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Original article

Patient-specific bolus for range shifter air gap reduction in intensity-modulated proton therapy of head-and-neck cancer studied with Monte Carlo based plan optimization

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ABSTRACT

Background & purpose: Intensity-modulated proton therapy (IMPT) of superficial lesions requires pre-absorbing range shifter (RS) to deliver the more shallow spots. RS air gap minimization is important to avoid spot size degradation, but remains challenging in complex geometries such as in head-and-neck cancer (HNC). In this study, clinical endpoints were investigated for patient-specific bolus and for conventional RS solutions, making use of a Monte Carlo (MC) dose engine for IMPT optimization.

Methods and materials: For 5 oropharyngeal cancer patients, IMPT spot maps were generated using beamlets calculated with MC. The plans were optimized for three different RS configurations: 3D printed on-skin bolus, snout- and nozzle-mounted RS. Organ-at-risk (OAR) doses and late toxicity probabilities were compared between all configuration-specific optimized plans.

Results: The use of bolus reduced the mean dose to all OARs compared to snout and nozzle-mounted RS. The contralateral parotid gland and supraglottic larynx received on average 2.9 Gy and 4.2 Gy less dose compared to the snout RS. Bolus reduced the average probability for xerostomia by 3.0%. For dysphagia, bolus reduced the probability by 2.7%.

Conclusions: Quantification of the dosimetric advantage of patient-specific bolus shows significant reductions compared to conventional RS solutions for xerostomia and dysphagia probability. These results motivate the development of a patient-specific bolus solution in IMPT for HNC.

Proton therapy (PT) can offer improved organ-at-risk (OAR) sparing compared to state-of-the-art photon radiotherapy. Combined with cost reduction of modern intensity-modulated proton therapy (IMPT) systems, this expected clinical advantage is currently driving a rapid increase in the number of proton therapy facilities [1]. Randomized clinical trials are being established for a wide range of indications [2]. For the often complex geometries of head-and-neck cancer (HNC) for instance, with close proximity of various OARs to the target volume, the improved conformity of IMPT is expected to result in reduced treatment-related side-effects [3,4].

In IMPT with pencil beam scanning (PBS), pencil beam spots are magnetically scanned across the target volume. The depths at which these spots are delivered, are selected layer-by-layer by varying the energy. Modern PT systems however are limited in the minimal energy they can deliver, ranging from 60 to 100 MeV which corresponds to a minimal range in water between 3.1 and 7.7 cm. For the treatment of more superficial lesions, such as in HNC, a pre-absorbing range shifter (RS) is typically attached to the nozzle. The air gap between the RS and the patient however is known to increase the PBS spot size, which can compromise the dose conformity of IMPT [5–7]. Also, various authors have reported on the sub-optimal modelling of RS air gaps by current treatment planning systems (TPS) [8,9].

To minimize these air gap effects, the RS is often positioned as close as possible to the patient using a movable snout extension. Careful attention however is needed to avoid any collision, especially when applying couch adjustments based on image guidance during patient positioning. Both et al. [10] implemented a universal bolus RS, a U-shape with a constant thickness positioned around the patient's head. Universal bolus' application mainly lies in cranial applications and is not always suited for HNC, since often the elective nodes extend beyond the lung apices. Also, such

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universal bolus has been reported to limit the close positioning of a prompt gamma camera, reducing the obtained useful signal for in vivo range verification in clinical conditions [11].

Novel solutions for on-skin range shifting tailored to the patient treatment would avoid air gaps altogether and could simplify the workflow for IMPT in HNC. The emerging 3D printing technology is already in clinical use for the creation of individualized devices such as bolus for electron radiotherapy [12]. This technology could also be used to create patient-specific range shifting bolus for IMPT, applicable to the complex curved geometries encountered in HNC while still allowing full flexibility in the selection of treatment beam angles. In a previous study, the potential of 3D printed materials was investigated for PT range shifting, possibly integrated in the immobilization structure [13]. Integration of RS in the immobilization device also ensures presence and correct placement of the RS for each IMPT treatment field. Issues related to the design and construction of such devices are subject of dedicated, ongoing studies and are not within the scope of this work.

In order to justify further investigation of 3D printed on-skin RS, the current study focused on the quantification of the dosimetric benefit compared to conventional RS solutions with air gaps. Although the influence of an air gap on the spot size has been subject of previous publications [5,6], the actual deteriorating effects on dose distributions and treatment plan quality were yet to be quantified. IMPT plan optimization in this study was fully based on Monte Carlo (MC) calculated beamlets to accurately account for RS air gap effects. The aim of this study was to quantify the potential gain of individualized bolus in terms of OAR sparing and normal tissue complication probability (NTCP) reduction in IMPT of HNC.

Materials and methods

Patient data and planning objectives

Computed tomography (CT) data of 5 patients with oropharyngeal cancer were used for the treatment planning study. A dose of 66 Gy_{RBE} (assuming a constant radiobiological effectiveness RBE of 1.1) was prescribed to the high-risk clinical target volume (CTV_{High}; primary tumour and positive neck levels) and 54 Gy_{RBE} to the low-risk CTV (CTV_{Low}; elective neck levels), to be delivered in a simultaneously integrated boost scheme of 30 fractions [14,15]. Planning target volumes (PTV) were defined as the CTVs with a 5 mm margin [15,16].

The PTV constraints were such that 98% of the volume received more than 95% of the prescribed dose D_{Prescr} ($D_{98\%} \geq 95\%$) and that no more than 2% of the volume received more than 107% ($D_{2\%} \leq 107\%$) [14,17,18]. The constraint on the spinal cord was a maximum dose of 40 Gy. A minimum mean dose D_{Mean} was used as objective for the parotid glands, submandibular glands, oral cavity, larynx, supraglottic larynx and superior pharyngeal constrictor muscle (PCM_{Sup}).

Range shifter configurations and plan optimization

A 3-beam arrangement with gantry angles 50, 180 and 310 degrees was used [15], with RS of 4 cm PMMA. For each patient, 3 different RS configurations were compared: applied as bolus or mounted either on a snout or on the nozzle. The bolus was created by expanding the body contour 4 cm parallel to the beam axis for each field. A 3 mm air gap was maintained between the body contour and the bolus to include the potential effect of non-ideal bolus set-up on the spot size in the modelling. For the snout RS, an extendable device attached to the nozzle that can hold accessories such as a RS or an aperture, a 25 cm diameter was chosen. This was the minimum size required to cover the total PTV for every gantry angle. For the nozzle RS, dimensions of 40 × 30 cm^2 were adopted from an IBA (Ion Beam Applications, Louvain-la-Neuve, Belgium) dedicated nozzle. For both the snout and nozzle RS, a safety distance, equal to the shortest distance between the RS and the patient, was maintained at 3 cm, to avoid collision with the patient (see Fig. 1). This translated into a maximum air gap of 10 cm and 12 cm for the snout and nozzle, respectively, on the more cranially located slices.

Treatment planning system and MC dose engine

To achieve the desired plan constraints ($D_{98\%} \geq 95\%$ of D_{prescr}) for the IMPT plans, an in–house TPS, MIROpt, was used for all RS configurations. MIROpt is fully coupled with the MC dose engine MCsquare, which has been validated in heterogeneous geometries [19] against GATE/GEANT4 [20], allowing to accurately model the effect of RS multiple Coulomb scattering and density heterogeneities within the patient. A clinical PBS system was modelled in MCsquare to reproduce commissioning data [20]. Initial spot sizes in air at isocenter were $\sigma = 7$ mm at 70 MeV and $\sigma = 2.5$ mm at 230 MeV.

In MIROpt, spots were placed on a hexagonal grid with 5 mm lateral spot spacing and 5 mm layer spacing. A CT number to tissue parameter conversion was applied to each voxel [21]. The dose deposition matrix was computed with MCsquare using 5×10^4 protons per spot. Simultaneous optimization of all spot weights was done using the large-scale non-linear solver IPOPT [22]. A final MCsquare forward dose calculation was performed with 5×10^8 protons on a $2 \times 2 \times 2$ mm^3 dose grid. A median statistical uncertainty of 0.19 Gy was found for the PTV voxels using a batch method [23].

Evaluation of different RS configurations

Target doses and OAR doses were compared between the patient-specific bolus, nozzle-mounted and snout-mounted RS configurations. In addition, expected endpoints for late toxicity in head-and-neck cancer patients receiving radiotherapy were evaluated in terms of their normal issue complication probability (NTCP). The probability of salivary flow <25% of pre-treatment after 1 year for the individual parotid glands was quantified based on Dijkema et al. [24]. Grade 2–4 patient-rated xerostomia probability after 6 months was calculated based on Beetz et al. [25]. Grade 2–4 physician-rated dysphagia probability after 6 months was calculated based on Christianen et al. [26].

Results

For the bolus plans, the average number of spots per field was 8596. The delivered energies ranged from 75 MeV to 207 MeV. Table 1 shows the target coverage metrics when the spot maps are optimized for each RS configuration individually, hence taking into account the air gap during optimization. The planning objectives for the PTVs were achieved for all RS configurations. The PTV homogeneity index however, calculated according to ICRU report 83 [18], was slightly higher for the snout and nozzle RS. More distinctively, achieving target coverage for the RS configurations with air gap (snout and nozzle RS) came at the expense of a decreased radiation conformity index as calculated according to Knöös et al. [27]. This resulted in an increased mean dose to all parallel OARs, as shown in Table 2. The mean dose to the contralateral parotid gland, for instance, increased on average by 2.9 Gy (snout RS) and 3.4 Gy (nozzle RS). The D_{mean} to the supraglottic larynx increased by 4.2 Gy (snout RS) and 5.5 Gy (nozzle RS). The dose distributions and dose–volume histograms for one representative patient are shown in Fig. 2.

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