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Probabilistic planning

An in silico comparison between margin-based and probabilistic target-planning approaches in head and neck cancer patients

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ABSTRACT

Background and purpose: To apply target probabilistic planning (TPP) approach to intensity modulated radiotherapy (IMRT) plans for head and neck cancer (HNC) patients.
Material and methods: Twenty plans of HNC patients were re-planned replacing the simultaneous integrated boost IMRT optimization objectives for minimum dose on the boost target and the elective volumes with research probabilistic objectives: the latter allow for explicit handling of systematic and random geometric uncertainties, enabling confidence level based probabilistic treatment planning. Monte-Carlo evaluations of geometrical errors were performed, with endpoints D98%, D2% and Dmean, calculated at a confidence level of 90%. The dose distribution was expanded outside the patient to prevent large bilateral elective treatment volumes ending up in air for probabilistic shifts.
Results: TPP resulted in more regular isodoses and in reduced dose, on average, to organs at risk (OAR), up to more than 6 Gy, while maintaining target coverage and keeping the maximum dose to limiting structures within requirements. In particular, when the surrounding OARs overlap with the planning target volume (PTV) but not with the clinical target volume (CTV), better results were achieved.
Conclusion: The TPP approach was evaluated in HNC patients, and proven to be an efficient tool for managing uncertainties.
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Head and neck cancer (HNC) patients generally have very complex target volumes, often large and overlapping with or in close proximity to radio-sensitive critical structures [1]. The ability to accurately shape dose in these patients becomes critical [2–4]. With intensity modulated radiotherapy (IMRT), treatments have significantly improved in terms of organs at risk (OARs) sparing while properly covering the target volumes [5]. This could allow for dose escalation strategies on the gross tumor volume (GTV) [6], e.g. using various tracers (such as 18[F]fluoro-deoxy-glucose [7]) to identify the most radioresistant areas inside the GTV [8] and drive the prescription dose distribution accordingly using either a dose painting by contours (DPBC) [9] or a dose painting by numbers (DPBN) [10] approach. For the latter, though, it is inherently impossible to apply standard margin expansions for the regions of interest (ROI) to account for uncertainties. These can be separated in systematic (Σ) and random (σ) components [11]. The first correspond to the difference between the planning geometry and the average geometry over all treatment fractions. In our study the systematic errors included a systematic component of setup uncertainty and a baseline shift. The latter are the differences between the average treatment geometry and the day-to-day geometries; the random errors refer to errors arising from the positioning of the patient for each fraction. In recent years, many techniques have been proposed to take such uncertainties into account during treatment planning optimization, e.g. probabilistic treatment planning, PP [12–16]. Only our approach, though, allows a confidence level (or probability) based plan optimization, producing results directly comparable to the conventional margin-based approach (for a detailed description of the method see [17]). The purpose for this in silico planning study was to apply target PP (TPP) to HNC cases and to assess if the results obtained were comparable with the traditional margin-based strategies. In case they were not, why and to what extent they differ. This way, also its application to DPBN planning, where no comparison with margin based planning is possible, can be considered reliable.

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Materials and methods

Patient data

In this study, 20 patients were retrieved from the ROCOCO database (www.mistir.info, [18]) who had undergone primary radiotherapy for HNC and elective or therapeutic treatment of both sides of the neck. The average age was 61 years (range 50–80 years); 20% were female and 80% were male. The primary tumor was located in the oropharynx and hypopharynx in 80% and 20% of the cases, respectively. T-stage was T1 in 13% of the patients, T2 in 20%, T3 in 27% and T4 in 40%; N stage was N0 in 13% of the patients, N1 in 20%, N2a in 7%, N2b in 20% and N2c in 40%.

Radiotherapy treatment planning was performed on a research version of the Philips Pinnacle[3] treatment planning system (version 9.100, Philips Radiation Oncology Systems, Fitchburg, WI, USA). Dose was always calculated using the Adaptive Convolve algorithm on computed tomography (CT) scans acquired in treatment position with slice thickness of 2 mm.

Geometrical uncertainties

The original plans, according to the ROCOCO protocol, were created with an expansion CTV to PTV of 0.5 cm in all directions. The hospital values for the standard deviations (SD) of Σ and σ were:

$$\begin{cases} \Sigma_X = 1.11 \text{ mm} \\ \Sigma_Y = 1.10 \text{ mm} \\ \Sigma_Z = 1.04 \text{ mm} \end{cases}$$

$$\begin{cases} \sigma_X = 1.79 \text{ mm} \\ \sigma_Y = 1.52 \text{ mm} \\ \sigma_Z = 1.68 \text{ mm} \end{cases}$$

Patient position deviations were determined from Electronic Portal Images (EPIs) of AP and lateral verification beams with respect to the Digitally Reconstructed Radiographs of these beams. The EPIs were acquired with Elekta iViewGT flat panels before start of treatment. An off-line Shrinking Action Level (SAL) protocol [19] was used for position correction with an initial action level of 6.2 mm (3D vector length) which decreased to 3.1 mm after four fractions. The position deviations of the vertebra were determined. 197 patients were analyzed. The hospital values for $\sum$ and σ were calculated from the patient position deviations with off-line corrections applied according to the method described in the appendix of [20].

These values, according to [21], would produce a margin expansion from CTV to PTV of:

$$\begin{cases} M_X = 4.03 \text{ mm} \\ M_Y = 3.81 \text{ mm} \\ M_Z = 3.77 \text{ mm} \end{cases}$$

This is a margin not comparable to that used for the original plans, which can be explained by the conservative approach of the ROCOCO protocol. But since the errors are then used in the TPP, for a fair comparison they were re-scaled to produce a final margin as close as possible to 0.5 cm.

So the values used were:

$$\begin{cases} \Sigma_X = 1. \text{ mm} \\ \Sigma_Y = 1.42 \text{ mm} \\ \Sigma_Z = 1.34 \text{ mm} \end{cases}$$

$$\begin{cases} \sigma_X = 2.31 \text{ mm} \\ \sigma_Y = 1.96 \text{ mm} \\ \sigma_Z = 2.17 \text{ mm} \end{cases}$$

Which would produce an anisotropic margin with values:

$$\begin{cases} M_X = 5.19 \text{ mm} \\ M_Y = 4.92 \text{ mm} \\ M_Z = 4.87 \text{ mm} \end{cases}.$$

Margin based plans

The original plans retrieved were IMRT plans created using the Direct Machine Parameter Optimization (DMPO) module [22], with seven coplanar 6-MV photon beams, at angles: 0°, 50°, 100°, 150°, 210°, 260°, 310°, and a fixed collimator rotation of 5°. To achieve results as general as possible, independent from the specific LINAC used, they were all reoptimized as pure fluence modulated plans, without segmentation.

Organs at risk (OARs), including the parotid glands, submandibular glands, spinal cord, brain stem, optic nerves, optical chiasm, superior and middle pharyngeal constrictor muscle (PCM), and supraglottic larynx, were outlined according to the previously described guidelines [23,24]. The targets in the original plans, the planning target volumes (PTVs), were created according to [25,26]: a PTV54, prescribed with 54.25 Gy in 35 fractions of 1.55 Gy; and a PTV70 prescribed with 70 Gy in 35 fractions of 2.00 Gy. A simultaneous integrated boost (SIB) technique was used where PTV54 was the prophylactic region and PTV70 was the therapeutic region.

Probabilistic planning

In the current work, the concept of PTV was discarded as in TPP the uncertainties are handled without margin expansion. So we created a copy of each of the originally delivered plans. Then we discarded any objective on PTVs or PTV related structures such as ring-like structures around or inside them (MinDose, MaxDose and Uniform Dose objectives in Pinnacle[2]). We used instead the corresponding CTV54 and CTV70 (mean volumes 127 cm^3 (range: 53–327 cm^3) and 376 cm^3 (range: 254–327 cm^3), respectively) as targets. As planning criteria, the ones in the original plans (corresponding to the ROCOCO planning protocol) were used, with the same weights. The same probabilistic coverage of the CTVs (evaluated using the endpoints described in Section 'Plan evaluation') was requested on both the original plans and on TPP. The maximum plan dose was 77 Gy and no hotspots (dose exceeding 107% of the prescribed dose) were allowed. After target coverage, the priority was set to not exceed the maximum dose to critical structures (spinal cord, 54 Gy; brainstem, 60 Gy; optic nerves, 54 Gy; and optic chiasm, 54 Gy). Finally, dose to other OARs was minimized as much as possible. In case of overlap between CTV and OAR, the overlapping region was considered as part of the tumor for the optimization process. For each of the newly created plans, the DMPO optimization was switched to Intensity Modulation, no conversion was applied and, after resetting the beams and running the first optimization procedure, two more warm runs (without beams reset) were performed to refine the results.

The TPP plugin provided a research version of all the standard optimization objectives in Pinnacle. We used a research objective named MinDosePP: this is equivalent to the original MinDose objective in Pinnacle, which is met when the region of interest has a minimum dose that is greater than or equal to the target dose. MinDosePP integrates also systematic and random geometric uncertainties during each cost computation. Random errors were simulated by blurring the dose while systematic errors by

[2] The three objectives are aimed at minimizing the quadratic distance between the minimum, maximum and mean calculated dose and the prescribed dose, respectively.