



Comparison of doses received in the mandibular condyle, cochlea, and parotid gland in neuroaxial treatment

Fernanda L. Oliveira^{1,2}, Fabiana F. de Lima², João Antônio Fo¹ e Êudice Vilela^{1,2}

¹ Universidade Federal de Pernambuco (UFPE)
Departamento de Energia Nuclear – DEN
Rua Professor Luiz Freire, 1000
50740-540 Recife-PE
fluoliveira@gmail.com / jaf@ufpe.br

² Centro Regional de Ciências Nucleares do Nordeste (CRCN-NE)
Comissão Nacional de Energia Nuclear (CNEN)
Av. Professor Luiz Freire, nº 200 - CDU
50740-540 Recife, PE
ecvilela@cnen.gov.br / falima@cnen.gov.br

ABSTRACT

Sensorineural hearing loss is a common side effect in patients who undergo radiotherapy for the treatment of cancer tumors in the head and neck. In fractionated doses of radiotherapy, in the majority of intracranial tumors, the cochlea is the most affected organ. In addition to the cochlea, the mandible and the parotid glands are also exposed to radiation, which commonly leads to Osteoradionecrosis of the mandible and Xerostomia. In the head and neck regions, this can be complicated by the semi-independence of the positioning in this region, as regards the rigid cranium, connected to the semi-rigid mandible, and successive levels of the upper cervical spine and thoracic spine, which can lead to uncertainty in rotation as well as in head-neck movements, both up and down and side to side. The present study performed an intercomparison of the doses applied through four radiotherapy planning techniques for the neuroaxial regions of the cochlea, mandible, and parotid glands, considering the changes carried out in each planning technique, including the protective shield, the angulations gantry and the field size. The results obtained by applying the half beam and angled field techniques varied in the cochlea by an average of 113.8% from the prescribed dose, whereas when applying the angled field technique with and without the mobile gap, the results varied in 104.5%. In the mandible, the half beam and angled field techniques showed that the dose varied an average of 16.5%, while in the techniques with and without the mobile gap, the variation showed an average of 116.4%. These values were also received by the parotid glands, which overlap the mandible. It can therefore be concluded that the protection shields of the first two techniques were less efficient in protecting the mandible due to its modeling.

Keywords: Radiotherapy, Neuroaxial treatment, Intercomparison

1. INTRODUCTION

In radiotherapy (RT), it is expected and accepted that in part of the treatment some of the normal tissue will undergo side effects and/or complications, so long as the normal tissues have received a dose at the same level as the dose applied to the tumor. The side effect is normally less harmful and temporary. Complications can arise in a shorter period of time and may be either acute or late and chronic. The side effect can be considered acceptable if the application frequency in patients is high, while complications are only considered acceptable if they occur with low-frequency applications [1].

Sensorineural hearing loss is a common side effect in patients who undergo RT for the treatment of cancer tumors in the head and neck. In the fractionated doses of RT, in the majority of intracranial tumors, the cochlea is the most affected organ. This is an important consequence of therapy for children with intracranial diseases, including medulloblastoma [3]. For Moeller B.J.[4] RT and chemotherapy are the greatest causes of ototoxicity in children with medulloblastoma.

RT can damage the cochlea and/or acoustic nerve, leading to sensorineural hearing loss (SNHL-PASN), which is defined by the significant increase in the bone conducting transducer (BCT), essential in the frequency of human speech with long-term impacts, in turn compromising the patient's quality of life [5].

Bhandare N.[5] suggests limits in the Dose-Volume (when possible, but maintaining the desired region covered), for which they recommend:

(1) In conventionally fractionated RT, the average dose to the cochlea must be limited to ≤ 45 Gy (or to a more conservative limit of ≤ 35 Gy) to minimize the risk of PASN. To block the PASN, the dose to the cochlea must be kept as low as possible.

(2) In stereostatic radiosurgery (SRS) in the treatment of vestibular sarcoma (VS), the prescribed dose must be limited to 12-14 Gy to preserve the patient's hearing.

(3) A hypofraction scheme is suggested for VS to establish tumor control and preserve the patient's hearing, for which the total prescribed dose is of 21-30 Gy in 3-7 Gy per fraction for 3 to 10 days.

In this region, in addition to the cochlea, other organs are also exposed to radiation, considered at-risk organs, such as the mandibular condyle and the parotid glands, which can lead to the manifestation of Osteoradionecrosis (ORN) of the mandible and Xerostomia.

The changes induced by radiation not only affect the mandible, but also the soft tissue surrounding it [6,7]. ORN of the mandible is the most serious sequela caused by radiation, as it causes strong pain, fistulas in the oral cavity, and pathological fractures. ORN is defined by the Schwartz classification as an exposure of the bone, which is weakened over a period of three months due to the necrosis of the soft tissue after radiotherapy [6].

Xerostomia is an important and predominant problem in patients after undergoing RT for head and neck cancers, since the acute and late effects provoked by xerostomia cause difficulty in speech, sense of taste, and even sleeping habits [8].

In one study carried out by Mebmer [8], it could be observed that, along with xerostomia, other collateral effects of irradiation, such as dysguesia, which influences the patient's life over the long term, can worsen after five years.

RT has played an important role in the treatment of patients with head and neck cancers, but with the risk of a reduction in salivary production and xerostomia in nearly all patients [9].

To reduce the incidence of ototoxicity in children, a wide range of methods to reduce radiation levels in the cochlea have been investigated, including the use of three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), and the more recent proton therapy [3].

Ahn H. P.[10] reported that with IMRT and related technologies it is possible to apply the dose with the intention of protecting the normal structures, as well as to increase the conformal dose within the patient. The head-neck and neuroaxial planning techniques serve to protect the parotid glands by creating impacts of xerostomia and dysguesia, as well as preserve the patient's hearing and sense of taste by limiting the dose applied to the cochlea and pharyngeal constrictor muscles.

In the head and neck regions, this procedure may be complicated by the semi-independence of their positioning in this area, with the rigid cranium connected to the semi-rigid mandible and successive levels of the cervical spine and the upper thoracic spine, joined by flexible ligaments, can lead to uncertainty concerning the head-neck rotation as well as their up-and-down and side-to-side movements. The methods of immobilization may not provide an adequate fixation in the interfraction of the patient's position at all levels of the head and neck when applying RT, including the variation in the positions used for rotation and up-and-down and side-to-side movements, and may cause lordosis and scoliosis, thus facilitating the increase in dosage in this region [10].

The overlapping of the parotid glands upon the mandible and their proximity to the cochlea (Figure 1) make it so that a dose, no matter how small the field may be, reaches the three organs.

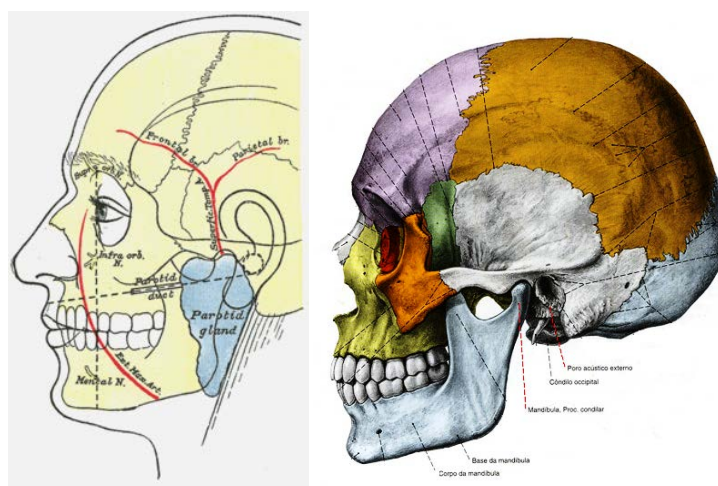


Figure 1 – Profile of the mandible, parotid glands, and acoustic pore (Sobotta, Johannes, 2000).

The present work therefore aims to compare the doses applied by four radiotherapy planning techniques within the neuroaxial regions of the cochlea, mandible, and parotid glands, considering the changes performed in each planning technique as: the protective shield in this region, the angulations gantry, and the field sizes.

2. METODOLOGY

To evaluate the techniques, medulloblastoma treatment simulations were performed in four distinct planning techniques, with RT treatment sessions carried out using two distinct linear accelerators, applied in a solid anthropomorphic simulator from the RANDO (Radiation Analog Dosimetry) Dosimetry Laboratory which represents the human body of a woman. The values of each RT planning technique for the positions are described in Table 1 below.

Table 1: Values of positions as radiotherapy planning.

Planning Technique	Gantry	Collimator	Table	Depth
1 st Planning Technique	270°/90°	11.3°/348.7°	Fixed	7.5 cm
2 nd Planning Technique	270°/90°	11.3°/348.7°	4.3° / 355.7°	7.5 cm
3 rd Planning Technique	270°/90°	171°/189°	5° / 355°	7.5 cm
4 th Planning Technique	270°/90°	351°/9°	355° / 5°	8.0 cm

The fields in the first and second planning techniques measured 30 x 18 cm. In the third session, the planning technique with mobile gap was applied, making it necessary to use three dimensions in the fields to record the oscillations, which measured 19 x 30 cm², 19 x 28 cm², and 19 x 26 cm², while in the fourth session, the fields measured 19 x 25 cm². In the first and second sessions, the protection used was a shield without lead, whereas in the third and fourth, the protection used was of a shield made of cerrobend alloy. These shields were modeled individually for each patient.

The experimental measurements were carried out using LiF:Mg,Ti (TLD-100) thermoluminescent dosimeters in the form of chips. These dosimeters were treated thermally in a PTW-TLDO annealing oven, manufactured by BICRON-NE, according to the specific parameters necessary for these, and the dosimeter readings were performed using a scanner manufactured by Harshaw-Bicron (model 5500) using synthetic air generated by an air compressor (model 4488) made by the same manufacturer.

3. RESULTS AND DISCUSSION

The results from the dose obtained in the cochlea in the first and second planning techniques are similar and slightly above the dose prescribed in the target volume. In the mandible, the doses are also quite similar and significantly lower than the prescribed dose. The parotid glands received the same doses as the mandibular condyle. In these two planning techniques, the collimator angles were the same on the left and right sides, 11.3° and 348.7° , respectively. The table in the first planning technique remained in the position of a 0° angle, whereas in the second planning technique, the table was angulated by 4.3° and 355.7° . The variation in the angle of the table caused no significant change in the dose received in this region.

In the third planning technique, both the dose from the cochlea and the dose from the mandible were above the prescribed dose for the target volume of 1.8 Gy, with values that were quite similar. The angles applied in the collimator were of 171° and 189° , while those in the table were of 5° and 355° . The 2° change in the collimator angle, as compared to the angles in the previous planning techniques, must have provoked a high dose within the mandibular condyle.

In the fourth planning technique, the collimator angles were of 351° and 9° , maintaining the table in the same position as the previous planning technique, and the gap did not oscillate. The doses were slightly lower, but the dose in the mandible remained high. These results can be observed in Table 2 below.

Table 2: Dose values in the four planning techniques

Sites	1 st Planning Technique	2 nd planning Technique	3 rd Planning Technique	4 th Planning Technique
Cochlea	(1.58 ± 0.05)	(1.54 ± 0.03)	(2.13 ± 0.06)	(1.89 ± 0.06)
	(1.72 ± 0.07)	(1.59 ± 0.05)	(2.13 ± 0.06)	(1.89 ± 0.05)
Mandible (Parotid glands)	(0.28 ± 0.02)	(0.23 ± 0.01)	(2.29 ± 0.10)	(1.96 ± 0.07)
	(0.20 ± 0.08)	(0.21 ± 0.01)	(2.46 ± 0.13)	(2.13 ± 0.04)

As expected, the dose identified in the cochlea was quite high, near the prescribed dose, since it can be found within the irradiation field and in a position that is slightly outside of the brain's

central symmetry plane. Fukunaga-Johnson [12] found values of 101% of the prescribed dose when applied to irradiation with parallel-opposed lateral fields. However, they perceived that by using the 3DCRT, in which non-coplanar fields were used, the dose in the cochlea can be found at approximately 65% of the prescribed dose. With this, the long-term complications of ototoxicity can be reduced, since the use of CRT allows for a better localization of the tumor and a reduction in the target volume, in addition to allowing for the normal structures to be “released”.

Another study [12] showed that, in adult patients with nasopharynx cancer, a significantly higher incidence of hearing loss could be observed for absorbed doses of above 50 Gy in the cochlea, as compared to lower doses. By contrast, Leach [11], analyzing a similar group of patients, had already reported that hearing loss could occur in patients who received a dose of 30 Gy or above. Considering the average values of doses/day evaluated in the present study, it could be observed that after 20 normally prescribed exposures, the patients who were submitted to the first two planning techniques would receive a dose in the cochlea region of nearly 34.2 Gy, while in the third and fourth, the patient commonly received a dose of around 37.6 Gy.

Nevertheless, Hus [2] carried out a study based on the longitudinal audiometric test (over a 6-month period) to determine the incidence and degree of hearing loss (average of 5 years) in a group of child patients undergoing radiotherapy for the treatment of head and neck cancers. The threshold of audiometry provided the quantitative measurement of the hearing damage through variations in the frequency from 250 to 8,000 Hz, and hearing loss after having received from 35 to 50 Gy in the cochlea region. With these results, the authors suggest that the dose received in the cochlea should be minimized and that the localization of the target volume should be improved, which can be achieved by applying highly conformed planning and distribution techniques, such as IMRT or radiation therapy that generates proton beams.

In the mandible, the doses diverge greatly between the two first planning techniques and the two final planning techniques. This difference can be attributed to the position of the table and the collimator angle. Hermans [13] reports that the breathing, taste, and speech can be severely compromised by mandibular necrosis. The mandible is a compact bone with a surface position.

Its high grade of calcium can lead to the spreading of radiation, in turn causing relatively higher damage to the endosteum cells, blood vessels, and the periosteum. The detection of a similar change in the bone on the contralateral side of the mandible increases the possibility of osteoradionecrosis. Contralateral osteoradionecrosis can be observed because many of the patients are commonly irradiated by opposing fields to reduce the dose on the entrance side.

Osteoradionecrosis of the mandible (OM) is a serious late complication of irradiation in high doses. The numbers published as regards the incidence of OM vary within an interval of <1% to >50%. The relation between the total dose using the conventional fractioning and the risk of OM is well-known. The dose of < 60 Gy using the fractioned model is rare, and a higher risk increases after 66 Gy [14].

It is important to emphasize that the doses in the mandible evaluated in this study resulted from the mandibular condyle region. The molar regions are the most common regions of complications in the mandibular bones; however, the condyles are a part of the temporary mandibular articulations that can be affected by fibroses and dysfunctions after irradiation. Jereczek-Fossa [15] affirms that a single dose is not enough to be representative of the dose in the mandibular region. In this author's work, many points of the mandible that received doses of higher than 74.4 Gy during treatment were evaluated, and no late complications were reported to have occurred in the bone.

Considering that for the treatment of medulloblastoma the prescribed dose is, on average, 65 Gy and the mandible is protected by protective shields, the dose in this region is minimal. However, the mandibular condyle region may continue to be exposed, as occurred in the third and fourth planning techniques, where, although the results were high, the total value of the doses in one treatment failed to reach to the critical value, given that the boost in treatment doses was carried out by excluding the mandibular region.

The parotid glands received the same doses as the mandibular condyle, since they are both located on the sides, covering part of the mandibular condyle. Dirix P.[16] affirmed that xerostomia is the most common complication resulting from RT applied to treat head and neck

cancers due to the irreparable damage caused to the salivary glands if they are included within the radiation field or poorly protected.

In a study by Chambers M [17], after a dose of 10 Gy, the patients had indeed developed a 50% reduction in the salivary flow. Upon receiving 50 Gy, the patients maintained only 10% of their salivary flow, and some patients did not recover their salivary functions. Chambers M [17] defined the radiation tolerance, setting the minimum tolerance of a 5/5 dose (tumor dose causing 5% of the rate of complications over a 5-year period) with 30 Gy, and the tolerance of a 50/5 dose with 50 Gy. Chambers M.[17] also reported a higher rate of xerostomia in patients whose parotid glands were irradiated with 40 Gy, but reported an insignificant rate in patients who received doses of less than 14 Gy. Thus, the dose tolerance of the glands can be found somewhere within this range.

4. CONCLUSION

The RT planning techniques for the treatment of neuroaxial, head, and neck regions must be performed more frequently with techniques that promote the preservation of organs that surround or overlap the tumor, such as the cochlea, the mandibular condyle, and the parotid glands.

In the present work, in the first two planning techniques, the doses in the cochlea region were slightly above the prescribed dose to treat the tumor, while the mandible received, on average, 16% of the prescribed dose. In the third and fourth planning technique, the doses were above the prescribed dose to treat the tumor both in the cochlea as well as in the mandible, especially in the third planning technique, where the dose was 18% higher than the prescribed dose. This result may well have occurred due to the variation in the collimator angle, which in the first two planning techniques was 11° and in the last two was 9°. In addition, in the first and second planning techniques, protective shields without lead were used, while in the third and fourth planning techniques, the modeling was carried out using shields made of cerrobend alloy.

These organs have a tolerance to radiation and a specific dose threshold that reacts in different manners and causes late effects and side effects that compromise the patients' quality of life.

REFERENCES

1. ICRP-86. *International Commission on Radiological Protection.*, Prevention of accidental exposures to patients undergoing radiation therapy. Bethesda: ICRP, 2000.
2. Hua C, Bass J. K., Raja Khan, Kun L. E. and Merchant T. E. "Hearing loss after radiotherapy for pediatric brain tumors effect of cochlear dose". *Int. j. radiation oncology biol. phys.*, **Vol. 72**, no. 3, pp. 892–899, 2008.
3. Paulino A.C., Lobo M, Teh B.S., Okcu M.F., South M., Butler E.B., Su J., Chintagumpala M. "Ototoxicity after intensity-modulated radiation therapy and cisplatin-based chemotherapy in children with medulloblastoma". *International Journal of Radiation Oncology Biology Physics*. Vol. 78, issue 5, Pages 1445-1450, 1 December 2010.
4. Moeller B. J, Chintagumpala M., Philip J. J, Grosshans D. R, McAleer M. F, Woo S. Y, Gidley P. W, Vats T. S. and Mahajan A. "Low early ototoxicity rates for pediatric medulloblastoma patients treated with próton radiotherapy" *Radiation Oncology* **Vol. 6**, pp 51-58, 2011.
5. Bhandare N., Jackson A., Eisbruch A, Pan C. C., Flickinger J. C., Antonelli P. and Mendenhall W. M.. "Radiation therapy and hearing loss". *Int. J. Radiation Oncology Biol. Phys.*, **Vol. 76**, No. 3, Supplement, pp. S50–S57, 2010
6. Lee I. J., Koom W. S., Lee C. G., Kim Y. B., Yoo S. W., Keum K. C., Kim G. E., Choi E. C. and Cha I. H. Risk factors and dose–effect relationship for mandibular osteoradionecrosis in oral and oropharyngeal cancer patients. *Int. j. radiation oncology biol. phys.*, **Vol. 75**, no. 4, pp. 1084–1091, 2009.
7. Gomez D. R., Estilo C. L, Wolden S. L., Zelefsky M. J., Kraus D. H. Wong, R. J., Shaha A. R., Shah J. P., Mechalakos J. G. and Lee N.Y. "Correlation of osteoradionecrosis and dental

- events with dosimetric parameters in intensity-modulated radiation therapy for head-and-neck cancer”. *Int. J. Radiation Oncology Biol. Phys.*, **Vol. 81**, No. 4, pp. e207–e213, 2011.
8. Meßmer M.-B., Thomsen A, Kirste S., Becke G., Momm F. “Xerostomia after radiotherapy in the head&neck area: Long-term observations”. *Radiotherapy and Oncology*, **Vol. 98**, 48–50, 2011.
 9. Wang Z-H., Yan C, Zhang Z-Y., Zhang C-P., Hu H-S., Tu W-Y, Kirwan J. and Mendenhall W. M. “Impact of salivary gland dosimetry on post-imrt recovery of saliva output and xerostomia grade for head-and-neck cancer patients treated with or without contralateral submandibular gland sparing: a longitudinal study”. *Int. J. Radiation Oncology Biol. Phys.*, **Vol. 81**, No. 5, pp. 1479–1487, 2011.
 10. Ahn P. H., Ahn A. I., Lee C. J., Shen J., Miller E., Lukaj A., Milan E., Yaparpalvi R., Kalnicki S. and Garg M. K.” Random positional variation among the skull, mandible, and cervical spine with treatment progression during head-and-neck radiotherapy”. *Int. j. radiation oncology biol. phys.*, **Vol. 73**, no. 2, pp. 626–633, 2009.
 11. Sobotta Johannes, “Atlas de anatomia Humana,” 21ed. Rio de Janeiro, Guanabara Koogan, 2000.
 12. Fukunaga-Johnson N., Sandler H.M., Marsh R.,Martel M.K.; “The use 3D conformal radiotherapy (3D CRT) to apare the cochlea in patients with medulloblastoma”. *Int.J.Radiat.Oncol.Biol.Phys.* **Vol. 41**,n° 1,pp.77-82,1998.
 13. Hermans R., Fossion E., Ioannides C., Van der Bogaert W., Ghekiere J., Baert A. L.” CT findings in osteoradionecrosis of the mandible”. *Skeletal radiol* (1996), **Vol. 25**: 31-36.
 14. Studer G., Grätz K. W., Glanzmann C. “Osteoradionecrosis of the mandíbula in patients treated with different fractionations”. *Strahlentherapie und onkologie.* **Vol. 180**: 233-240. 2004.
 15. Jereczek-Fossa B.; Garibaldi C.; Catalano G.; d’ Onofrio A.; DE Pas T.; Bocci C.; Ciocca M.; DE Paoli F.; Orecchia R. “Analisis of mandibular dose distribution in radiotherapy for

oropharyngeal cancer: dosimetric and clinical results in 18 patients”; *Radiotherapy and Oncology*. **Vol. 66**, pp 49-56, 2003.

16. Dirix P., Nuyts S., Poorten V.V., Delacre P., Van der Bogaert W. “The influence of xerostomia after radiotherapy on quality of life”. *Support care cancer*. **Vol. 16**: 171-179, 2008
17. Chambers M.S., Garden A. S., Rosnethal D., Ahamad A., Schwartz D. L., Blanco A. I., Chao K.S. C., Morrison W. H., Ang K.K., Weber R. S. “Intensity-modulated radiotherapy: Is xerostomia still prevalent?”. *Current Oncology report*. **Vol. 7**, 131-136, 2005.