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Original Article

Dose Measurements of Parotid Glands and Spinal Cord in Conventional Treatment of Nasopharyngeal Carcinoma Using RANDO Phantom and Thermoluminescent Dosimeters

Mohammad Taghi Bahreyni Toossi[1], Eftekhar Rajab Bolookat[1*], Raham Salek[2], Mohsen Layegh[2]

Abstract

Introduction
Radiotherapy is regarded as the first treatment of choice for nasopharyngeal carcinoma. Despite the advantages of radiotherapy, patients may suffer from a wide range of side-effects due to the presence of many sensitive normal tissues in these regions. If the absorbed dose exceeds the tolerance level in parotid glands and the spinal cord, myelopathy, Lhermitte's sign and xerostomia cannot be avoided.
Materials and Methods
The head and neck of a RANDO phantom (reference man), which was regarded as a hypothetical patient with nasopharyngeal carcinoma was evaluated. The full course of treatment consisted of three phases. At the beginning of each phase, an oncologist marked conventional fields on the RANDO phantom using a simulator. For measuring the absorbed dose, Thermoluminescent Dosimeters (TLD) chips (TLD-100) were utilized.The absorbed dose by TLDs was read by Harshaw 3500 TLD reader.
Results
The total absorbed dose was calculated by measuring the absorbed dose in each phase, multiplied by the fraction numbers of each phase; the obtained values were summed up. The results showed that the received doses by spinal cord ranged from 15.24 to 54.56 Gy. Also, the absorbed dose of parotid glands was approximately 39.23 Gy.
Conclusion
Considering the minimum tolerance dose the absorbed doses in the spinal cord and parotid glands were above the tolerance level. The incidence rate of xerostomia and myelopathy were higher in patients, treated by conventional methods.

Keywords: Nasopharyngeal Carcinoma, Radiotherapy, RANDO Phantom, Thermoluminescent Dosimetry

1- Medical Physics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2- Radiation Oncology Department, Omid Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
*Corresponding author: Tel: +982122718081, E-mail: eftekhar.bolookat@gmail.com

1. Introduction

Nasopharyngeal carcinoma (NPC) is one of the most common cancers of the head and neck regions. This type of cancer is endemic to South East Asia and its incidence ranges between 15 and 50 cases per 100,000 [1]. Considering the anatomical position of the nasopharynx, radiation therapy is regarded as the first treatment of choice.[2]

Despite the fact that radiotherapy is widely applied for head and neck regions, it may lead to many side-effects due to the presence of sensitive organs in these regions [3]. In fact, if the absorbed dose exceeds the tolerance level in parotid glands and spinal cord, Myelopathy, Lhermitte's sign (LS) and xerostomia may occur as late response [4-8].

In 1999, the permitted level of scattered radiation to the spinal cord due to head and neck radiotherapy was evaluated. Twenty patients with head and neck cancers treated by cobalt 60 or a 6MV linear accelerator, the total dose absorbed by the spinal cord was calculated based on direct and scattered radiation doses. The cord was removed from the radiation field at tumor doses below 4,400 cGy. The total tumor dose ranged from 5400 to 7400 cGy (mean: 6060 cGy). [5]

In the mentioned study, all patients received the prescribed dose and none missed the follow-up assessments (mean follow up duration: 36 months). As the results indicated, scattered radiation could produce as much as 20% extra dose to the spinal cord. It was concluded that the scattered radiation could cause a significant additional dose to the spinal cord, which may in turn contribute to a higher incidence of myelopathy; this was in fact contrary to the previous assumptions. [5]

In another study, LS was assessed among NPC patients, following radiotherapy. In this study, 1,171 patients with NPC were studied from 1979 through 1990. LS was reported in 121 patients (10.3%) and the median time of its development was 3.0 months after the completion of radiotherapy (range: 0.2–72 months), LS manifestation among patients lasted for 1-82 weeks (median:17 weeks). A correlation was noted between the increased incidence of LS and radiotherapy dose received by the cervical spinal cord when the cord absorbed dose exceeded 48.9 Gy.[6]

Xerostomia is the most common post-radiotherapy complication in (NPC) patients. In a study by Wu, the relationship between the received dose and post-radiotherapy changes in parotid glands was evaluated. Data from 18 NPC patients, treated by radiotherapy between 1997 and 2001, were collected. The volumes of parotid glands were compared before and after the treatment [7].

In the study by Wu, a questionnaire was used to assess patients' reactions and Xerostomia status. Radiotherapy treatment plans or participants were retrieved from the Eclipse Treatment Planning System which radiation doses delivered to the parotid glands was estimated. The correlation between the parotid gland dose and post-radiotherapy changes was evaluated. The results showed that parotid glands were significantly smaller after radiotherapy, compared to the pre-radiotherapy period ($P<0.001$) [7].

In the mentioned study, changes in gland volume and the subjective severity of Xerostomia could be evaluated based on the dose delivered to parotid glands in NPC patients. The damage to the glands was long-lasting with significant effects on patients' quality of life[7]. In all mentioned studies, the dose received by organs' was estimated by the treatment planning system. However, in the current study, dose measurements were carried out by Thermoluminescent Dosimeters (TLDs) and a RANDO phantom that has been used in several studies as a reference patient[8,9,10].

2. Materials and Methods

2.1. TLD

To measure the absorbed dose by the spinal cord and parotid glands, TLD-100 (LiF: Mg, Ti) chips (dimension of $3.0\times3.0\times0.9$ mm^3) were used. The effective atomic number of TLD material is about 8.2, which is nearly the

same as that of soft tissues. TLDs' were calibrated by gamma rays from CO-60 machine.

Before the measurements, 100 TLDs were exposed to 1 Gy dose by CO-60 machine (THERATRON 780C) to obtain the Element Correction Coefficient (ECC). ECC indicates the deviation of each TLD from its mean reading at a constant dose. Also, reader calibration factor (RCF) was calculated as follows:

$$RCF = \langle Q \rangle / L \quad (1)$$

Where Q is the mean charge measured in a set of calibration dosimeters and L denotes the radiation quantity expressed in generic units (gU). One gU is the radiation delivered in one second at a specific geometry by a specific source at a constant distance from the source. Finally, the absorbed dose (Gy) was measured by the following formula:

$$D = ECC*(Q)/RCF \quad (2)$$

The calibration of TLDs was performed at a depth of 5 cm in a polymethylmethylmethacrylate (PMMA) phantom with a dimension of 30×30×20 cm^3 to account for the full scatter.

2.2. RANDO phantom

In this study, RANDO phantom was used as a hypothetical patient with NPC. This phantom is made of a natural human skeleton cast, and the inside material is radiologically equivalent to soft tissue [11]. This phantom consists of soft tissue, bone and lung-equivalent tissues.

The soft tissue in phantom is manufactured with a proprietary urethane formulation with an effective atomic number of 7.3 and a mass density of 0.985 g/ml^3; this tissue closely simulates muscle tissues with randomly distributed fat. RANDO phantom is sliced into 35 sections, each with a 2.5 cm thickness. Several holes are made in the slices, which allow the insertion of several TLDs [11].

In the present study, the location of spinal cord and parotid glands was determined in the phantom by an oncologist and CT images. Since no holes were located exactly at the center of the spinal cord, TLD chips were inserted in holes nearest to the spinal cord (Figure1).

2.3. Phantom irradiation

The full course of treatment was carried out in three phases. According to Fletcher's method, each phase was delineated on the surface of the phantom by an oncologist and the use of a simulator. In phase I, the treatment included two lateral neck fields (15.5*18.5 cm^2) and an anterior supraclavicular field (16.5*10 cm^2). In phase II, two lateral and an anterior face field (8*9 cm^2), plus an anterior supraclavicular field (17.5*16.5 cm^2) were included.

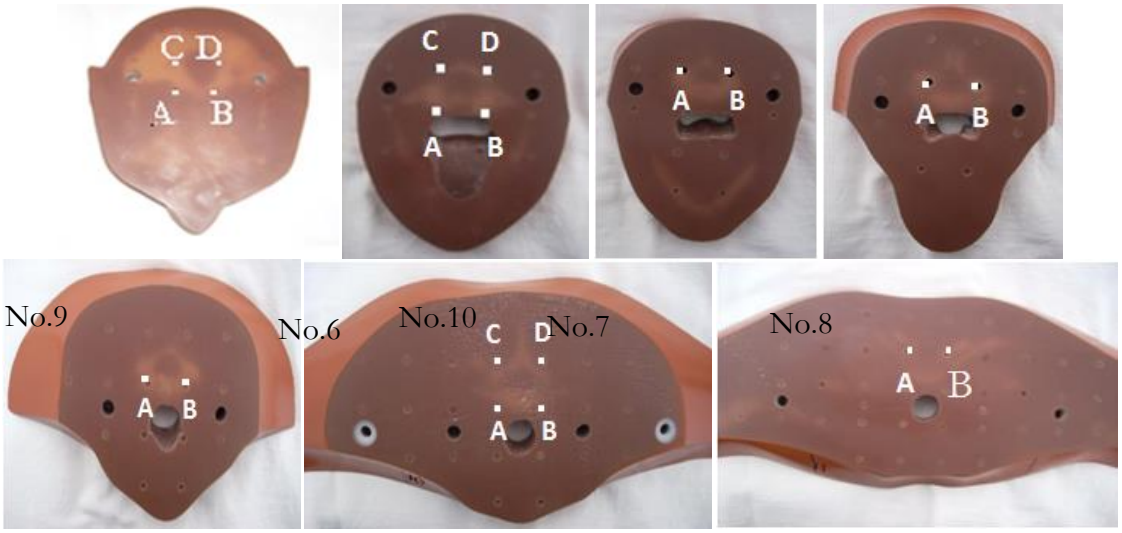

Figure 1. Location of TLDs in the RANDO phantom

The full course of treatment was planned as follows: phase I: 44Gy in 22 fractions, phase II: 6 Gy in three fractions, and phase III: 16 Gy in eight fractions. Then, the RANDO phantom was irradiated by gamma rays from CO-60 machine at Mashhad Omid Hospital. The first fraction of each phase was performed on the phantom. The ends of irradiation, TLDs were removed and the absorbed dose was read by Harshaw 3500 TLD reader. For higher accuracy, each fraction was repeated three times. To determine the total absorbed dose, the absorbed dose of each fraction was multiplied by the number of fractions in that phase.

3. Results

Firstly, the dose-response diagram was plotted. The response of TLDs to radiation was linear in the dose range applied in NPC treatment (Figure 2).

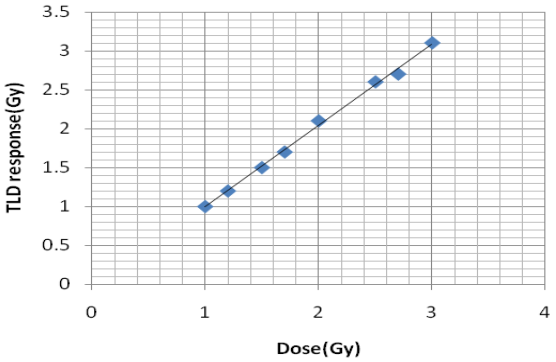

Figure2. TLD dose-response curve

The dose received by parotid glands and spinal cord was measured after the completion of each treatment stage. The absorbed doses of parotid glands after the first fraction for each phase were 1.16±0.04, 1.29±0.05 and 1.23±0.08 Gy, respectively. The total absorbed dose of these organs was approximately 39.23±1.53 Gy. The absorbed doses of the spinal cord are presented in tables 1-7.

Table 1. The absorbed dose (Gy) of the spinal cord adjacent to the fourth and fifth thoracic vertebrae

	A	**B**
Phase I	1.71±0.02	1.78±0.02
Phase II	1.22±0.02	1.21±0.02
Phase III	0.31±0.01	0.32±0.01
Total absorbed dose (Gy)	45.1±0.45	

Table 2. The absorbed dose (Gy) of the spinal cord adjacent to the second and third thoracic vertebrae

	A	B	C	D
PhaseI	1.71±0.02	1.78±0.02	1.71±0.1	1.52±0.19
PhaseII	1.22±0.02	1.21±0.02	1.22±0.01	1.21±0.04
PhaseIII	0.31± 0.01	0.32±0.01	0.41±0.01	0.40±0.02
Total absorbed dose(Gy)		45.1±0.45	42.41±3.35	

Table 3. The absorbed dose (Gy) of the spinal cord adjacent to the first thoracic vertebrae

	A	**B**
Phase I	2.21±0.10	2.22±0.14
Phase II	1.48±0.03	1.46±0.03
Phase III	0.16±0.03	0.17±0.02
Total absorbed dose(Gy)	54.56±2.60	

Table 4. The absorbed dose (Gy) of the spinal cord adjacent to the seventh cervical vertebra

	A	B
Phase I	1.92±0.07	1.92±0.06
Phase II	1.21±0.06	1.19±0.11
Phase III	0.20±0.01	0.21±0.01
Total absorbed dose(Gy)	47.48±1.42	

Table 5. The absorbed dose (Gy) of the spinal cord adjacent to the fifth and sixthcervical vertebrae

	A	B
Phase I	2.06±0.12	2.19±0.10
Phase II	0.27±0.001	0.29±0.01
Phase III	0.20±0.01	0.19±0.01
Total absorbed dose(Gy)	49.15±2.77	

Table 6. The absorbed dose (Gy) of the spinal cord adjacent to the third and forth cervical vertebrae

	A	B	C	D
PhaseI	2.14±0.11	2.10±0.09	2.08±0.04	2.05±0.05
PhaseII	1.64±0.01	1.70±0.06	0.46±0.02	0.45±0.01
PhaseIII	0.96±0.09	0.98±0.04	0.43±0.01	0.45±0.01
Total absorbed dose(Gy)	62.91±1.99		50.31±1.06	

Table 7. The absorbed dose (Gy) of the spinal cord adjacent to the second cervical vertebrae

	A	B	C	D
PhaseI	1.14±0.01	1.31±0.02	0.57±0.01	0.57±0.01
PhaseII	1.13±0.03	1.22±0.02	0.53±0.01	0.55±0.01
PhaseIII	0.96 ±0.05	0.97±0.06	0.41±0.04	0.42±0.08
Total absorbed dose(Gy)	34.30±1.24		15.24±1.31	

Repeated measurement test in SPSS was used for data analysis. The difference between the absorbed dose of parotid glands in the first fraction of each phase was not significant. However, in the spinal cord, the difference between the absorbed doses in phases I, II and III was significant due to replacing the anterior field with lateral fields and spine sparing.

4. Discussion

Xerostomia is one of the most common late complications of NPC resulting in a decline patients' quality of life after curative radiotherapy. Many studies have shown that conventional radiotherapy increases the risk of Xerostomia among patients. In this regard, Nishioka et al. indicated that use of CT simulation and a treatment planning system, combined with three-field irradiation, for delineating targets and organs at risk could significantly reduce radiation-induced xerostomia, compared to conventional simulation and bilateral opposed treatment methods[12].

In a previous study, Pow et al directly compared the effects of intensity-modulated radiotherapy (IMRT) versus conventional radiotherapy (CRT) on salivary flow and quality of life in patients with early-stage NPC. IMRT was significantly more advantageous than CRT in terms of parotid sparing and quality of life in the early-stage o the disease [13].

Moreover, Tribius et al. compared intensity-modulated radiotherapy versus conventional and three dimensional (3D) conformal

radiotherapy in patients with head and neck cancers. Based on the study finding, patients treated with IMRT experienced significant improvements in several important domains of quality of life, compared to two-dimensional radiotherapy and 3D conformal radiotherapy [14].

In this study, the total absorbed dose of parotid glands was 39.29 Gy, which was above the tolerance level according to the minimum tolerance dose (TD5/5). The risk of complications within five years after radiotherapy was estimated at 5%. Therefore, patients may probably complain of xerostomia following radiotherapy. This measurement was in good agreement with findings reported by Kuhnt and colleagues (36.9 Gy) [15].

LS is another side-effect occurring in the spinal cord in patients with head and neck cancers [16, 17]. In a study by Leung W et al. During 1979-1990, 1,171 patients with NPC completed radiotherapy with or without chemotherapy. LS was observed in 121 patients (10.3%). The median development time of LS was 3 months after the completion of radiotherapy (range: 0.2-72 months), and its manifestation lasted for 1-82 weeks (median: 17 weeks) [6].

A correlation was detected between the increased incidence of LS and radiotherapy dose received by the cervical spinal cord was when the cord dose exceeded 48.9 Gy. Therefore, wherever possible, a CT simulator and a 3D treatment-planning system should be used to verify the dose distribution of electron-beam radiotherapy and diminish the risk of radiation overdose on the cervical cord [17]. In this study, although the spinal cord was excluded at the end of phase I, no significant change in the absorbed dose was observed at the end of phases I and II. In phase III, the anterior neck field was replaced by a lateral field, and therefore, the absorbed dose by the spinal cord considerably reduced.

According to our findings, the absorbed dose of spinal cord segments, corresponding to the region confined between the third cervical and third thoracic vertebrae, was higher than 47 Gy. Also, 70% of the spinal cord received more than 44 Gy, while the average absorbed dose was 51.20 Gy. In a study by Martel et al. the spinal cord absorbed dose was equal to 52 Gy, which was in consistence with our findings [18].

There are many studies that show the probability of uncomplicated tumor control is increased with 3D treatment planning compared to the 2D approach. The dose received by normal structures also reduced with 3D planning and IMRT technique in head and neck cancers [19-23].

5. Conclusion

The obtained findings showed that conventional radiation therapy which is still popular in some developing countries, delivers higher doses to normal organs. Some radiotherapy centers still have neither access to modern devices nor treatment planning software and should continue using conventional techniques. Consequently, patients may suffer from the side-effects of radiotherapy, which might have significant effects on their quality of life, as discussed earlier. In conclusion, it is highly recommended that modern high-conformal techniques such as 3D-Conformal radiotherapy and IMRT must be applied in order to reduce the unnecessary absorbed dose by the spinal cord and parotid glands.

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