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PHYSICS CONTRIBUTION

A TREATMENT PLANNING COMPARISON OF COMBINED PHOTON–PROTON BEAMS VERSUS PROTON BEAMS–ONLY FOR THE TREATMENT OF SKULL BASE TUMORS

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Purpose: To compare treatment planning between combined photon–proton planning (CP) and proton planning (PP) for skull base tumors, so as to assess the potential limitations of CP for these tumors.
Methods and Materials: Plans for 10 patients were computed for both CP and PP. Prescribed dose was 67 cobalt Gray equivalent (CGE) for PP; 45 Gy (photons) and 22 CGE (protons) for CP. Dose–volume histograms (DVHs) were calculated for gross target volume (GTV), clinical target volume (CTV), normal tissues (NT), and organs at risk (OARs) for each plan. Results were analyzed using DVH parameters, inhomogeneity coefficient (IC), and conformity index (CI).
Results: Mean doses delivered to the GTVs and CTVs with CP (65.0 and 61.7 CGE) and PP (65.3 and 62.2 Gy CGE) were not significantly different ($p > 0.1$ and $p = 0.72$). However, the dose inhomogeneity was drastically increased with CP, with a mean significant incremental IC value of 10.5% and CP of 6.8%, for both the GTV ($p = 0.01$) and CTV ($p = 0.04$), respectively. The $CI_{80\%}$ values for the GTV and CTV were significantly higher with PP compared with CP. Compared with CP, the use of protons only led to a significant reduction of NT and OAR irradiation, in the intermediate-to-low dose (≤80% isodose line) range.
Conclusions: These results suggest that the use of CP results in levels of target dose conformation similar to those with PP. Use of PP significantly reduced the tumor dose inhomogeneity and the delivered intermediate-to-low dose to NT and OARs, leading us to conclude that this treatment is mainly appropriate for tumors in children. © 2007 Elsevier Inc.

Skull base tumors, Comparative treatment planning, Conformity index, Proton beam therapy.

INTRODUCTION

Over the last decades, significant improvement has been achieved in dose distribution for radiation therapy (RT). Technical advances have emerged from the transition of two-dimensional to three-dimensional (3D) RT planning, with a wide spectrum of modern techniques including (but not limited to) 3D conformal radiotherapy, stereotactic radiosurgery, fractionated stereotactic radiotherapy, and, more recently, intensity-modulated RT (IMRT). These techniques have led to better tumor dose conformation and increased normal tissue (NT) sparing (1, 2). The aims of all 3D irradiation techniques are to increase the dose delivered to the target volume and to decrease the irradiation of nontarget structures so as to decrease radiation-induced complications.

Advances in RT techniques have been associated with an incremental tumor control rate and decreased toxicity in a substantial number of cancers (3–10). Currently, IMRT is gaining widespread use in the radiation therapy community (11). The advantage of IMRT compared with 3D conformal radiotherapy is that dose delivery can be further sculpted (or "painted") to conform to the tumor volumes. However, this technique delivery results in a substantial greater volume of NT receiving intermediate-to-low doses of radiation

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(12–14). This dose delivery may increase the risk of radiation-induced second malignancies, especially in children (15–17). This dilemma has been an incentive to develop more conformal irradiation techniques such as proton beam therapy, which results in an optimal dose distribution, sparing substantially more NT and offering the opportunity to increase the dose to the target volume. Several series have also shown an improvement of dose distributions and NT-sparing with protons compared with IMRT and other 3D conformal techniques (18–21). Protons are characterized by their rapid dose fall-off at the distal end of the Bragg peak (80% to 20% over 4 mm with the proton beam at the Centre de Protonthérapie d'Orsay [CPO], Paris) and their sharp lateral penumbra (90–20% over 3.5–9 mm), depending on the energy, depth, and delivery (22).

Chordomas and chondrosarcomas of the skull base are uncommon, slow-growing neoplasms (23–25) that are challenging tumors for neurosurgeons and radiation oncologists alike. Total resection can rarely be achieved as the critical structures (optic nerves, optic chiasm, and brainstem) are usually in the direct vicinity of the tumor volume. The use of conventional radiation therapy is also limited because of the tolerance of these organs at risk (OARs) to ionizing radiation and has consequentially resulted in suboptimal long-term tumor control (26–29). As such, surgery followed by charged-particle irradiation is the gold standard of treatment for patients with chordoma or chondrosarcoma of the cervical spine or skull base (30–35).

By the end of 2006, more than 55,000 patients have been treated worldwide (Marin Jermann, personnal communication) in 26 different proton therapy centers (36), demonstrating the rapidly increasing use of particle therapy. Irradiation of skull base tumors has been achieved with combined photon–proton treatments or proton-only treatments (21, 24, 30–33, 37).

At the CPO, our choice to combine photon beam and proton beam is secondary to several considerations: (*1*) increasing the availability of proton therapy and the number of treated patients; (*2*) decreasing the number of fractions to limit the constraining and time-consuming seated position for patients; and (*3*) limiting the high costs of proton therapy (38). This treatment strategy is questionable, however, as the photon RT component of the radiation treatment will always decrease the overall ‘‘quality’’ of the irradiation. The present study was thus undertaken to assess the treatment planning intercomparison between a combined photon–proton planning (CP) and proton-only planning (PP) as applied to 10 patients with skull base tumors. The aim was to quantify this decremented radiation quality with CP for this tumor location.

METHODS AND MATERIALS

Patient selection and treatment planning

Ten (9 chordoma and 1 chondrosarcom) skull base tumor patients were selected for this study. All patients were selected because the target volume abutted or was in close vicinity (<5 mm) of the optic chiasm. Planning CT scans were performed with a 3-mm-slice spacing acquisition and matched or fused with a 1.5-mm (T1WGado+) skull base magnetic resonance imaging (MRI). Target volumes (TV) and OARs were delineated on the computed tomography (CT)–MRI datasets. The NT is defined by all tissue minus the target and OAR volumes. The OARs were brainstem, optic nerves, eyes, optic chiasm, and cochleas. The TVs were gross tumor volume (GTV), clinical target volume (CTV), and planning target volumes (PTV_1 and PTV_2). The GTV was defined as the macroscopic disease observed on CT and/or MRI. The CTV automatically included a 3D automatic 5- to 10-mm margin around the GTV, correcting manually to take into account anatomy and natural barriers. The PTV_1 was defined as the CTV plus an additional 3D automatic 3- to 6-mm margin. The PTV_2 was the GTV without additional margin as inter- and intrafractional motion was considered negligible considering the set-up immobilization techniques and verifications implemented at CPO. The median GTV volume was 8.5 cm^3 (range, 1.4–92.3); and the median CTV volume 32.7 cm^3 (range, 11.0–185.8). The NT in the vicinity of the target volumes was defined as the nontarget tissue in the vicinity of the GTV or CTV, encompassed by the 80% to 95% isodose lines.

The CP plans were the actual treatments delivered to patients, whereas the PP plans were computed for the purpose of this study. The photon component was delivered with a linear accelerator delivering 10 to 20 MV. The proton irradiation was delivered using the 201-MeV fixed horizontal proton beam of the CPO-synchrocyclotron (39).

Algorithms for dose calculation included the electron density information provided by the CT dataset. Treatment plans were generated using the ISIS 3D treatment planning system (technology diffusion 1997). With a conventional scheme (1.8 Gy/fraction for photons and 2 cobalt Gray equivalent (CGE)/fraction for protons), prescribed dose was 67 CGE for the PP and 45 Gy (photons) and 22 CGE (protons) for CP. A dose of 55 and 67 CGE was prescribed to PTV_1 and PTV_2, respectively. Treatment plans were optimized with the requirement that at least 95% of the target volume received the prescribed dose according to the International Commission on Radiation Units and Measurements (ICRU) criteria (40). A relative biologic effectiveness factor for protons of 1.1 (relative to 60 Co) was used, and proton doses were expressed in CGE (CGE = proton Gy $\times$ 1.1) (41). Dose constraints to the organs at risk were applied both to the proton-only plans and the combined plans, and are listed in Table 1.

CP and PP comparison

The PP and CP intercomparison was undertaken on TVs (GTV, CTV), NT, and OARs. Dose–volume histograms (DVHs) were

Table 1. Dose prescription for the target volumes and dose constraints for organs at risk

PTV_2 = GTV	67 Gy CGE
PTV_1 = CTV + 3–6 mm margin	55 Gy CGE*
Optic nerves	55 Gy-CGE max
Optic chiasm	55 Gy-CGE max
Anterior surface of the brain stem	63 Gy-CGE max
Center of the brain stem	53 Gy-CGE max

Abbreviations: CGE = cobalt Gray equivalent; CTV = clinical target volume; GTV = gross tumor volume; PTV = planning target volume.

* Photons: 45 Gy + protons: 10 CGE for combined photon–proton planning.