

Radiological and radio-therapeutic nuances in skull base tumors

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Thesis scientific impact

1 Objectives and findings

As a contribution to the broader aim of providing patients with skull base chordoma and large vestibular schwannoma (VS) with the safest and most reliable care, this thesis was set out to achieve the following specific objectives:

- To assess the safety and efficacy of proton therapy (PT) in skull base chordoma and identify patterns of recurrence after treatment failure.
- To assess the safety and efficacy of Gamma Knife (GK) after partial resection of large vestibular schwannoma (VS), with special attention to tumor control, facial nerve (FN) preservation, and treatment-related complications.
- To provide the most optimal sequence for FN visualization using diffusion-weighted imaging (DWI).
- To determine the degree of uncertainties in dose distribution between the AAA and Acuros XB dose calculation algorithms at low dose regions in the brain.

The research findings and conclusions are summarized as follows:

- The systematic review demonstrated that recurrence rates in skull base chordoma remain high despite advances in PT. Moreover, early and late toxicities after PT tend to be similar to those after photon-based radiation therapy.
- By studying the patterns of recurrence in skull base chordoma, a greater burden was placed on surgery with regards to the treatment failure. In our cohort, most of the loco-regional recurrences were identified in the surgical trajectories at areas not intended to receive a curative radiation dose. Our theory is that these recurrences are perhaps due to the tumor spill during surgery. This conclusion was reinforced when multiple recurrences were detected after treating the first visible recurrence by surgery. Moreover, the anatomical changes after surgery have made it difficult to distinguish between tumor progression and radiation necrosis.
- The effectiveness and safety of GK radiosurgery after partial resection of large VS (combined approach) appear high and therefore can be the treatment of choice. The efficiency and safety are made obvious with the good growth control (88% control rate) and the excellent FN functional preservation (100%). In our cohort, the absence of post-surgery complications after the partial resection of VS and the low number of observed radiation-induced effects after GK irradiation imply the high safety of this approach.

- The response of VS to GK radiosurgery may be more related to the biological differences that exist among VSs.
- Conventional DWI sequencing is able to show a distinctive visualization of the FN from the vestibulocochlear nerve.
- The AAA and Acuros XB dose calculation algorithms could be used interchangeably in neuro patients for low dose regions. However, Acuros XB remains superior to AAA in terms of computation time.

2 Research relevance and contribution to science

This thesis describes two types of skull base tumors that, once diagnosed, constitute a burden on both the patient and the management team. These are the skull base chordoma and a distinct subset of VS, the large VS. Despite extensive efforts to improve the quality of life of patients with skull base chordoma, these patients may not enjoy relief after treatment for a long time. The patient's life is possibly at risk in two ways. First, post-surgery complications, including recurrence [1], neurological deficits and depression [2] may occur. Second, there is a high chance of developing serious side effects after exposure to a high dose of radiation [1]. Given the rareness of skull base chordoma, a retrospective evaluation for our cohort could be of significant contribution, which may allow for pooling analysis from many centers to achieve an evaluable study population. Moreover, defining the prognostic factors and risks associated with any therapeutic strategy is extremely helpful in designing and assessing the feasibility of conducting a prospective study.

With regard to the large VS, this thesis showed that advances in microsurgery approaches and optimizations in the prescribed radiation doses have eased its management and resulted in encouraging outcomes. The retrospective study in Chapter 5 has strengthened the feasibility of partial resection and the use of GK in preserving FN function and controlling the residual VS, with minimal surgical and radio-surgical morbidities. Consequently, it is relevant to the decision to keep following this treatment approach at MUMC. Moreover, publishing these data may probably increase awareness among other medical centers across the globe. On the relevance of imaging the FN, such informational resources have the potential to add more protection to the FN during VS surgery by adding value to the planning process.

The difficulty in planning radiation dose delivery for brain tumors lies in the fact that healthy tissues or critical structures usually surround these tumors. This is a concern, as the dose-response curves are steeper in normal tissue than they are for tumors [3,4]. There is also growing interest in the low-dose region of certain parts of the brain in relation to cognitive decline, a serious side effect after radiotherapy to the brain, but rare after stereotactic radiotherapy [5,6]. Therefore, validating the use of one dose calculation algorithm to the other is highly relevant to ensuring an accurate distribution in high- and low-dose regions.

3 Target groups and the way of targeting them

As stated in the discussion, skull base tumors and large VS should be treated by a multidisciplinary effort. Therefore, the research findings could be interesting to the disciplines that are mainly involved in planning and actual treatment. These disciplines include neurosurgery, otorhinolaryngology, radiation therapy, radiology, and medical physics. It could also be relevant to other scientific communities who may use them to build on and conduct further studies. However, the most appropriate and efficient way to inform this wide community is by publishing the results in relevant scientific journals.

The secondary target group is the patients themselves, as they should be aware of the limitations associated with the current treatment in case one has been diagnosed with skull base chordoma, or the advantages of the conservative treatment in case of large VS. Apparently, these findings may be relayed to them indirectly at the time of discussing treatment options with the management team.

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