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Original article

Assessment of improved organ at risk sparing for meningioma: Light ion beam therapy as boost versus sole treatment option

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ABSTRACT

Purpose: To compare photons, protons and carbon ions and their combinations for treatment of atypical and anaplastical skull base meningioma.
Material and methods: Two planning target volumes ($PTV_{initial}$/PTV_{boost}) were delineated for 10 patients (prescribed doses 50 Gy(RBE) and 10 Gy(RBE)). Plans for intensity modulated photon (IMXT), proton (IMPT) and carbon ion therapy (^{12}C) were generated assuming a non-gantry scenario for particles. The following combinations were compared: IMXT + IMXT/IMPT/^{12}C; IMPT + IMPT/^{12}C; and ^{12}C + ^{12}C. Plan quality was evaluated by target conformity and homogeneity (CI, HI), $V_{95\%}$, $D_{2\%}$ and $D_{50\%}$ and dose-volume-histogram (DVH) parameters for organs-at-risk (OAR). If dose escalation was possible, it was performed until OAR tolerance levels were reached.
Results: CI was worst for IMXT. HI < 0.05 ± 0.01 for ^{12}C was significantly better than for IMXT. For all treatment options dose escalation above 60 Gy(RBE) was possible for four patients, but impossible for six patients. Compared to IMXT + IMXT, ion beam therapy showed an improved sparing for most OARs, e.g. using protons and carbon ions $D_{50\%}$ was reduced by more than 50% for the ipsilateral eye and the brainstem.
Conclusion: Highly conformal IMPT and ^{12}C plans could be generated with a non-gantry scenario. Improved OAR sparing favors both sole ^{12}C and/or IMPT plans.
 Radiotherapy and Oncology xxx (2014) xxx–xxx

Total resection of atypical and anaplastical skull base meningioma is often limited due to the proximity of organs at risk (OARs). These tumors show a high tendency to recur repeatedly and therefore require adjuvant radiotherapy after surgery [1,2]. Intensity modulated radiotherapy (IMXT) or fractionated stereotactic radiotherapy have become attractive treatment options. Although the majority of the meningiomas are benign, atypical and anaplastical meningiomas constitute about 10% of the cases. These tumors show a high recurrence rate with a low overall 5 year survival [3–6]. It is recommended to administer at least 60 Gy to improve the progression-free survival [7]. However, cranial nerve toxicities have to be considered when applying high doses [4,8,9].

Particle beam therapy centers offer promising new treatment options for these patients [10–15]. At present, limited dosimetric data are available that compare the different treatment options using advanced photon beam and light ion therapy in patients suffering from meningioma. Arvold et al. [16] compared photon vs. proton radiotherapy for benign intracranial meningioma and showed a significant dose reduction in the involved brain structures for proton plans. With regard to corresponding clinical data, different authors reported on the outcome of patients with meningioma receiving combined proton and photon radiotherapy [17–20]. A recently initiated Phase II study using a carbon ion boost in patients with atypical and anaplastical meningioma [21] was based on previously published results that proved carbon ion therapy as a safe and promising treatment option [22]. A prospective light ion therapy study was recently published covering seventy patients with meningioma [23] showing no severe treatment-related side effects.

In Europe two synchrotron based cancer treatment and research centers are in operation i.e. HIT in Heidelberg and CNAO in Pavia, which offer both proton and carbon ion therapy. A third one, MedAustron, is planned to follow in 2015. In all these centers proton and light ion treatments will be relying heavily on fixed beam lines where robotic positioners provide additional degrees of freedom. The unique carbon ion gantry at HIT and the proton

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only gantry at MedAustron are exceptions, also when compared to Asian facilities (e.g. Shanghai and Hyogo) that provide more than one particle species.

The aim of this planning study was to compare state-of-the art intensity modulated photon beam therapy (IMXT) to proton and carbon ion treatments that are based on beam delivery options with fixed beam lines for patients with atypical and anaplastical skull base meningioma. Due to the high WHO grades of these tumors and based on the outcomes of the studies by Combs et al. [21–23] an aggressive treatment scheme with a dose of at least 60 Gy(RBE) was simulated in this planning study. For the reasons mentioned above fixed beam lines are considered to be representative delivery options, even if suboptimal from a theoretical point of view. In this study the various combinations using light ion beams as sole treatment options or as boost option were investigated as well.

Patients and methods

Treatment plans for 10 patients (9 female, 1 male) with atypical and anaplastical skull base meningioma were created. All patients were actually treated with photon beam therapy. At the time of the initial diagnosis, the median patient age was 57 years (37–81 years). Tumor size ranged from 11–1111 cm^3 with a median value of 49 cm^3. The tumors were localized at the sphenoid bone (3 pts.), as well as the dorsum sellae (1 pt.), the fossa cranii media (2 pts.), the fossa pterygopalatina (1 pt.), the sinus cavernosus (2 pts.) and the sphenoorbital region (1 pt.). The study protocol was approved by the institutional review board.

Target volumes and organs at risk (OAR)

Structure segmentation was based on CT and MR images according to ICRU recommendations [24]. The gross tumor volume (GTV) was determined as the macroscopically visible tumor extent on contrast enhanced MRI. In case of resection the topography of post-surgery imaging was adopted to those pre-surgery. The clinical target volume ($CTV_{initial}$) included the GTV and areas of subclinical tumor extend (e.g. the pre- or post-operative tumor bed, pathological dural enhancement in the CT/MRI images or regions with peritumoral edema) plus a 1 cm safety margin [21]. To construct the planning target volume ($PTV_{initial}$ or PTV_{boost}) a 3 mm isotropic margin was added to the $CTV_{initial}$ or GTV, assuming a high precision mask system [25,26]. Median $PTV_{initial}$ and PTV_{boost} were 147 ± 85 cm^3 (range 44–1272 cm^3) and 94 ± 46 cm^3 (range 31–182 cm^3), respectively.

The following structures were delineated as OAR: chiasm, optical nerve, temporal lobe, hippocampus, hypothalamus, brainstem, pituitary gland, cerebellum, eye, lens, brain hemisphere, amygdala, cochlea and thalamus. Where applicable ipsilateral (subscript "i") and contralateral (subscript "c") OARs were considered separately.

Treatment planning goals

Since photon, proton and carbon ion treatment plans were compared, RBE weighted doses (product of absorbed dose and RBE) were reported [24]. Treatment plans were optimized considering the following OAR constraints with the aim to maximize CTV coverage: Chiasm $D_{2\%} < 60$ Gy(RBE) and $D_{50\%} < 54$ Gy(RBE); optical nerve (contralateral) $D_{2\%} < 60$ Gy(RBE) [27,28]. Due to the close proximity of the target to these OARs rather aggressive constraints needed to be chosen, i.e. serious visual toxicity of 3–7% was accepted for some patients [27,29]. Furthermore, for some patients the optical pathway constraints needed to be relaxed due to tumor geometry. Similar strategies for unfavorably located targets were described in clinical studies [30,31]. The ipsilateral optical nerve was not considered since it was included in the CTV in 9/10 patients. Further constraints were: temporal lobe $D_{2cc} \leqslant 71.4$ Gy(RBE) [32]; brainstem $D_{50\%} < 53$ Gy(RBE) and brainstem surface $D_{2\%} < 64$ Gy(RBE) [30,31]; pituitary gland $D_{2\%} < 56$ Gy(RBE) [33]; cerebellum V45 < 10cm; eye $D_{50\%} \leqslant 6$ Gy(RBE), V35 < 50%; lense $D_{2\%} < 6$ Gy(RBE); cochlea $D_{50\%} \leqslant 45$ Gy(RBE) [29,34].

Adequate dose coverage of at least 95% of $PTV_{initital}$ with $D_{pres} = 50$ Gy(RBE) was aimed for. PTV_{boost} was treated with a dose of at least 10 Gy(RBE). A fractionation scheme with 2 Gy(RBE) per fraction was assumed. The maximum allowed dose to $PTV_{initial}$ and PTV_{boost} was 107% of the prescribed dose [35]. In a second step and if possible, dose escalation to PTV_{boost} – up to 68 Gy [21] – was aimed for by respecting the maximum dose levels to OAR as specified above.

Treatment techniques and planning systems

For both PTVs three different treatment techniques and their combinations were investigated, i.e. intensity-modulated photon (IMXT), proton (IMPT) and carbon-ion therapy (^{12}C). More specifically, the following combinations of the initial and the boost plans were considered:

- IMXT 50 Gy(RBE) ($PTV_{initial}$) and IMXT or IMPT or ^{12}C boost (PTV_{boost}).
- IMPT 50 Gy(RBE) ($PTV_{initial}$) and IMPT or ^{12}C boost (PTV_{boost}).
- ^{12}C 50 Gy(RBE) ($PTV_{initial}$) and ^{12}C boost (PTV_{boost}).

For IMXT 6 static beams on the tumor infiltrated side of the head (from ipsilateral to cranio-caudal direction) were used for $PTV_{initial}$ and 4 static beams for PTV_{boost}. The beam angles were consistent for all patients. The TPS Monaco v.3.2 (Elekta, CMS software, St. Louis, US) was utilized.

For IMPT and ^{12}C options two beams were applied from ipsilateral direction for the $PTV_{initial}$ and from cranio-caudal direction for the PTV_{boost}, to avoid having the same entrance regions. Beam directions were always separated by a couch angle of 20–30°. Starting from the horizontal beam line all respective couch angle combinations between ±30° were investigated and the best beam positions were chosen. In the attempt to find the best beam arrangement, optimal couch angles for IMPT and ^{12}C differed sometimes slightly.

IMPT plans were created with the software XiO v4.4.1 (Elekta, CMS software, St. Louis, US) assuming spot scanning. The spacing between the IMPT energy layers was 0.8 cm, the spot size (FWHM) 0.3 cm and the spot spacing was 0.5 cm.

The treatment planning system TRiP98 (Version 1001c), developed at the GSI, was used to generate ^{12}C treatment plans [36]. A spot size (FWHM) of 4–6 mm was used in combination with a Bragg peak width of 3 mm. Biological treatment plan optimization and dose calculation in this TRiP98 version was based on the local effect model LEM I [14,37]. For dose calculation the allpoints algorithm was employed, which takes all neighboring raster beam spots into account that may explicitly contribute to a considered voxel. All treatment plans were optimized employing multiple field optimizations using intensity modulation.

Treatment plan analysis

With the MATLAB (MathWorks, Natick, Massachusetts (USA)R2009, 64 bit) based software platform CERR (v4.1) the dose matrices of the initial and the boost plans were summed up on a voxel by voxel basis. Furthermore a software tool was used to create patient averaged dose–volume-histograms and to assess dosimetric differences. Dosimetric comparisons for the PTV were performed separately for the $PTV_{initial}$ and PTV_{boost} plans.

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