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Sonographic Assessment of Parotid and Submandibular Glands in Patients Undergoing 3D Conformal Radiotherapy

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ABSTRACT

The aim of this study was to evaluate sonographic changes in parotid and submandibular salivary glands in patients undergoing radiotherapy for head and neck malignancies. In addition, salivary changes subsequent to radiotherapy were evaluated objectively and subjectively. Twenty patients(13males and 7females) with head and neck malignancies, who had been referred to the Radiotherapy/Oncology Department of the Shahid Madani Hospital in Tabriz, Iran, were included in the study. Length, width, echotexture, echogenicity and margins of parotid and submandibular glands were evaluated before and after radiotherapy using sonography. Peak-systolic velocity(PSV),end-diastolic velocity(EDV) and resistive index(RI) were also assessed by Doppler sonography. Xerostomia subsequent to radiotherapy was evaluated with the use of two techniques: patients' self-reported scoring and objective measurement of resting saliva. There was a significant decrease in the width of the parotid gland after radiotherapy compared to baseline(P=0.005).Although the length of the parotid gland and the dimensions of submandibular gland decrease, the differences were not significant. In addition, the echogenicity, echotexture and the margin of the glands change to hypoechoic, heterogenic and irregular, respectively, subsequent to radiotherapy. The Doppler technique showed decrease in PSV and RI and an increase in EDV; however, only the decrease in RI in the submandibular gland was statistically significant(P=0.002).The results showed a significant decrease in salivary flow after radiotherapy(P<0.001).In addition, based on the patients reports, the severity of xerostomia increased significantly after radiotherapy(P<0.001). Songraphic changes of parotid and submandibular glands after radiotherapy should be considered in ultrasound examinations. The damages to the parotid and submandibular glands had significant influence in patient post 3D-CRT.

Key words: Ultrasonography, Conformal radiotherapy, Parotid glands, Submandibular glands, Xerostomia.

INTRODUCTION

Radiotherapy is the main treatment modality for head and neck malignancies[1].An important complication of radiotherapy for head and neck malignancies is its potential to damage the major salivary glands[2] because salivary gland parenchyma is very sensitive to radiation[3].A decrease in salivary function is a common toxicity and decreases the patient's quality of life. Several studies have shown that over 90% of patients with head and neck malignancies develop some degree of xerostomia after radiotherapy. Often, permanent xerostomia is associated with oral discomfort, increase drates of dental caries and oral infection, and problems with speaking and swallowing[4,5]. Limited studies have been conducted using ultrasound to measure radiation-induced parotid injuries in spite of its wide use as a diagnostic tool for parotid neoplasms and infections[6-11]. Recently, the Doppler technique and sonographic appearance of the parotid glands were suggested for the evaluation of parotid glands after radiotherapy[12-14].

In a Doppler study of late toxicity (3–8 years after radiotherapy), significant differences were shown in high peak systolic velocity (PSV), resistive index (RI) and pulsatility index (PI) between the irradiated and healthy parotid glands[14]. Conversely, no significant differences regarding PSV, end diastolic velocity (EDV) and RI in the parotid glands were found at 2 weeks or 6–7 weeks after radiotherapy[13].In addition, sonographic features of the parotid glands, such as echogenicity, showed significant differences in both late toxicity[14] and acute toxicity groups[13]. Furthermore, another research showed that salivary glands after radiotherapy have been reported to be hypoechoic and heterogenic in sonography[14-16]. Peak systolic velocity (PSV), end-diastolic velocity (EDV) and resistive index (RI) also showed sub-normal values in sonography[14].

All of the published studies have been used Cobalt Radiotherapy(2D) before sonographic evaluation of patients. 3D Conformal Radiotherapy is now routinely used at the most of radiotherapy centers [17]However, there is inadequate data on changes in salivary glands following 3D conformal radiotherapy for head and neck malignancies. This study was designed and conducted to evaluate changes in parotid and submandibular glands in patients with head and neck malignancies undergoing Three-Dimensional Conformal Radiation Therapy (3D-CRT), using grayscale and Doppler sonography.

MATHERIALS AND METHODS

This study involved humans and all participants were informed about the aims of the study and the procedures prior to evaluations, and written consent was received from each patient. The protocol of the study was approved by the Ethics Committee of Tabriz University of Medical Science (registration code: TBZMED.REC.1394.1194).

Inclusion criteria: patients who had a tumor in the head and neck region and received 3D conformal radiotherapy treatment using 6 MV photon energy (ONCOR, Siemens, USA). The patients received 10 Gy of radiation in a week (2 Gy daily for 5 days/week) and a total of 60–66 Gy. All the patients also simultaneously received chemotherapy with 100 mgm^{-2} cisplatinonce every 3 weeks.

Exclusion criteria: a history of background salivary gland disease, including salivary gland malignancy and Sjögren’s disease, history of HIV virus or autoimmune diseases and history of previous radiotherapy or surgical procedures in the head and neck region.

In this study, 20 patients (13 males and 7 females) with head and neck malignancies referred to the Radiotherapy/Oncology Department of Shahid Madani Hospital in Tabriz, Iran, were evaluated. The age range of the patients was 18–82 years. Parotid and submandibular glands of the patients were evaluated by grayscale and Doppler sonography. Parameters including length, width, echotexture, echogenicity and gland margins for grayscale sonography and PSV, EDV and RI for Doppler sonography were measured in two stages.

All the ultrasound examinations were performed with the ultrasound unit in conjunction with a 7–12 MHz linear transducer (Mindray DC-8, North America). Sonographic evaluations were accomplished by a professional radiologist at Imam Reza Hospital in two stages: one, prior to the radiotherapy; and two, 6–7weeks after radiotherapy.

The length and width were measured for each parotid and submandibular gland. The longest longitudinal and transverse dimensions of parotid and submandibular glands were measured in order to determine their dimensions (Figures 1 and 2). In cases in which the size of the gland was larger than the field of view dual images were prepared and placed next to each other.

Gland margins, echogenicity and echotexture were also evaluated. Echogenicity is described as hyperechoic, isoechoic and hypoechoic in comparison with the adjacent muscles[13]. Echotexture was classified as homogeneous or heterogeneous. Gland margins were considered as regular or irregular. PSV, EDV and RI were also measured using Doppler sonography (Figure 3).

To evaluate the severity of xerostomia, the subjects underwent a 'resting whole saliva' collection test. The patients were asked to avoid smoking, eating and drinking any liquids for 1.5 hours from 9□12 in the morning to avoid circadian effects. They were asked to swallow their saliva before collecting their salivary samples and be seated in a calm manner; then the spitting method was used to collect their saliva for 5 minutes. During the sampling procedure the subjects were asked to avoid swallowing and talking.

In addition, the subjects were asked to complete a valid and structured questionnaire [18](Figure 4) prior to and subsequent to radiotherapy. The patient scores each question from zero to 10, with zero indication the minimum severity and 10 indicating the maximum severity.

Statistical analysis
The level of significance of the difference in length, width, PSV, EDV and RI for each parotid and submandibular gland before and after radiotherapy was calculated by paired-sample t-test.

Chi-squared test was used to analyse the values of qualitative variables. P-values of <0.05 were considered significant. Paired-sample t-test was employed to evaluate the relationship between the questions on xerostomia and the saliva volume before and after radiotherapy. Statistical significance was set at (P<0.05).

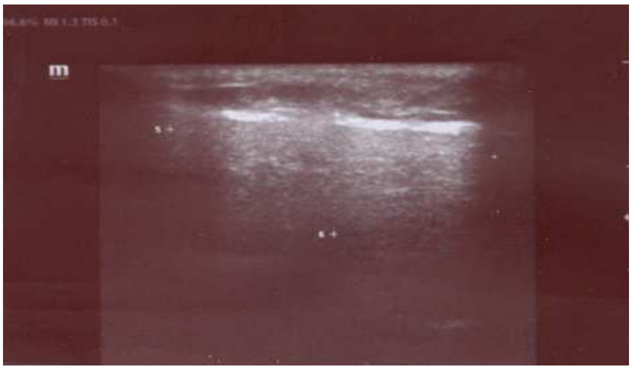

Figure 1. Measurement of the dimensions of parotid gland

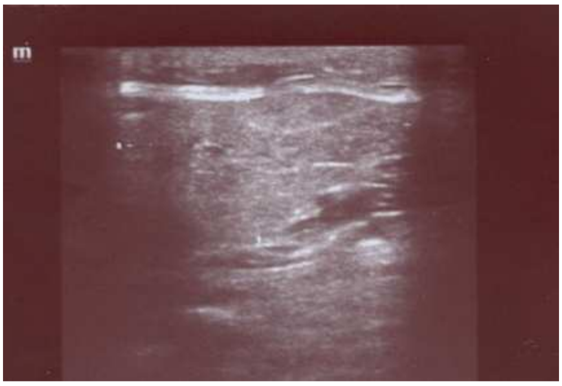

Figure 2. Measurement of the dimensions of submandibular gland

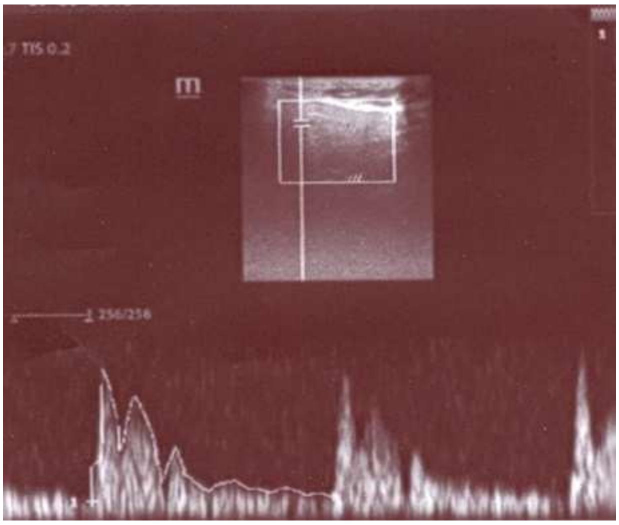

Figure 3. Doppler sonogram of a parotid gland showing measurement of blood flow velocity (peak systolic velocity and end diastolic velocity) and vascular resistance (resistive index) of the gland

Below are several questions which will help describe the dryness in your mouth and how that dryness interferes with aspects of your daily life? Please make one vertical mark across the line and choose a number of 0-10 to show your condition.

1. During the last three days, overall, your mouth or tongue was:
   Not dry (0 ---10) Very dry
2. In general, during the daytime hours of the last three days, the feeling of your mouth and tongue was:
   Comfortable (0 ---10) Extremely uncomfortable
3. During the last three nights, due to the dryness of your mouth and tongue, how difficult was it to sleep? Consider such factors as how difficult it was for you to go to sleep, the duration and quality of your sleep, and how often you woke up to drink or to urinate.
   Easy (0 ---10) Very Difficult
4. During the last three days, overall, due to the dryness of your mouth and tongue, how difficult was it to speak without drinking liquids?
   Easy (0 ---10) Very Difficult
5. During the last three days, overall, due to the dryness of your mouth and tongue, how difficult was it to chew and swallow food?
   Easy (0 ---10) Very Difficult

Figure 4. Xerostomia Questionnaire[18]

RESULTS

Of 20 patients evaluated, 10 had nasopharyngeal carcinomas, 5 had laryngeal squamous cell carcinoma, 3 had hypopharyngeal carcinomas and 2 had tongue squamous cell carcinoma. The parotid and submandibular glands of all the 20 patients were successfully imaged with high-resolution grayscale and Doppler sonography. The total evaluated glands included 39parotid and 39 submandibular glands due to the bilateral sonographic evaluations and also the qualitative and quantitative differences between the glands on both sides. The patients were 18–82 years of age (mean, 60.9±17.6).

We found decrease in the length and width of both glands after radiotherapy but decrement in the width in only parotid gland was statistically significant (P=0.005)(Table 1). In both parotid and submandibular glands, echotexture, echogenicity and gland margins significantly altered to heterogenic, hypoechoic and irregular, respectively, during radiotherapy (P=0.000) (Table 2).

Table 1. Correlation of the longitudinal and transverse dimensions of parotid and submandibular glands with sonographic stages

Type of gland	Dimension	Stage		Mean ± SD (mm)	P-value
Parotid	Longitudinal	I		3.47(±0.46)	
		II		3.38(±0.41)	0.252
	Transverse	I		1.63(±0.45)	
		II		1.42(±0.46)	0.005
Submandibular	Longitudinal	I		2.99(±0.47)	
		II		2.93(±0.43)	0.280
	Transverse	I		1.22(±0.29)	
		II		1.14(±0.42)	0.536

D, standard deviation.
Stages: I, before radiotherapy; II, 6–7 weeks after radiotherapy.

Table 2. Frequency distributions of the parotid and submandibular glands echotexture and echogenicity in sonographic stages

Type of gland	stage	Echotexture		Echogenicity			Margins	
		Homogen	Heterogen	Hyperecho	Isoecho	Hypoecho	Regular	Irregular
parotid	I	37	2	35	4	0	37	2
	II	4	35	0	11	28	0	39
Submandibular	I	38	1	34	5	0	37	2
	II	1	38	0	2	37	0	39

Chi-squared P=0.000. Stages: I, before radiotherapy; II, 6-7 weeks after radiotherapy

PSV, EDV and RI were measured for 39 parotid and 39 submandibular glands. In this study PSV and RI values decreased after radiotherapy but EDV increased. There were significant differences in RI in submandibular glands between different sonography stages whereas there were no significant differences in PSV and EDV (Table 3).

The means and standard deviations of salivary flow before and after radiotherapy were 82.7±28.7 and 39.9±34.5, respectively. The results of paired-sample t-test showed a significant decrease in mean salivary flow after radiotherapy (P value < 0.001). In addition, the same test showed that the mean scores of all the questions on xerostomia after radiotherapy were significantly higher than those before radiotherapy (P<0.001) (Table 4).

Table 3. Correlation of the parotid and submandibular glands' peak systolic velocity (PSV), end-diastolic velocity (EDV) and resistive index (RI) with sonographic stages

Type of gland	Vascular index	Stage		Mean ± SD	P-value
Parotid	EDV	I		4.50±3.01	0.812
		II		4.63±3.33	
	PSV	I		14.62±9.30	0.529
		II		13.30±9.19	
	RI	I		0.74±0.24	0.195
		II		0.68±0.08	
Submandibular	EDV	I		4.24±2.71	0.861
		II		4.35±3.13	
	PSV	I		12.34±8.82	0.828
		II		11.89±9.07	
	RI	I		0.67±0.12	0.002
		II		0.65±0.10	

SD, standard deviation
Stages: I, before radiotherapy; II, 6–7 weeks after radiotherapy.

Table 4. The means and standard deviations of scores of questions on xerostomia before and after radiotherapy

Type of question	Stage	Mean ± SD	P-value*
Tongue and mouth dryness	I	1.25(±1.55)	P<0.001
	II	4.75 (±2.37)	
The feeling of the tongue or the mouth	I	1.10 (±1.48)	P<0.001
	II	4.80 (±2.35)	
Sleep	I	0.50 (±1.05)	P<0.001
	II	3.25 (±2.65)	
Talking without drinking liquids	I	0.6 (±0.99)	P<0.001
	II	5 (±2.34)	
Mastication and deglutition	I	0.85 (±1.23)	P<0.001
	II	4.90 (±2.51)	

DISCUSSION

Conventional(2D) Radiotherapy consists of a single beam from one to four directions (usually lateral fields). There are few studies about sonographic changes of salivary glands in patient treated with conventional radiotherapy[14,19,20].3D or CT based planning took into account axial anatomy and complex tissue contours and allowed for accurate dose calculation and precise targeted[21].Jen et al, concluded that 3D conformal radiotherapy delivered a higher dose to the tumor and it spared the parotid gland significantly better than the conventional treatment[22]. Due to the inadequate of published data about sonographic changes in salivary glands following 3D conformal radiotherapy, and the importance of mentioned issue, the present study evaluated these changes, employing sonography as the evaluation technique.

Ultrasonography is useful in assessment of the superficial soft tissue structures including parotid and submandibular glands. It is safe, noninvasive, inexpensive, widely available and carries no radiation danger[23].We observed some changes, including the decrease in length and width of parotid and submandibular glands in patients treated with 3D-CRT during the two stages of sonography. This reduction was statistically significant for the width of parotid glands. However, generally there is inflammation and swelling after radiotherapy, which result in an increase in organ size[24].It has also been reported that the reduction in size of the gland may be a result of parenchymal damage and acinar atrophy[25,26]. Some studies have shown that smaller size of salivary glands found in radiotherapy patients was due to acinar atrophy after irradiation[25,27]. Volume reduction of parotid glands after radiotherapy has been documented in previous studies using computed tomography (CT)[28,29] and magnetic resonance imaging (MRI)[30,31]. Orloff et al, Imanimoghaddam et al, Burke et al and Ying et al studies also yielded similar results [13,14,16,31]Ying et al reported a significant difference only in the width of parotid glands[14].In our study, most of the normal glands had homogenic echotexture, which changed to heterogenic after radiotherapy. A number of similar studies have reported similar results[14,16,32].

Orderly and homogeneous position of acini in normal salivary glands might explain their homogenic echotexture; in this context, loss of acini in association with residual acini that are larger than normal and exhibit a disrupted pattern might justify the heterogenic echotexture of the gland after chemotherapy.[26,33] Radiotherapy-associated chronic sialadenitis might result in inflammation and fibrosis[25,34-36].

The heterogenic echotexture of salivary glands after radiotherapy might be due to the presence of such inflammatory areas that are manifested as hypoechoic areas in ultrasound examinations[15].In this study, salivary glands before radiotherapy were relatively hyperechoic compared with adjacent muscles. After radiation, there was a decrease in echogenicity of parotid and submandibular glands, which changed some of them to isoechoic and most of them to hypoechoic compared with adjacent muscles. Previous studies yielded similar results[8,14,15,37].

In normal salivary glands the acini and granules might function as reflexive interfaces to reflect ultrasound waves; therefore, they appear hyperechoic than muscles. In addition, hyperechoic nature of normal salivary glands might be associated with fatty infiltration of the gland [38] and a decrease in the echogenicity of the gland after radiotherapy might be attributed to the inflammatory infiltration within the gland[24,38].

The regular margins of the salivary glands before radiotherapy altered to irregular mode after radiotherapy. We found few published data regarding this matter, such as Imanimoghaddam et al research that reported similar results [13]this regularity may be caused by acinar irregular atrophy.

The Doppler results in the present study showed that PSV and RI decreased and EDV increased after radiotherapy. However, only the decrease in RIin submandibular gland was significant. Ying et al reported similar results[14]. However, they only evaluated PSV, EDV and RI for parotid glands. Imanimoghaddam et al [13]reported that PSV and RI in the parotid and submandibular glands reduced after conventional radiotherapy but the values were insignificant. In addition, they found no statistically significant changes in EDV values of parotid and submandibular glands after radiation.

Normal salivary glands have densely packed acini structures and the vessels are encased. After radiotherapy there is a reduction in the number of acini and granules. Therefore, the pressure is lifted from the vessels and they can easily dilate and pulsate, resulting ina decrease in PSV and vascular resistance.

Ying et al reported insignificant differences in EDV between parotid glands before and after conventional radiotherapy[14]. EDV changes may be a result of tissue and RI changes after irradiation. Ying et al reported that RI values decreased significantly after radiotherapy, which was similar to our findings. This reduction could be a result of acini destruction which leads to removal of pressure from the vessels, the same way as described in PSV[14].

Assessment of dry mouth in the present study was done with two different techniques. In the first technique, the salivary volume was measured using an objective method and in the second technique the patient self-reported scoring method was used. The results of both techniques indicated a significant increase in the severity of xerostomia subsequent to 3D-CRT. Jen et al concluded that incidence of severe xerostomia decreased after 3D-CRT compare with conventional radiotherapy[22].

In this study the most prevalent complaints reported by the patients were related to talking without drinking water, followed by problems with mastication and deglutition.

It seems that despite several advances in radiation techniques including 3D-CRT, xerostomia treatment in patient undergoing radiotherapy is needed.

It is suggested that similar studies be carried out in patient undergoing radiotherapy with IMRT and also with larger sample sizes.

CONCLUSION

To avoid incorrect interpretation of ultrasound images, changes in sonographic images of parotid and submandibular glands after radiotherapy of the head and neck region should be taken into account in the ultrasound examinations of these patients. Radiation induced damages to the parotid and submandibular glands had significant influence in patient undergoing 3D-CRT.

REFERENCES

[1] Eisbruch A. Clinical aspects of IMRT for head-and-neck cancer. Med Dosim. 2002; 27:99–104.
[2] Dirix P, NuytsS, Van den Bogaert W. Radiation inducedxerostomia in patients with head and neck cancer. Cancer 2006;107: 2525–2534.
[3] White SC, PharoahMJ. Radiobiology. In:White SC, PharoahMJ, eds. Oral radiology—principles and interpretation. 7th edn.Maryland Heights, MO: Mosby Elsevier; 2014. p. 23–25.
[4] Braam PM, Roesink JM, Raaijmakers CP, Busschers WB, Terhaard CH. Quality of life and salivaryoutput in patients with head-and-neck cancer five years after radiotherapy. RadiatOncol. 2007; 2:3.
[5] Wada A, Uchida N, Yokokawa M, Yoshizako T, KitagakiH. Radiation-induced xerostomia. Objectiveevaluation of salivary gland Injury using MR sialography. Am J Neuroradiol. 2009; 30:53–58.
[6] Bhatia KSS, Rasalkar DD, Lee YP, Wong KT, King AD, Yuen HY, Ahuja AT. Evaluation of real-timequalitative sonoelastography of focal lesions in the parotid and submandibular glands. Applicationsand limitations. EurRadiol. 2010; 20:1958–1964.
[7] Brennan PA, Herd MK, Howlett DC, Gibson D, Oeppen RS. Is ultrasound alone sufficient forimaging superficial lobe benign parotid tumours before surgery?.Br J Oral Maxillofac Surg. 2011; E-pub ahead of print.
[8] Howlett DC. High resolution ultrasound assessment of the parotid gland. Br J Radiol. 2003; 76:271– 277.

[9] Katz P, Hartl DM, Guerre A. Clinical ultrasound of the salivary glands. OtolaryngolClin North Am.2009; 42:973–1000.
[10] Sodhi KS, Bartlett M, Prabhu NK. Role of high resolution ultrasound in parotid lesions in children. IntJ PediatrOtorhinolaryngol. 2011; 75: 1353–1358.
[11] Yoo DS, Wong TZ, Brizel DM. The role of adaptive and functional imaging modalities in radiationtherapy: Approach and application from a radiation oncology perspective. Semin Ultrasound Ct.2010; 31:444–461.
[12] Cheng SC, Ying MT, Kwong DL, Wu VW. Sonographic appearance of parotid glands in patientstreated with intensity-modulated radiotherapy or conventional radiotherapy for nasopharyngealcarcinoma. Ultrasound Med Biol. 2011a; 37: 220 230.
[13] Imanimoghaddam M, Rahrooh M, Tafakhori Z, Zahedanaraki S, Homaeieshandiz F.Changes of parotid and submandibular glands caused by radiotherapy—an ultrasound evaluation. Dentomaxillofacial Radiology. 2012; 41: 379-384.
[14] Ying M, Wu VWC, Kwong DLW. Comparison of sonographic appearance of normal and postradiotherapyparotid glands: A preliminary study. Ultrasound Med Biol. 2007; 33:1244–1250.
[15] Bialek EJ, Jakubowski W, Zajkowski P, Szopinski KT, Osmolski A. US of the major salivary glands: anatomy and spatial relationships,pathologic conditions, and pitfalls. Radiographics. 2006; 26: 745–763.
[16] Orloff LA, Hwang HS, Jecker P. The role of ultrasound in thediagnosis and management of salivary disease. Operative techniques in otolaryngology 2009; 20: 136–144.
[17] Vaezzadeh SA, Allahverdi M, Nedaie HA, Aghili M, Esfehani M. Comparison of conventional and 3D conformal treatments using linac energies for prostate cancer. Iran J Radiat Res. 2012; 10: 145-150.
[18] Zimmerman RP, Mark RJ, Tran LM, Juillard GF. Concomitant pilocarpine during head and neck irradiation is associated with decreased posttreatment xerostomia. Int J RadiatOncolBiolPhys 1997; 37: 571-5
[19] Dirix P, Nuyts S, Van den Bogaert W. Radiation—inducedxerostomia in patients with head and neck cancer. Cancer 2006;107: 2525–2534.
[20] Wu VW, Ying MT, Kwong DL. Evaluation of radiation-inducedchanges to parotidglandsfollowingconventionalradiotherapy in patients with nasopharygnealcarcinoma. Br J Radiology. 2011; 84(1005): 843-849.
[21] Kara Bucci M, Bevan A, Roach M. Advances in radiation therapy: conventional to 3D, to IMRT, to 4D and beyond. CA Cancer J Clinic 2005; 55: 117-134
[22] Jen YM, Shih R, Lin YS, Su WF, Ku CH et al. Parotid gland-sparing 3-dinemsional conformal radiotherapy results in less severe dry mouth in nasopharyngeal cancer patients: a dosimetric and clinical comparison with convetional radiotherapy. RadiotherOncol 2005; 75: 204-9.
[23] Kotecha S, Bhatia P, Rout PGJ. Diagnostic ultrasound in thehead and neck region. Dent Update 2008;35:529–34.
[24] McBride WH, Roney Withers H. Biologic basic of radiationtherapy. In: Halperin E, Perez C, Brady L, eds. Principles andpractice of radiation oncology. 5th edn. Philadelphia, PA:Lippincott Williams and Wilkins; 2008. p. 79.
[25] Radfar L, Sirois DA. Structural and functional injury in minipigsalivary glands following fractionated exposure to 70 Gy ofionizing radiation: An animal model for human radiationinducedsalivary gland injury. Oral Surg Oral Med Oral PatholOral RadiolEndod 2003; 96: 267–274.
[26] Nagler Rm, Baum Bj, Fox PC. Effects of X irradiation on thefunction of rat salivary glands at 3 and 40 days. Radiat Res 1993;1363: 392–396.
[27] Henriksson R, Frojd O, Gustafsson H, Johansson S, Yi-Qing C, Franzen L, Bjermer L. Increase inmast cells and hyaluronic acid correlates to radiation-induced damage and loss of serous acinarcells in salivary glands: The parotid and submandibular glands differ in radiation sensitivity. Br JCancer. 1994; 69:320–326.
[28] Barker JL, Garden AS, Ang KK, O'Daniel JC, Wang H, Court LE, et al. Quantification of volumetric and geometric changes occurringduring fractionated radiotherapy for head-and-neck cancerusing an integrated CT/linear accelerator system. Int J RadiatOncolBiolPhys 2004;59:960–970.
[29] Lee C, Langen KM, Lu W, Haimerl J, Schnarr E, Ruchala KJ, et al. Evaluation of geometric changes of parotid glandsduring head and neck cancer radiotherapy using daily MVCT andautomatic deformable registration. RadiotherOncol 2008;89:81–88.
[30] Nomayr A, Lell M, Sweeney R, Bautz W, Lukas P. MRI appearance ofradiation-induced changes of normal cervical tissues. EurRadiol 2001;11:1807–1817.
[31] Burke CJ, Thomas RH, Howlett D. Imaging the major salivaryglands. Br J Oral MaxillofacSurg 2011; 49: 261–269.

[32] Gritzmann N, Rettenbacher T, Hollerweger A, Macheiner P,Hubner E. Sonography of the salivary glands. EurRadiol 2003;13: 964–975
[33] Grehn AL, Gustafsson H, Franzen L, Thomell LE, HenrikssonR. Ultrastructural morphometry of parotid acinar cells followingfractionated irradiation. Oral Oncol 1997; 33: 23–28.
[34] Konings AW, Faber H. Secondary radiation damage as the maincause for unexpected volume effects: A histopathologic study ofthe parotid gland. Int J RadiatOncolBiolPhys 2006; 64: 98–105.
[35] Teymoortash A, Simolka N, Schrader C, Tiemann M, WernerJA. Lymphocyte subsets in irradiation-induced sialadenitis of thesubmandibular gland. Histopathology 2005; 47: 493–500.
[36] Seifert G. Etiology and differential diagnosis of sialadenitis.Laryngorhinootologie 1995; 74: 274–281.
[37] Evans RM, Ying M, Ahuja AT. Ultrasound. In: Ahuja AT,Evans RM, King AD, van Hasselt CA, eds. Imaging in head andneck cancer. A practical approach. London: Greenwich MedicalMedia Limited; 2003. pp. 3–16.
[38] Turner MD, Ship JA. Salivary secretion in health and disease. In:Wong DT, ed. Salivary diagnostics. 1st edn. Hoboken, NJ: Wiley-Blackwell; 2008. p. 60.
[39] Kotecha S, Bhatia P, Rout PGJ. Diagnostic ultrasound in thehead and neck region. Dent Update 2008;35:529–34.