Radiotherapy and Oncology 124 (2017) 263–270

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Knowledge-based selection

Using a knowledge-based planning solution to select patients for proton therapy

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ARTICLE INFO

Article history:
Received 29 September 2016
Received in revised form 12 January 2017
Accepted 21 March 2017
Available online 12 April 2017

Keywords:
Proton therapy
Knowledge-based planning
Patient selection
Head and neck cancer

ABSTRACT

Background and purpose: Patient selection for proton therapy by comparing proton/photon treatment plans is time-consuming and prone to bias. RapidPlan™, a knowledge-based-planning solution, uses plan-libraries to model and predict organ-at-risk (OAR) dose-volume-histograms (DVHs). We investigated whether RapidPlan, utilizing an algorithm based only on photon beam characteristics, could generate proton DVH-predictions and whether these could correctly identify patients for proton therapy.

Material and methods: $Model_{PROT}$ and $Model_{PHOT}$ comprised 30 head-and-neck cancer proton and photon plans, respectively. Proton and photon knowledge-based-plans (KBPs) were made for ten evaluation-patients. DVH-prediction accuracy was analyzed by comparing predicted-vs-achieved mean OAR doses. KBPs and manual plans were compared using salivary gland and swallowing muscle mean doses. For illustration, patients were selected for protons if predicted $Model_{PHOT}$ mean dose minus predicted $Model_{PROT}$ mean dose (ΔPrediction) for combined OARs was ≥6 Gy, and benchmarked using achieved KBP doses.

Results: Achieved and predicted $Model_{PROT}$/$Model_{PHOT}$ mean dose R^2 was 0.95/0.98. Generally, achieved mean dose for $Model_{PHOT}$/$Model_{PROT}$ KBPs was respectively lower/higher than predicted. Comparing $Model_{PROT}$/$Model_{PHOT}$ KBPs with manual plans, salivary and swallowing mean doses increased/decreased by <2 Gy, on average. ΔPrediction ≥ 6 Gy correctly selected 4 of 5 patients for protons.

Conclusions: Knowledge-based DVH-predictions can provide efficient, patient-specific selection for protons. A proton-specific RapidPlan-solution could improve results.

Proton therapy utilizes the steep dose gradient of proton beams after the dose maximum ("Bragg-Peak") to provide conformal dose distributions around the target which may lead to increased organ-at-risk (OAR) sparing in comparison with photon plans. Ideally, patients would receive the best treatment, based for example, upon a comparison of the risk of toxicity and probability of tumor control. However, the limited capacity of proton centers and higher cost associated with proton treatments necessitates patient selection.

The Netherlands has adopted a model-based approach to select patients based on estimated reductions in normal-tissue complication probability (NTCP) [1]. A key requirement is high quality photon and proton treatment plans for individual patients using the same planning-CT and contours. However, despite recent improvements [2], treatment planning remains time consuming and plan quality can vary substantially among planners and institutions [3–6]. This variation might be exacerbated for less-established treatments such as intensity-modulated proton therapy (IMPT), which could render proton–photon comparisons unreliable.

Knowledge-based planning solutions, such as RapidPlan™ (Varian Medical Systems, Palo Alto, USA), semi-automate the treatment planning process with good results [7–9]. RapidPlan uses the dosimetric and geometric information contained in a library of previously created plans to construct a model which is used to predict a range of achievable OAR dose-volume histograms (DVHs) for future patients. These prediction ranges can be used to create knowledge-based plans (KBPs) by placing optimization objectives along the inferior boundary of the prediction range, guiding the optimization process. The DVH of the calculated plan typically lies within the prediction range. Previous work demonstrated the accuracy of RapidPlan DVH-predictions and showed that predictions alone could be used to assess the quality of volumetric modulated arc therapy (VMAT) plans [10]. We hypothesized that RapidPlan could offer a semi-automated and efficient methodology for selecting patients who may benefit from IMPT by comparing DVH-predictions generated for a patient by individual IMPT and VMAT photon models. This method may be less susceptible to bias than comparing manually created proton and photon plans, and

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http://dx.doi.org/10.1016/j.radonc.2017.03.020
0167-8140/

would not require creation of actual treatment plans. In this proof-of-principle study we investigated whether the RapidPlan approach can be used to create KBPs for proton therapy treatments in head-and-neck cancer (HNC); whether the predicted DVH-range accurately reflected what was achieved in the calculated plan; and whether patients could be selected for VMAT or IMPT therapy, solely by using DVH-predictions.

Materials and methods

Treatment plans

All HNC patients were planned using a simultaneous integrated boost technique, delivering 70/54.25 Gy to the boost/elective planning target volume (PTV_B/PTV_E) in 35 fractions. A 5 mm transition-region (PTV_T) was created to allow for gradual dose fall-off between PTVs. Plans included sparing of multiple organs, including the salivary glands and swallowing muscles [11]. Certain structures could be sacrificed by the physician depending on the degree of overlap with PTVs.

Clinical VMAT (RapidArc, Varian Medical Systems, Palo Alto, USA) plans utilized 2 full arcs and 6MV photons. The aim was to deliver 95% of the prescribed dose to 99%/98% of PTV_B/PTV_E while limiting PTV volume receiving >107% of the prescription dose. Optimization was performed using the progressive resolution optimizer (PRO) v10.0.28, followed by dose calculation using AcurosXB v11.0.31 or the anisotropic analytical algorithm (AAA) v10.0.28/11.0.31 using a 2.5 mm calculation grid. A subsequent continue-previous optimization (CPO) was performed for all plans to improve PTV dose homogeneity [12]. RapidArc optimization for HNC was carried out using manual or automated interactive optimization (AIO), as described previously [2].

Intensity-modulated proton plans were created using the non-linear universal proton optimizer (NUPO) and proton convolution superposition algorithm (PCS) v13.7.14 with a 2.5 mm dose calculation grid. Spot sigma in air at the isocenter was 3.9 mm for 240 MeV proton beams. Spot spacing was 0.425 of the energy dependent in-air full width half maximum spot size at the isocenter. Plans incorporated three-field multi-field optimization (MFO), with gantry angles at 35–55°, 180° and 305–330° determined by the geometry of PTVs. A range shifter of 5.7 cm water equivalent material was used to allow for irradiation of proximal portions of the PTV [13]. For each beam direction, typical target margins were 0.2 cm proximal, 0.3 cm distal, and 0.5 cm lateral to the target volume. Optimization was performed interactively during planning by manually adjusting optimization-objectives to maintain an approximately fixed diagonal distance to DVH-lines displayed in the optimization-window [12]. If target dose coverage and homogeneity did not meet the aforementioned criteria, a subsequent optimization was performed with increased priorities on PTV optimization-objectives. In both proton and photon optimizations, maximum point dose-objectives were used for the spinal cord, brainstem and their planning-at-risk volumes.

Models and model cleaning

RapidPlan currently utilizes an algorithm which does not account for the physical characteristics of proton therapy (e.g. no dose beyond Bragg peak). It may therefore not predict OAR DVHs as accurately for protons as it does for photons. However, this was not expected to detract from the primary goals of this study, namely to demonstrate the principle of applying such a knowledge-based planning solution to proton treatment planning and show how the predicted dosimetry could be used as the basis for proton–photon comparisons.

Clinical VMAT photon plans for 30 HNC patients were used to construct the photon model library ($Model_{PHOT}$) and each patient also had an IMPT plan made, so that 30 plans were available for

Table 1
Volumetric and dosimetric details of both the proton ($Model_{PROT}$) and photon ($Model_{PHOT}$) models after outlier removal. The R^2 values for each OAR indicate the quality of regression models, with a value of 1 indicating a perfect fit between dosimetry and geometric features.

Target/OAR	$Model_{PROT}$				$Model_{PHOT}$			
	#	Average Volume Range	Average Mean Dose (Gy)	R^2	#	Average Volume Range	Average Mean Dose (Gy)	R^2
PTVB	30	193.3 ± 102.6 35.8–417.6	70.2 ± 0.3		30	193.3 ± 102.6 35.8–417.6	71.01 ± 0.5	
PTVE	30	573.0 ± 121.9 327.8–840.7	54.9 ± 0.3		30	573.0 ± 121.9 327.8–840.7	55.3 ± 0.5	
PTVT	29	251.4 ± 132.7 55.9–554.5	63.5 ± 0.8		29	251.4 ± 132.7 55.9–554.5	63.3 ± 0.6	
C. Parotid	27	26.3 ± 7.3 12.0–40.1	13.9 ± 5.5	0.82	25	27.4 ± 8.0 12.0–41.5	18.2 ± 4.0	0.75
I. Parotid	28	27.8 ± 7.1 11.2–45.8	22.6 ± 9.4	0.85	30	28.2 ± 6.8 11.2–45.8	25.7 ± 8.5	0.68
C. Submandibular	25	9.0 ± 2.2 5.5–12.5	34.8 ± 14.7	0.86	25	9.1 ± 2.2 5.5–12.5	37.0 ± 15.3	0.85
I. Submandibular	29	9.3 ± 2.1 4.9–12.6	61.9 ± 9.8	0.88	20	9.4 ± 2.4 4.9–13.8	66.5 ± 4.0	0.71
Oral Cavity	25	104.5 ± 55.4 20.8–259.5	10.3 ± 4.7	0.73	25	99.5 ± 32.1 55.1–172.0	25.9 ± 7.6	0.82
Cricoph	29	2.4 ± 1.2 0.7–4.8	14.0 ± 6.5	0.8	22	2.4 ± 1.2 1.0–4.9	20.4 ± 5.3	0.83
L Larynx	27	6.7 ± 6.7 1.5–26.8	10.3 ± 4.6	0.85	22	6.2 ± 5.9 1.8–24.1	17.4 ± 3.8	0.67
U Larynx	27	10.2 ± 4.8 3.8–24.7	30.2 ± 14.6	0.72	27	10.2 ± 4.8 3.8–24.7	38.0 ± 14.0	0.75
PCM Inf	25	3.4 ± 1.5 1.2–6.2	20.09 ± 8.1	0.85	23	3.6 ± 1.5 1.3–6.2	30.3 ± 11.3	0.79
PCM Med	24	1.2 ± 0.7 0.5–2.6	50.8 ± 16.3	0.97	30	1.4 ± 1.0 0.5–5.8	58.4 ± 13.8	0.95
PCM Sup	27	2.6 ± 1.0 0.7–6.0	56.4 ± 15.8	0.95	22	2.7 ± 1.1 0.7–6.0	60.2 ± 9.7	0.92
UES	29	1.6 ± 0.9 0.8–5.6	9.7 ± 5.3	0.73	21	1.7 ± 1.1 0.9–5.6	15.2 ± 4.1	0.46