ACU Sağlık Bil Derg
https://dx.doi.org/10.31067/0.2018.75

ARAŞTIRMA YAZISI / ORIGINAL ARTICLE **Radyoloji** / Radiology

Radiotherapy Induced Changes of Masticatory Muscles and Parotid Glands on MRI in Patients with Nasopharyngeal Carcinoma

Taner Arpacı[1], Gamze Uğurluer[2], Gülhan Örekici[3], Tuğana Akbaş[1], Meltem Serin[2]

[1]SHMYO Acıbadem University, Acıbadem Adana Hospital, Radiology, Adana, Turkey
[2]Acıbadem University School of Medicine, Acıbadem Adana Hospital, Radiation Oncology, Adana, Turkey
[3]Mersin University School of Medicine, Department of Statistics, Mersin, Turkey

Taner Arpacı
Gamze Uğurluer
Gülhan Örekici
Tuğana Akbaş
Meltem Serin

Correspondence:
Taner Arpacı
SHMYO Acıbadem University, Acıbadem Adana Hospital, Radiology, Adana, Turkey
Phone: +90 322 455 43 25
E-mail: taner.arpaci@acibadem.edu.tr

Received : February 01, 2018
Revised : March 06, 2018
Accepted : March 14, 2018

ABSTRACT

Objective: The aim of this study was to identify radiotherapy (RT) induced changes of masticatory muscles and parotid glands on magnetic resonance imaging (MRI) in patients with nasopharyngeal carcinoma (NPC).

Patients and Methods: Thirty-one patients treated with RT for NPC between 2009-2016 in our instution were included in the study. MRI examinations performed before and after RT were reviewed retrospectively. Transverse diameters and signal intensities of masticatory muscles and parotid glands were evaluated on T2 weighted axial MR images. Normal (hypointense) signal was scored as 0, mild hyperintensity as 1 and severe hyperintensity as 2.

Results:The mean interval between pre-RT MRI and last control MRI was 44 months (12-84 months). Reductions of transverse diameters were; right masseter (RM):2.32mm (15%), left masseter (LM):2.42mm (15.4%), right medial pterygoid (RMP):1.26mm (8.7%), left medial pterygoid (LMP):1.71mm (12%), right lateral pterygoid (RLP):1.35mm (9.6%), left lateral pterygoid (LLP):1.32mm (9.4%), right parotid gland (RP):8.22mm (26%), left parotid gland (LP):8.87mm (28%). T2 signal changes were; RM: mild 8 cases (26%), LM: mild 5 cases (16%), RMP: mild 5 cases (16%), severe 1 case (3.5%), LMP: mild 4 cases (13%), severe 2 cases (6.5%), RLP and LLP: mild 8 cases (26%), severe 3 cases (9.7%), RP: mild 10 cases (32%), severe 18 cases (58%), LP: mild 10 cases (32%), severe 17 cases (55%).

Conclusion: Volume loss and hyperintensity were mostly seen in parotid glands. Masseter was the muscle with highest rate of volume loss and lateral pyterygoid showed the highest rate of hyperintensity in masticatory muscles.

Key words: Magnetic resonance imaging, masticatory muscle, nasopharyngeal carcinoma, parotid gland, radiotherapy.

NAZOFARENKS KANSERLİ OLGULARDA RADYOTERAPİ SONRASI MASTİKATÖR KASLARDA VE PAROTİS BEZLERİNDE GELİŞEN DEĞİŞİKLİKLERİN MRG İLE DEĞERLENDİRİLMESİ

Amaç: Bu çalışmada, nazofarenks kanserli olgularda radyoterapi (RT) sonrası mastikatör kaslarda ve parotis bezlerinde ortaya çıkan değişikliklerin manyetik rezonans görüntüleme (MRG) ile değerlendirilmesi amaçlandı.

Hastalar ve Yöntem: Kurumumuzda 2009-2016 yılları arasında nazofarenks kanseri tanısıyla RT verilen 31 olgunun RT öncesi ve sonrası çekilen MRG'leri retrospektif olarak değerlendirildi. T2 ağırlıklı aksiyel imajlarda mastikatör kasların ve parotis bezlerinin maksimum transvers çapları ve sinyal özellikleri kaydedildi. Normal (hipointens) sinyal 0, hafif sinyal artışı 1 ve belirgin sinyal artışı 2 olarak skorlandı.

Bulgular: RT öncesi çekilen ve takipte en son çekilen MRG arasındaki ortalama süre 44 aydı (12-84 ay). Sağ masseter kası (RM):2.32mm (15%), sol masseter (LM):2.42mm (15.4%), sağ medial pterygoid (RMP):1.26mm (8.7%), sol medial pterygoid (LMP):1.71mm (12%), sağ lateral pterygoid (RLP):1.35mm (9.6%), sol lateral pterygoid (LLP):1.32mm (9.4%), sağ parotis bezi (RP):8.22mm (26%) ve sol parotis bezi (LP):8.87mm (28%) oranında incelme gösterdi. RM 8 olguda (26%) hafif, LM 5 olguda (16%) hafif, RMP 5 olguda (16%) hafif ve 1 olguda (3,5%) belirgin, LMP 4 olguda (13%) hafif ve 2 olguda (6,5%) belirgin, RLP ve LLP 8'er olguda (26%) hafif ve 3'er olguda (9,7%) belirgin, RP 10 olguda (32%) hafif ve 18 olguda (58%) belirgin, LP 10 olguda (32%) hafif ve 17 olguda (55%) belirgin sinyal artışı gösterdi.

Sonuç: Hacim kaybı ve sinyal artışı en sık parotis bezlerinde gözlendi. Mastikatör kaslar arasında en sık hacim kaybı masseterde ve en sık sinyal artışı lateral pterygoid kasta saptandı. Radiotherapy induced changes of masticatory muscles and parotid glands on MRI in patients with nasopharyngeal carcinoma

Anahtar sözcükler: Manyetik rezonans görüntüleme, mastikatör kas, nazofarenks kanseri, parotis bezi, radyoterapi.

Ionising radiation leads to fibrosis, inflammation and atrophy of the masticatory muscles, restricts jaw mobility and induces trismus (1). Trismus is defined as restriction in the opening of mouth due to reasons like radiation, trauma, surgery or tetanus (2). It may affect the quality of life with difficulties in nutrition, communication and oral hygiene (3). Radiation may also cause mucositis, loss of salivary gland function, dental decay and osteoradionecrosis (ORN) in addition to systemic complications (1). Radiation induced damage and atrophy of the parotid glands result **s** in persistent xerostomia which is related with problems in mastication, swallowing and dental complications (4,5). Masticatory muscles and temporomandibular joint (TMJ) are late-responding tissues to the radiation when compared with other oral tissues. Because of their late response, radiation induced tissue alterations emerge after months or years and are usually mistaken as recurrent tumor (6). Magnetic resonance imaging (MRI) demonstrates radiotherapy (RT) related soft tissue changes such as muscle fibrosis, inflammation and denervation atrophy (7-9). Early detection of these findings enables timely management of the clinical symptoms (10). However, there are only a few reported studies evaluating these findings. The aim of this retrospective study was to identify RT induced changes of masticatory muscles and parotid glands on MRI in patients with nasopharyngeal carcinoma (NPC).

Materials and Methods

We received approval from our institutional ethical committee and included 31 patients from our institution treated with RT and followed up periodically for NPC between 2009 and 2016. Intensity Modulated Radiotherapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT) techniques were used for the radiation therapy. Radiotherapy planning was performed by using linear accelerator and 6 MV (megavoltage) photon energy. Seventy Gy was delivered for primary nasopharyngeal tumor and metastatic lymph nodes, 60 Gy to the high-risk regions and 46-54 Gy for elective irradiation. Fraction dose was 165-212 cGy for 33 days. The patients received concurrent cisplatin weekly. Magnetic resonance imaging examinations performed before the beginning of RT and annual control MRI scans after RT were reviewed by the same radiologist retrospectively. Magnetic resonance imaging (1.5 Tesla, Siemens Magnetom Avanto Tim 76x18, Erlangen, Germany) protocol of the nasopharynx included axial T1W, axial and sagittal T2W, axial and coronal T2W with fat saturation, axial and coronal T1W post-gadolinium with fat saturation sequences, diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) map. Maximum transvers diameters and signal intensities of the masticatory muscles (masseter, medial and lateral pterygoid, temporalis) and parotid glands were evaluated on T2-weighted turbo spin-echo (TSE) axial MR images (TR, average 3100 ms; TE, average 100 ms; slice thickness, 4 mm; gap, 1 mm; FOV, 190-240 mm; matrix, 384x384) and were recorded. For masticatory muscles and parotid glands, normal (hypointense) signal was scored as "0", mild hyperintensity was scored as "1" and severe hyperintensity with atrophy were scored as "2" (Figure 1-5). Contrast enhancement of masticator muscles and parotid glands were evaluated on post-gadolinium T1-weighted turbo spin-echo (TSE) with fat saturation axial MR images. Mild enhancement was rated as "1" and prominent enhancement was rated as "2". Magnetic resonance imaging abnormalities of the mandibula, maxilla,

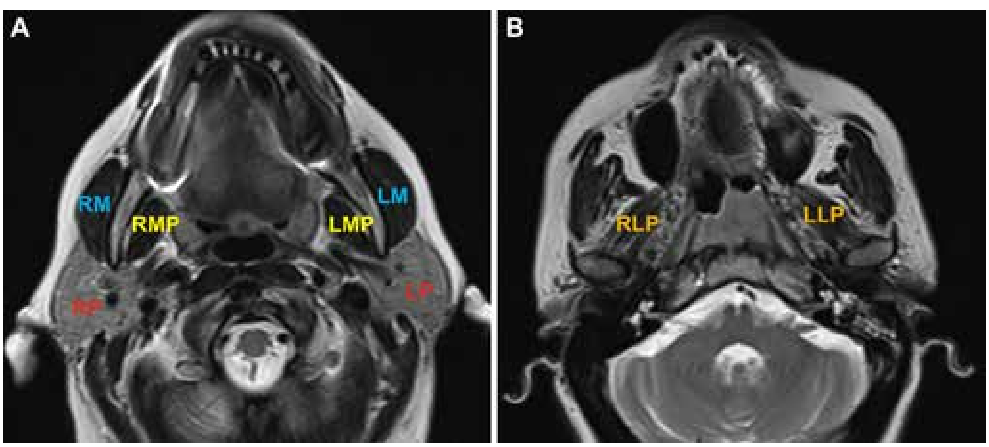

Figure 1 (A,B). Axial T2-weighted MR images demonstrate normal width and signal intensity of the masticatory muscles and parotid glands. **(A) RM:** right masseter muscle, **LM:** left masseter muscle, **RMP:** right medial pterygoid muscle, **LMP:** left medial pterygoid muscle, **RP:** right parotid gland, **LP:** left parotid gland. **(B) RLP:** right lateral pterygoid muscle, **LLP:** left lateral pterygoid muscle.

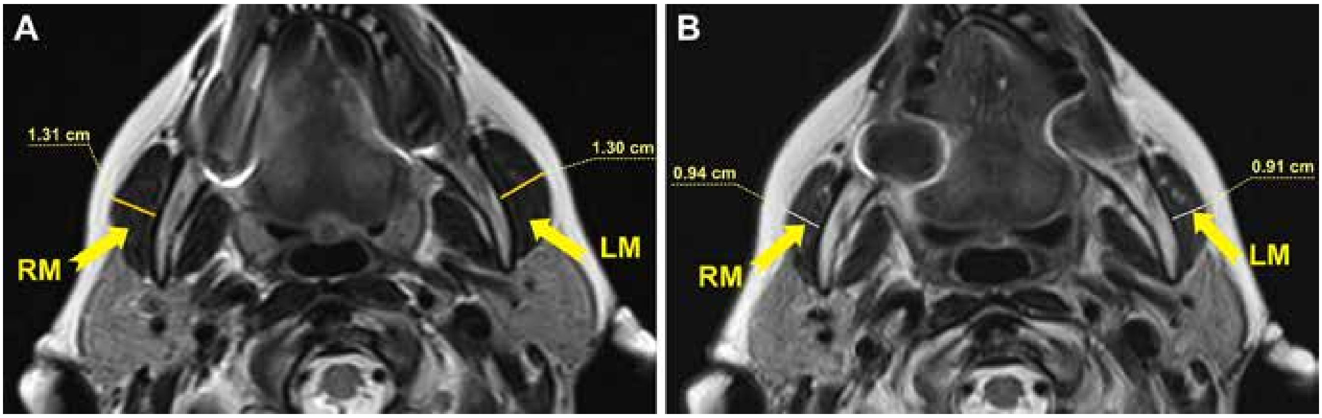

Figure 2 (A,B). 54 year-old woman with nasopharyngeal carcinoma (NPC) who was treated with RT (70 Gy for primary NPC and metastatic lymph nodes, 60 Gy to the high-risk regions and 46-54 Gy for elective irradiation) and concurrent weekly cisplatin 62 months ago. Axial T2-weighted MR image performed before RT **(A)** and 60 months after RT **(B)** show mild reduction of transverse diameters and mild increase *(score 1)* of signal intensity in bilateral masseter muscles (arrows).

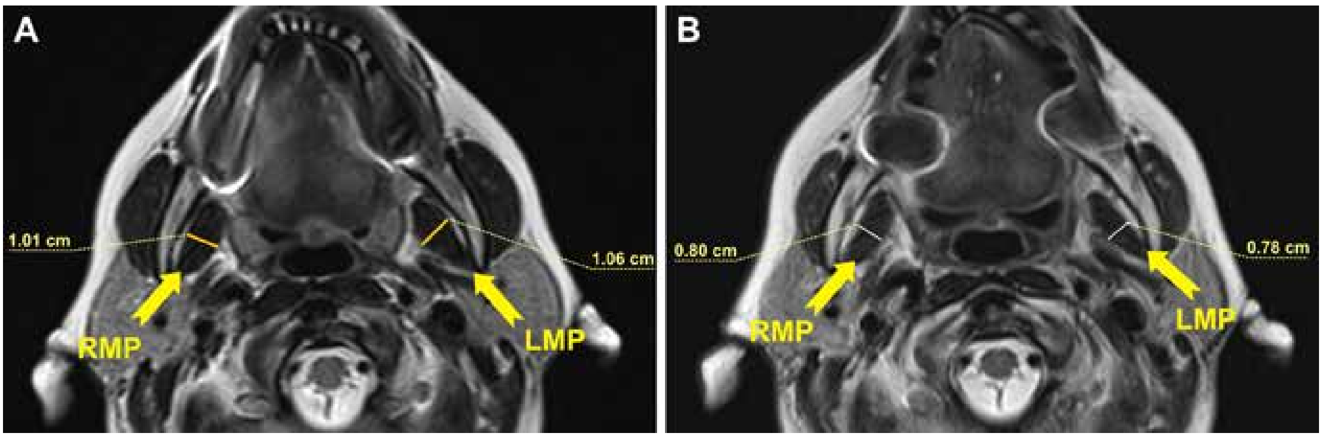

Figure 3 (A,B). Axial T2-weighted pre-RT **(A)** and post-RT **(B)** MR images of the same patient with figure 2 reveal mild decrease of transvers diameters and mild increase *(score 1)* of signal intensity in bilateral medial pterygoid muscles (arrows).

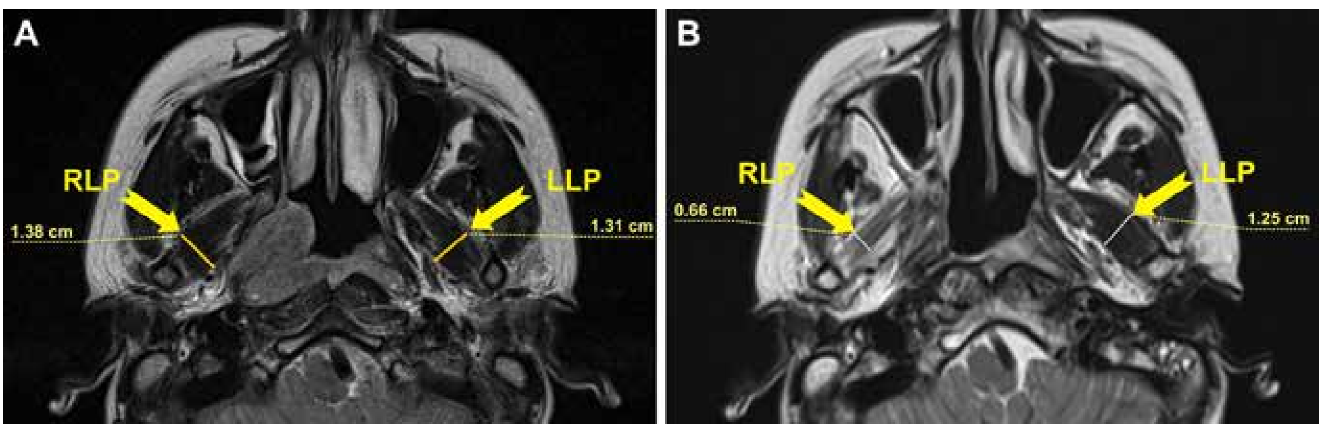

Figure 4 (A,B). 33 year-old woman with nasopharyngeal carcinoma (NPC) who was treated with RT (70 Gy for primary NPC and metastatic lymph nodes, 60 Gy to the high-risk regions and 46-54 Gy for elective irradiation) and concurrent weekly cisplatin 81 months ago. Axial T2-weighted MR image taken before RT **(A)** and 72 months after RT **(B)** demonstrate prominent volume loss and severe hyperintensity *(score 2)* in right lateral pterygoid muscle (arrow). Note complete regression of the right NPC after RT.

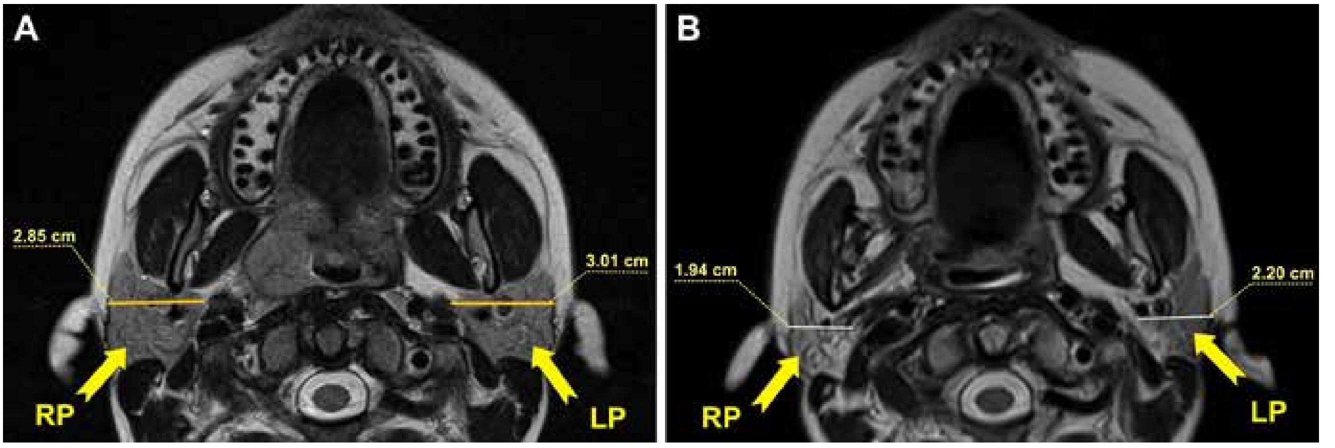

Figure 5 (A,B). Axial T2-weighted pre-RT **(A)** and post-RT **(B)** MR images of the same patient with figure 4 reveal marked reduction of transvers diameter and severe hyperintensity (score 2) in right parotid gland (arrow). Left parotid gland (arrow) shows moderate reduction of transvers diameter and mild hyperintensity *(score 1)* after RT.

skull base and TMJ- like marrow edema, bone destruction and ORN were recorded. It was recorded if the patients developed clinically trismus or not. The patients who had invasive disease involving the masticator structures during or after RT and had undergone previous surgery of the nasopharynx, skull base or maxillofacial region were excluded from the study. The Statistical Package for the Social Sciences for Windows (SPSS Inc.; version 20, IBM, Chicago, USA), Student's T Test and Chi-Squared analysis were used for statistical evaluation. P value less than 0.05 was considered as statistically significant.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Informed consent was obtained from all patients participating in the study.

Results

Thirty-one patients (20 men, 11 women; median age 45 years, range 19–80 years) with a total of 62 MRI exams were included in this study. Table 1 lists the characteristics of the patients. The mean interval between the first MRI performed before the beginning of RT and the last post-RT annual control MRI was 44 months (12-84 months). The reductions in transverse diameters of masticatory muscles and parotid glands between the first and last MRI are listed in Table 2. These results were statistically significant (p<0.05). Changes of the T2 signal intensity in masticatory muscles and parotid glands between the first and last MRI are mentioned in Table 3. Volume loss and hyperintensity were mostly seen in the parotid glands, which were more prominent in the deep lobes than the superficial lobes. Except temporalis, all masticatory muscles showed statistically significant volume loss. Masseter muscles demonstrated the most amount of volume loss

Table 1. Patient characteristics

Number of patients	***n:31***
Median Age	45 years (range 19–80)
Gender	20 men (65%) 11 women (35%)
The mean interval between MRI exams	44 months (12-84)

Table 2. Reductions of maximum transvers diameter in masticator muscles and parotid glands

	Pre RT mm	***Post RT mm***	***Mean difference mm / (%)***	***P***
MUSCLE				
RM	15.42±2.70	13.10±2.83	2.32±1.58 (15%)	p<0.01
LM	15.68±3.02	13.26±2.85	2.42±1.59 (15.4%)	p<0.01
RMP	14.42±2.91	13.16±3.23	1.26±1.18 (8.7%)	p<0.01
LMP	14.29±2.53	12.58±2.51	1.71±1.10 (12%)	p<0.01
RLP	14.00±1.77	12.65±1.87	1.35±1.30 (9.6%)	p<0.01
LLP	13.97±2.67	12.65±1.87	1.32±2.10 (9.4%)	p<0.01
PAROTIS				
RP	31.94±5.44	23.71±6.31	8.22± 4.55 (26%)	p<0.01
LP	32.23±5.50	23.35 ±5.41	8.87±5.72 (28%)	p<0.01

RM: right masseter muscle, **LM:** left masseter muscle, **RMP:** right medial pterygoid muscle, **LMP:** left medial pterygoid muscle, **RLP:** right lateral pterygoid muscle, **LLP:** left lateral pterygoid muscle, **RP:** right parotid gland, **LP:** left parotid gland.

Table 3. Increase of T2 signal in masticator muscles and parotid glands.

	Normal T2 signal (score0) number of paients (n) / (%)	*Mild T2 signal (score1) number of paients (n) / (%)*	*Severe T2 signal (score2) number of paients (n) / (%)*	*TOTAL n / (%)*
MUSCLE				
RM	23 (74%)	8 (26%)	0	8 (26%)
LM	26 (84%)	5 (16%)	0	5 (16%)
RMP	25 (80.5%)	5 (16%)	1 (3.5%)	6 (19.5%)
LMP	25 (80.5%)	4 (13%)	2 (6.5%)	6 (19.5%)
RLP	20 (64%)	8 (26%)	3 (9.7%)	11 (35.7%)
LLP	20 (64%)	8 (26%)	3 (9.7%)	11 (35.7%)
PAROTIS				
RP	3 (10%)	10 (32%)	18 (58%)	28 (90%)
LP	4 (13%)	10 (32%)	17 (55%)	27 (87%)

RM: right masseter muscle, **LM:** left masseter muscle, **RMP:** right medial pterygoid muscle, **LMP:** left medial pterygoid muscle, **RLP:** right lateral pterygoid muscle, **LLP:** left lateral pterygoid muscle, **RP:** right parotid gland, **LP:** left parotid gland.

and lateral pyterygoid muscles showed the highest rate of hyperintensity in masticatory muscles. Significant contrast enhancement was not detected in the masticatory muscles and parotid glands (p>0.05). There was not a statistical correlation between the tumor location (right-left) and mentioned changes of masticatory muscles and parotid glands (p>0.05). Trismus occured in 15 (10 men, 5 women) cases (48%). Statistical correlation was not detected between the occurence of trismus and masticator muscle volume loss/ hyperintensity (p>0.05).

Discussion

Radiation therapy is crucial in the treatment of head and neck cancers but frequently damages the adjacent healthy tissues immediately or after many years (11). Dose of radiation, fraction time interval and the ratio of radiation dose/tissue volume identify the intensity of the complications (11). Although radiation-induced tissue injuries usually occur and recover immediately after the end of RT, residual tissue ischemia and fibrosis may be asymptomatic for months or years (12,13). Masticator muscle fibrosis is most likely the main reason of RT induced trismus and there is direct correlation between RT dose and restriction of the dental gap (14). Radiotherapy induced MRI findings of the masticatory muscles has been mentioned rarely in the literature. Magnetic resonance imaging enables evaluation of thickness, area, signal intensity and contours of the masticatory muscles and allows diagnosis of RT induced muscle damage by determining edema, fibrosis, inflammation and denervation (7,8,11,15). Masticatory muscles usually demonstrate increased T2 hyperintensity and post-gadolinium enhancement after RT (11). In their study of 35 NPC patients, with retrospective MRI analysis and without considering the correlation of RT doses, Bhatia et al. (16) reported these findings in pterygoid, masseter and temporalis muscles in 45% of patients suffering trismus. They believed, MRI probably could not determine muscular fibrosis or different diseases that have participated in trismus in remaining 55% of their patients. In our sudy, 70% of MRI series showed no signal abnormality in the masticatory muscles. The most frequent signal abnormality was detected in lateral pterygoid (RLP-LLP) muscles when compared with the other masticatory muscles, this result was consistent with the study of Bhatia et al. (16). We did not qualify the RT dose of each muscle, but probably lateral pterygoid muscles were exposed to a higher dose. Direct relation between the masticatory RT dose and restriction of mouth opening were reported in a few previous studies (14). Chong et al. (17) reported that 3 of their 5 patients (60%) with radiation induced mandibular ORN demonstrated T2 hyperintensity in the ipsilateral masseter and pterygoid muscles and two of these three patients also showed marked thickening of the mentioned masticatory muscles close to the ORN. In our study of 31 patients, RT induced mandibular marrow edema, bone destruction and ORN were not detected. In their single case, Ariji et al. (18) published prominent hyperintensity of whole masticatory muscles showing denervation atrophy caused by mandibular nerve damage a few months after RT. Denervation of masticatory muscles demonstrate edema, inflammation, fatty infiltration and atrophy respectively (8,15). In our study, all masticatory muscles showed statistically significant volume loss except temporalis muscle. Masseter muscles demonstrated the highest rate of volume loss. We did not find muscle size to be a significant finding to detect radiation induced trismus which was consistent with the study of Bhatia et al. Statistical correlation was not detected between the occurence of trismus, masticatory muscle volume loss and hyperintensity. Significant contrast enhancement was not detected in the masticatory muscles. We also evaluated the RT induced size and signal abnormalities of the parotid glands which were found more frequent than the masticatory muscles. This was probaly related with the anatomical proximity of parotid glands and masticator muscles in planning RT (19). Wu et al. (20) reported that all of their 18 patients showed reduction in parotid gland volumes after RT. Their overall mean volume reduction was about 35% and was related with the mean doses of the parotid glands. In our study, the average reduction in transvers diameter of parotis were about 27%. Our study had several limitations due to the technical difficulties. First, we did not calculate the RT dose given to the each masticatory muscle and parotid gland. We should have evaluated the relationship between the RT dose and RT induced MRI changes. Also, we should have measured the pre-RT and post-RT volumes instead of muscle and gland thickness for more accurate comparison.

Conclusion

RT leads to atrophy of the masticatory muscles and induces trismus which is defined as restriction in mouth opening and may affect the quality of life with difficulties in nutrition, communication and oral hygiene (1-3). RT induced damage and atrophy of the parotid glands results in persistent xerostomia which is related with problems in mastication, swallowing and dental complications (4,5). RT induced muscle and salivary gland changes can be detected by using MRI (8). This retrospective study has determimed two main MRI abnormalities like volume loss and increased signal in the masticatory muscles and parotid glands. Early detection of these findings enables timely management of the clinical symptoms like trismus and xerostomia.

References

1. Parliament M, Alidrisi M, Munroe M. Implications of radiation dosimetry of the mandible in patients with carcinomas of the oral cavity and nasopharynx treated with intensity modulated radiation therapy. Int J Oral Maxillofac Surg 2005; 34:114–21.
2. Johnson J, van As-Brooks CJ, Fagerberg-Mohlin B, Finizia C. Trismus in head and neck cancer patients in Sweden: incidence and risk factors. Med Sci Monit 2010; 16: CR278–82.
3. Louise Kent M, Brennan MT, Noll JL. Radiation-induced trismus in head and neck cancer patients. Support Care Cancer 2008; 16:305–9.
4. Jellema AP, Slotman BT, Doomaert P, Leemans CR, Langendijk JA. Impact of radiation-induced xerostomia on quality of life after primary radiotherapy among patients with head and neck cancer. Int J Radiat Oncol Biol Phys 2007; 69:751–60.
5. Chambers MS, Harden AS, Kies MS, Martin JW. Radiation induced xerostomia in patients with head and neck cancer: pathogenesis, impact on quality of life, and management. Head Neck 2004;26:796–807.
6. Vissink A, Jansma J, Spijkervet F, Burlage F. Oral Sequelae of Head and Neck Radiotherapy. CROBM 2003; 14:199–212.
7. Farrugia M, Bydder G, Francis J, Robson M. Magnetic resonance imaging of facial muscles. Clin Radiol 2007; 62:1078–86.
8. D'Ippolito S, Borri Wolosker A, D'Ippolito G, Herbert De Souza B, Fenyo- Pereira M. Evaluation of the lateral pterygoid muscle using magnetic resonance imaging. Dentomaxillofac Radiol 2010;39:494–500.
9. Kato K, Tomura N, Takahashi S, Watarai J. Motor denervation of tumors of the head and neck: changes in MR appearance. Magn Reson Med Sci 2002; 1:157–64.
10. Al-Saleh MA, Jaremko JL, Saltaji H, Wolfaardt J, Major PW. MRI findings of radiation-induced changes of masticatory muscles: a systematic review. J Otolaryngol Head Neck Surg. 2013; Mar 28:42:26. doi: 10.1186/1916-0216-42-26.
11. Yeh SA, Tang Y, Lui CC, Huang YJ, Huang EY. Treatment outcomes and late complications of 849 patients with nasopharyngeal carcinoma treated with radiotherapy alone. Int J Radiat Oncol Biol Phys 2005;62:672–9.
12. Stone H, Coleman C, Anscher M, McBride W. Effects of radiation on normal tissue: consequences and mechanisms. Lancet Oncol 2003;4:529–36.
13. Bennett M, Feldmeier J, Hampson N, Smee R, Milross C. Hyperbaric oxygen therapy for late radiation tissue injury. Cochrane Database Syst Rev 2012; 5:CD005005.
14. Liu Y, Chen M, Zhao C, et al. Radiation-induced temporomandibular joint damage in nasopharyngeal carcinoma patients after intensity-modulated radiotherapy. Chinese journal of cancer 2007; 26:64–7.
15. Fukui T, Tsuruta M, Murata K, Wakimoto Y, Tokiwa H, Kuwahara Y. Correlation between facial morphology, mouth opening ability, and condylar movement during opening-closing jaw movements in female adults with normal occlusion. Eur J Orthod 2002; 24:327–36.
16. Bhatia KS, King AD, Paunipagar BK. MRI findings in patients with severe trismus following radiotherapy for nasopharyngeal carcinoma. Eur Radiol 2009; 19: 2586–93.
17. Chong J, Hinckley L, Ginsberg L. Masticator space abnormalities associated with mandibular osteoradionecrosis: MR and CT findings in five patients. AJNR Am J Neuroradiol 2000; 21:175–8.
18. Ariji Y, Fuwa N, Tachibana H, Ariji E. Denervation atrophy of the masticatory muscles in a patient with nasopharyngeal cancer: MR examinations before and after radiotherapy. Dentomaxillofac Radiol 2002; 31:204–8.
19. Hsieh LC, Chen JW, Wang LY. Predicting the severity and prognosis of trismus after intensity-modulated radiation therapy for oral cancer patients by magnetic resonance imaging. PLoS One. 2014;9(3):e92561.
20. VWC Wu, MTC Ying, DLW Kwong. Evaluation of radiation-induced changes to parotid glands following conventional radiotherapy in patients with nasopharygneal carcinoma. Br J Radiol 2011 Sep; 84(1005): 843–9.