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FULL PAPER

A study on the post-radiotherapy changes of temporomandibular joint in nasopharyngeal carcinoma patients

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Objective: Radiation-induced trismus, which is resulted from damage of the temporomandibular joint (TMJ), is one of the common late complications in nasopharyngeal carcinoma (NPC) patients after radical radiotherapy. This study investigated the radiation induced TMJ changes using ultrasonography in post-radiotherapy (post-RT) NPC patients.

Methods: 114 NPC patients, who had completed radiotherapy for more than 4 years, were assessed with the maximum incisal distance (MID) and ultrasonography examination of TMJ from which the maximum disc thickness of the joint disc, the condyle irregularity (CI), joint vascularity (JV) and relative muscle echogenicity were assessed. The same assessments were conducted on 100 age-matched normal subjects. The results were compared among the patients with and without trismus, and the control group. The mean doses to the TMJ were estimated using the treatment planning system and their correlation with the magnitude of MID was also investigated by the Pearson correlation test.

Results: 39 out of the 114 patients (34.2%) presented with trismus. The average mean TMJ for all patients was 41.4 Gy, in which patients with trismus was significantly higher than patients without trismus (p = 0.017). The mean MID of patient group was significantly lower than control group (p < 0.001). The mean maximum disc thickness of the patient group was significantly smaller than the control group, whereas the mean CI and JV were significantly higher in patient group. For relative muscle echogenicity, a higher percentage of the control group showed hyperechoic pterygoid muscle than the patient group. The mean total dose to the TMJs for the patient group was 41.4 Gy and there was a mild negative correlation between the mean TMJ dose and the MID (r = −350).

Conclusion: The TMJ in post-RT NPC patients showed reduction of disc thickness, increase of CI and JV. Patients with trismus demonstrated thinner disc thickness and higher JV than those without trismus.

Advances in knowledge: Our study was the first cross-sectional comparative study involving over 100 patients and normal subjects that used ultrasound to assess the radiation-induced morphological changes of TMJ. Post-RT TMJ changes characterized by the reduction of disc thickness, increase of CI and JV were detected in the NPC patients. The parameters used in this study were able to detect the morphological differences between the patient group and control group, and therefore can be effectively used to monitor the TMJ condition of post-RT NPC patients.

INTRODUCTION

Due to the close proximity between target volume of nasopharyngeal carcinoma (NPC) and the temporomandibular joint (TMJ), external beam radiotherapy often delivers high radiation dose to the TMJ. This may result in joint dysfunction such as radiation-induced trismus, which is one of the common late complications in NPC patients after treatment. This affects about 35–45% of the post-radiotherapy (post-RT) patients[1–3] with a mean decrease in initial interincisal distance of 32% in 4 years after treatment.[4] Trismus adversely affects quality of life such as speech impairment and diminished vocal quality to difficulty in mastication and swallowing, leading to poor nutritional status and oral hygiene. The severity of trimus can be classified into three grades measured by the maximum interincisal distance (MID), in which the ranges of MID for Grade 1 to 3 are 3.5–2.5, 2.5–1.0 and <1.0 cm in adults, respectively.[5] Although it has been reported that radiation-induced trismus is mainly due to fibrosis and scarring of the muscles around the TMJ,[6,7] the understanding about the changes of TMJ after radiation treatment is still limited.

Other possible associations are the changes in joint morphology including vascularization and joint disc dimension. Acquiring such information can facilitate early diagnosis and regular monitoring of the condition for patients. Treatment of radiation-induced trismus is much more effective if conducted at early stage. Unfortunately this condition usually develops slowly and silently, and not noticed by patient until late stage.[8]

Early stage trismus cannot be easily diagnosed only based on clinical examination, but requires the help of a suitable imaging modality. Ultrasonography is one of the effective imaging tools for TMJ, which is non-invasive, readily available, and has the potential to provide assessment of joint vascularization and real-time dynamic examination. Therefore the aim of this study was to investigate the radiation-induced TMJ changes in terms of joint morphology using ultrasonography in post-RT) NPC patients.

MATERIALS AND METHODS

114 adult NPC patients (male = 75, female = 39, average age = 53.0 years), who had completed radiotherapy for more than 4 years with no sign of disease recurrence, were recruited between April 2013 and August 2014 in the Clinical Oncology Department of Queen Mary Hospital, Hong Kong. Ethics approval was obtained from the Institutional Review Board IRB of the hospital. Informed consent was obtained from the patients before they joined the study. Since trismus could be one of the symptoms of NPC if the tumour involved the TMJ, patients with pre-RT trismus or joint defect were excluded from the study. The patient characteristics are shown in Table 1.

Table 1. Patient characteristics

	Patient number (%)	
	Patient-T (n = 39)	Patient-NT (n = 75)
Age (Year)		
≤50	8 (20.5%)	17 (22.7%)
51–55	7 (17.9%)	14 (18.7%)
56–60	8 (20.5%)	21 (28.0%)
61–69	11 (28.2%)	20 (26.7%)
≥70	5 (12.8%)	3 (4.0%)
Gender		
Male	24 (61.5%)	51 (68.0%)
Female	15 (38.5%)	24 (32.0%)
Post-RT duration (Year)		
4–10	5 (12.8%)	24 (32.0%)
11–20	17 (43.6%)	35 (46.7%)
≥21	17 (43.6%)	16 (21.3%)
Radiotherapy technique		
Conventional 2D/3D	26 (66.7%)	33 (44.0%)
IMRT	13 (33.3%)	42 (56.0%)
Stage		
I	4 (10.3%)	14 (18.7%)
II	15 (38.5%)	24 (32.0%)
III	11 (28.2%)	21 (28.0%)
IVa	8 (20.5%)	13 (17.2%)
Unknown	1 (2.7%)	2 (4.0%)

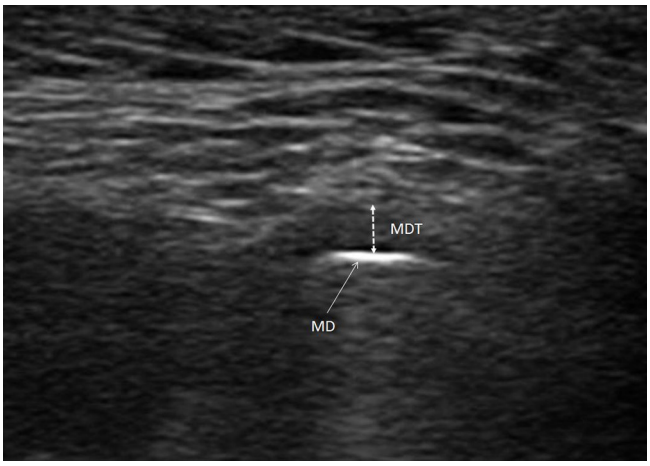
IMRT, intensitymodulated radiotherapy; Patient-T, patients with trismus; Patient-NT, patients without trismus; Post-RT, post radiotherapy.

The radiation dose to the TMJ was estimated by retrieving their treatment plans from the treatment planning system. Mean doses of the left and right TMJs in each patient were generated from their respective dose volume histogram. The MID of the patients was measured using a caliper when the patients opened their mouth to the greatest extent, which was an indication of the severity of trismus. The measurement was carried out three times and the average value was calculated for analysis. The correlation between the TMJ dose and MID in the patients was also investigated using the Pearson correlation test.

In addition, each subject received ultrasonography examination of TMJ using the Esaote MyLab Twice ultrasound unit in conjunction with a 4–13 MHz linear transducer (Esaote, Genoa, Italy). The left and right TMJs were scanned separately with the patient lying on a couch and head turned to the opposite side of scanning. Both transverse and longitudinal scans of each TMJ were taken. In each scan, the thickness of the joint disc, the irregularity of the mandibular condyle, echogenicity of lateral pterygoid muscle and the joint vascularity (JV) were assessed.

The maximum disc thickness (MDT) was measured by the perpendicular line joining the "peak" of the mandibular condyle and the uppermost part of the corresponding point at the glenoid fossa of the temporal bone using the electronic caliper (Figure 1). The condyle irregularity (CI) was assessed by inspecting the whole surface of the mandibular condyle and identifying the regions of irregularity (Figure 2). It was expressed in percentage of the portion of irregularity over the entire length of the condyle and multiplied. The echogenicity of lateral pterygoid muscle was a relative parameter and it was assessed by comparing the echogenicity of the pterygoid muscle with that of the patient's thumb muscle (thenar eminence), which had not received any radiation (Figure 3). The relative muscle echogenicity (RME) was classified as hyperechoic when it appeared to be "brighter" than the thumb muscle in the ultrasound image, and the opposite condition would be graded as hypoechoic. Isoechoic was used to describe the condition that both muscle demonstrated similar brightness. Power Doppler ultrasound was used to assess the JV. The Doppler setting was standardized for high sensitivity in the detection of blood vessels and with minimum artefact: pulse repetition frequency was 750 Hz and low wall filter. The colour gain was first increased to a level which showed colour noise and then decreased to the level that the noise was just disappeared. A standard colour box of 1 cm height x 2 cm width was placed over the centre of the TMJ (Figure 4). For each power Doppler

Figure 1. Ultrasound image showing the measurement of MDT of TMJ. MD = mandibular condyle. MDT, maximum disc thickness; TMJ, temporomandibular joint.



ultrasound image, the degree of JV expressed in percentage was calculated by a customized program using MATLAB® software (MathWorks, MA, USA). Using the software Microsoft Paint (v. 5.1; Microsoft Corporation, Redmond, WA), the colour box covered the TMJ (*i.e.* region of interest, ROI) were manually outlined on the power Doppler ultrasound image. The image with the ROI outlined was then analysed with MATLAB®. Using the customized algorithm, the ROI was firstly extracted from the image and the total number of pixels of the ROI was counted by the algorithm. Subsequently, the colour pixels coded by power Doppler ultrasound were extracted from the ROI, and the number of colour pixels was counted. The JV was then calculated by the following equation:

$$JV = \frac{\text{Number of colour pixels within the ROI}}{\text{Total number of pixels within the ROI}} \times 100$$

100 normal adult subjects (male = 53, female = 47, average age = 48.1 years), age matched with the patient group within ±5 years and with no previous irradiation and injury in the TMJ, were recruited as the control group. Informed consent was obtained before they joined the study. Each normal subject underwent the same TMJ assessments as for the patient group. All the ultrasound examinations and measurements for both patient and control groups were carried out by the same operator.

Based on the definition of trismus suggested by previous reports,[9,10] patients with MID ≤3.5 cm were defined as presenting with trismus and they were classified into the "Patient-T" group, while the other patients with MID ≥3.5 cm were classified as the "Patient-NT" group. Comparison was made among the patients with and without trismus and the control group, which was useful to detect the characteristic morphological features of the TMJ in post-RT patients presenting with trismus and how they were different from the normal subjects. One way analysis of variance was used to test the significance of their differences in MDT, CI, JV and MID. The post hoc Tukey test was used to provide the ranking in case there was significant difference among the three groups.

RESULTS

A total of 228 and 200 TMJs were scanned for the patient and control groups respectively. The patient characteristics are shown in Table 1. The MID of the patient group ranged from15 to 53 mm (mean = 35.0 ± 9.4 mm), which was significantly lower than that of the control group (range: 27–61 mm, mean = 47.2 ± 6.5 mm) ($p < 0.001$). Besides, higher percentage of trismus (MID ≤3.5) incidences were found in the patient group (Figure 5), in which 39 out of the 114 patients (34.2%) presented with trismus; whereas it was only 4.0% in the control group, which were likely caused by other factors such as exceptional small month size, prior joint infection or dental treatment. The mean total dose to the TMJs for the entire patient group was 41.4 Gy, with the majority lied between 41–45 Gy (Figure 6). When comparing between patients with and without trismus, higher percentage of patients in the Patient-T group were treated by conventional radiotherapy (66.7%) than intensity modulated radiotherapy (IMRT) (44.0%; Table 1). Furthermore, the mean TMJ doses in the Patient-T group were higher than the Patient-NT group, with the difference of the right TMJ reaching statistical significance ($p = 0.017$) (Table 2). In addition, there was a mild negative correlation between the mean TMJ dose and the MID based on the Pearson correlation test ($r = -350$).

For the ultrasound examination, the mean MDT of the patient groups was smaller than that of the control group in both transverse and longitudinal scans ($p = 0.039$ and 0.04, respectively) (Table 3). When comparing between the patients with and without trismus, the Patient-T group showed significantly smaller mean MDT than the Patient-NT group in the transverse

Figure 2. Ultrasound image showing the CI of TMJ. CI, condyle irregularity; TMJ, temporomandibularjoint.

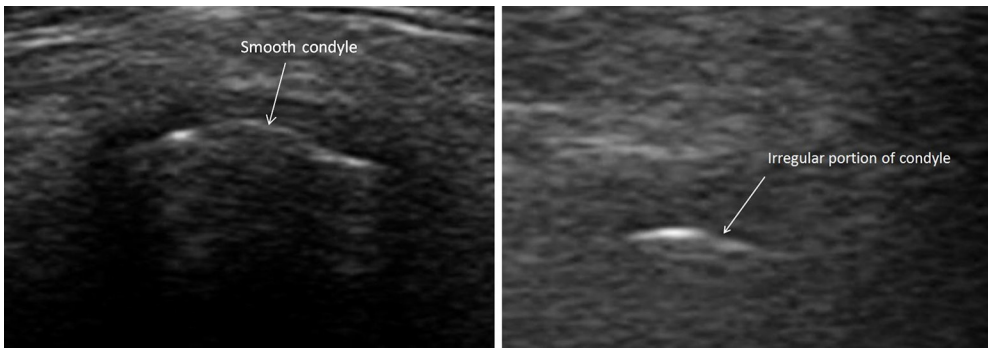
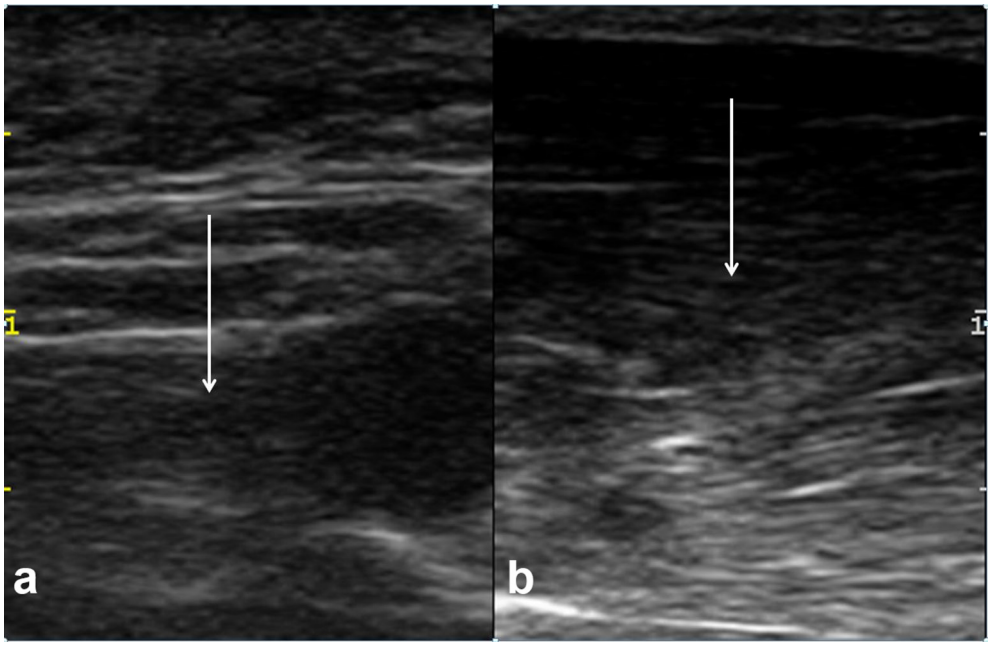
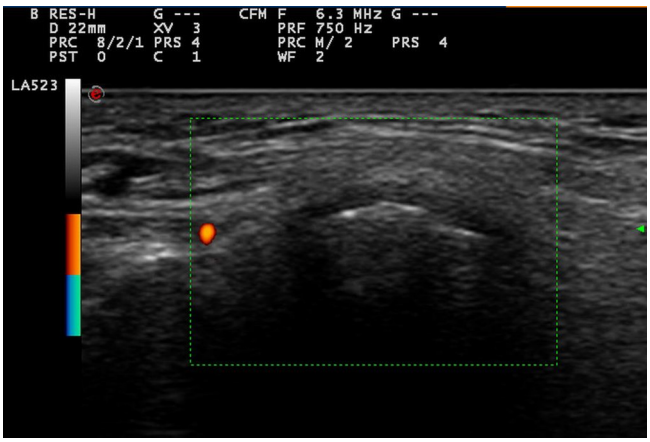


Figure 3. Ultrasound image showing the assessment of RME of TMJ. (a) pterygoid muscle; (b) the thumb muscle. The arrows indicate the muscles. This is an example of hypoechoic RME. RME, relativemuscle echogenicity; TMJ, temporomandibularjoint.



scan and marginally in the longitudinal scan. For CI, the mean values of the control group were significantly lower than those of the patient groups in both transverse and longitudinal scans (p = 0.10 and <0.001, respectively), but no significant difference was observed between the Patient-T and Patient-NT groups. For JV, the control group demonstrated significantly lower percentage than that of the patient groups in the longitudinal scans (p = 0.042) and the Patient-T group was marginally higher JV than the Patient-NT group. For the RME of the lateral pterygoid muscle, majority of the subjects (over 60%) in both the patient and control groups belonged to hypoechoic (Table 4). However, slightly higher percentage of hypoechoic and lower percentage of hyperechoic RME were found in the patient groups compared with the control group. Little difference was observed between the patients with and without trismus.

Figure 4. Diagram showing the assessment of JV of TMJ using MatLab software on Doppler ultrasound image. JV, joint vascularity; TMJ, temporomandibular joint.



DISCUSSION

Our study was the first cross-sectional comparative study that used ultrasound to assess the radiation-induced morphological changes of TMJ. We obtained a post-RT trismus incidence of about 35%, which was similar to those data reported in previous related studies.[1,2] Since the patients of this cohort were treated with either conventional or IMRT, there was a relatively wide range of mean dose delivered to the TMJ. This could explain that there was fairly large variation of MID in the patient group as the severity of trismus was reported to be associated with the TMJ dose.[11] This phenomenon was reflected by the mild negative correlation between mean TMJ dose and MID. This implied that minimizing the dose to the TMJ in radiotherapy treatment planning could reduce the severity of trismus. The significantly higher mean TMJ dose in the Patient-T group over the Patient-NT group was because a higher percentage of the Patient-T group patients were treated by the conventional techniques which were less effective in sparing the TMJ compared with IMRT. The irradiation of the TMJ to relatively high dose in NPC patients could explain for the fact that there was significant higher incidence of trismus with a reduction of mean MID by about 26% the in the patient group (35.0 mm) compared with the control group (47.2 mm).

About the ultrasound findings, the joint disc was thinner in the patient group than the control group by around 11.0%, which was consistent between the longitudinal and transverse scans. Since the cartilage of the disc is mainly composed of collagen fibres and proteoglycans, the thinning of the disc could be the result of the loss of collagen fibres due to radiation damage to the TMJ. Since the fibre system of the disc served as stress distribution function,[12] loosing of the fibres in the disc could affect the joint movement and subsequently leading to trismus.

Figure 5. Histograms showing the spread of MID for the patient and control group. MID, maximum incisal distance.

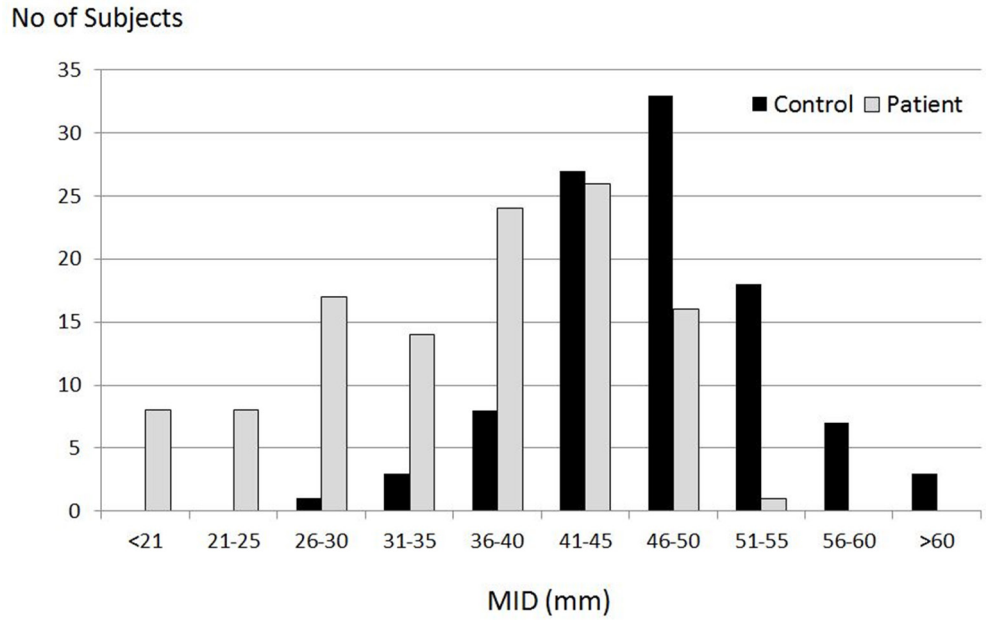


Figure 6. Histogram showing the spread of mean TMJ doses in patient group. Each bar indicates the absolute number of patients. The grey bar represents the patients presenting with trismus whereas the black bar represents patients without trismus. TMJ, temporomandibular joint.

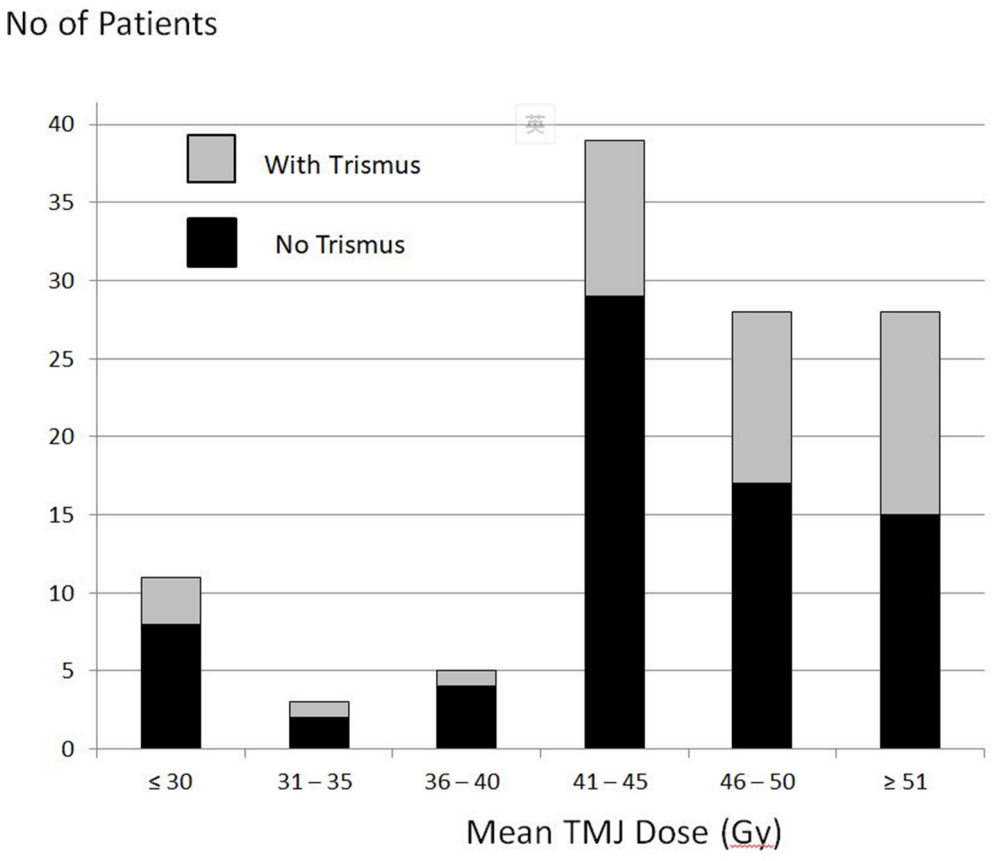


Table 2. Comparison of mean TMJ doses between patients with and without trismus

	Mean dose ± SD (Gy)			
	Patient-T (n = 39)	Patient-NT (n = 75)	p-value	All patients (n = 114)
L TMJ	43.1 ± 8.4	39.5 ± 10.4	0.065	41.3 ± 9.4
R TMJ	44.1 ± 10.1	38.6 ± 12.2	0.017	41.4 ± 11.2

Patient-T, patients with trismus; Patient-NT, patients without trismus; TMJ, temporomandibular joint.

This explained why the trismus patients (Patient-T) presented with thinner joint disc than patients without trismus.

Mandibular condyle erosion and sclerosis caused by radiation induced inflammatory process, which was associated with CI, have been reported in patients after radiotherapy.[13] This phenomenon was also observed in our study in which the mandibular condyle was more irregular in the post-RT patients than the normal subjects. Mandibular condylar cartilage is important in TMJ function which facilitates the articulation of the joint disc and reduces point loads on the underlying bone.[14,15] Therefore, irregular condyle would cause articulation problem leading to limitation of joint movement. However, such condition was not found to be related to the severity of trismus as there was no difference between the Patient-T and Patient-NT groups.

A significant increase in JV was observed in the patient group relative to the control group in the longitudinal scan. This condition was likely caused by the chronic inflammatory process induced by radiation, which has been reported by some previous studies that used Doppler ultrasound to investigate various inflammatory conditions of joints.[16,17] Based on our results, we could say that inflammatory condition was observed in all the post-RT patients leading to increase in JV. This also explained the result that patients with trismus showed more inflammatory condition than those without trismus in the longitudinal scans, as their JV was marginal higher than the non-trismus patients.

With regard to RME of the pterygoid muscle, the difference between the patient and control groups was not obvious in which a majority portion of the subjects showed hypoechoic condition. The main difference between the two groups was the relatively lower percentages of hyperechoic condition (higher percentage of hypoechoic condition) found in the patient groups. This could be explained by the fact that chronic inflammation was induced by radiation on the muscle fibres in the post-RT patients, which was associated with edematous changes of the muscles. With the higher chance of fluid accumulation, the muscle tended to appear either hypoechoic or isoechoic when compared with other muscle which did not receive any radiation.

Our study has demonstrated the morphological changes of the TMJ in post-RT NPC patients using ultrasonography, which is a non-invasive imaging modality. These changes such as the disc thickness and CI could be associated with the development of trismus and measurement of these parameters can be used to monitor the TMJ condition. For NPC patients after radiotherapy, ultrasound examination of the TMJ using these parameters can be conducted at follow up visits so as to detect early sign of trismus and facilitate timely management for patients who present with trismus. Examples of treatment interventions for trismus include physiotherapy, use of pharmaceuticals, micro-current therapy and oxygen therapy.[18] In addition, a longitudinal study starting from the beginning of radiotherapy course would be suggested so to assess the pattern of TMJ changes with respect to time.

Table 3. Comparison of TMJ parameters among the patients with and without trismus and the control group in the transverse and longitudinal scans of ultrasonography

Transverse scan (mean ± SD)					
	Patient-T (T) (n = 39)	Patient-NT (N) (n = 75)	Control (C) (n = 100)	ANOVA p-value	Post hoc test
MDT (mm)	1.39 ± 0.46	1.62 ± 0.54	1.72 ± 0.83	0.039	C > N >T
CI (%)	8.16 ± 11.2	7.88 ± 10.4	4.16 ± 6.80	0.010	C < N = T
JV (%)	0.41 ± 0.42	0.34 ± 0.33	0.30 ± 0.36	0.271	–
Longitudinal scan (mean ± SD)					
MDT (mm)	1.36 ± 0.52	1.55 ± 0.54	1.65 ± 0.70	0.04	C > N ≥ T
CI (%)	14.0 ± 14.3	12.4 ± 12.7	6.82 ± 7.28	0.001	C < N = T
JV (%)	0.35 ± 0.34	0.27 ± 0.31	0.22 ± 0.21	0.042	C < N ≤ T

ANOVA, analysis of variance; C,control group; CI, condyle irregularity; JV, joint vascularity; MDT, maximum disc thickness; Patient-T, patients with trismus; Patient-NT, patients without trismus; SD, standard deviation.

Table 4. Comparison of RME of the pterygoid muscle among patient groups and control group

	All scans (transverse + longitudinal)		
RME	Patient-T (n = 156) No (%)	Patient-NT (n = 300) No (%)	Control (n = 400) No (%)
Hyperechoic	30 (17.9)	59 (19.6)	99 (24.8)
Isoechoic	27 (17.3)	51 (17.3)	60 (15.0)
Hypoechoic	101 (64.7)	190 (63.3)	241 (60.3)

Patient-T, patients with trismus; Patient-NT, patients without trismus; RME, relative muscle echogenicity.

CONCLUSIONS

Post-RT TMJ changes characterized by the reduction of disc thickness, increase of CI and vascularity were detected in the NPC patients. Furthermore, patients with trismus demonstrated thinner disc thickness and higher JV than those without trismus. Our results showed that disc thickness, CI and JV provided from ultrasonography were useful parameters for monitoring the TMJ condition in post-RT NPC patients.

REFERENCES

1. Bhatia KS, King AD, Paunipagar BK, Abrigo J, Vlantis AC, Leung SF, et al. MRI findings in patients with severe trismus following radiotherapy for nasopharyngeal carcinoma. *Eur Radiol* 2009; **19**: 2586–93. doi: https://doi.org/10.1007/s00330-009-1445-z
2. Louise Kent M, Brennan MT, Noll JL, Fox PC, Burri SH, Hunter JC, et al. Radiation-induced trismus in head and neck cancer patients. *Support Care Cancer* 2008; **16**: 305–9. doi: https://doi.org/10.1007/s00520-007-0345-5
3. Lindblom U, Gärskog O, Kjellén E, Laurell G, Levring Jäghagen E, Wahlberg P, et al. Radiation-induced trismus in the ARTSCAN head and neck trial. *Acta Oncol* 2014; **53**: 620–7. doi: https://doi.org/10.3109/0284186X.2014.892209
4. Wang CJ, Huang EY, Hsu HC, Chen HC, Fang FM, Hsiung CY. The degree and time-course assessment of radiation-induced trismus occurring after radiotherapy for nasopharyngeal cancer. *Laryngoscope* 2005; **115**: 1458–60. doi: https://doi.org/10.1097/01.mlg.0000171019.80351.46
5. Becker W, Naumann HH, Pfaltz CR. Mouth and Pharynx. In: *Ear, Nose and Throat Diseases: A Pocket Reference*. New York: Thieme Medical Publishers; 1989. pp. 320–71.
6. Steelman R, Sokol J. Quantification of trismus following irradiation of the temporomandibular joint. *Mo Dent J* 1986; **66**: 21–3.
7. Vissink A, Jansma J, Spijkervet FK, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. *Crit Rev Oral Biol Med* 2003; **14**: 199–212.
8. Bensadoun RJ, Riesenbeck D, Lockhart PB, Elting LS, Spijkervet FK, Brennan MT. A systematic review of trismus induced by cancer therapies in head and neck cancer patients. *Support Care Cancer* 2010; **18**: 1033–8. doi: https://doi.org/10.1007/s00520-010-0847-4
9. Dijkstra PU, Huisman PM, Roodenburg JL. Criteria for trismus in head and neck oncology. *Int J Oral Maxillofac Surg* 2006; **35**: 337–42. doi: https://doi.org/10.1016/j.ijom.2005.08.001
10. Scott B, Butterworth C, Lowe D, Rogers SN. Factors associated with restricted mouth opening and its relationship to health-related quality of life in patients attending a Maxillofacial Oncology clinic. *Oral Oncol* 2008; **44**: 430–8. doi: https://doi.org/10.1016/j.oraloncology.2007.06.015
11. VWC W, Ying MTC, Tam SY, Kwong DLW. A study of the factors affecting radiation-induced temporomandibular joint changes in post-radiotherapy nasopharyngeal carcinoma patients. *J Radiat Oncol* 2016; **5**: 41–6.
12. Scapino RP, Obrez A, Greising D. Organization and function of the collagen fiber system in the human temporomandibular joint disk and its attachments. *Cells Tissues Organs* 2006; **182**(3-4): 201–25. doi: https://doi.org/10.1159/000093969
13. Mercado CE, Little SB, Mazewski C, Schwaibold FP, Esiashvili N. Mandibular condyle erosion and sclerosis in pediatric patients treated with radiotherapy to the head and neck region. *Pediatr Blood Cancer* 2014; **61**: 1479–80. doi: https://doi.org/10.1002/pbc.24941
14. Kuroda S, Tanimoto K, Izawa T, Fujihara S, Koolstra JH, Tanaka E. Biomechanical and biochemical characteristics of the mandibular condylar cartilage. *Osteoarthritis Cartilage* 2009; **17**: 1408–15. doi: https://doi.org/10.1016/j.joca.2009.04.025
15. Singh M, Detamore MS. Tensile Properties of the Mandibular Condylar Cartilage. *J Biomech Eng* 2008; **130**: 11009. doi: https://doi.org/10.1115/1.2838062
16. Kristoffersen H, Torp-Pedersen S, Terslev L, Qvistgaard E, Holm CC, Ellegaard K, et al. Indications of inflammation visualized by ultrasound in osteoarthritis of the knee. *Acta Radiol* 2006; **47**: 281–6. doi: https://doi.org/10.1080/02841850600551508
17. Klauser AS, Faschingbauer R, Kupferthaler K, Feuchnter G, Wick MC, Jaschke WR, et al. Sonographic criteria for therapy follow-up in the course of ultrasound-guided intra-articular injections of hyaluronic acid in hand osteoarthritis. *Eur J Radiol* 2012; **81**: 1607–11. doi: https://doi.org/10.1016/j.ejrad.2011.04.073
18. Wranicz P, Herlofson BB, Evensen JF, Kongsgaard UE. Prevention and treatment of trismus in head and neck cancer: A case report and a systematic review of the literature. *Scand J Pain* 2010; **1**: 84–8. doi: https://doi.org/10.1016/j.sjpain.2010.01.006