase-shift NDs, ICD and temperature after the first FU exposure were lower than those after the second FU exposure. For the shelled MBs, ICD and temperature after the first FU exposure were higher than those after the second FU exposure.

**CONCLUSIONS:** These results suggested that lipid-shelled MBs may have a greater efficiency than polymer-shelled MBs in heating and cavitation during focused ultrasound exposures. The trends of cavitation and heating for the nanodroplets were the reverse of those for the shelled MBs. Further studies are necessary to investigate the treatment efficiency of different shelled MBs and phase-shift NDs in cavitation and heating.



## Oral session 12A

2013/5/15 11:06:00

**CONTROL ID:** 1671724

**TITLE:** Time lapse observation of phase change nano droplet after vaporization stimulated by ultrasound

**AUTHORS/INSTITUTIONS:** K. Takehara, T. Azuma, Y. Matsumoto, Bioengineering, the University of Tokyo, Tokyo, JAPAN|S. Takagi, Mechanical engineering, the University of Tokyo, Tokyo, JAPAN|S. Yamaguchi, T. Nagamune, Chemistry and Biotechnology, the University of Tokyo, Tokyo, JAPAN|I. Sakuma, Precision Engineering, the University of Tokyo, Tokyo, JAPAN|M. Maezawa, Olympus Corporation, Tokyo, JAPAN|K. Yoshinaka, National Institute of Advanced Industrial Science and Technology, Ibaraki, JAPAN|

### **ABSTRACT BODY:**

**OBJECTIVES:** Small enough to permeate through tumor blood vessel, and can be detected by ultrasound, phase change nano droplet (PCND) have been studied as contrast agents and therapeutic sensitizer for cancer. To investigate performance for both purposes above mentioned, we investigated physical behavior of PCND, especially a lifetime of microbubbles generated by ultrasound stimulation.

**METHODS:** PCND, which is submicron size, is a droplet of perfluorocarbon covered with phospholipid layer. When ultrasound is applied, PCND becomes microbubble. To investigate bubble's behavior after phase change, we observed a time-lapse change of bubble population with following method. Focused transducer with a frequency of 3.3 MHz was placed in a water bath of 37 degrees. At the focal point, polyacrylamide gel including PCND was placed. Focused hydrophone was placed perpendicularly to the direction of ultrasound propagation. Two kinds of ultrasound pulse wave were used; phase change pulse at the beginning and observation pulse at every 500  $\mu$ s. The amplitude of scattering signal (SS) reflects the sum of scattering cross-section of bubbles. As index of time-lapse change of bubble population, the degree of remained bubbles (DRB) is defined as this;  $DRB = \text{Integral of SS} / \text{Initial amplitude} / \text{Time width}$ .

**RESULTS:** DRB was not related to the amplitude of acoustic pressure of phase change pulse while that amplitude was above the threshold of phase change, and the average of DRB increased as the number of cycles increased. In some cases of 1000 cycles, the amplitude of SS increased during monitoring phase after the phase change. This unique behavior is thought to be relating to following two phenomena; the increase of detectable size bubble due to bubbles coalesce and/or change of shielding effects due to a change of bubble spatial distribution.

**CONCLUSIONS:** The time lapse observation of PCND after phase change showed two kinds of behavior, quick and slow decay of scattering signal from the bubbles. The unique increase of SS from the phase-changed bubbles in the monitoring phase was observed.



**Oral session 12A**

**2013/5/15 11:18:00**

**CONTROL ID:** 1671740

**TITLE:** DYNAMICS OF STEMBELLS IN AN ULTRASOUND FIELD

**AUTHORS/INSTITUTIONS:** T. Kokhuis, A. van der Steen, N. de Jong, Biomedical Engineering, Erasmus Medical Center, Rotterdam, NETHERLANDS|T. Kokhuis, B. Naaijken, L. Juffermans, O. Kamp, A. van der Steen, N. de Jong, ICIN, Netherlands Heart Institute, Utrecht, NETHERLANDS|B. Naaijken, Pathology, VU Medical Center, Amsterdam, NETHERLANDS|L. Juffermans, Physiology, VU Medical Center, Amsterdam, NETHERLANDS|O. Kamp, Cardiology, VU Medical Center, Amsterdam, NETHERLANDS|M. Versluis, Physics of Fluids Group, University of Twente, Enschede, NETHERLANDS|M. Versluis, MIRA Institute of Biomedical Technology and Technical Medicine, University of Twente, Enschede, NETHERLANDS|

**ABSTRACT BODY:**

**OBJECTIVES:** The conjugation of targeted microbubbles to stem cells creates echogenic cells, dubbed StemBells. The objective of this study was to investigate the dynamics of these StemBells in an ultrasound (US) field using high-speed optical imaging. A modified Rayleigh-Plesset model was developed to corroborate our experimental findings.

**METHODS:** StemBells were created by fully decorating adipose-derived stem cells (mean size 16  $\mu\text{m}$ ) with CD90targeted microbubbles (mean size 3.5  $\mu\text{m}$ ) under continuous rotation. The StemBells were insonified at frequencies in between 0.4 - 3 MHz at various pressures (50 - 200 kPa). Dynamics were imaged with the ultra-fast Brandaris128 camera. To investigate the dynamics of the StemBells numerically, a modified Rayleigh-Plesset equation was derived. A StemBell was modeled as a liquid globule surrounded by a thin gas shell, mimicking respectively the stem cell and the layer of microbubbles around. The gas shell was assumed to have an effective shell elasticity  $\chi$  and effective shell viscosity  $\kappa \cdot s$

**RESULTS:** The StemBells were found to be very stable during repetitive US insonifications. Interestingly, StemBells appeared to be pulsating as one big entity (i.e. resembling one big bubble). The presence of neighboring targeted bubbles was found to lower the frequency of maximum response (fMR) of the individual bubbles (normally 1.5 - 2 MHz) drastically, causing an apparent shift in the fMR of the StemBells, typically towards 600 kHz. The experimental resonance curves of the StemBells were predicted by our model including values of  $\kappa$  of the order 10<sup>-7</sup> kg/s and  $\chi$  of 3.5 N/m.

**CONCLUSIONS:** The dynamics of StemBells in an US field was investigated both experimentally and numerically. The dense packing of targeted microbubbles around the cell resulted in a low fMR for the StemBells (~600 kHz). This behaviour was predicted by our model. Understanding the dynamics of these StemBells in an US field is important for optimizing the acoustical parameters for US-mediated stem cell tracking and for facilitating localized delivery of stem cells using acoustic radiation force.



**Oral session 12A**

**2013/5/15 11:30:00**

**CONTROL ID:** 1671839

**TITLE:** MICROBUBBLE MANIPULATION USING ULTRASOUND STANDINGWAVE GENERATED IN SQUARE COLUMN TRANSDUCER

**AUTHORS/INSTITUTIONS:** K. Inoue, H. Kaji, R. Masuda, H. Ushijima, T. Azuma, S. Takagi, Y. Matsumoto, Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN | K. Yoshinaka, National Institute of Advanced Industrial Science and Technology, Tsukuba, Ibaraki, JAPAN |

**ABSTRACT BODY:**

**OBJECTIVE:** In the field of biotechnology, the method for manipulating micro-particle remotely has been developed and practically used in recent years. If this micro-manipulation can apply to microbubbles (MBs), they will contribute to the mechanism investigation on the drug delivery system or the gene transfer. In a previous work, MBs were manipulated precisely by using optical tweezers. This method is limited to in vitro case because the laser cannot transmit through thick overlapping cell layers. On the other hand, there are many papers presenting the MBs manipulation with acoustic radiation force that is called Bjeknes force. However, this force cannot manipulate MBs precisely. In this research, to develop the MB manipulation method with Bjeknes force, we try to control the position of MBs in a two dimensional ultrasound field.

**METHODS:** Bubbles in the ultrasound field are subjected to the Bjeknes force. In standing wave field, this force drives bubbles to certain direction that is to the node if MBs are larger than resonant radius. Our method aimed that MBs were trapped at the antinode or the node and manipulated with moving the position of the antinode or node. We prepared the device which had four flat transducers with the frequency of 2.06 MHz on all side of a square column. We confirmed that ultrasound field inside the device made a latticed pattern by computing and Schlieren picture. The position of the antinode or node could be moved with the phase shift.

**RESULTS:** MBs were trapped at certain position just after making ultrasound standing wave field. The position was thought to be node since the interval between the crowds of bubbles corresponds approximately with 0.4 mm which was the half of wave length. However, MBs did not move to the desired direction with phase shift. This was because MBs were trapped at the node. Since the node was not isolated with the neighbor node, MBs transited to the neighbornode and moved around the original position.

**CONCLUSIONS:** In this research, to develop the MB manipulation method with Bjeknes force, we tried to control the position of MBs on the two dimensional surface. We confirmed the aggregation of MBs at the node in the ultrasound standing wave field inside the device but could not move MBs effectively with phase shift.



# 13<sup>th</sup> International Symposium on Therapeutic Ultrasound

Shanghai, China

May 12-16, 2013

**Poster**

**(Abstract)**

**Tuesday 15:00-18:00**





## NO.1

**CONTROL ID:** 1672429

**TITLE:** HOW SONOPORATION DISRUPTS CELLULAR STRUCTURAL INTEGRITY: MORPHOLOGICAL AND CYTOSKELETAL OBSERVATIONS

**AUTHORS/INSTITUTIONS:** X. Chen, Y. Hu, R. Leow, A.C. Yu, Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG|J.M. Wan, School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG|

### **ABSTRACT BODY:**

**OBJECTIVES:** In considering sonoporation for drug delivery applications, it is essential to understand how living cells respond to this puncturing force. Here we seek to investigate the effects of sonoporation on cellular structural integrity. We hypothesize that the membrane morphology and cytoskeletal behavior of sonoporated cells under recovery would inherently differ from that of normal viable cells.

**METHODS:** A customized and calibrated exposure platform was developed for this work, and the ZR-75-30 breast carcinoma cells were used as the cell model. The cells were exposed to either single or multiple pulses of 1 MHz ultrasound (pulse length: 30 or 100 cycles; PRF: 1kHz; duration: up to 60s) with 0.45 MPa spatial-averaged peak negative pressure and in the presence of lipid-shelled microbubbles. Confocal microscopy was used to examine insitu the structural integrity of sonoporated cells (identified as ones with exogenous fluorescent marker internalization). For investigations on membrane morphology, FM 4-64 was used as the membrane dye (red), and calcein was used as the sonoporation marker (green); for studies on cytoskeletal behavior, CellLight (green) and propidium iodide (red) were used to respectively label actin filaments and sonoporated cells. Observation started from before exposure to up to 2 h after exposure, and confocal images were acquired at real-time frame rates. Cellular structural features and their temporal kinetics were quantitatively analyzed to assess the consistency of trends amongst a group of cells.

**RESULTS:** Sonoporated cells exhibited membrane shrinkage (decreased by 61% in a cell's cross-sectional area) and intracellular lipid accumulation (381% increase compared to control) over a 2 h period. The morphological repression of sonoporated cells was also found to correspond with post-sonoporation cytoskeletal processes: actin depolymerization was observed as soon as pores were induced on the membrane. These results show that cellular structural integrity is indeed disrupted over the course of sonoporation.

**CONCLUSIONS:** Our investigation shows that the biophysical impact of sonoporation is by no means limited to the induction of membrane pores: e.g. structural integrity is concomitantly affected in the process. This prompts the need for further fundamental studies to unravel the complex sequence of biological events involved in sonoporation.



## NO.2

**CONTROL ID:** 1672434

**TITLE:** DEVELOPMENTAL DELAYS AND SUBCELLULAR STRESS AS DOWNSTREAM EFFECTS OF SONOPORATION

**AUTHORS/INSTITUTIONS:** X. Chen, W. Zhong, A.C. Yu, Medical Engineering Program, The University of Hong Kong, Pokfulam, HONG KONG|J.M. Wan, School of Biological Sciences, The University of Hong Kong, Pokfulam, HONG KONG|

### **ABSTRACT BODY:**

**OBJECTIVES:** The biological impact of sonoporation has often been overlooked. Here we seek to obtain insight into the cytotoxic impact of sonoporation by gaining new perspectives on anti-proliferative characteristics that may emerge within sonoporated cells. We particularly focused on investigating the cell-cycle progression kinetics of sonoporated cells and identifying organelles that may be stressed in the recovery process.

**METHODS:** In line with recommendations on exposure hardware design, an immersion-based ultrasound platform has been developed. It delivers 1 MHz ultrasound pulses (100 cycles; 1 kHz PRF; 60 s total duration) with 0.45 MPa peak negative pressure to a cell chamber that housed HL-60 leukemia cells and lipid-shelled microbubbles at a 10:1 cell-to-bubble ratio (for 1e6/ml cell density). Calcein was used to facilitate tracking of sonoporated cells with enhanced uptake of exogenous molecules. The developmental trend of sonoporated cells was quantitatively analyzed using BrdU/DNA flow cytometry that monitors the cell population's DNA synthesis kinetics. This allowed us to measure the temporal progression of DNA synthesis of sonoporated cells. To investigate whether sonoporation would upset subcellular homeostasis, post-exposure cell samples were also assayed for various proteins using Western blot analysis. Analysis focus was placed on the endoplasmic reticulum (ER): an important organelle with multi-faceted role in cellular functioning. The post-exposure observation time spanned between 0-24 h.

**RESULTS:** Despite maintaining viability, sonoporated cells were found to exhibit delays in cell-cycle progression. Specifically, their DNA synthesis time was lengthened substantially (for HL-60 cells: 8.7 h for control vs 13.4 h for the sonoporated group). This indicates that sonoporated cells were under stress: a phenomenon that is supported by our Western blot assays showing upregulation of ER-resident enzymes (PDI, Ero1), ER stress sensors (PERK, IRE1), and ER-triggered pro-apoptotic signals (CHOP, JNK).

**CONCLUSIONS:** Sonoporation, whilst being able to facilitate internalization of exogenous molecules, may inadvertently elicit a cellular stress response. These findings seem to echo recent calls for reconsideration of efficiency issues in sonoporation-mediated drug delivery. Further efforts would be necessary to improve the efficiency of sonoporation-based biomedical applications where cell death is not desirable.



### NO.3

**CONTROL ID:** 1680297

**TITLE:** REAL-TIME MONITORING OF THE TEMPERATURE DURING HIFU TREATMENT BY ACOUSTIC RADIATION FORCE IMPULSE IMAGING

**AUTHORS/INSTITUTIONS:** P. Yang, C. Wang, C. Zeng, R. Qiu, S. Lin, M. Qian, H. Zheng, J. Wang, Paul C. Lauterbur Research Center for Biomedical Imaging, Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guang, CHINA|

#### **ABSTRACT BODY:**

**OBJECTIVES:** The high-intensity focused ultrasound (HIFU) is often considered as a promising technology used for non-invasive or minimally invasive therapy. However, real-time monitoring of the temperature during HIFU heating is strongly required but many problems about this kind of technology has not been fully solved. Acoustic radiation force impulse (ARFI) imaging is an attractive method for tissue stiffness assessment and has a potential to be used to monitor the heating of tumors during HIFU treatment on account of its non-invasive, non-ionizing, convenient and

inexpensive advantages. In this study, a self-made ARFI device was used to investigate the relationship between tissue stiffness and tissue temperature preliminarily.

**METHODS:** Focused ultrasound beam was used to generate acoustic radiation force in the tissue and therewith shear wave was generated and propagation to the surrounding tissues. Simultaneously, the displacements caused by shear wave propagation were tracked and strain was estimated. From shear wave velocity, tissue stiffness could be estimated and used to evaluate the temperature change in the region of HIFU treatment. Thus, real-time monitoring of temperature could be achieved since a temperature depend tissue stiffness change could be monitored. Experiments were performed on a tissue of porcine muscle sample which was heated by water-bath and its stiffness was measured by our ARFI device. Temperature were raised from 25 degree centigrade to 60 degree centigrade.

**RESULTS:** The results clearly demonstrated that as temperature increased, the tissue stiffness was considerably decreased while the value of measured shear wave velocity was also decreased. The value of the shear wave velocity was 2.1 m/s at the normal room temperature (25 degree centigrade) and decreased to 1.8 m/s when the temperature raised to 60 degree centigrade.

**CONCLUSIONS:** These preliminary experimental results of using ARFI to monitor the tissue stiffness as an indicator of temperature change has proved that this method has a potential to be an effective way to be used in the guidance and monitoring of HIFU treatment. Detailed studies are necessary to verify its applicability in real HIFU treatment environment and will be performed in the future.





#### NO.4

**CONTROL ID:** 1680329

**TITLE:** A STUDY ON THE CHANGE IN PLASMA MEMBRANE POTENTIAL DURING SONOPORATION

**AUTHORS/INSTITUTIONS:** P. Qin, P. Cai, Department of Instrumentation Science and Engineering, Shanghai Jiaotong University, Shanghai, CHINA|L. Du, L. Jin, Department of Ultrasound, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, CHINA|A. Yu, Medical Engineering Program, The University of Hong Kong, Hong Kong, CHINA|

#### **ABSTRACT BODY:**

**OBJECTIVES:** There has been validated that the correlation of sonoporation with calcium transients is generated by ultrasound-mediated microbubbles activity. Besides calcium, other ionic flows are likely involved in sonoporation. Our hypothesis is the cell electrophysiological properties are related to the intracellular delivery by ultrasound and microbubbles. In this study, a real-time live cell imaging platform is used to determine whether plasma membrane potential change is related to the sonoporation process at the cellular level.

**METHODS:** Hela cells were cultured in DMEM supplemented with 10% FBS in Opticell Chamber at 37 °C and 5% CO<sub>2</sub>, and reached 80% confluency before experiments. The Calcein Blue-AM, DiBAC4(3) loaded cells in the Opticell chamber filled with PI solution and Sonovue microbubbles were immersed in a water tank on a inverted fluorescence microscope. Pulsed ultrasound (1MHz freq., 20 cycles, 20Hz PRF, 0.2-0.5MPa PNP) was irradiated at the angle of 45° to the region of interest for 1s. The real-time fluorescence imaging for different probes was acquired by a cooled CCD camera every 20s for 10min. The time-lapse fluorescence images were quantitatively analyzed to evaluate the correlation of cell viability, intracellular delivery with plasma membrane potential change.

**RESULTS:** Our preliminary data showed that the PI fluorescence, which indicated intracellular delivery, was immediately accumulated in cells adjacent to microbubbles after exposure, suggesting that their membranes were damaged by ultrasound-activated microbubbles. However, the fluorescence reached its highest level within 4 to 6 minutes and was unchanged thereafter, indicating the membrane was gradually repaired within this period. Furthermore, using DiBAC4(3), which detected the change in the cell membrane potential, we found that the loss of membrane potential might be associated with intracellular delivery, because the PI fluorescence accumulation was usually accompanied with the change in DiBAC4 (3) fluorescence.

**CONCLUSIONS:** Our study suggests that there may be a linkage between the cell membrane potential change and intracellular delivery mediated by ultrasound and microbubbles. We also suggest that other ionic flows or ion channels may be involved in the cell membrane potential change in sonoporation. Further efforts to explore the cellular mechanism of this phenomenon will improve our understanding of sonoporation.



**NO.5**

**CONTROL ID:** 1681799

**TITLE:** Comparative effectiveness of different frequencies ultrasound on inflammatory pain release

**AUTHORS/INSTITUTIONS:** C. She, H. Qiao, J. Bai, Z. Wang, College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** The purpose of this study was to investigate the effects of ultrasound on hyperalgesia that occur during the inflammation.

**METHODS:** Thirty-five Zelanian rabbits were randomly allocated into 5 groups: group 1 that injected with carrageenan in the paw was applied with nothing to be the control group; Group 2 and 3, both injected with carrageenan in the paw, were applied with 0.2 MHz and 1 MHz ultrasound irradiation for 20min respectively, to investigate the effects of ultrasound on hyperalgesia; Group 4 and 5 that injected with carrageenan in the paw were injected intramuscularly with naltrexone (opioid antagonist) 10 min before 0.2 MHz and 1 MHz ultrasound administration respectively.

**RESULTS:** Both 0.2 MHz and 1 MHz ultrasound have amelioration of hyperalgesia. However, 0.2 MHz ultrasound presented longer lasting effect compared with 1 MHz one. Naltrexone-treated ones have shown the decay of the analgesic effect induced by 0.2 MHz ultrasound, but There was no difference between the two groups treated with 1 MHz ultrasound, which were injected with Naltrexone or not.

**CONCLUSIONS:** The treatment effect of ultrasound on hyperalgesia, especially the 0.2 MHz one, which associate with endogenous opioid peptide post a new method of inflammation-associated analgesia.



**NO.6**

**CONTROL ID:** 1681973

**TITLE:** Effect of low intensity ultrasound on ER and cyclinE Expression in Rats'uterine after Abortion Induced by Medication

**AUTHORS/INSTITUTIONS:** W. Dan, L. Fang, Z. Wang, College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** To study the effect of low intensity ultrasound on ER and cyclinE Expression in Rats'uterine after abortion induced by medication and discuss the mechanism of treating uterine delivery after abortion.

**METHODS:** 20 pregnant SD rats were divided into treatment groups and control groups, and Complete abortion models after abortion were made by using Mifepristone and Misoprostol at 7th day. Experimental group were treated by low intensity ultrasound 30 min every day after delivery one day to seventh day. Each group of models were killed after 7 days and then expression of ER and cyclinE were tested by Immunohistochemistry method and detected histopathological change.

**RESULTS:** The expression of ER and cyclinE in treatment group significantly higher in experimental group than that in the control group( $P < 0.05$ ).

**CONCLUSIONS:** Low intensity ultrasound can promote uterine involution and rising ER and cyclinE expression.



**NO.7**

**CONTROL ID:** 1671481

**TITLE:** HIFU THERAPY FOR LOCAL RECURRENCE OF PROSTATE CANCER AFTER EXTERNAL BEAM RADIOTHERAPY AND RADICAL PROSTATECTOMY – 5,5 YEARS EXPERIENCE

**AUTHORS/INSTITUTIONS:** V. Solovov, Y. Matyash, D. Fesenko, R. Khametov, Interventional Radiology, Samara Oncology Center, Samara, RUSSIAN FEDERATION |

**ABSTRACT BODY:**

**OBJECTIVES:** To evaluate the clinical efficacy of high-intensity focused ultrasound ablation (HIFU) for local recurrence of prostate cancer after external beam radiotherapy (EBRT) and radical prostatectomy (RPE).

**METHODS:** During 2007-2013 years 47 patients with local recurrence of prostate cancer after EBRT and RPE undertook HIFU therapy on the system "Ablaterm» (EDAP, France). Relapse arose an average of 2 years after EBRT and RPE. Median follow-up after HIFU therapy was 38 (12-60) months. The mean age was  $68.5 \pm 5.8$  years. The median PSA level before HIFU – 15.4 (7-48) ng / mL.

**RESULTS:** In 34 patients (72.3%) at six months after treatment the median PSA was 0.4 (0-3.2) ng / mL, in 48 months - 0.9 (0.4-7.5) ng / mL . In 13 patients (27.7%) at 6 months was observed progression of the disease. In general, after a 5,5 years follow-up 72.3% of the patients had no data for the progression and recurrence.

**CONCLUSIONS:** HIFU therapy in patients with local recurrence of prostate cancer after EBRT and RPE is minimally invasive and effective technology.



**NO.8**

**CONTROL ID:** 1679125

**TITLE:** Dynamic contrast-enhanced MR imaging: predictor for treatment effect of ultrasound-guided high intensity focused ultrasound ablating uterine fibroids with hyperintense on T2-weighted MR imaging

**AUTHORS/INSTITUTIONS:** W. Zhao, W. Zhao, College of Biomedical Engineering, Chongqing Medical University, Chongqing, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** To retrospectively investigate the role of dynamic contrast-enhanced MR imaging (MRI) in predicting treatment effect of ultrasound-guided high intensity focused ultrasound (USgHIFU) ablating uterine fibroids with hyperintense on T2-weighted MRI.

**METHODS:** 74 symptomatic uterine fibroids with hyperintense in 74 patients were analyzed. Uterine fibroids were subjectively divided into three types on pretreatment dynamic contrast-enhanced MRI in the arterial phase (in less than 60s after the injection): slight, irregular and regular enhancement. Non-perfused volume (NPV) which was represented as non-perfused area inside uterine fibroids on enhanced MRI after the treatment was used as the indices of treatment effect. The treatment time, treatment efficiency, energy efficiency ratio and adverse events were also analyzed.

**RESULTS:** The mean NPV ratio was 67.3% in all uterine fibroids. The mean NPV ratio was 85.1%, 68.2%, 49.8% in fibroids with slight, irregular and regular enhancement respectively. Regular enhancement had the lowest NPV ratio and treatment efficiency, but the highest energy effect ratio and risk of severe adverse effects.

**CONCLUSIONS:** Hyperintense uterine fibroids amenable to treatment with USgHIFU could be predicted by pretreatment dynamic contrast-enhanced MRI.



**NO.9**

**CONTROL ID:** 1667403

**TITLE:** ENHANCEMENT OF FOCUSED ULTRASOUND WITH MICORBUBBLES ON THE DELIVERY AND TREATMENTS OF ANTICANCER NANODRUG IN DIFFERENT STAGES OF BRAIN TUMORS

**AUTHORS/INSTITUTIONS:** H. Hung, Y. Hsu, S. Wu, W. Lin, Institute of Biomedical Engineering, National Taiwan University, Taipei, TAIWAN|T. Lin, Institute of Pharmacology, National Taiwan University, Taipei, TAIWAN|

**ABSTRACT BODY:**

**OBJECTIVES:** In this study, we tried to employ focused ultrasound (FUS) with microbubbles (MB) to enhance the delivery of PEGylated liposomal doxorubicin (PLD) into different stages of brain tumors in rodent model, and then quantified the amount of drug accumulated in tumor tissues and evaluated the treatment results.

**METHODS:** The ultrasound frequency and peak pressure at the focal zone were 0.5 MHz and 0.5 MPa, respectively.

The doses of MB and PLD through IV injection were 100 ul/kg, and 6 mg/kg, respectively. C6 glioma cells (10<sup>6</sup> cells) were injected into the right hemisphere and same volume of saline were into the left hemisphere (sham). PLD solution was injected on Day 8, Day 11, or Day 14 after tumor inoculation for the early-, medium-, or late-staged tumors, respectively, and a shot on both Day 8 and Day 11 was also studied for both with and without FUS/MB. Half the number of rats were sacrificed 24 hours after PLD injection to quantify the amount of PLD accumulated in tumor tissue and the other were sacrificed on Day 16 to evaluate the tumor growth response. We also injected Evan's blue (EB, 100 mg/kg) on Day 15 and N was equal to 6 for each group.

**RESULTS:** The amount of PLD accumulated in tumor tissues was significantly enhanced by FUS/MB sonication on Day 8 but not so drastically enhanced by sonication on Day 11 or Day 14, due to a high vascular permeability for medium- and late-staged tumors. The vascular permeability of brain tumor for PLD was very low on Day 8. The tumor size on Day 16 was much smaller for an early-staged tumor with PLD+FUS/MB treatment, and an additional treatment on Day 11 would cause a much further inhibition.

**CONCLUSIONS:** FUS/MB is able to enhance the delivery of nanodrug into brain tumors and can produce an effective inhibition for tumor growth. A better hinder for early-staged tumors can be seen and multiple treatments can further damage the tumor.



**NO.10**

**CONTROL ID:** 1669244

**TITLE:** FOCUSED ULTRASOUND INDUCED BLOOD-BRAIN BARRIER OPENING TO ENHANCE TEMOZOLOMIDE DELIVERY FOR GLIOMA TREATMENT IN RAT

**AUTHORS/INSTITUTIONS:** H. Liu, P. Chu, P. Lee, Department of Electrical Engineering, Chang-Gung University, Taoyuan, TAIWAN|C. Huang, P. Chen, K. Wei, Department of Neurosurgery, Chang-Gung University and Memorial Hospital, Taoyuan, TAIWAN|H.J. Wang, Department of Biological Sciences, National Sun Yat-sen University, Kaohsiung, TAIWAN|

**ABSTRACT BODY:**

**OBJECTIVES:** To report the preclinical therapeutic results of using MRI-monitored focused ultrasound induced BBB disruption to enhance TMZ delivery for improving glioma treatment in rats.

**METHODS:** MRI-monitored FUS was used to transcranially disrupt the blood–brain barrier (BBB) in rat brains in the presence of microbubbles. Cultured 9L glioma cells implanted into Fisher rats were used as the tumor model. FUS-BBB opening efficiency was evaluated by using the leakage of substitute dyes into brain, and the concentration of Temozolomide were quantified by using LC-MS\MS analysis in the cerebrospinal fluid and plasma. MRI was used to evaluate the effect of treatments longitudinally, including analysis of tumor progression and animal survival, and brain tissues were examined histologically.

**RESULTS:** We demonstrated that the FUS-BBB opening was beneficiary for increasing local concentration in brain parenchyma examined by dye substitutes via spectrophotometric analysis (380%/ 210% increase in normal/ tumor tissues); The TMZ concentration in cerebrospinal fluid (CSF) and plasma was measured via LC-MS/MS analysis, and confirm the TMZ CSF/ plasma ratio can be effectively increased (38.6% versus 22.7%). The tumor progression as well as animal survival when compared with TMZ alone were significantly improved (7-day tumor progression ratio was reduced from 24 to 5, with animal median survival extended), suggesting the enhanced TMZ delivery can improve therapeutic efficacy, including the tumor shrinkage and animal survival.

**CONCLUSIONS:** This study provides preclinical evidence that the use of FUS-BBB opening to locally can successfully increase local TMZ concentration, and may have clinical potential for improving current brain tumor treatment.



**NO.11**

**CONTROL ID:** 1671645

**TITLE:** TARGETED DRUG DELIVERY AGAINST BETA-AMYLOIDOSIS IN ALZHEIMER'S DISEASE MOUSE MODELS BY USING FOCUSED ULTRASOUND TECHNOLOGY

**AUTHORS/INSTITUTIONS:** L.L. Strobel, R.M. Nitsch, Division of Psychiatry Research, University of Zurich, Zurich, SWITZERLAND|B. Werner, E. Martin-Fiori, MR-Center, University Children's Hospital, Zurich, SWITZERLAND|

**ABSTRACT BODY:**

**OBJECTIVES:** Administration of a recombinant human A $\beta$ -antibody has been shown to decrease the  $\beta$ -amyloid load and restore cognitive impairment. Successful transport of antibodies across the BBB is a critical issue for A $\beta$  immunotherapy. Recent developments in magnetic resonance image-guided focused ultrasound (MRgFUS) have shown promising results for the induced disruption of the BBB for the delivery of antibodies as well as other pharmacological and physiological approaches. Noninvasive MRI-guided focal delivery of energy may allow for low doses of antibodies to enter the brain.

**METHODS:** Animals were fixed on top of a transducer that is positioned within a waterbath for noise-free sonication. We chose focus points for BBB opening after localization MR imaging. Microbubble injection was given i.v. during sonication. We then monitored extravasation with MR imaging of previously i.v. injected gadolinium as an in vivo BBB opening control.

**RESULTS:** We successfully demonstrate that FUS can be used to facilitate noninvasive antibody delivery to the brain. By targeting delivery to the choroid plexus of the 3rd ventricle, IgG is delivered to the CSF and elegantly distributed throughout the entire brain in areas abundant of A $\beta$  plaques. Delivery of antibody at 0.41 MPa pressure amplitude results in an increased delivery of antibody to the target tissue compared to regular intravenous delivery. Further findings include the cognitive improvement of animals receiving the FUS induced treatment antibody delivery accompanied by a decrease of A $\beta$  load measured biochemically and histologically. Additionally the FUS application does not lead to an increase of intracerebral microhemorrhages at the BBB opening site.

**CONCLUSIONS:** Focused ultrasound facilitates therapeutic antibody entry into the brain of an Alzheimer's disease mouse model. The application enables a safe and noninvasive approach to obtain therapeutic treatment effects.





## NO.12

**CONTROL ID:** 1671077

**TITLE:** EFFECTS OF MULTIPLE ULTRASOUND EXPOSURES ON CISPLATIN DELIVERY IN IN VITRO OPTICELL SETUP

**AUTHORS/INSTITUTIONS:** N. Sasaki, C. Bos, R. Deckers, B. Lammertink, C. Moonen, Division Imaging, UMC Utrecht, Utrecht, NETHERLANDS|

### **ABSTRACT BODY:**

**OBJECTIVES:** As ultrasound (US) disrupts microbubbles (MBs) only in the exposed area, in vivo disruption of bloodcirculating MBs in the target region can be repeated after an appropriate refilling time. This strategy may be useful to increase the efficiency of US-mediated drug delivery. Indeed, some in vivo studies used repetition of destructive US pulses and intermittent periods [1,2]. To improve our understanding of this strategy, we assessed the delivery efficiency in vitro.

**METHODS:** Human breast cancer cells (MDA-MB-468, ATCC) were seeded into Opticell (Thermo Scientific) and incubated for 48hr. Then, just before US exposure, 10  $\mu$ l Sonovue<sup>®</sup> (Bracco) and 5  $\mu$ g Cisplatin (Sigma-Aldrich) were added. Cells were exposed US for 1 sec by a mono-element transducer (Precision Acoustics), with a frequency of 1.3 MHz, 10-cycle pulses, 1msec pulse repetition time, and 1 MPa peak-to-peak pressure. US exposures were performed once or four times: after every exposure, the Opticell was gently shaken and inverted to refill MBs in the exposed

area. Disruption and replenishment were confirmed by light microscopy. Cells from the exposed area were harvested and seeded into a 96-well plate within 15 min after the last exposure. Cytotoxic effects were evaluated by MTT assay after 48hr.

**RESULTS:** The inhibition rate of single MB disruption and cisplatin was  $25.7 \pm 5.2\%$ , and that of repeated MB disruption and cisplatin was  $35.9 \pm 5.9\%$ . However, even without cisplatin, repeated MB disruption alone showed an inhibition rate of  $32.9 \pm 4.6\%$ . Light microscopy revealed mild cell detachment after multiple US exposures and severe cell wash-out during washing and harvesting.

**CONCLUSIONS:** Repetition of MB disruption might deliver cisplatin in larger quantities to more cells than single MB disruption. However, the present in vitro setup may not be appropriate for evaluating effects on viability due to cell detachment. MB disruption may weaken cellular attachment to the membrane and result in detaching cells in subsequent washing steps. Currently, we plan to measure DNA-binding cisplatin to partly overcome this problem. Alternatively, we may have to use a different in vitro setup, such as a sealed well plate, that allows collecting all cells, detached cells included, to measure viability.

[1] A. Carson, et al. Cancer Res 2012;72:6191-6199.

[2] S. Tinkov, et al. J Control Release 2010;148:368-372.



**NO.13**

**CONTROL ID:** 1671548

**TITLE:** CONFORMAL DRUG DELIVERY AND INSTANTANEOUS MONITORING BASED ON AN INVERSE SYNTHESIS METHOD AT A DIAGNOSTIC ULTRASOUND PLATFORM

**AUTHORS/INSTITUTIONS:** S. Xu, Z. Xu, H. Jiang, M. Lu, M. Wan, Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Xi'an, Shaanxi, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** In this work, a strategy that disruption of drug-encapsulated microbubbles at 5MHz, not kilohertz scale, in a focal region synthesized on a diagnostic ultrasound platform based on an inverse synthesis method, and instantaneous monitor was proposed.

**METHODS:** First of all, a low intensity focused ultrasound (LIFU) region, where acoustic pressure was well above fragmentation threshold of microbubble, was synthesized using all elements of a linear array transmitting a release pulse at pre-defined time delays based on an inverse synthesis method, in which excitation parameters were theoretically derived from an efficient field calculation formula together with a genetic optimization algorithm. Secondly, a subsequent conventional imaging frame was used to interrogate surviving microbubbles in LIFU region. Afterwards, the "composite" sequence comprising focused release pulse and imaging frame was repeated on demand. Thirdly, intensity of backscattered signals from region of interest (ROI) corresponding to LIFU region, defined as integration of squared amplitude of backscattered RF signals, was calculated for each imaging frame, eliciting a time-intensity-curve (TIC) characterizing dynamics of microbubble disruption. Similarly, a time-rms-curve (TRC) describing inertial cavitation activity of microbubbles in LIFU region was deduced by registering rms of broadband noise for each backscattered RF signal of release pulse to time trace. Lastly, we tested effects of time-delay sets of release pulse calculated from different modes of LIFU region on decay rates of TIC and TRC. Experiments were performed in suspension of lipid shelled drug-encapsulated microbubbles filled in latex-tube.

**RESULTS:** The simulation results of 128-element linear array show capability of deriving excitation parameters and size of synthesized LIFU region given its location. The experiment results actually confirm feasibility of microbubble disruption within synthesized LIFU region from both TIC and TRC. Furthermore, for the fixed excitation voltage, microbubbles were disrupted more efficiently in smaller LIFU region.

**CONCLUSIONS:** This work showed potential in adaptively conformal drug-delivery as needed in therapeutic application of ultrasound on a diagnostic ultrasound scanner, which was considered to expand functions of conventional diagnostic scanner to integration of delicate therapy and imaging.



**NO.14**

**CONTROL ID:** 1671569

**TITLE:** INVESTIGATION ON CAVITATION CONTRIBUTION IN SCLERAL PERMEABILITY ENHANCEMENT

**AUTHORS/INSTITUTIONS:** A. Razavi, A. Birer, F. Chavier, J. Mestas, J. Chapelon, C. Lafon, LabTAU - Thérapie et Applications des Ultrasons, INSERM, Lyon, Rhone alpes, FRANCE | A. Razavi, D. Clement, F. Romano, A. Begle, EYETECHCARE, Rillieux la pape, Rhone alpes, FRANCE |

**ABSTRACT BODY:**

**OBJECTIVES:** Due to the low permeability of the sclera, efficient local administration of drugs into the eye is challenging. It has been shown that application of pulsed focused ultrasound can enhance the permeability of the sclera with minimal damage. Cavitation is thought to be a major contributor to permeability enhancement; however, limited research has been performed to test this hypothesis in ocular drug delivery. The goal of the present work was thus to assess the contribution of cavitation activity to the ultrasound-induced sclera permeability enhancement.

**METHODS:** Dissected samples of rabbit sclera were placed between the two chambers of a diffusion cell. The transscleral route was the only passage between the two chambers of the cell. The donor and receiver chambers were filled with sodium Fluorescein (376 Daltons) and phosphate buffered saline solution, respectively. A

piezoceramic ultrasound transducer (5 cm in diameter and focal length) operating at a frequency of 1.1 MHz was mounted above the donor chamber. The ultrasonic beam was normally incident to the membrane which was placed at the focal plane. Pulses 250 and 25  $\mu$ s in length were applied at a repetition frequency (PRF) of 100 and 1000 Hz (2.5% duty cycle) for a sonication duration of 10 minutes. Time-averaged acoustic powers of 2.2 and 5.7 W were used and corresponded to peak negative pressures at the focus of 9.3 and 12.5 MPa. A needle hydrophone was positioned in the donor chamber to passively detect the broadband noise associated with inertial cavitation. A cavitation dose (CD) was calculated from the received hydrophone signals and used to quantify the level of bubble activity during sonications. The level of diffused Fluorescein into the receiver chamber was measured by fluorometry.

**RESULTS:** Fifty samples were tested under the 4 exposure conditions and no macroscopic damage was observed. The CD and permeability was a maximum at a PRF of 100 and an acoustic power of 5.7W and decreased significantly (<30% and 50%) at a higher PRF of 1000. The CD and permeability were both significantly lower at the sonications 2.2W and did not show a dependence on the PRF.

**CONCLUSIONS:** The performed acoustic measurements demonstrate that the scleral permeability can be enhanced significantly with cavitation activity.



**NO.15**

**CONTROL ID:** 1678274

**TITLE:** ULTRASOUND TARGETED MICROBUBBLE DESTRUCTION STIMULATES CELLULAR ENDOCYTOSIS IN ENHANCING ADENO-ASSOCIATED VIRUS DELIVERY

**AUTHORS/INSTITUTIONS:** L. Jin, F. Li, L. Du, Department of Ultrasound, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, Shanghai, CHINA|H. Wang, F. Wei, Experimental Research Center, Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, Shanghai, CHINA|P. Qin, Department of Instrumentation Science and Engineering, Shanghai Jiaotong University, Shanghai, Shanghai, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** The generally accepted mechanism for ultrasound targeted microbubble destruction (UTMD) to enhance drug and gene delivery is through sonoporation. However, passive uptake of adeno-associated virus (AAV) into cells following sonoporation does not adequately explain observations of enhanced transduction by UTMD. This study investigated alternative mechanisms of UTMD enhancement in AAV delivery.

**METHODS:** Three various doses of AAV were used in UTMD-mediated AAV transduction to illustrate the doseresponse of UTMD enhancement. Dynamic AAV uptake following UTMD was detected by immunofluorescence, western blotting and real-time PCR to compare with the time-course of uptake through endocytosis. The cellular clathrin-mediated endocytosis activity was demonstrated when cells were infected by AAV and/or treated with UTMD. Transmission electron microscopy was applied to display the form and quantity of endosomes near cell membranes. Clathrin-mediated endocytosis was inhibited to observe the inhibition of UTMD enhancement in AAV-mediated transduction.

**RESULTS:** UTMD significantly enhanced transduction efficiency of AAV at the middle dose only ( $P=0.002$ ). UTMD stimulated a prolonged uptake of AAV into the cytoplasm and nucleus with the peak time 45 min to 2h post infection, which was consistent with the peak time of cellular uptake through endocytosis. Additionally, UTMD enhanced clathrin expression and accumulation at the plasma membrane. Transmission electron microscopy revealed that UTMD stimulated increasing formation of clathrin-coated pits (CPs) and uncoated pits (nCPs). Furthermore, inhibition of clathrin-mediated endocytosis partially blocked the enhancement of AAV uptake following UTMD.

**CONCLUSIONS:** The results of this study implicate endocytosis of viral particles as a major contributor to UTMD-enhanced AAV delivery.



**NO.16**

**CONTROL ID:** 1666133

**TITLE:** PERMEABILITY IMPROVEMENT AND ACOUSTIC CHARACTERIZATION FOR PLA FOAMS BY ULTRASOUND

**AUTHORS/INSTITUTIONS:** G. Guo, D. Zhang, Key Laboratory of Modern Acoustics, Institute of Acoustics, Nanjing University, Nanjing, Jiangsu Province, CHINA|Q. Ma, Key Laboratory of Optoelectronics of Jiangsu Province, School of Physics and Technology, Nanjing Normal University, Nanjing, Jiangsu Province, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** In the present study, power ultrasound is applied to improve the permeability of the solid-state fabricated PLA foams with different pore sizes. In addition, an insert-substitution testing approach is put forward to perform acoustic measurement and property characterization for the PLA foams before and after ultrasound radiation.

**METHODS:** In the permeability improvement experimental setup, a commercial ultra-sonic processor is used to send out power ultrasound at the frequency of 20 kHz with a maximum power of 750W. Burst ultrasound pulses with an on/off ratio 3:3 are applied on PLA foams for 1 min with the ultrasound radiation intensity varied from 20% to 100% Pmax. Enhanced by a circular ultrasonic horn and coupled by water, the power ultrasound radiates to PLA foams at a distance of about 1 mm. The PLA foams are held by two rubber clips.

In this study, each cell of the fabricated PLA foams can be regarded as a gas filled cavity with corresponding acoustic attenuation, reflection and absorption, and the integrated affect of the micro-cellular structure can be estimated by the acoustic impedance  $z=r_0*c$ , which is determined by the density  $r_0$  and the acoustic velocity  $c$ . Because the acoustic impedance of gas is much smaller than that of the solid PLA raw material, higher acoustic attenuation coefficient, stronger acoustic reflection and greater acoustic attenuation can be achieved for the bigger cell-sized PLA foams.

**RESULTS:** The permeability improvement experimental results indicate that with the increase of ultrasound radiation intensity, the strengthened cell rupture can improve the permeability of the PLA foams by enhancing the interconnectivity of cells.

The attenuation coefficients of the PLA foams increase linearly with the increasing ultrasound radiation intensity. Besides a 4.3 dB/cm attenuation, the attenuation coefficient of the 2.5-MPa PLA foams has a similar linear increase slope as that of the 4-MPa PLA foams when the ultrasound radiation intensity is lower than 70%. But the attenuation coefficient goes down rapidly with the radiation intensity over 70% and it is even lower than that of the 4-MPa PLA foams with 100% ultrasound radiation.

**CONCLUSIONS:** The permeability of the PLA foams could be improved by power ultrasound and the property characterization could be measured by insert-substitution for the PLA foams before and after ultrasound radiation.



**NO.17**

**CONTROL ID:** 1666881

**TITLE:** REFINED ULTRASOUND-MEDIATED GENE DELIVERY USING CUSTOMIZED MICROBUBBLES

**AUTHORS/INSTITUTIONS:** R.R. Sun, M.L. Noble, S. Min, S.S. Sun, C.H. Miao, Immunity & Immunotherapies, Seattle Children's Research Institute, Seattle, WA|

**ABSTRACT BODY:**

**OBJECTIVES:** Ultrasound (US)-targeted microbubble (MB) destruction (UTMD) has emerged as a promising method for safe and selective gene delivery. When enhanced by the cavitation of MBs, US exposure can induce elevated sonoporation that transiently increases cell membrane permeability, allowing efficient and localized delivery of DNA. The goal of this study is to synthesize and characterize customized MBs for enhancing the efficiency of US-mediated gene delivery.

**METHODS:** We explored MB improvements in two ways: 1) Increasing the chain length of phospholipids which help increase overall MB stability and resist spontaneous and acoustic dissolution. 2) Adding cationic charge on MB surface with which MBs can electrostatically couple with DNA, increasing the concentration of genetic payload in the vicinity of target cells to allow amplified gene transfer upon sonoporation. To evaluate the effectiveness of various MBs in enhancing gene transfection, 293T cells were incubated with pGL4 (a reporter luciferase plasmid)/MB mixtures and exposed to US for 3 mins (1 MHz frequency, 20% duty cycle, 2W/cm<sup>2</sup>). Luciferase expression was examined 48 hrs after transfection.

**RESULTS:** The customized neutral MB (RN18) and cationic MB (RC5K) are comparable in concentrations and sizes with the surface charge of RN18 at -1.8mV and RC5K at a significantly more positive +6.4mV. After incubation with Cy5-labeled plasmid DNA, RN18 did not associate strongly with DNA (MFI=53), whereas RC5K showed significant binding after incubation with DNA (MFI=289).

The results showed that cells exposed to US with RN18 and RC5K MBs had 302 and 346-fold higher luciferase activity than cells treated with US only, respectively. As the US intensity increased, gene expression was further increased. Prior MB-DNA incubation did not enhance gene delivery efficiency with neutral RN18, but promoted 1.6-fold increase with cationic RC5K, reaching 8.1E7 RLU/mg.

**CONCLUSIONS:** Our data indicate that the addition of MBs is necessary for effective gene delivery, and that the efficiency can be further optimized by tailoring MB properties for therapeutic purposes. Both customized MBs are more effective than the standard clinically available Definity MBs, and the cationic MB can induce even greater transgene expression by increasing payload capacity with prior DNA incubation. Further MB customizations are underway to generate MBs best suited to facilitate US-mediated gene delivery.



**NO.18**

**CONTROL ID:** 1681568

**TITLE:** EFFECT OF ULTRASOUND INTENSITY FOR BUBBLE ENHANCED HIFU WITH HEATING LOCATION CONTROL METHOD

**AUTHORS/INSTITUTIONS:** K. Yoshinaka, Human technology Research Institute, AIST, Tsukuba, JAPAN|H. Utashiro, T. Azuma, A. Sasaki, S. Takagi, Y. Matsumoto, The University of Tokyo, Tokyo, JAPAN|

**ABSTRACT BODY:**

**OBJECTIVES:** High-intensity focused ultrasound (HIFU) is widely used for therapeutic applications because it is an attractive and non-invasive tool by which to provide thermal therapy. We used microbubbles to enhance the heating effect at the focal point of HIFU treatments. However, when microbubbles exist on the ultrasound pathway, they disturb the ultrasound propagation and distort the acoustic field. Distortion of the acoustic field leads to defocus and causes unexpected damage to tissue in the body. So, we developed a method for destroying microbubbles on the ultrasound pathway by irradiating repetitive high-intensity short-burst waves, where the durations of the intervals between burst waves are on the order of microseconds. High intensity burst waves are for oscillating and fragmenting microbubbles. We established the bubble destruction method with burst wave sequence on the pathway of the focused ultrasound. Previous study we proposed an advanced method, which is irradiating high intensity burst waves and weak waves in turn for consideration of blood flow model. In this study, we evaluated various intensities of weak waves

**METHODS:** Recent study we combined below two steps. The first step is irradiating repetitive high intensity short burst waves for destroying the microbubbles on the pathway. In the second step, low amplitude continuous waves were sent for heating the focal point. In this study we evaluated the various intensities of weak waves. We observed heat up region using thermal liquid crystal sheet.

**RESULTS:** In this experiment we observed the heat up region at the focus point when an irradiation intensity was  $500\text{W}/\text{cm}^2$ . When we set the intensity of  $1000\text{W}/\text{cm}^2$ , we couldn't observe the heat up region on the geometric focus point. Because microrobubules couldn't dissolved while weak wave (for heat up)were irradiating. Fragmented bubbles are dissolved during the subsequent weak waves, which are for heating the focal point. Weak waves should be decided enough weak not to oscillate and enlarge smaller microbubbles fragmented by high intensity ultrasound.

**CONCLUSIONS:** In our advanced bubble enhanced HIFU method, weak waves should be decided enough weak not to oscillate and enlarge smaller microbubbles fragmented by high intensity ultrasound. Our bubble enhanced HIFU with heating location control method has the possibility to use in the liver treatment with intravascular bubble flow.



**NO.19**

**CONTROL ID:** 1668941

**TITLE:** THE DEVELOPMENT OF MAGNETIC RESONANCE SURFACE COIL FOR HIFU ABLATION IN A MINI-PIG MODEL

**AUTHORS/INSTITUTIONS:** S.C. Hwang, P.H. He, H. Chang, I.Y. Kuo, C. Yao, T.H. Fang, Division of Medical Engineering Research, National Health Research Institutes, Zhunan, Miaoli, TAIWAN | L.Y. Shyu, Biomedical Engineering, Chung-Yuan Christian University, Chung Li, Taoyuan, TAIWAN |

**ABSTRACT BODY:**

**OBJECTIVES:** In MR-guided HIFU ablation, the accuracy of temperature measurement was directly proportional to the signal-to-noise (SNR) ratio of the MRI image. In this study, an MRI receive-only surface coil was fabricated and used to provide higher SNR MRI signal, where was around the hot spot, to improve the accuracy of MRI temperature measurement of HIFU ablation in a mini-pig model.

**METHODS:** A movable hole-circle surface coils with 14cm diameter of wire loop was fabricated and mounted onto the HIFU transducer package. The dynamic temperature images during HIFU ablation of porcine meat and living mini-pig leg were measured by this home-made surface coils. MR temperature measurements were made based on proton resonance frequency (PRF) shift method. A spoiled gradient echo sequence was applied for temperature mapping in a 1.5 Tesla MRI scanner (TR = 13ms, TE = 7 ms, flip angle = 30 deg, matrix 128x128, FOV= 256 x 256 mm, slice thickness = 8 mm).

**RESULTS:** The standard deviations of temperature measured by the 14cm diameter circle surface coils were 0.3, 0.6 deg C for porcine meat and pig leg, respectively.

**CONCLUSIONS:** The results of the experiments showed that the signal-to-noise ratio would be improved and the higher precision of the temperature measurement could be obtained. It showed the advantage and feasibility of using a smaller and mobile surface coil for MR-guided HIFU ablation.





**NO.20**

**CONTROL ID:** 1682062

**TITLE:** INVESTIGATION ON THE ACOUSTIC SIGNAL CHARACTERISTICS OF BOILING BUBBLE PRODUCED IN EX VIVO BOVINE LIVER DURING HIFU IRRADIATION

**AUTHORS/INSTITUTIONS:** Y. Li, F. Li, H. Ai, M. Zhong, W. Qi, College of Biomedical Engineering, Chongqing Medical University, Chongqing, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** To investigate the relativity between the fourth harmonic detected by passive cavitation detection, echogenicity in B-mode ultrasound image and bubbles formed in boiling ex vivo bovine liver tissue fluid during high intensity focused ultrasound irradiation.

**METHODS:** Set four groups of HIFU irradiation parameters. Group 1 and 2 were exposed to 50W acoustic power for 10s and 80s respectively, while group 3 and 4 were exposed to 200W acoustic power for 2s and 5s respectively. During HIFU exposure which is realtime monitored in B-mode ultrasound image, the temperature in the focal region was measured by thermocouple, acoustic signals were collected by passive cavitation detection system.

**RESULTS:** During the exposure, inertial cavitation was generated in the focal region in group 3 and 4 but not in group 1 and 2. The focal region temperature was high enough to make tissue fluid boiling in group 2 and 4, but not in group 1 and 3. Enhanced echogenicity occurred and the fourth harmonic amplitude significantly increased in group 2 and 4, but not in group 1 and 3.

**CONCLUSIONS:** During HIFU irradiation, the fourth harmonic amplitude increase detected by PCD system and enhanced echogenicity may due to HIFU-caused boiling bubble.



**NO.21**

**CONTROL ID:** 1683977

**TITLE:** Dual CCD high-precision positioning method of focused ultrasound body sculpting system

**AUTHORS/INSTITUTIONS:** D. Li, Research, Company, Shanghai, Shanghai, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** The non-invasive focused ultrasound body sculpting system is a new clinical application which is being accepted by the public gradually. The basic principle is: with high-precision positioning system, a specific frequency focused ultrasound sonication from in vitro to patient's subdermal fat, so that the fat cells membrane were broken by cavitation effect and mechanical force, then fat cells were crushed, dissolved and emulsified gradually, so as to achieve the purpose of the body sculpting.

About the body sculpting system, the accuracy of positioning method affects the safety and effectiveness of body sculpting treatment directly. Positioning method is one of the key technologies in non-invasive focused ultrasound body sculpting treatment.

**METHODS:** According to the binocular imaging principle, dual CCD image sensor is the main part of positioning method for non-invasive focused ultrasound body sculpting treatment. The principle of binocular imaging technology is that the relationship between the three-dimension coordinates of a point in space and the two-dimensional coordinates captured in the image could have been identified after the dual CCD is fixed. with the known calibration template, the dual CCD were taken calibration template image, three dimensional coordinates obtained by calculating their correspondence relationship between the two-dimensional coordinates in the captured image and dual CCD system calibration parameters. The three-dimensional coordinates of a point in space can be calculated by the two-dimensional coordinates of the point corresponding points in the two captured images and dual-CCD system calibration parameters.

**RESULTS:** The technical solution based on the principle of binocular imaging is achieved by dual CCD image acquisition technology. The use of the dual CCD acquisition image can calculate with three-dimensional information within the treatment area (surface) treatment of patient. This solution overcomes only flat graphic information calculated from the treatment point in the treatment area by single CCD, which is lack of existence of a certain error.

**CONCLUSIONS:** Dual CCD high-precision positioning method of body sculpting system make non-invasive body sculpting treatment more safely, reliably, usably and credibly, and also has the advantages of low manufacturing cost, easy-to-use.



**NO.22**

**CONTROL ID:** 1671571

**TITLE:** ROBOTIC ASSISTANCE IN THE EVALUATION OF THE POSITION OF A HIFU LESION DURING IMAGE GUIDED FUS

**AUTHORS/INSTITUTIONS:** A. Melzer, Institute for Medical Science and Technology, University of Dundee, Dundee, UNITED KINGDOM|X. Xiao, Z. Huang, School of Engineering, University of Dundee, Dundee, UNITED KINGDOM|

**ABSTRACT BODY:**

**OBJECTIVES:** For image guided high-intensity focused ultrasound (HIFU) therapy, the position of the HIFU transducer usually should be assessed if the HIFU transducer has to be moved during treatment. And this situation is very common especially when the sizes of the sonications are much smaller than the sizes of the tumors or the target tissue is moving during the treatment. This paper has investigated and compared the validation of positioning method of HIFU transducers both in MRgFUS and USgFUS. This job can be took as the previous work for image guided organ motion tracking in HIFU therapy.

**METHODS:** In this paper, the validation of positions for HIFU transducers in MR is using active tracking sequence which takes less than 0.01s. To prove its efficiency and accuracy, a MR-compatible robotic arm InnoMotion™ (IBSMM, Engineering spol. s r.o. / Ltd, Czech) was employed to move the HIFU transducer, which offers five pneumatically driven degrees of freedom (DOF) with a range of 170mm\*200mm\*200mm within the magnet bore. The robotic arm will guide the HIFU transducer to all the reference positions which were provided by an agar phantom. The coordinates recorded from the micro-coils which are fixed on the robotic arm will be compared with the reference positions to evaluate the performance of the validation method. For the ultrasound guided focused ultrasound (USgFUS), the validation for positions of HIFU transducer is based on stereo vision. To test its performance, an industrial robot with 6-DOF was used to control the HIFU transducer. The performance to validate the HIFU transducer positions could be assessed after comparing the coordinates computed from stereo vision method and the position information recorded from the robot system.

**RESULTS:** The positioning accuracy of using MR active tracking technique is dependent on the distance from the micro-coils to the iso-center of MR bore. In the central area which is 150mm\*150mm\*150mm, the accuracy could be higher than 0.5mm. For the USgFUS, the positioning precision is related to the distance between the monitoring cameras and the HIFU transducers. The accuracy of this validation method is around 1.0mm.

**CONCLUSIONS:** The validation of positions for HIFU transducers in MRgFUS and USgFUS were both assessed. This job is crucial for organ motion tracking in clinical trials.



**NO.23**

**CONTROL ID:** 1672167

**TITLE:** WHAT ARE THE BEST METHODS OF ASSESSING ADVANCEMENT IN THE FIELD OF FOCUSED ULTRASOUND?

**AUTHORS/INSTITUTIONS:** D. Tyshlek, A. Hananel, N. Kassell, H. Huff-Simonin, Focused Ultrasound Foundation, Charlottesville, VA|N. Kassell, Department of Neurosurgery, University of Virginia, Charlottesville, VA|

**ABSTRACT BODY:**

**OBJECTIVES:** The Focused Ultrasound Foundation has created a dashboard including various metrics to monitor the advancement of focused ultrasound from bench to bedside.

**METHODS:** We have collected information on publications, citations, abstracts presented at dedicated academic conferences, NIH funding dedicated to Focused Ultrasound, general awareness as measured by web hits and social media and number of indications reaching the stage of first in human.

**RESULTS:** As will be presented in a graph format at the meeting, all metrics evaluated show continuous increase.

**CONCLUSIONS:** The Focused Ultrasound Dashboard demonstrates progress in the field of Focused Ultrasound for clinical applications. This demonstration is important as a tool to validate the technology, in the eyes of the general medical community, insurance companies and governmental sources of funding as well as heighten awareness of focused ultrasound among the general population.



**NO.24**

**CONTROL ID:** 1666024

**TITLE:** MAGNETIC RESONANCE IS PROMISING IN CONTRIBUTING TO FIND AN ULTRASOUND DOSE DEFINITION

**AUTHORS/INSTITUTIONS:** J. Kramme, M. Günther, J. Jenne, Fraunhofer MEVIS - Institute for Medical Image Computing, Bremen, GERMANY|M. Günther, Faculty of Physics and Electronics, University of Bremen, Bremen, GERMANY|J. Haller, Physikalisch-Technische Bundesanstalt, Braunschweig, GERMANY|J. Jenne, Mediri GmbH, Heidelberg, GERMANY|

**ABSTRACT BODY:**

**OBJECTIVES:** Even though ultrasound (US) is widely used in diagnostic as well as in therapeutic applications there is so far no standardized and appropriate US dose quantification. At the moment several partners are working on a definition of a dose term for therapeutic US applications in the framework of the project “Dosimetry for Ultrasound Therapy” [1]. Magnetic resonance imaging (MRI) is promising to quantify such a dose term.

**METHODS:** Seven standard MRI temperature measurement methods like diffusion imaging or proton resonance frequency shift (PRFS) were theoretically evaluated to find the most promising one for a thermal dose definition. Attempts for mechanic dose definitions are rare, for example acoustic radiation force imaging (MR-ARFI) [2], while MR-elastography (MRE) and MR-shear wave imaging were to our knowledge not evaluated relating to dose definitions yet.

**RESULTS:** For temperature measurements it seems most promising to use PRFS phase mapping [3]. From one image taken before and after heating the temperature difference can be calculated. An advantage over the other temperature imaging methods is that no time consuming calibration measurements are needed, because the temperature coefficient is almost the same for all tissue types when using PRFS. However, it is recommended to use fat suppression [5].

MR-ARFI seems to be the choice for mechanical dose definition approaches. A directed displacement is measurable here.

**CONCLUSIONS:** The use of MRI for US dose measurements is fully non invasive, the propagation of the US field is not influenced by the MRI measurement and it does not cause any viscous heating effects or additional US absorption, as observed with small sensors. Since 3D temperature imaging is time consuming, often fast echo planar imaging techniques are used to gain 3-5 slices out of the volume of interest. MRI is an easy tool especially considering the aspect that the number of MR guided HIFU applications is rising. The results suggest that at least quantitative temperature but possibly also mechanical measurements are possible. In the next step the practicability will be verified in a phantom study. Our final goal is to develop practical and standardized MR-methods to measure adequate dose terms.

[1]<http://www.duty-project.eu/emrp/dosultrasound-home.html>

[2]Kaye et al. Magn Reson Med 2011;65:738–743

[3]Hindman. J. Chem. Phys. 1966;44:4582

[4]Zwart et al. Magn Reson Med 1999;42:53–59



**NO.25**

**CONTROL ID:** 1671161

**TITLE:** ELECTROMAGNETIC HYDROPHONE FOR HIGH INTENSITY FOCUSED ULTRASOUND MEASUREMENT

**AUTHORS/INSTITUTIONS:** P. Grasland-Mongrain, J. Mari, B. Gilles, C. Lafon, LabTau, INSERM, Lyon, FRANCE|P. Grasland-Mongrain, J. Mari, B. Gilles, C. Lafon, Université Claude Bernard, Lyon, FRANCE|

**ABSTRACT BODY:**

**OBJECTIVES:** The goal of the present study is to describe an electromagnetic hydrophone based on the Lorentz force.

**METHODS:** This electromagnetic hydrophone is made of a thin wire and eight magnets. The wire is vibrating while exposed to an ultrasound wave, which induces by Lorentz force an electrical current proportional to the integral of pressure along the wire. 2D pressure field mapping is achieved by performing a tomography through wire translations and rotations in the imaging plane. Characteristics of such type of hydrophone are assessed in this study.

**RESULTS:** Signal is linear over pressure from 10 kPa to at least 10 MPa with a determination coefficient  $R^2$  above 0.997. Excellent resistance to cavitation has been observed. Upper cutoff frequency was measured against four different wire diameters: 70  $\mu\text{m}$ , 100  $\mu\text{m}$ , 200  $\mu\text{m}$  and 400  $\mu\text{m}$ . Wire tension has no visible effect on the signal. Due to its resistance, the electromagnetic hydrophone should be convenient for High-Intensity Focused Ultrasound.

**CONCLUSIONS:** An electromagnetic hydrophone was designed. Measured pressure fields were in agreement with simulated fields and measurements with a conventional piezoelectric hydrophone.



**NO.26**

**CONTROL ID:** 1683862

**TITLE:** The research on image denoising in sound field measurement based on infrared imaging

**AUTHORS/INSTITUTIONS:** Z. Su, G. Shen, Y. Yu, S. Qiao, X. Ji, H. Wu, M. Zhu, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA|Y. Yu, School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** The background of the research is to explore the distribution of focused ultrasound field. Making use of the heat property of focused ultrasound, we can measure the distribution of heat sources to calculate the distribution of focused ultrasound field. During the exploration, we found that the temperature rise rate have a liner relation to sound intensity, so the distribution of temperature rise rate is directly relate to the distribution of focused ultrasound field. After the experiments, we can get the infrared charts with noise. In order to obtain an accurate distribution of focused ultrasound field, it's necessary to find out a solution to get rid of the noise in infrared charts. The traditional method to explore the distribution of focused ultrasound field is measuring it directly by hydrophone, but it can't be used in the nonlinear area. So the present investigation was focused on the experimental validation of a filter which is most suitable for image process of infrared chart, as a consequence, most noise is removed and the distribution of temperature rise rate is not changed.

**METHODS:** The purpose of the analysis is to compare the effects of different common filtering techniques. After processing the raw data, we compared the distribution of the temperature rise rate, the measurement index is -6dB width of temperature rise charts. By comparing the distribution of temperature rise rate, we can tell which kind of filter is better in keeping the distribution of focused ultrasound field in steady.

**RESULTS:** All simulations, semi-simulations and experiments use six kind filters to deal with the raw data to obtain related information, and the related information of noise and noise-free temperature rise charts can be obtained from the raw data processed and unprocessed.

**CONCLUSIONS:** From the experiment results of simulation, semi-simulation and experiment, we can draw a conclusion that gauss filter is superior to the others filter, it has a better ability to keep the distribution of focused ultrasound field in steady.



**NO.27**

**CONTROL ID:** 1679865

**TITLE:** DEVELOPMENT OF ULTRASOUND GUIDED HIGH INTENSITY FOCUSED ULTRASOUND SYSTEM WITH ROBOT MANIPULATOR FOR TREATMENT OF EARLY BREAST CANCER

**AUTHORS/INSTITUTIONS:** K. Fujiwara, H. Takeuchi, K. Itani, Engineering R&D Dept, Hitachi Aloka Medical, Ltd., Ome-Shi, Tokyo, JAPAN | N. Abe, Application Development Office, Hitachi Medical Corporation, Kashiwa-Shi, Chiba, JAPAN | K. Yoshinaka, Human Technology Research Institute, National Institute of Advanced Industrial Science and Technology, Tsukuba-Shi, Ibaraki, JAPAN | T. Yonetsuji, T. Azuma, A. Sasaki, S. Takagi, I. Sakuma, Y. Matsumoto, School of Engineering, the university of Tokyo, Bunkyo-Ku, Tokyo, JAPAN |

**ABSTRACT BODY:**

**OBJECTIVES:** For treatment of early breast cancer, we are trying to develop an ultrasound guided High Intensity Focused Ultrasound (HIFU) system which is safe, precise, and noninvasive. Then we made a prototype system combined with the position control and monitoring of HIFU beam.

**METHODS:** The prototype was designed based on following concepts; 1). The patient's breasts were placed on the top part of a water tank with the patient in a prone position. 2). The HIFU transducer with the imaging array were set on a tip of a rotary multi-joint 4-axis robot manipulator in the water tank and its position was controlled by the manipulator. 3). A difference between a planned and an actual focal-position of HIFU was confirmed by HIFU Beam Imaging (HBI) developed previously by us. HBI was imaging method for displaying a HIFU focal point and its beam path in real time on the ultrasound image. A pulse transmitted from a HIFU transducer was used as an imaging pulse for this method. To demonstrate the performance of the prototype system, two experiments were performed by using hemispherical tissue-mimicking phantoms.

1). The phantom was scanned with the imaging array under the control of the manipulator. Ultrasound 3D volume image of the phantom was structured using the acquired 2D image data.

2). The position of HIFU transducer was controlled by using the manipulator and HBI. Then HIFU was exposed to the seven target points and each exposure time was 40 s.

Imaging and HIFU frequency were 7.5 and 2.0 MHz. HIFU transducer was irradiated 2-cycle burst wave for HBI. Total acoustic power of HIFU was 100 W in the case of heating and HBI mode.

**RESULTS:** The ultrasound 3D volume data and HBI images acquired by the prototype system was useful to plan the target and adjust the focal point. As a result of HIFU exposure to the targets, seven ellipse-shape thermal volumes were coagulated at equal distance in accordance with the position control and HIFU beam monitoring. Its total volume was approximately 2.1 cm<sup>3</sup>.

**CONCLUSIONS:** We made a prototype ultrasound guided HIFU system with the robot manipulator and performed some experiments using tissue mimicking phantom. As a result, the treatment planning on the basis of the acquired ultrasound images and precise position control and monitoring of HIFU beam were realized by the system.





**NO.28**

**CONTROL ID:** 1681256

**TITLE:** ASSESSMENT AND CORRECTION OF PHASE ABERRATIONS IN THE BREAST FOR MRGFUS

**AUTHORS/INSTITUTIONS:** A. Farrer, D.A. Christensen, Department of Bioengineering, University of Utah, Salt Lake City, UT|A. Farrer, S. Almquist, D.L. Parker, A. Payne, Utah Center for Advanced Imaging Research, University of Utah, Salt Lake City, UT|S. Almquist, School of Computing, University of Utah, Salt Lake City, UT|D.L. Parker, A. Payne, Department of Radiology, University of Utah, Salt Lake City, UT|D.A. Christensen, Department of Electrical and Computer Engineering, University of Utah, Salt Lake City, UT|

**ABSTRACT BODY:**

**OBJECTIVES:** MR-guided focused ultrasound surgery (MRgFUS) has the potential to non-invasively treat breast cancer. Our group has designed and built a 1.0-MHz breast-specific MRgFUS system that employs a laterally mounted phased-array transducer with 256 elements within a 14.4 x 9.8-cm aperture[1]. In a study of beam focusing in the heterogeneous breast using another MRgFUS system with a larger aperture phased-array circular transducer surrounding the breast, it was shown that phase aberration caused by varying tissue acoustic properties can lead to significant broadening of the pressure pattern at the focus[2]. The work presented here employed simulations to assess whether such focusing distortions would be present using a system with a smaller numerical aperture transducer in a breast with multiple fibroadenomas.

**METHODS:** A 3D breast image volume (165x117x112 mm<sup>3</sup> at 1.0 mm isotropic resolution, zero-fill interpolated to 0.5 mm<sup>3</sup> isotropic voxel spacing) was obtained from a female volunteer (61.2 kg, 31 y.o.) and was segmented into five tissue types (skin, breast fat, fibroglandular, fibroadenoma, and water). Simulations were performed using the Hybrid Angular Spectrum method[3] implemented in MATLAB to model the propagation of the ultrasound beam in this breast both with and without a phase correction technique[4]. The aberration correction method individually modeled the beam from each transducer element, and then inverted the phase found at the desired focus for each element's excitation to maximize constructive interference.

**RESULTS:** For this particular breast model, phase aberration correction sharpened the focus, reduced side lobes, and increased peak intensity by 36%. Mean deviation of the beam's focus from the desired location decreased from about 1.1 mm to less than 0.4 mm with correction.

**CONCLUSIONS:** Correction of phase aberration results in an improved beam focus and positioning accuracy for our system. In the breast anatomy analyzed, the expected phase aberration causes enough distortion to the beam's focus to make phase aberration correction advantageous for treatment accuracy. Continuation of this work will analyze phase aberration and subsequent phase correction in experimental phantoms and ex vivo tissues.

References

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3. U. Vyas and D. Christensen, IEEE Proc. UFFC 59(6), 2012
4. S. Almquist et al., ISTU Symposium, 2012



**NO.29**

**CONTROL ID:** 1672005

**TITLE:** DEDICATED 8 CHANNEL HEAD RECEIVE ARRAY FOR TRANSCRANIAL MR GUIDED FOCUSED ULTRASOUND SURGERY

**AUTHORS/INSTITUTIONS:** B. Werner, E. Martin, Center for MR-Research, University Children's Hospital, Zurich, ZH, SWITZERLAND|F. Resmer, T. Lanz, Rapid Biomedical GmbH, Rimpar, GERMANY|

**ABSTRACT BODY:**

**OBJECTIVES:** Transcranial MR guided Focused Ultrasound Surgery (TcMRgFUS) is a new treatment modality for image-guided, non-invasive neurosurgery. However, while intra-interventional high-quality MR imaging is a mission-critical prerequisite it remains challenging due to mechanical constraints and electronic complexity imposed by the ultrasound transducer setup. Here, a dedicated 8 channel MR head receive array has been developed to support the TcMRgFUS intervention.

**METHODS:** The front-end of the InSightec ExAblate 4000 Brain system (InSightec Ltd., Tirat Carmel, Israel) consists of a large phased array transducer supported by a mechanical 4-axis positioner. A stereotactic frame immobilizes the patient's cranium inside the transducer. The MR array (inner diameter 345mm, outer diameter 375mm, length 240mm) wraps tightly around the transducer. It comprises an anterior section and a posterior section of 4 receive channels each. Every channel contains an active and a passive decoupling circuit and is connected to a low impedance preamplifier [1] via a 50  $\Omega$  matching network followed by a phase shifter for preamplifier decoupling [1]. Next neighbor elements are decoupled with shared inductors [2].

**RESULTS:** Compared to the system BODY coil the image SNR is improved by a factor of 3-4 in phantom tests and in clinical treatments, allowing to significantly reduce acquisition time of navigation images while still supporting the neurosurgeon by improved image quality. The MR array was certified as a medical device and has been successfully tested in ongoing clinical phase I studies for functional TcMRgFUS neurosurgery [3] and TcMRgFUS tumor surgery. It offers full head coverage and parallel imaging capability.

**CONCLUSIONS:** The TcMRgFUS environment is very challenging for MR imaging owing to the system electronics of the phased array ultrasound transducer, its copper shielded transducer surface with water bath and the stereotactic fixation of the patient head. Here we demonstrate the advantages of integrating an MR array into the TcMRgFUS frontend: handling, image stability and SNR are significantly improved.

This work was supported by NCCR Co-Me and Gönnerverein Kinderspital Zürich.

[1] P. Roemer et al., MRM 16: pp.192 (1990)

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**NO.30**

**CONTROL ID:** 1672086

**TITLE:** FUS-COMPATIBLE MR IMAGING COIL FOR LARGE ANIMAL BRAIN APPLICATIONS

**AUTHORS/INSTITUTIONS:** M.D. Eames, J.W. Snell, Focused Ultrasound Foundation, Charlottesville, VA | M. Jones, HighField, LLC, St. Paul, MN |

**ABSTRACT BODY:**

**OBJECTIVES:** Neurosurgical preclinical MRg-FUS research necessitates in-vivo studies in the large animals to approximate the scale of the proposed clinical application. However, with a reduced brain volume as compared to humans, the body coil built into clinical MR systems provides sufficiently low SNR – especially for functional neurosurgery targets – to hamper research progress. Existing, commercially-available coils are not suited to the research environment for such studies, which require a water bath in close proximity to the imaging volume and acoustic continuity between transducer and target. Given that commercial head coils are not designed for submerged use and would obstruct the acoustic path, in addition to the lack of commercial availability of an appropriately-sized flex array for use in a 3T magnet, there exists a need for the development of a custom imaging coil for these experimental applications. In this work we present the imaging results of a FUS-compatible head coil for large animal research.

**METHODS:** Animal studies involving the InSightec ExAblate Neuro system require that the transducer be positioned on the MR table such that the range axis is directed vertically upwards. The transducer is then filled with chilled and degassed water, and the research animal is positioned on its back with the top of its head submerged in this water bath in order to couple the FUS transducer to the subject's head. Coil design was centered around the need for a flex array that would be positioned on the animal's neck in order to image its brain. Overall array dimensions and loop diameters were assessed in conjunction with HighField, LLC, the coil designer involved in this study. After promising results from a prototype coil were achieved, the design was finalized for production.

**RESULTS:** Imaging SNR improved by a factor of three to four as compared to body coil imaging, yielding an associated reduction in thermometry standard deviation. Penetration depth is sufficient (>10cm) to provide fine detail of the animal brain in the experimental setup.

**CONCLUSIONS:** This project resulted in the successful design and fabrication of an effective, FUS-compatible MR imaging coil for use in large animal brain research. The coil is easily positioned relative to the animal and associated ventilation and monitoring equipment, and remains above water level throughout the studies.



**NO.31**

**CONTROL ID:** 1681615

**TITLE:** Wireless energy transmission using ultrasound for implantable devices

**AUTHORS/INSTITUTIONS:** : Z. Yang, H. Wang, D. Zeng, Z. Wang, College of Biomedical Engineering, Chongqing Medical University, Chongqing, Chongqing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Implantable devices used to replace or assist the operation of certain organs have been widely used in human body. The power supply which can provide long-term, stable and efficient electric energy for Implantable devices is a tough issue in medical applications. The traditional power supply method for implantable devices, such as disposable batteries or energy transmission by a puncture through the skin tissue, could damage the skin resulting in infections of the body. Once the power of the battery that powered the implantable device run out, the battery should be replaced by a new one through re-operation, which would cause the secondary pains to patients. To overcome these problems above, a new energy supply method for the implantable devices operating in the body was proposed.

**METHODS:** The ultrasound was used to wirelessly transmit energy to the implantable devices in a non-invasive manner. A piezoelectric transducer was set on the recharging batteries that power implantable devices to receive the ultrasonic energy.

**RESULTS:** In this paper, we presented our recent modeling results on power transmission through an elastic wall by piezoelectric transducers and ultrasound. This included the case of finite piezoelectric transducers on plates, power transmission through circular cylindrical shells. The results demonstrated the operating principles of using ultrasound for implantable devices

**CONCLUSIONS:** Transmission of electric energy to implantable devices using ultrasound is feasible.



**NO.32**

**CONTROL ID:** 1682072

**TITLE:** Radiation Force Calculation of Cylindrical Focusing Transducer and Array on Ray Acoustics Model

**AUTHORS/INSTITUTIONS:** S. Duan, Center for Certification & Evaluation, Shanghai Food and Drug Administration, Shanghai, Shanghai, Shanghai, CHINA|W. Shou, B. Hu, Shanghai Jiao Tong University affiliated 6th People's Hospital, Shanghai, Shanghai, Shanghai, CHINA|Z. Zhan, Florida International University, Miami, Miami, FL|W. Shou, B. Hu, Shanghai Institute of Ultrasound in Medicine, Shanghai, Shanghai, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Using the method of ray acoustics, a general formula for calculating the radiation force  $F$  on the target with reflection coefficient  $r$  in cylindrically focused acoustic field was derived. Based on the superposition principle the radiation forces on absorbing target in spherically and cylindrically focused multi-beam fields of arrays as well as in two moving focusing scan beam fields were calculated based on ray acoustic model.

**METHODS:** ray acoustics

**RESULTS:** A general formula for calculating the radiation force on the target with partial reflection coefficient in cylindrically focused acoustic field was derived. Then the radiation force on the totally reflecting and absorbing target can easily calculated using the reflection coefficient of 1 or 0. Based on the superposition principle the radiation forces on absorbing target in spherically and cylindrically focused multi-beam fields of arrays as well as in two moving focusing scan beam fields were calculated based on ray acoustic model.

**CONCLUSIONS:** The calculation based on ray acoustic model for radiation force on the target at the focus of a spherically focusing beam or at the focal line of a cylindrically focusing beam meets difficulty in theory because it is impossible that the focal region at focus or focal line have unlimited small across-area where the acoustic intensity is unlimited large to satisfy Equation in the model. So in measurement the target should place at the position away from the focal region. Indeed because of the diffraction effect the true focal angle is smaller than the geometric focal angle. So the calculated power using these formulas are over-valuation. The diffraction correction should be taken in measurement. Previous formulas can be applied as useful tools for correction and uncertainty evaluation in practical power measurements based on radiation force for cylindrically focused field.



**NO.33**

**CONTROL ID:** 1682403

**TITLE:** Characterization of 1-3 single crystal/epoxy composite ultrasonic transducer for elevated temperature application

**AUTHORS/INSTITUTIONS:** Z. Wu, X. Kui, S. Li, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** There is an increasing demand for high performance transducers to operate at higher temperatures, which either are required to work under elevated temperature conditions or encounter the issue of self-heating from high power operation. Relevant biomedical applications include high intensity focused ultrasound (HIFU) therapy, elastic wave imaging excitation, and acoustic radiation force etc. Compared to traditional piezoelectric ceramic materials for ultrasonic transducers, lead magnesium niobate-lead titanate (PMN-PT) as a novel relaxor-based ferroelectric single crystal has attracted considerable attention for its higher piezoelectric coefficients and electromechanical coupling factors, and wider bandwidth. Further improved characteristics of high performance transducers can be achieved with PMN-PT/epoxy composite materials. These materials allow greater flexibility to design mechanical, piezoelectric and dielectric properties of ultrasonic transducers with optimization of single crystal volume fraction and structure mode. However, there is very rare thorough investigation in elevated temperature properties of ultrasonic transducers with single crystal/epoxy composite materials. In this paper, high temperature characteristics of ultrasonic transducer with 1-3 PMN-PT/epoxy composite are to be studied.

**METHODS:** The electrical impedance characteristics around resonant frequency of the composite, which are prepared with “dice and fill” technique, will be measured under stable temperature conditions ranging from ambient to 150°C. These measured results will be fitted with a Simulated Annealing optimization algorithm to accurately calculate various complex material parameters comprising loss characteristics. The elastic, piezoelectric and dielectric constants of the PMN-PT/epoxy piezoelectric composite at different temperatures are to be analyzed.

**RESULTS:** The fundamental acoustic and electric properties of the composite ultrasonic transducer will be theoretically simulated and analyzed with calculated complex material parameters at various temperatures.

**CONCLUSIONS:** The theoretical and experimental results of this investigation will offer a support to design and optimization of high performance ultrasonic transducers for elevated temperature biomedical applications with single crystal/epoxy 1-3 composite piezoelectric materials.



**NO.34**

**CONTROL ID:** 1683856

**TITLE:** AN IMPROVED MRI GUIDED ULTRASOUND SYSTEM FOR SUPERFICIAL TUMOR HYPERTHERMIA

**AUTHORS/INSTITUTIONS:** S. Chen, G. Shen, Z. Su, M. Zhu, S. Qiao, Y. Bo, Y. Chen, Biomedical Instrument Institute, Shanghai Jiao Tong University, Shanghai , CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Ultrasound hyperthermia is one of the most important methods in tumor treatment and characterized by high safety and non-invasiveness. Magnetic resonance temperature imaging (MRTI) is non-invasive and is widely applied in the field of tissue temperature monitoring. The proton resonance frequency (PRF) method is relatively advanced among various MRTI methods, which is near-independence of tissue composition and is able to provide accurate temperature information. This research is conducted on an MRI guided ultrasound superficial tumor hyperthermia instrument based on PRF method.

**METHODS:** Based on the feedback of temperature, the system calculates the proper output power of the amplifier and the flow rate of circulating cooling water using strategically advanced PID algorithm, adjusts the overall treatment time and by the excited transducer, submits ultrasound wave, which goes through water, the coupling agent layer and skin to the lesions and keeps the temperature of the targeted area at 42-43 degrees C while skin surface not scalded. The transition of the signals mentioned above is completed by the upper controller and the lower control chip. The former sets controlling parameters of ultrasound output amplifier and by RS232 communication interface sends them to the latter, which executes the instructions. The temperature measurement module consists of an MR scanner and a module, located in the control system, receives specific images from the scanner and deduces the temperature change of skin and the targeted area from the phase difference of between reference data and data acquired during heating. This precise temperature information then is transmitted to the upper controller, guiding tumor hyperthermia. Some essential components are used for the sake of electromagnetic leakage or interference between the MR scanner and the rest part of the system.

**RESULTS:** Up to now this system is on the research with animal experiment, during which its performance has reached our first-level expectations.

**CONCLUSIONS:** Ultrasound can be used to heat lesions non-invasively and MR scanning is harmless to human body and helpful in accurate positioning and non-invasive temperature measurement. In conclusion, this system can heat the targeted tumor area safely and effectively, achieving non-invasive and secure hyperthermia.



**NO.35**

**CONTROL ID:** 1666043

**TITLE:** FINITE ELEMENT SIMULATION OF ACOUSTIC WAVE PROPAGATION AND ENERGY DEPOSITION IN BONE DURING EXTRACORPOREAL SHOCK WAVE TREATMENT

**AUTHORS/INSTITUTIONS:** X. Wang, D. Zhang, J. Tu, School of Physics, Nanjing University, Key Laboratory of Modern Acoustics, Nanjing, Jiangsu, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** It is well known that extracorporeal shock wave treatment is capable of providing a non-surgical and relatively pain free alternative treatment modality for patients who suffer from musculoskeletal disorders but do not respond well to conservative treatments. However, the presence of musculoskeletal structures might significantly distort the propagation of incoming shock wave (SW) pulses in the body, which might make the acoustic energy be deflected and/or absorbed by intervening bones to induce undesired side-effects. The major objective of current work is to investigate how the SW field would change if a bony structure exists in the path of the acoustic wave.

**METHODS:** (1) based on linear elasticity and acoustic wave propagation equations a model of finite element method (FEM) was developed to examine SW propagation and deflection with the presence of a mimic musculoskeletal bone; (2) high-speed photography experiments were performed to record cavitation bubbles generated in the phantom gel with the presence of mimic bone; and (3) strain energy distributions in the bone were also calculated by numerical simulations.

**RESULTS:** (1) the SW field will be deflected with the presence of bony structure and varying deflection angles can be observed as the bone shifted in the z-direction relative to SW geometric focus (F2 focus); (2) SW deflection angles calculated by the FEM model agree well with experimental results obtained from high-speed photographs; and (3) based on FEM model temporal evolutions of strain energy distribution in the bone can also be evaluated with varied vertical distance between F2 focus and intended target point on the bone surface.

**CONCLUSIONS:** The present work indicates the proposed FEM model should be able to effectively predict SW propagation properties with taking into account of the interaction between shock wave and elastic bony structure. Combining MRI/CT scans and FEM model, it is possible to better understand SW propagation characteristics and energy deposition in musculoskeletal structure during ESWT, which is important for standardizing the treatment dosage, optimizing treatment protocols, and even providing patient-specific treatment guidance in clinic.





**NO.36**

**CONTROL ID:** 1699660

**TITLE:** Dose-effect Study of Pancreatic Cancer Cell Apoptosis Induced by Focused Ultrasound in Vitro

**AUTHORS/INSTITUTIONS:** Q. Guo, L. Jiang, B. Hu, Department of Ultrasound in Medicine, the Sixth People's Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA | Q. Guo, L. Jiang, B. Hu, Shanghai Institute of Ultrasound in Medicine, Shanghai, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** To investigate the optimal sonication protocol of focused ultrasound to induce pancreatic cancer cell apoptosis. Acquire the peak time of cell apoptosis after focused ultrasound sonication and provide the foundation for detection of focused ultrasound induced cell apoptosis in vivo.

**METHODS:** Human pancreatic cancer PaTu 8988t cell suspension was exposed to focused ultrasound sonication. Control group and focused ultrasound treatment group were established. According to the focused ultrasound doses, the treatment group was divided into low, medium and high dose group. For each group, pulsed sonication pattern and continuous sonication pattern were used. The cells after focused ultrasound sonication were stained with Alexa Fluor<sup>®</sup> 488 annexin V and propidium iodide (PI). The cell apoptosis and necrosis rate was counted using flow cytometry, and the apoptotic and necrotic cells was observed using fluorescence microscopy. The colony formation analysis was used to observe the proliferation inhibition caused by different focused ultrasound sonication.

**RESULTS:** The apoptosis rate of PaTu 8988t cell peaked at 24 hours after focused ultrasound sonication. Apoptotic cells increased significantly after focused ultrasound sonication. The highest cell apoptosis rate achieved with the medium dose group using continuous sonication pattern, in which the temperature of the cell suspension was 50°C - 60°C. The results of colony formation analysis showed that with the same sonication pattern, higher sonication dose resulted in greater inhibition of cell proliferation; and with the same sonication dose, continuous sonication pattern could inhibit cell proliferation much stronger than pulsed sonication pattern.

**CONCLUSIONS:** Medium dose focused ultrasound sonication with continuous pattern could maximally induce pancreatic cancer cell apoptosis in vitro and inhibit the cell proliferation.



**NO.37**

**CONTROL ID:** 1671053

**TITLE:** SONOLUMINESCENCE AND SONOCHEMILUMINESCENCE STUDY OF CAVITATION FIELD IN A 1.2MHZ FOCUSED ULTRASOUND

**AUTHORS/INSTITUTIONS:** H. Yin, Y. Qiao, H. Cao, M. Wan\*, The Key Laboratory of Biomedical Information Engineering of Ministry of Education, Department of Biomedical Engineering, School of Life Science and Technology, Xi' an Jiaotong University , Xi'an, Shanxi, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** We have investigated cavitation field in water, bubbles near a water-parenchyma interface in the focal region. In addition, two different shells coated UCAs were studied through this method.

**METHODS:** It was found that SL emissions were located in the post-focal region. The intensity of SCL in the focal region is usually the weakest because of "oversaturation". SL/SCL emissions located in the post-focal region and formed branch-like streamers. It is the connatural acoustic radiation force (ARF) that pushes the cavitation bubbles away from the source transducer. So an ARF offset appliance which could partly reduce the influences of ARF on bubbles was necessary to simulate the cavitation field in tissue where bubbles cannot easily move. Acoustic pressure mapping have been done to make sure that the acoustic field would not change in overall outline. We found that the SCL in the pre-focal region was the same as that in the post-focal region when the electric power was below 50W. However, when the electric power was 70W and 90W, bubbles broke the limitation of the acoustic potential well.

SCL was also employed to measure cavitation does and map the spatial distribution of cavitation near a water- parenchyma interface. It turns out that a short pulse length and a high duty cycle lead to high-efficiency erosion. Mechanical damage was also observed near the boundary of vessel in an acrylamide phantom.

Two different shells coated UCAs, lipid-shelled and polymer-shelled UCAs, were studied and compared. Due to its thin and soft coat, the lipid-shelled group had a maximum SCL intensity in pre-focal region at lower electric power than that of polymer-shelled group, and a brighter SCL intensity in post-focal region at high electric power.

**CONCLUSIONS:** Through this method, we found that the spatial distribution organized into special structures under different acoustic amplitudes. And as polymer-shelled UCAs are more resistant to acoustic pressure, they had a higher destruction power and showed less reactivation than lipid-shelled ones.



**NO.38**

**CONTROL ID:** 1682190

**TITLE:** : High-speed imaging of ultrasound-mediated bacterial biofilm removal

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**ABSTRACT BODY:**

**OBJECTIVES:** Bacterial biofilm infections on medical implants tend to have invasive treatment options with increasing recurrence rate, complications and costs with each treatment [1]. Ultrasound has been shown to be effective in bacterial biofilm disruption or enhancing the efficacy of antimicrobial agents against bacterial biofilm [2-4]. However, the mechanisms behind this behaviour are not fully understood. One of the objectives of this project is to study and report the cavitation activity or micro-bubbles interactions with bacterial biofilm during high frequency ultrasound exposure.

**METHODS:** We use a focused ultrasound transducer driven at 1.0 MHz with a 50  $\mu$ s burst pulse submerged in a water tank with de-ionized water. The p.n.p is kept at 2 Mpa across all experiments. E. coli is cultivated on Cell-Tak treated coverslips for 72 hours in TSB+0.2% Glucose at 30oC. Clean or biofilm-attached coverslips are placed vertically in the sonoporation chamber. SonoVue<sup>®</sup> ultrasound contrast agent micro-bubbles are added the sonoporation chamber filled with de-ionized water. Using a laser optical trapping setup we are able to trap and position a microbubble around 3  $\mu$ m initial bubble radius ( $R_0$ ) close to the vertical coverslip and more than 20  $R_0$  away from all other boundaries. The images are taken at up to 2 Million frames per second (Mfps) by the Cordin 550-62 high-speed camera. Our setup is similar to that used by Prentice, P. et al. (2005) [5].

**RESULTS:** We are able to capture high-speed image sequences of an oscillating microbubble with liquid jet towards a coverslip (with and without bacterial biofilm). For the case of ultrasound with microbubble on a coverslip with bacterial biofilm, we are able to capture the disruption of the biofilm due to cavitation.

**CONCLUSIONS:** Ongoing work focuses on different experimental configurations for the ultrasound frequency and intensity, intial bubble radius and stand-off distance etc. Computational simulations can also be undertaken to evaluate on this physical mechanism of ultrasound-mediated removal of bacterial biofilm.

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**NO.39**

**CONTROL ID:** 1669268

**TITLE:** STUDY OF THERML DOSE BEHIND RIBS CAUSED BY FOUSED ULTRASOUND

**AUTHORS/INSTITUTIONS:** X. Liu, F.Zhang, X. Gong, Institute of Acoustics, Nanjing, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Although the application of ultrasound has great potential, many outstanding issues still restrict their development, such as non-invasive temperature measurement, cavitation effects of HIFU treatment and so on. For example, ultrasound for the treatment of liver tissue, the impact of the ribs at this stage has not been taken into account. The high intensity ultrasound will induce nonlinear effects. The sound absorption of bone is usually an order, even in some specific cases, two orders larger than that of soft tissues. Furthermore, because the acoustic impedance of tissue and bones has large differences in the sound impedance, the bone interface will encounter a strong reflection, which will influence the distribution of acoustic energy.

**METHODS:** In order to describe the ribs on the nonlinear acoustic effects, we developed a three-dimensional model in the frequency domain and solve Khokhlov-Zabolotskaya-Kuznetsov (KZK) equation by the alternating direction implicit backward difference combination of forecasts and calibration method and get the non-linear sound field behind ribs. We also studied in detail the temperature change by the ribs block.

**RESULTS:** The results showed that: If there is no barrier ribs, the time of the ultrasound heat tissue to reach the critical thermal maximum dose of 240 min required 31 s, while if there are ribs on both sides of ultrasound propagation path, it required 43 s, a difference of more than 30%. If the rib is placed in the middle of the sound propagation path, after a 60 s of ultrasound irradiation, the maximum temperature rise of only about 1.7 degree Celsius, the temperature almost does not produce any effective thermal dose and can not achieve the desired therapeutic effect.

**CONCLUSIONS:** Ribs have great influence on the thermal dose during the ultrasound thermay. For hyperthermia application concerned, we also concerned about the thermal dose by the influence of the ribs.The authors would like to acknowledge the National Basic Research Program of China (No.2012CB921504, No.2011CB707902),financial support of the National Natural Science Foundation of China (No. 11274166), fundamental Research Funds for the Central Universities (No.1113020403, No.1101020402), State Key Laboratory of Acoustics, Chinese Academy of Sciences(SKLA201207).



**NO.40**

**CONTROL ID:** 1699514

**TITLE:** NUMERICAL SIMULATION OF TEMPERATURE DISTRIBUTION DURING TRANSCRANIAL TUMOR THERAPY OF HIGH INTENSITY FOCUSED ULTRASOUND

**AUTHORS/INSTITUTIONS:** Q. Zhang, Y. Wang, W. Zhou, F. Xue, J. Zhang, X. Jian, Biomedical Engineering , Tianjin Medical University, Tianjin, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Due to the strong phase and amplitude aberration of the acoustic wave induced by the skull, the brain tumor therapy using the high intensity focused ultrasound (HIFU) is limited. However, the time reversal method could correct the aberration and produce a focus. To provide a reference for clinical therapeutic dose formulation, the temperature distribution and lesion volume are analyzed using the numerical simulation.

**METHODS:** The adopted numerical simulation is based on a transcranial ultrasound therapy model, including an 8 circle-element curved phased array transducer and the normal brain tissue. The acoustic pressure and temperature elevation are calculated using the approximation of Westervelt Formula and the Pennes bio-heat Transfer Equation. In addition, the Time Reversal theory combined with eliminating hot spot technique is applied to optimize the temperature distribution. The lesion volume is evaluated according to temperature threshold theory after setting different input power and exposure time.

**RESULTS:** When the input intensity and exposure time is  $3\text{W}/\text{cm}^2$  and 20s, the lesion volume is  $44\text{mm}^3$  and the temperature inside and outside of skull surface is  $54.3^\circ\text{C}$  and  $43.5^\circ\text{C}$  without eliminating the peak temperature in the skull. However , the lesion volume is  $31\text{mm}^3$  and the temperature inside and outside of skull surface is  $40^\circ\text{C}$  and  $38^\circ\text{C}$  with eliminating the peak temperature. After a second time eliminating operation, a lower temperature in skull is obtained, but the lesion volume is smaller than the one before. Compared with non-skull model, it is necessary to increase the input power and exposure time for realizing the same size lesion volume in transcranial model due to the attenuation, reflection and refraction effect.

**CONCLUSIONS:** The lesion region could be restored at the expected location by the time reversal method. Although the lesion volume reduces after eliminating the peak temperature in the skull and more input power and exposure time is required, the normal tissue around skull could be avoided injury during HIFU therapy. The prediction of thermal deposition in the skull and the lesion region would provide a reference for clinical treatment.



**NO.41**

**CONTROL ID:** 1699634

**TITLE:** EVALUATION OF HIFU-INDUCED LESION REGION USING TEMPERATURE THRESHOLD AND EQUIVALENT THERMAL DOSE METHODS

**AUTHORS/INSTITUTIONS:** S. Chang, F. Xue, W. Zhou, J. Zhang, X. Jian, School of Biomedical Engineering, Tianjin Medical University, Tianjin, Tianjin, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** Usually, numerical simulation is used to predict the acoustic field and temperature distribution of high intensity focused ultrasound (HIFU). To acquire an effective evaluation method for lesion region in the simulation, the lesion volume obtained by the temperature threshold (TRT) and equivalent thermal dose (ETD) methods were compared using simulation and animal tissue experiment *in vitro*.

**METHODS:** In the simulation, considering the non-linear characteristics of the ultrasound and the influence of tissue acoustic properties, a model was established according to the *in vitro* tissue experiment. The Westervelt formula and Pennes bio-heat transfer equation were used along with the Finite Difference Time Domain (FDTD) method, to get the temperature distribution induced by HIFU, and then the lesion volume was calculated based on the TRT and ETD method respectively. 60 degree C was selected as the threshold in the TRT method, and 240min was selected as the time threshold in the ETD method. In the experiment, the fresh bovine liver was exposed for 8s, 10s, 12s under different power conditions (150W, 170W, 190W, 210W), and the exposure was repeated 6 times under the same dose. After the exposures, the liver was sliced and photographed every 0.2mm, and the area of the lesion region in every photo was calculated. Then, every value of the areas was multiplied by 0.2mm, and summed to get the approximation volume of the lesion region.

**RESULTS:** The lesion volume of the region calculated by TRT method in simulation was much closer to the lesion volume obtained in the experiment, and the lesion volume above 60 degreeC was larger than the experimental results, but the volume deviation was not exceed 10%. The volume of the lesion region calculated by ETD method was larger than that calculated by TRT method in simulation, and the volume deviations were ranged from 4.9% to 23.7%.

**CONCLUSIONS:** In HIFU simulation, the TRT method can better evaluate the lesion region than the ETD method. Therefore, this method (threshold= 60 degreeC) could be used to determine the therapeutic dose in the clinical treatment plan.



**NO.42**

**CONTROL ID:** 1678259

**TITLE:** Research on the lesion segmentation of breast tumor MR images based on FCM-DS theory

**AUTHORS/INSTITUTIONS:** L. Zhang, W. Ma, X. Shen, Y. Li, L. Chen, Y. Zhu, S. Zhang, School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA|Y. Yu, School of Computer, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi, CHINA|

**ABSTRACT BODY:**

**OBJECTIVES:** Magnetic resonance imaging (MRI) plays an important role in the treatment of breast tumor by high intensity focused ultrasound (HIFU). The doctors evaluate the scale, distribution and the statement of benign or malignancy of breast tumor by analyzing variety modalities of MRI, such as the T2, DWI and DCE images for making accurate preoperative treatment plan and evaluating the effect of the operation.

**METHODS:** This paper presents a method of lesion segmentation of breast tumor based on FCM-DS theory. Fuzzy c-means clustering (FCM) algorithm combined with Dempster-Shafer (DS) theory is used to process the uncertainty of information, segmenting the lesion areas on DWI and DCE modalities of MRI and reducing the scale of the uncertain parts.

**RESULTS:** Experiment results show that FCM-DS can fuse the DWI and DCE images to achieve accurate segmentation and display the statement of benign or malignancy of lesion area by Time-Intensity Curve (TIC).

**CONCLUSIONS:** FCM-DS algorithm could be beneficial in making preoperative treatment plan and evaluating the effect of the therapy.



**NO.43**

**CONTROL ID:** 1699111

**TITLE:** HEATING SIMULATIONS OF PULSED HIGH-INTENSITY FOCUSED ULTRASOUND IN THE PRESENCE OF HETEROGENEOUS TISSUE

**AUTHORS/INSTITUTIONS:** H. Zhou, Y. Zheng, H. Duan, Key laboratory of Biomedical Engineering of Ministry of Education, Zhejiang University, Hangzhou, Zhejiang, CHINA |

**ABSTRACT BODY:**

**OBJECTIVES:** To propose a numerical model for evaluating the distribution of the acoustic pressure, acoustic intensity, and temperature beneath the heterogeneous abdominal wall or the heterogeneous chest wall under nonablative pulsed high-intensity ultrasound treatments.

**METHODS:** A k-space pseudospectral method was developed on the staggered-grid to solve the first-order nonlinear acoustic equations. The heterogeneous tissue in the simulation was represented by the digital tissue cross sections.

**RESULTS:** The presents of the heterogeneous tissue can influence the distribution of the acoustic intensity and temperature of the focus area. The intensity decreased by 3.8 dB on the focal point compared with homogeneous tissue. Furthermore, compared with Abersim and conventional FDTD methods, the proposed method is still stable when the high dissipative tissue (e.g., bone) presents.

**CONCLUSIONS:** The temperature of the focused region in the tissue is probably low in most situations.





**NO.44**

**CONTROL ID:** 1672005

**TITLE:** DEDICATED 8 CHANNEL HEAD RECEIVE ARRAY FOR TRANSCRANIAL MR GUIDED FOCUSED ULTRASOUND SURGERY

**AUTHORS/INSTITUTIONS:** B. Werner, E. Martin, Center for MR-Research, University Children's Hospital, Zurich, ZH, SWITZERLAND|F. Resmer, T. Lanz, Rapid Biomedical GmbH, Rimpfing, GERMANY|

**ABSTRACT BODY:**

**OBJECTIVE:** Transcranial MR guided Focused Ultrasound Surgery (TcMRgFUS) is a new treatment modality for image-guided, non-invasive neurosurgery. However, while intra-interventional high-quality MR imaging is a mission-critical prerequisite it remains challenging due to mechanical constraints and electronic complexity imposed by the ultrasound transducer setup. Here, a dedicated 8 channel MR head receive array has been developed to support the TcMRgFUS intervention.

**METHODS:** The front-end of the InSightec ExAblate 4000 Brain system (InSightec Ltd., Tirat Carmel, Israel) consists of a large phased array transducer supported by a mechanical 4-axis positioner. A stereotactic frame immobilizes the patient's cranium inside the transducer. The MR array (inner diameter 345mm, outer diameter 375mm, length 240mm) wraps tightly around the transducer. It comprises an anterior section and a posterior section of 4 receive channels each. Every channel contains an active and a passive decoupling circuit and is connected to a low impedance preamplifier [1] via a 50 Ω matching network followed by a phase shifter for preamplifier decoupling [1]. Next neighbor elements are decoupled with shared inductors [2].

**RESULTS:** Compared to the system BODY coil the image SNR is improved by a factor of 3-4 in phantom tests and in clinical treatments, allowing to significantly reduce acquisition time of navigation images while still supporting the neurosurgeon by improved image quality. The MR array was certified as a medical device and has been successfully tested in ongoing clinical phase I studies for functional TcMRgFUS neurosurgery [3] and TcMRgFUS tumor surgery. It offers full head coverage and parallel imaging capability.

**CONCLUSIONS:** The TcMRgFUS environment is very challenging for MR imaging owing to the system electronics of the phased array ultrasound transducer, its copper shielded transducer surface with water bath and the stereotactic fixation of the patient head. Here we demonstrate the advantages of integrating an MR array into the TcMRgFUS frontend: handling, image stability and SNR are significantly improved. This work was supported by NCCR Co-Me and GAKF Innoververein Kinderspital Zürich. [1] P. Roemer et al., MRM 16: pp.192 (1990) [2] J. Wang, Proc. ISMRM 4 p.1434 (1996) [3] E. Martin, et al., Annals of Neurology Vol 66 No 6 December 2009



**NO.45**

**CONTROL ID:** 1671966

**TITLE:** STUDY OF MECHANISM OF SONOPORATION USING LIPID BILAYER AND SURFACE-MODIFIED MICROBUBBLE

**AUTHORS/INSTITUTIONS:** K. Hirose, T. Azuma, A. Sasaki, S. Takagi, Y. Matsumoto, Department of Mechanical Engineering, Faculty of Engineering, The University of Tokyo, Tokyo, JAPAN|K. Yoshinaka, National Institute of Advanced Industrial Science and Technology, Tsukuba, JAPAN|

**ABSTRACT BODY:**

**OBJECTIVE:** Gene therapy has been expected as an advanced therapy for genetic diseases. Micro-bubble enhanced sonoporation is one of these therapies and expected to be a good controllability, less invasive, and localization of treatment area, but its efficiency is not enough. In previous research, it was reported that induction rates depend on conditions of ultrasound burst wave, but more detailed mechanism remains explained. The objective of this research was to analyze the mechanism and obtain an optima designing method to increase induction efficiency on the basis of an observation of an interaction between microbubbles and lipid bilayer, which was used as artificial cell membrane.

**METHODS:** We used the lipid bilayer instead of cell membrane to set up experiment system in which we could observe phenomenon stably, and used biotin-avidin binding to fix position of microbubble near lipid bilayer. First we will build lipid bilayer bound with biotin by Black Lipid Membrane (BLM) method. Then, ultrasound irradiation system and observation system will be built and microbubble and lipid bilayer will be observed under ultrasound sonication.

**RESULTS:** We built lipid bilayer using BLM method. The thickness of layer was evaluated by measuring a capacitance of layer. The capacitance of lipid layer was 3.3 nF which was as same as that of theoretical value of the experiment system in this research (3.28 nF). From this experiment, we confirmed that lipid bilayer was built by BLM method. Using this experiment system, we also found that the duration of lipid bilayer was more than an hour, which confirmed that lipid bilayer could endure through process such as binding microbubble with lipid bilayer and irradiation of ultrasound.

**CONCLUSIONS:** We confirmed that stable lipid bilayer could be built using BLM method. We are trying to modify biotin to lipid bilayer and bind microbubble to lipid bilayer, and considering experiment system in which we can observe microbubble and lipid bilayer under ultrasound.



**NO. 46**

**CONTROL ID:** 1668988

**TITLE:** TEMPERATURE MEASUREMENT OF HIFU USING A THIN-FILM THERMOCOUPLE ARRAY

**AUTHORS/INSTITUTIONS:** K. Matsuki, R. Narumi, T. Azuma, A. Sasaki, T. Kanagawa, S. Takagi, Y. Matsumoto, Mechanical Engineering, The University of Tokyo, Tokyo, JAPAN | K. Yoshinaka, National Institute of Advanced Industrial Science and Technology, Tsukuba, JAPAN | K. Okita, Mechanical Engineering, Nihon University, Tokyo, JAPAN |

**ABSTRACT BODY:**

**OBJECTIVE:** A temperature distribution measurement of HIFU with a sufficient temperature, spatial and temporal resolution was not available. When metal thermocouples are inserted in an ultrasound field, artificial heating occurs, which is referred to as viscous heating. It occurs because of a steep velocity gradient of a traverse wave on the surface of a thermocouple. We aim to realize the measurement method of temperature distribution free from viscous heating.

**METHODS:** A prototype thin-film thermocouple (TFTC) array with 49 measurement points was developed. Thermocouple printed wires (200 nm diameter, 50  $\mu\text{m}$  long) were fabricated on a 25- $\mu\text{m}$ -thick polyimide film. The printed wire and film were sufficiently thin so as to not disturb ultrasonic propagation. In addition, the wire diameter was approximately one-thousandth that of conventional fine thermocouples, so that viscous heating was minimized. It is necessary to clarify influence on thermal measurement error caused by the TFTC array. It was difficult to estimate independently both heating sources, ultrasound absorption in propagation media and viscous heating at the surface of the thermocouple. The width of temperature increase distribution by ultrasound absorption was much wider than that by viscous heating. These effects were separable by measuring the integration value of temperature distribution because the effect of ultrasound absorption was dominant in this value. In the study, the peak temperature and the width of heating area estimated by a shift of propagation time passing through temperature rise area were measured. A remaining unknown parameter, ratio of these two quantities, was estimated from the comparison between propagation time shifts in the experiment and calculation, which was calculated by solving the thermal diffusion equation in several different ratios of these two quantities.

**RESULTS:** The ratio of the quantity of heat by viscous heating at the surface of the thermo-couple to that of heat by ultrasound absorption in the propagation media was 1 to 3 % when ultrasound frequency was 2.2 MHz and focal intensities were 190 and 320 W/cm<sup>2</sup>. It succeeded in evaluating the influence by the TFTC quantitatively.

**CONCLUSIONS:** We proposed the way to evaluate the effect of viscous heating by measuring the propagation time through heating area. The independent estimation of the both effect of viscous heating and media absorption was realized.



**NO.47**

**CONTROL ID:** 1681677

**TITLE:** LOW FIELD HOME-BUILT PERMANENT MR GUIDED FOCUSED ULTRASOUND INTEGRATION SYSTEM

**AUTHORS/INSTITUTIONS:** G. Li, D. Li, J. Dong, Oncology, Weifang medical school, Weifang, Shandong, CHINA | D. Li, J. Dong, Sales, Shanghai A&S Co.Ltd, Shanghai, Shanghai, CHINA |

**ABSTRACT BODY:**

**OBJECTIVE:** High-intensity focused ultrasound (HIFU) is used for cure tumor by producing high temperature in the body. The positioning method is the key factor of safety and efficiency in the HIFU treatment. After using ultrasound scanner positioning method in the previous generation, the latest HIFU system use magnetic resonance (MR) to position generally. The use of magnetic resonance is high field superconducting MR in the world at present, we hope to develop the system of low field home-built permanent MR guided HIFU integration system, which can improve the image quality compared with the ultrasound scanner guided HIFU, and is inexpensive compared with high field MR.

**METHODS:** We have done so a lot of research on low field home-built permanent MR and HIFU that the two system as one, to achieve a real integration system. Traditional MR is C-shaped, so we transform magnet to U-shaped, and then place HIFU treatment head above the opening on the MR. This idea is the first, unique in the world. At the same time, we do a lot of research in the magnetic compatibility, fast magnetic resonance imaging, magnetic resonance temperature measurement, phased array transducers, HIFU treatment plan by the latest technology and a breakthrough. After complete the integration system, we verify the system performance in type test, and validate function in experiments.

**RESULTS:** By type test and related experiments to validate that the integration system can provide the following features: diagnostic by MR, positioning by MR, therapy by HIFU, monitoring by MR, thermometry or imaging for efficacy assessment by MR; and the performance of the system has completed the intended requirements, the design is accord with clinical applications.

**CONCLUSIONS:** In the low field home-built permanent MR guided, the integration system can achieve all the functions, the positioning image is much clearer than ultrasound scanner, and the price of low field MR is much cheaper than high field MR, means that the integration system reduce the cost of products greatly and improve the practicability. But there is a certain gap of the image quality needs to be further improved in the integration system compare with high field superconducting MR.