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Review

Review of photon and proton radiotherapy for skull base tumours

Piero Fossati[a,b,*], Andrea Vavassori[a], Letizia Deantonio[c,d], Eleonora Ferrara[c], Marco Krengli[b,c,d], Roberto Orecchia[a,b]

[a] Radiotherapy Division, IEO, Milan, Italy
[b] Centro Nazionale Adroterapia Oncologica (CNAO), Pavia, Italy
[c] Radiotherapy Division, University Hospital "Maggiore della Carità", Novara, Italy
[d] Department of Translational Medicine, University of "Piemonte Orientale", Novara, Italy

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ABSTRACT

An extremely large variety of benign and malignant tumours occur at skull base; these tumour lesions are in the proximity to structures deputed to relevant physiologic functions, limiting extensive surgical approaches to this body district. Most recent progresses of surgery and radiotherapy have allowed to improve local control with acceptable rates of side effects. Various photon radiotherapy techniques are employed, including 3-dimensional conformal radiotherapy, intensity modulated radiotherapy (IMRT), stereotactic radiotherapy (SRT) and brachytherapy that is manly limited to the treatment of primary or recurrent nasopharyngeal carcinoma. Proton beam radiotherapy is also extensively used thanks to its physical characteristics. Our review, focusing in particular on meningioma, chordoma, and chondrosarcoma, suggests that proton therapy plays a major role in the treatment of malignant tumours whereas photon therapy still plays a relevant role in the treatment of benign tumour lesions.

1. Background

The base of skull is a structure at the interface between the intracranial content and the rest of the body where a number of neoplasms can arise from tissues of various origin including meningeal sheets, bone, cartilage, soft tissues, muscles, lymphatic tissue, mucosal epithelium, nerves and nerve sheets and embryonic remnants. This explains the extremely large variety of benign and malignant tumours occurring at this anatomic site. A peculiar aspect of the skull base lesions is the proximity to structures deputed to relevant physiologic functions, like the temporal lobes, brainstem, cranial nerves, major vessels, pituitary gland, and inner and middle ears, limiting extensive surgical approaches aimed to achieve a really radical oncologic result, otherwise possible in other body districts. For these reasons, only the most recent progresses of surgery and radiotherapy have allowed to improve the results in terms of local control with acceptable rates of side effects and complications.[1] In order to obtain acceptable

* Corresponding author at: Radiotherapy, Istituto Europeo di Oncologia, via Ripamonti, 435, 20141 Milano, Italy. Tel.: +39 0382 078505.
E-mail address: piero.fossati@ieo.it (P. Fossati).

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Table 1 – Dose constraints for the principal organs at risk.

OAR	Photon conventional fractionation (1.8–2 Gy)	Photon single fraction	Protons conventional fractionation	Source
Brainstem	Entire organ < 54 Gy, D_{max} < 64 Gy	D_{max} < 15 Gy D_{1cc} < 10 Gy	D_{max} Centre ≤ 53 Gy (RBE) Surface ≤ 64 Gy (RBE)	Mayo 2010[2], Timmerman 2008[7], Munzenrider 1999[9]
Optic pathways	Entire organ < 55 Gy	D_{max} < 10 Gy $D_{0.2cc}$ < 8 Gy	D_{max} ≤56–60 Gy (RBE)	Mayo 2010[3], Timmerman 2008[7], Noel 2005[10], Munzenrider 1999[9]
Cochlea	Entire organ < 45 Gy	D_{max} < 12–14 Gy	D_{max} ≤55 Gy (RBE)	Bhandare 2010[4], Timmerman 2008[7], Noel 2005[10]
Temporal lobe	Not well established: constraints in the range from V_{45} < 15 cc to V_{40} < 55 have been suggested	(Brain) V_{12} < 5–10 cc	D_{max} ≤63 Gy (RBE)	Zhou 2014[5], Su 2013[6], Lawrence 2010[8], Wenkel 2000[11]

rates of local control, malignant tumours in the skull base must be irradiated to a dose that exceeds the constraints of the above listed organs at risk (OARs). In case of a benign disease, doses employed can be lower and comparable to the tolerance of OARs but the long prognosis raises the issues of long-term side effects. A complete review of skull base dose constraints is beyond the scope of the present work; however, Table 1 summarizes dose constraints to the most significant OARs commonly used in clinical practice for photons and protons, considering both conventional fractionation and short course treatments for photons.[2–11]

2. Aim

The purpose of this paper is to review the techniques and the main results of photon and proton radiotherapy for the treatment of skull base tumours. To highlight strengths and disadvantages of different techniques, we have selected meningioma and chordoma/chondrosarcoma as examples of benign and malignant diseases in this region.

3. Materials and methods

A literature search was performed in Pubmed using the following keywords (meningioma or chordoma or chondrosarcoma or skull-base or nasopharyngeal carcinoma and radiotherapy or radiation or radiosurgery or SRT or brachytherapy or proton therapy). In principle, papers published since 2000 were selected, listed and analysed for relevance based on their abstract. Case reports were excluded, whereas review papers were analysed.

4. Results

4.1. *Photon radiotherapy*

4.1.1. *Intensity modulated radiation therapy (IMRT)*

Intensity modulated radiotherapy (IMRT) represents an advanced modality of 3-dimensional conformal radiotherapy (3D-CRT) and it is employed for the treatment of many different tumours, in particular in the case of irregular target shapes and closeness to critical structures.[12] The advantage of using IMRT for skull base tumours is evident because of the proximity of various sensitive anatomic structures, such as the brainstem, optic nerves and chiasm and brain tissue.[13]

IMRT involves a treatment delivery employing hundreds or thousands of small beams, created by a multi leaf collimator (MLC), each with intensity generated using an inverse treatment planning system. Inverse planning involves a process that uses computer optimization techniques aimed to modulate intensities across the target volume and normal tissues, starting from a specified dose distribution[14] and reaching the desiderate outcome.[15] As a result, a high dose conformation is reached and delivered to irregularly shaped targets, while the dose to surrounding non-target structures is minimized.[12]

IMRT can be delivered in different ways: (a) IMRT with static field segments (step and shoot), where the field is divided into different segments and radiation is delivered after the leaves movement to create the next segment; (b) with dynamic delivery (sliding windows), in which the leaves move across the field during treatment and the time-dependent position of each leaf determines the intensity; and (c) with rotational technique using volumetric modulated arc therapy (VMAT) or tomotherapy; in VMAT, the MLC has the leaf pattern changing continuously as the gantry rotates, allowing the simultaneous variation in dose rate, and in tomotherapy, the gantry continuously rotates while the patient couch is translated in the rotation plane.[16]

A pre-requisite of such a sophisticated technology is the importance of precise targeting and delivering of daily RT because of the steep gradients between high and low-dose regions. The advent of image guided RT (IGRT) allowed a target position correction, performing imaging prior to each radiation fraction.[17]

4.1.2. *Stereotactic radiotherapy*

Stereotactic radiotherapy (SRT) dates back to the early '50s with the pioneering experience of Leksell in Sweden.[18] Originally, it was defined as the delivery of high RT dose with multiple entrance portals, a steep dose gradient, optimal sparing of surrounding tissues and a precise patient immobilization. Immobilization was achieved with invasive fixation of the patient anatomy to an external rigid stereotactic frame, which made fractionated treatment impractical. Treatment