

# Evaluation of Radiotherapy Effect on Auditory System in Patients with Head and Neck Tumors

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## Abstract

**Introduction:** Radiotherapy in patients with head and neck tumors may result in damage of different organs such as eyes and ears. However, there is no consensus regarding the level of damage, especially its effect on hearing threshold. This study has been designed to determine the effect of radiotherapy on auditory system of patients with head and neck tumors.

**Methods:** In a prospective cohort study, 36 patients receiving radiotherapy were examined before and after radiotherapy and variations in the threshold of hearing of radiotherapy-receiving ears (encounter group) and the other ears (witness group) were compared using OAE and High-frequency audiometry.

**Findings:** After radiotherapy, according to OAE the threshold of hearing of radiotherapy-receiving ears increased significantly, but the threshold of hearing of the other ears increased significantly just at 2000Hz ( $P < 0.05$ ). The mean of the threshold of hearing variations in all frequencies between the two groups had the significant differences ( $P < 0.001$ ). According to High frequency audiometry method, the variations in threshold of hearing in the three studied frequencies had a significant difference for both groups.

**Conclusion:** Radiotherapy had related with hearing loss in patients with head and neck tumors. So, preventive measures such as ear protective shields and providing new radiotherapy devices and method sand informing the personnel of radiotherapy units about the standard way of radiation exposure are required.

**Keywords:** Radiotherapy; Head and neck tumors; Hearing loss

## Introduction

Radiotherapy is one of the most effective ways of treating head and neck tumors in such a way that its results are comparable to surgery in many instances. In some tumors, radiotherapy is preferred method to achieve better results. However, based on the anatomic location of the lesion, radiotherapy can cause different complications for the patient [1]. One of the important complications of radiotherapy is ototoxicity [2].

The dose of radiotherapy is another factor that influences the level of complication. For more advanced and more aggressive tumors we may need higher doses which lead to more complications [3]. Hearing loss is one of the main complications of radiotherapy in head and neck tumors [4]. In recent years, the standard treatment for many tumors has been radiotherapy and chemotherapy with Cisplatin; both are well-known causes of ototoxicity [5,6]. Many studies have evaluated the irreversible hearing loss in these patients, and results showed a great variability in the incidence of ototoxicity, varying between 18% and 50% [7,8].

Factors like the dose of radiotherapy, tumor stage, placing cochlea in radiotherapy field and the patients' age) the older the patient, the more the ototoxicity), influence ototoxicity [9,10]. Also, these studies have shown contradicting results about the influence of radiotherapy on ototoxicity.

Besides hearing loss other complications such as external ear necrosis, temporal bone osteoradionecrosis, otitis media, otalgia, and Tinnitus has been attributed to head and neck radiotherapy [11,12]. So, regarding the relatively large frequency of head and neck tumors and performing radiotherapy on most of the patients, the aim of current study is to determine the effect of radiotherapy on hearing in these patients.

## Materials and Methods

This study is a prospective cohort study, which has been conducted in 2015 and 2016 on patients who underwent radiotherapy to cure head and neck tumors in Isfahan Milad Hospital. The inclusion criteria were: suffering from head and neck tumors

and receiving radiotherapy, 30-80 years of age, no previous hearing malady, no primary tumors in hearing apparatus, no previous radiotherapy and chemotherapy and the patients' agreement to be enrolled in the study. Also, patients who died before the completion of the study, or had ear surgery during the study or were lost to follow up visits or needed adjuvant chemotherapy were excluded from the study. The proposal of the study was approved by medical ethics committee of Isfahan University of medical sciences.

The qualified patients were entered the study by simple sampling and their demographic data was extracted and registered. Also, the information regarding their tumors such as imaging studies performed, previous diagnostic tests, pathology and grading and staging of their tumors, anatomic location, number of radiotherapy sessions and the dose of radiation was determined and recorded.

Before radiotherapy, the hearing of both the ears of the patients was evaluated using OAE and High-frequency audiometry. In the study, the radiotherapy-receiving ear was considered the case and opposite ear (ear not receiving radiation) was considered control and hearing level of both ears were documented. Hearing level of the patients was measured at the end of the radiotherapy with OAE and

with High-frequency audiometry three months after radiotherapy and finally, the differences in hearing levels were compared.

The obtained data were analyzed with observation repetition using SPSS version 24, Chi-square statistical test, independent T-test, paired T-test and One-way ANOVA with repeated measures, also data were showed as mean±SD and frequency (percent) and  $P < 0.05$  was considered as significant.

## Results

In this study, 43 patients with head and neck cancer who received radiotherapy were included. During the study, 7 patients were excluded (4 patients died, 1 patient needed chemotherapy and 2 patients didn't return for follow up visit) and finally data of 36 patients were analyzed.

The mean age of the patients was  $57.1 \pm 9.4$  years and the range was 45-76 years. 16 patients were male (44.4%) and 20 (55.6%) were female. Table 1 shows the demographic and clinical variables of the patients. According to Table 1, patients with  $\geq 60$  years old, male, parotid mass, hard palate tumor, ACC pathology, stage III disease and left-side involvement were the most common demographic and clinical variables.

**Table 1:** The distribution of demographic and clinical variables in the study.

Variable	Number	Percent	
Age Distribution	Younger than 50	9	25
	50-59	13	36.1
	60 years old and older	14	38.9
Gender	male	16	44.4
	Female	20	55.6
Reason of Referring	Palate mass	9	25
	parotid mass	13	36.1
	Jaw tumor	8	22.1
	Scalp tumor	6	16.7
Location of the Tumor	Hard palate	16	44.4
	Parotid	12	33.3
	Maxillary sinus	4	11.1
	Scalp	4	11.1
Tumor Pathology	ACC	20	55.6
	BCC	7	19.4
	SCC	9	25
Tumor Stage Involved Side	II	16	44.4
	III	20	55.6
	right	13	18.1
	left	23	31.9

ACC: Adenoid Cystic Carcinoma; BCC: Basal Cell Carcinoma; SCC: Squamous Cell Carcinoma.

The mean number of radiotherapy sessions was  $30.5 \pm 2.9$  and the mean of radiation dose was  $5961 \pm 615.6$  CGY. Table 2 showed the means of hearing threshold at different frequencies using OAE before and after radiotherapy in the two groups. According to T-paired test, hearing threshold of ears receiving radiotherapy increased significantly ( $P < 0.05$ , for all) but on the other side (control ear) hearing threshold increased significantly just in 2000Hz ( $P = 0.007$ ).

On the other hand, according to T-test, hearing threshold before radiotherapy didn't have any meaningful difference between the two ear sat all frequencies. But after treatment, the difference between the ears was significant at all the frequencies ( $P < 0.05$ ) (Table 2). Also, according to One-way ANOVA with repeated measures, the mean of hearing threshold change had a significant difference at all frequencies between the two groups ( $P < 0.05$ ).

**Table 2:** Means of hearing threshold before and after radiotherapy in the two groups according to OAE test.

Frequency	Time	Group		P-Value*
		Encountered or involved ear	Not- encountered or control ear	
500	Before radiotherapy	$0.86 \pm 0.14$	$1.06 \pm 0.92$	0.35
	after radiotherapy	$3.69 \pm 1.69$	$1.47 \pm 1.13$	$< 0.001$
1000	Before radiotherapy	$1.25 \pm 0.15$	$1.22 \pm 1.07$	0.18
	after radiotherapy	$5.78 \pm 2.47$	$1.56 \pm 1.03$	$< 0.001$
1500	before radiotherapy	$1.08 \pm 0.13$	$1.22 \pm 0.99$	0.51
	after radiotherapy	$5.17 \pm 2.05$	$1.22 \pm 0.76$	$< 0.001$
2000	before radiotherapy	$1.14 \pm 0.83$	$0.92 \pm 1.02$	0.031
	after radiotherapy	$3.86 \pm 3.36$	$1.58 \pm 0.87$	$< 0.001$
4000	before radiotherapy	$0.86 \pm 0.54$	$0.72 \pm 0.57$	0.29
	after radiotherapy	$2.67 \pm 0.68$	$0.89 \pm 0.83$	0.02

\*Independent t test.

High-frequency audiometry test showed that in X-ray encountered group, hearing thresholds were increased significantly at 8000, 10000 and 16000Hz ( $P < 0.001$ , for all three) and in the not-encountered group, hearing threshold was increased significantly only at 10000Hz ( $P = 0.003$ ) in the after compared to before radiotherapy. On the other hand, before the treatment, there were

no significant differences between the two groups at these three frequencies ( $P > 0.05$ ), but after treatment, there were significant differences at 10000 and 16000Hz ( $P < 0.001$ , for both) (Table 3). Also, the trend of hearing threshold change at the frequencies had the significant difference between the groups ( $P < 0.001$ , for three frequency).

**Table 3:** Means of hearing threshold before and after radiotherapy in the two groups according to High Frequency Audiometry test.

Frequency	Time	Group		P-Value*
		Encountered	Not- encountered	
High frequency (8000Hz)	Before radiotherapy	$25.4 \pm 9.8$	$28.8 \pm 9.7$	0.15
	3 months after radiotherapy	$48.5 \pm 6.3$	$30.3 \pm 5.5$	0.12
High frequency (10000Hz)	Before radiotherapy	$23.2 \pm 9.6$	$26.9 \pm 10.1$	0.35
	3 months after radiotherapy	$57.8 \pm 8.4$	$32.3 \pm 5.1$	$< 0.001$
High frequency (16000Hz)	Before radiotherapy	$28.1 \pm 11.5$	$28.7 \pm 12.4$	0.11
	3 months after radiotherapy	$70.1 \pm 12.3$	$33.3 \pm 6.5$	$< 0.001$

\*Independent t test.

## Discussion

Patients with head and neck tumors who receive radiotherapy are exposed to the dangers of radiotherapy complications from which the effects of radiotherapy on ears can be mentioned. The effect of radiotherapy on ears appears as hearing loss and the

amount of hearing loss depends on the duration of radiotherapy, radiation dose, personal characteristics, treatment technique, and the place of tumor and radiation angle. Although protective shields are used to protect organs during radiotherapy but the amount of the complications is high. Enough studies has been done about

harmful effects of radiotherapy on organs like eyes [12] but little attention has been paid to its influence on hearing. So, this study was conducted to determine the effect of radiotherapy on hearing in patients with head and neck tumors.

In this study 72 ears of 36 patients suffering from cancer who received radiotherapy were evaluated from which radiation-receiving ear was considered the case and the other ear was considered control and hearing conditions of both ears were examined and compared before and after radiation using OAE and high frequency audiometry tests. According to the results of our study, after treatment hearing threshold of patients had a significant difference at all frequencies and most of the patients suffered from hearing loss, while the other ear had no significant hearing loss and only at 2000Hz the control ear had hearing loss.

In three independent studies conducted by Pearson [7], Dell'Aringa [8] and Zuur [9], radiotherapy had a significant effect on hearing loss in patients with head and neck tumors. Schultz et al reported hearing loss in 72.3% of patients in their study of 282 patients with head and neck tumors receiving radiotherapy and in this study the prevalence and severity of hearing loss was a lot in the patients who received radiotherapy [2]. In a study, Chen et al. [10], investigated on 44 ears of 22 patients receiving head and neck radiotherapy for 28 months and the results indicated that 57% of the patients suffered from hearing loss. In this study receiving X-ray dosage more than 48.5 Grays, significantly increased hearing loss danger [10]. Bhandare et al. [11] have investigated the complications of radiotherapy and reported its effect on hearing loss in patients. In the other study, indicated radiotherapy of laryngeal carcinoma decreased hearing loss and had related with tumor side and adjuvant therapy of chemotherapy [4]. In a study, patients with nasopharyngeal carcinomas following radiotherapy had hearing loss and poor response to treat and this sensorineural hearing loss was related with posterior circulation disorders [13].

## Conclusion

According to our study and other study, the patients with head and neck tumors who received radiotherapy had hearing loss in the ipsilateral and opposite side ears but the hearing loss in the ipsilateral ear was more severe than opposite side ear. So, preventive measures such as ear protective shields and providing new radiotherapy devices and informing the personnel of radiotherapy units about the standard way of radiation exposure and controlling the radiation dose and other related standards are required. Also, concerning the hearing loss mechanism in radiotherapy, it is recommended that in future studies the influence of antioxidant

compounds on reducing the complications of radiotherapy be investigated. Moreover, regarding the limitations of our study such as paucity of number of samples, there should be more studies with more sample size.

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