



Retrospective Prostate Treatment Plan Comparison for Proton, Tomotherapy, and Cyberknife Therapy

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Abstract

Background: Twenty-eight cases from patients previously treated for prostate cancer using helical tomotherapy (22 patients) or Cyberknife (6 patients; Accuray, Sunnyvale, California) linear accelerators were selected chronologically between 2009 and 2011 and were replanned using parallel-opposed beam geometry for proton therapy (PT).

Methods: Proton data used an IBA (Louvain-La-Neuve, Belgium) beam model that was made available from the Philips Radiation Oncology System (Fitchburg, Wisconsin) as a pre-510(k)-approved Pinnacle treatment planning system. Comparison for the coverage of the planned target volume (expanded clinical target volume) and doses to bladder, rectum, and femoral heads were used to evaluate the plans. Radiation Therapy Oncology Group (RTOG, Philadelphia, Pennsylvania) trial 0815, a prostate intensity-modulated radiation therapy protocol, and trial 0938, a prostate stereotactic radiation therapy protocol, were used as an independent “benchmark” for plan robustness.

Results: In a head-to-head comparison, PT planning results showed greater uniformity in coverage of the expanded clinical target volume because helical tomotherapy and Cyberknife planning criteria customarily required the prescribed dose to the 75% to 85% isodose line, whereas PT has been prescribed to at least to the 95% line as specified in the RTOG protocols. In the group of 15 eligible patients, 93% of the plans were able to meet RTOG protocol normal tissue dose constraints for all 3 modalities.

Conclusions: Summary findings indicated that, for the patients selected, RTOG benchmark for inclusion was met in a substantial majority of cases for all 3 modalities. Conformality indices for the prescription dose/target volume for helical tomotherapy and Cyberknife were marginally, but consistently, superior compared with parallel-opposed passive scatter PT plans. It is hypothesized that PT targeting ability is lessened because of the beam’s rapid distal falloff, whereas increased conformality for the helical tomotherapy and Cyberknife treatment plans is attributed to the 360° helical delivery and out-of-plane convergent-beam configuration, respectively.

Submitted 13 Feb 2015

Accepted 02 Jun 2015

Published 16 Oct 2015

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Original Article

DOI
10.14338/IJPT-15-00004.1

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<http://theijpt.org>

Introduction

The treatment for prostate cancer using simple, parallel-opposed, proton radiation fields from double-scattering machines with a nominal proton energy of 200 to 250 MeV has been in selective practice since Massachusetts General Hospital and Loma Linda Proton Therapy came online in the late 1970s and 1980s [1, 2]. The superior properties of the

How to cite this article Wessels BW, Brindle JM, Cheng CW, Rhodes CR, Albani DM, Sohn JW, Lo SS, Ellis RJ, Mansur DB. Retrospective Prostate Treatment Plan Comparison for Proton, Tomotherapy, and Cyberknife Therapy. *Int J Particle Ther.* 2015;2(2):XX–XX.

distal falloff in a proton beam spread-out Bragg peak, resulting in approximately one-third the dose to surrounding tissues compared with x-ray radiation, were thought to result in treatment plans that were vastly superior to the conventional 4-field “box therapy” and the many intensity-modulated radiation therapy (IMRT) techniques using high-energy x-rays [3]. The advent and clinical maturation of IMRT from 2002 to 2008 [4], helical tomotherapy (HT) from 2004 to 2012 [5], Cyberknife (CK; Accuray, Sunnyvale, California) from 2005 to 2012 [6], and volumetric-modulated arc therapy (VMAT) from 2010 to the present [7] have led to an increase in targeting properties of these modalities and the resulting high-quality treatment plans. Hence, the presumed superiority of proton therapy (PT) irradiation for prostate cancer has been called into question [8]. However, current literature still supports the notion that dose to tissues that receive < 50% of the prescription dose appears to be delivered favorably by PT [9]. This property is clearly advantageous in decreasing the potential risk of secondary malignancy generation, which is important for pediatric irradiation [10–12]. The target population of potential patients with prostate cancer is much older on average compared with pediatric patients. A reduction in the integral low-dose region for secondary malignancy generation in this older population with prostate cancer is, therefore, of marginal utility. Furthermore, modern imaged-guided radiation therapy using x-ray beams are producing highly conformal volumes of irradiation. It is now thought that only scanning proton beam or IMPT techniques could compete with image-guided IMRT in prostate irradiation [13]. The importance of cost and the time required for irradiation, both intrafractionally and interfractionally, is of increasing consideration [14]. Increases in plan conformality, robustness, and sparing of healthy tissues is thought to be correlated with increased survival and decreased toxicity to healthy organs and is the objective of previous and ongoing cooperative clinical trials for comparing IMRT to PT [15, 16].

Treatment planning comparison studies for prostate irradiation between PT (passive scattering, uniform scanning, and pencil beam scanning) [4, 5, 17] and external beam therapy using a variety of treatment techniques (RapidArc, IMRT, 4-field box, and very high-energy electron therapy) have been reported [18–20]. The general conclusion was that PT provides comparable and, in some cases, better sparing of organs at risk (OARs) compared with the external beam techniques. Comparison of IMPT and HT was also studied for patients with early stage prostate cancer in a single institution experience, which found similar dose target coverage, normal tissue sparing, and dose homogeneity between the 2 modalities [5]. More recently, 10 patients irradiated with stereotactic body radiation therapy CK treatment were replanned and compared with 3-field double-scatter (DS) PT for prostate irradiation. The result has been presented in abstracted data [21]. However, further comparison to evolving modern irradiation techniques (VMAT, HT, and CK) and double scattering or IMPT proton irradiation at the multiinstitutional level is needed to complement existing prostate plan comparison studies in the literature.

In this work, direct comparison of plans for 2 forms of current, state-of-the art prostate irradiation methods with PT were made using common planning metrics available from the Radiation Therapy Oncology Group (RTOG, Philadelphia, Pennsylvania) and other cooperative groups as clinically relative benchmarks for setting planning goals or control points. We have provided quantitative planning comparison using a relatively small sample size of patients previously treated with HT and CK. These patients were replanned for “theoretical” patient treatment using PT by the double-scattering method using outlined structures and computed tomography (CT) anatomy data available from the HT or CK treatment-planning data sets. Standard PT plan evaluation methodology adopted from RTOG relevant protocols were employed, in which the dose-volume histograms (DVH) of the planned target volume (PTV) and OARs, conformality indices (CIs), and healthy-tissue tolerance doses were compared.

Methods and Materials

Patient Selection

Twenty-eight previously treated patients (HT, 22 HT patients; CK, 6 patients) were selected chronologically between the years of 2009 and 2011 and anonymized from an existing database of HT and CK cases at the University Hospitals Case Medical Center. This institutional review board–approved analysis was initially designed to test the proton planning capabilities of the pre-510(k) version of Pinnacle treatment planning software (Version 9.0, Philips Radiation Oncology Systems, Fitchburg, Wisconsin). Because the original intent of work was to explore the utility and robustness of the pre-510(k) version of the software for potential, subsequent clinical use, uniformity of prescribed dose to the target volume, standardized PTV designation, healthy organ tolerance, and uniformity definitions were adopted from the original method of treatment (HT or CK). However, it became apparent that high-quality plans available from this unique combination of radiation therapy treatment equipment for prostate cancer at this institution provided an opportunity for direct comparison of proton planning. Hence, subselection criteria were developed for plan comparison purposes after the first 10 patients entered into the treatment

planning system (TPS), which were then restricted to 79.2 to 81.0 Gy in 44 to 45 fractions with HT or 36.25 Gy in 5 fractions or 51.6 in 12 fractions for CK to conform to the dose criteria outlined in RTOG trials 0815 or 0938, respectively [22, 23]. These plan doses were considered a full, definitive course of treatment for early and intermediate-grade prostate cancer.

Simulation

Patients who received treatment with the tomotherapy unit were imaged with 3-mm slice thickness using a 40-slice Brilliance Siemens CT scanner (Global Siemens Healthcare, Erlangen, Germany) or the Phillips AcQsim single slice system (Phillips Healthcare, Andover, Massachusetts). Patients who received treatment with the Cyberknife unit were scanned with a slice width of 1 mm. Patients were immobilized with a CIVCO 2-pin localization system in conjunction with a vac-Loc bag or body-fix system (Elekta, Stockholm, Sweden).

Image fusion with the MIM software (version 6.0.5; Cleveland, Ohio) was performed when magnetic resonance or radionuclide imaging exams and CT were indicated for target delineation and potential boost therapy. At the CT simulator, laser marks were used to align patients by visual inspection after bony landmarks were imaged with kV-CT to set the patients' positions reproducibly when reimaged and aligned in either the HT or CK treatment units.

All patients had a couch-indexed knee positioner in place for simulation and treatment without rectal balloons or Foley catheters. For the patients treated with CK, 4 to 5 fiducials had been placed in the prostate at least 1 week before the simulation.

Volume Definition

The expanded clinical target volume (CTV) used for PT planning was obtained using the previously defined PTV for either the HT or CK because these patients were already treated by 1 of these 2 modalities. The PTV was typically defined as the CTV plus an expanded 5-mm margin in all directions, except 3 mm posterior for CK and 8 mm in all directions, except 5 mm posterior for HT. For plan comparison, conformity index (CI) of the PTV relative to the volume of the prescription isodose volume (PITV) was computed by 2 methods. The first method designated as CI_RTOG indicated the ratio of the PITV divided by the PTV [24]. This method works well if the prescription isodose line of 95% or greater is used [25]. Because HT and CK dose prescription lines may be as low as 70% with only a partial volume of the PTV covered and where PTV and PITV may not overlap, a second and more-rigorous Paddick CI was used [26]. Prescription dose defined as the mean PTV dose (eg, for HT) may also result in values of the PITV < 95% of the PTV. The Paddick method provides for a linear penalty function for underlap, overlap, and nonconformality of the PITV isocenter with the PTV. Mathematically, the inverse Paddick ratio (CI_IP) was used to directly compare with the CI_RTOG because the radiation therapy and the neurosurgical communities adopted CIs, which have an inverse relationship (Gamma Knife [Elekta Inc, Stockholm, Sweden] versus stereotactic body radiation therapy).

Planning Approach

Planning for Proton

Traditional PT planning for prostate cancer comprises 2 parallel-opposed lateral beams using automatic selection of maximal range and modulation (spread-out Bragg peak) by TPS. The proton beams were modeled from an IBA (Louvain-La-Neuve, Belgium) cyclotron delivered via a passive-scattering nozzle. Once imported, a treatment isocenter is placed at the center of the patient's HT- or CK-defined PTV1. Range compensator and proton aperture selection is also part of the automatic optimization scheme by TPS where distal and proximal treatment margins, smearing, and range uncertainty parameters are usually set by the operator after default presets used by TPS. Selections of snout sizes of 10, 18, or 25 cm were available and are machine dependent.

If the patient's original treatment prescription for HT was between 79.2 Gy and 81.0 Gy delivered in 1.8-Gy fractions, a PT plan was created using the constraints specified in RTOG trial 0815. The PT dose prescription was assigned to not < 95% isodose line (plan normalization). The prescribed dose had to cover a minimum of 95% of the PTV volume and contain a hot spot no higher than 107%. Further, 15%, 25%, 35%, and 50% of the bladder could not receive > 80, 75, 70, and 65 Gy, respectively. Similarly, > 15%, 25%, 35%, and 50% of the rectum could not receive > 75, 70, 65, and 60 Gy, respectively, to maintain RTOG study guidelines. Because no patients were to be treated with PT comparison plans, monitor units were not computed. Therefore, the customary RBE of 1.1 was not applied for protons, and the plan dose

Table 1. Comparison of helical tomotherapy and proton therapy plans for 10 patients according to RTOG 0815 guidelines, averaged data.

| Treatment modality | Treatment volume | Fx | | Total dose, Gy | PTV volume, cm ³ | PTV coverage, % | Rectum | | | Bladder | | |
|--------------------------|-----------------------------|----------|-------|---------------------|-----------------------------|-----------------|----------|-----------|---------------------------|----------|-----------|---------------------------|
| | | dose, Gy | Fx | | | | Dose, Gy | Volume, % | RTOG 0815 volume limit, % | Dose, Gy | Volume, % | RTOG 0815 volume limit, % |
| Helical tomotherapy | Prostate PTV (expanded CTV) | 1.8 | 44/45 | 80.3 (79.2 to 81.0) | 153.5 | 84.70 | ≤ 80 | 3.0 | — | ≤ 80 | 2.1 | 15.0 |
| | | | | | | | ≤ 75 | 8.7 | 15.0 | ≤ 75 | 8.3 | 25.0 |
| | | | | | | | ≤ 70 | 14.1 | 25.0 | ≤ 70 | 12.5 | 35.0 |
| | | | | | | | ≤ 65 | 19.0 | 35.0 | ≤ 65 | 16.4 | 50.0 |
| | | | | | | | ≤ 60 | 24.2 | 50.0 | ≤ 60 | 22.9 | — |
| Double-scattered protons | Prostate PTV (expanded CTV) | 1.8 | 44/45 | 80.3 (79.2 to 81.0) | 159.2 | 96.50 | ≤ 80 | 7.8 | — | ≤ 80 | 5.2 | 15.0 |
| | | | | | | | ≤ 75 | 12.5 | 15.0 | ≤ 75 | 8.7 | 25.0 |
| | | | | | | | ≤ 70 | 15.5 | 25.0 | ≤ 70 | 10.8 | 35.0 |
| | | | | | | | ≤ 65 | 18.1 | 35.0 | ≤ 65 | 12.2 | 50.0 |
| | | | | | | | ≤ 60 | 21.2 | 50.0 | ≤ 60 | 14.0 | — |

Abbreviations: RTOG, Radiation Therapy Oncology Group; Fx, fractions; PTV, planned target volume; CTV, clinical target volume.

comparisons were made directly for all computed DVHs (with plan normalization included in the DVH calculations) for each machine type in cobalt-equivalent Gy. Pinnacle uses a pencil-beam algorithm with a dose calculation grid size of 4 × 4 × 4 mm.

The initial shape of the aperture was created by adding a uniform margin. Similarly, proximal and distal margins were also computed initially by the TPS using the automatic setting typically ranging from 0.5 to 1.5 cm. Upon obtaining acceptable PTV coverage, the margins of the aperture, proximal margins, and distal margins were manually adjusted in an attempt to meet normal tissue constraints and to increase plan conformality. The typical range-uncertainty value (including straggling, Hounsfield Unit to relative stopping power [HU-RSP] calibration uncertainty, etc) of ~3 % of the total range or approximately 9 mm constitutes part of the distal margin. Aperture blocking was initially set at 1 cm around the PTV, except near the bladder and rectum, where manual margins were planned such that minimal rectal and bladder dose was achieved while coverage of the PTV was maximized (> 95 %). These resulted in lateral penumbra as small as 5 mm to a maximum of 12 mm in this study.

A minimum source-surface distance (220 to 230 cm) was set within 5 cm of the snout to minimize proton penumbra around the target while avoiding collision between patient and treatment snout. With the Pinnacle TPS, the compensator profile can be manipulated by “smearing,” which smoothes or averages compensator pixel thickness based on the user-specified values of neighboring pixels and “border smoothing,” which smoothens the compensator thickness from the edge of the PTV to the aperture’s edge by a user-specified step-size. Values used for the smearing and smoothing were between 5 to 10 mm.

Planning for HT

Image segmentation methods were the same as those used in treatments using other treatment machines. Tomotherapy Hi-Art version 4.0.4 (TomoTherapy Inc, Madison, Wisconsin) was used for planning. The collapsed-cone convolution algorithm was used for dose calculation with a grid size of 3.1 mm × 3.1 mm × 3.1 mm. Because HT is specially designed for IMRT, it has a unique radiation delivery system. It has 40 multileaf collimator pairs across the body axis, and selects multiple beam thicknesses (1, 2.5, and 5 cm). Rotational IMRT using linear accelerators is optimized in a 3-dimensional volume; however, helical rotation with a thin-beam thickness allows 2-dimensional optimization, which produces highly conformal dose distribution. For prostate treatments, a 2.5-cm field length was used. Prostate was defined as CTV, and PTV was created by applying an 8-mm margin to CTV. The posterior margins were typically 5 mm in the original plans. In some cases, a prescribed mean dose for the patients planned with HT was assigned to the PTV, and tolerance doses to bladder and rectum were optimized using the HT inverse-treatment planning. Hence, the percentage of PTV that received the prescription dose ranged from 73.2% to 98.5%. The limiting doses used in HT planning for OARs were set at 75 Gy to volumes < 75% and 70 Gy to volumes < 75% of bladder and rectum, respectively. All treatments for the 22 patients were completed with a 1.8-Gy fractional dose and the subset of patients (n = 10) prescribed to a total dose of 79.2 or 81 Gy were included in the results (Table 1).

Planning for CK

Accuray MultiPlan version 3.5.2 was used for the treatment planning of the CK cases. Contouring of all structures specified in RTOG 0938 protocol was performed within the MultiPlan TPS. Upon delineation of the prostate volume, CTV, a planning target volume (PTV1) was created based on the following margin around the CTV, 3 mm posteriorly and 5 mm in all other directions. Inverse-planning, targeting the PTV1, was used to create a satisfactory plan per the treating physicians and the RTOG 0938 protocol when 95% of the PTV was specified to be covered by the normalized 100% isodose line. The CK ray tracing algorithm was employed for prostate dose planning with variable grid spacing, $0.5 \times 0.5 \times 0.5$ mm for the target and $1 \times 1 \times 1$ mm for the rest of the contours. In some cases, the mean dose to the PTV was used to optimize the plan. The treatment delivery used the Iris collimator and comprises approximately 150 to 200 beams, taking approximately 60 to 90 minutes to deliver.

The treatment directive for the original CK plans was a fractional dose of 7.25 Gy to be delivered in 5, or 4.3 Gy delivered in 12, fractions, resulting in a total prescription dose of 36.25 or 51.6 Gy for 5 of 6 patients, respectively. Guidelines set forth in RTOG 0938 also provided for both arms of the CK irradiation to be matched with PT with accompanying OAR limits.

When the CK plans were originally performed and evaluated, they were optimized according to the dose directives (both target and critical structure) in the 5-fraction arm of the RTOG 0938 protocol. In particular, for the bladder, the maximum dose (D_{max}), the dose to 90% of the bladder volume (D_{10}), and the dose to 50% of the bladder volume (D_{50}) were assessed. For the rectum, the maximum dose (D_{max}), the dose to 80% of the rectum volume (D_{20}), and the dose to 50% of the rectum volume (D_{50}) were assessed. These 3 parameters were used to compare the CK plans against the PT plans. A CI was also included in the evaluation of the plan comparison as described above. Dose to the femoral heads were also recorded in the DVH analysis.

Results

Plan Comparison

Of the 22 patients selected and planned with the HT planning system, only 14 were treated with a full course of radiation therapy to PTV1 mean or V95 PTV dose between 79.2 and 81 Gy. The remaining 8 patients had undergone additional therapy designed to include more complex PTV2 or PTV3 boost volume per physician's prescription to accommodate structures of interest (seminal vesicle [SV] and nodal volumes). Additionally, 4 more patients were excluded from the HT and PT comparison data set because of either (1) ranging out of the protons in larger patients because the planning data set provided did not have high enough energy protons (Bragg peak maximum, 28.0 g/cm^2), or (2) planning volume included specialized structures (eg, prostate bed, SV, lymph nodes, etc) and was not well-suited for passive 2-field PT planning using RTOG 0815 guidelines. Hence, for comparison simplicity, 10 patients were included in the current HT/PT analysis. Similarly, of the 6 patients selected, planned, and treated with the CK system, 5 patients were eligible for this comparison study, where the remaining patient was excluded for similar reasons of complex PTV geometry. One of the 5 patients in the comparison group included SV structures to show how, and to what extent, both CK and PT plans failed to achieve RTOG criteria. Additionally, the 5 CK planned patient were divided into 2 separate treatment arms, 5 fractions at 7.35 Gy and 12 fractions at 4.3 Gy per RTOG 0938 protocol. The 12-fraction arm had 3 patients and the 5-fraction arm included 2 patients. The 5-fraction arm contained the patient with the expanded SV coverage.

In general, proton plans produced results comparable to existing plans generated for HT- and CK-treated patients, which were evaluated according to guidelines set forth by the RTOG protocols 0815 and 0938, respectively. Specifically, the PTV coverage, limits on normal critical structures (bladder and rectum) (**Tables 1** through **3**), and the CI of the treatment plans (**Table 4**) were used in the comparative analysis.

Target Volumes

Plan results showed that the GTV coverage for both HT and PT was $> 98\%$. However, because of the prescription dose being specified, in many cases, to the mean PTV for HT, coverage fell to 84.5% for the PTV, which is noncompliant with RTOG 0938. To meet the PTV constraints specified in RTOG, PTV coverage for PT plans were specified to not $< 95\%$. Additionally, the HT plans were not replanned to try to meet the higher coverage criteria because treatments were already performed. In **Table 4**, CIs for the PTV were provided for the CI_RT0G and the CI_IP, as previously defined. The CI_RT0G method of calculation for volumes that are substantially undercovered by the PITV associated with a PTV was found to be an inadequate method of evaluating the conformality of an HT plan. When the CI_IP method was used as a comparison indicator, undercoverage and

Table 2. Cyberknife versus proton RTOG 0938 comparison data, 5-fraction arm (n = 2), averaged data.

| Treatment modality | Treatment volume | Fx dose, Gy | Fx | Total dose, Gy | PTV volume, cm ³ | PTV coverage volume, % | Rectum | | | Bladder | | |
|--------------------------|-----------------------------|-------------|----|----------------|-----------------------------|------------------------|-----------------------------|-----------|-----------|-----------------------------|-----------|-----------|
| | | | | | | | Dose, Gy | Volume, % | limit, Gy | Dose, Gy | Volume, % | limit, Gy |
| Cyberknife | Prostate PTV (expanded CTV) | 7.25 | 5 | 36.25 | 100.1 | 99 | Max (0.03 cm ³) | 37.8 | < 38.1 | Max (0.03 cm ³) | 40.8 | < 38.1 |
| | | | | | | | 90 | 32.3 | < 32.6 | 90 | 34.6 | < 32.6 |
| | | | | | | | 80 | 28.2 | < 29 | 50 | 20.9 | < 18.1 |
| | | | | | | | 50 | 19.5 | < 18.1 | — | — | — |
| Double-scattered protons | Prostate PTV (expanded CTV) | 7.25 | 5 | 36.25 | 100.9 | 95 | Max (0.03 cm ³) | 37.0 | < 38.1 | Max (0.03 cm ³) | 37.2 | < 38.1 |
| | | | | | | | 90 | 33.7 | < 32.6 | 90 | 36.3 | < 32.6 |
| | | | | | | | 80 | 26.9 | < 29 | 50 | 20.4 | < 18.1 |
| | | | | | | | 50 | 8.1 | < 18.1 | — | — | — |

Abbreviations: RTOG, Radiation Therapy Oncology Group; Fx, fractions; PTV, planned target volume; CTV, clinical target volume; Max, maximum.

overcoverage of the PTV and PTV are equally weighted in terms of the “goodness” of coverage. Values of CI_IP (Table 4) HT and PT plans were 1.34 and 1.57, respectively, and show that HT plans were more conformal ($P < 0.0158$). For the comparison of CK and PT treatments, Table 4 results show that CK consistently had more conformal plans than PT plans did using both the CI_RTOG and CI_IP CIs but were not statistically significant because of sample size.

Normal Tissue Volumes for the Rectum, Bladder, and Femoral Heads

Table 1 shows that for the HT and PT comparison, the average of 10 plans consistently met RTOG 0815 for bladder and rectum dose constraints where results were slightly better using HT. Because the average coverage in the HT PTV plans is 85%, the difficulty in meeting these OAR constraints is also proportionally relaxed. Tables 2 and 3 show the results for CK plan comparison replanned using PT. Table 2 compares CK and PT for the 2 patients in the 5-fraction arm with the dose of 7.25 Gy per fraction for a total dose of 36.25 Gy. Both CK and PT plans did not meet dose-constraint criteria for RTOG 0938 mainly because of the excessive bladder exposure. The simple average for the 2 plans was weighted substantially by the inclusion of a PTV volume in the single plan that included the SV structures. The SV structure inclusion caused the bladder to wrap around the PTV at the superior aspect, which created a large concave surface that neither planning modality was able to successfully separate out and target. Table 3 shows the results of the 12-fraction arm for the remaining 3 patients treated with CK, where the fractional dose was 4.3 Gy for a total dose of 51.6 Gy. For these patients, all RTOG 0938 dose constraints were met for the bladder and rectum. There was no inclusion of SV into the PTV for these patients.

Both HT and CK produce a smaller high-dose region (80 Gy) than PT does (2-tailed Student *t* test, $P < 0.05$, 2-tailed Wilcoxon). On the other hand, there is no statistically significant difference between HT/CK and PT in the rectal and bladder volumes receiving a dose in the range of 60 to 75 Gy ($P > 0.05$). The PT plans were marginally better in sparing of the rectum

Table 3. Cyberknife versus proton RTOG 0938 comparison data, 5-fraction arm (n = 3), averaged data.

| Treatment modality | Treatment volume | Fx dose, Gy | Fx | Total dose, Gy | PTV volume, cm ³ | PTV coverage volume, % | Rectum | | | Bladder | | |
|--------------------------|-----------------------------|-------------|----|----------------|-----------------------------|------------------------|-----------------------------|-----------|-----------|-----------------------------|-----------|-----------|
| | | | | | | | Dose, Gy | Volume, % | limit, Gy | Dose, Gy | Volume, % | limit, Gy |
| Cyberknife | Prostate PTV (expanded CTV) | 4.3 | 12 | 51.6 | 81.2 | 96.6 | Max (0.03 cm ³) | 53.0 | < 54.2 | Max (0.03 cm ³) | 53.7 | < 54.2 |
| | | | | | | | 90 | 39.0 | < 46.4 | 90 | 44.7 | < 46.4 |
| | | | | | | | 80 | 27.8 | < 41.3 | 50 | 20.6 | < 25.8 |
| | | | | | | | 50 | 10.9 | < 25.8 | — | — | — |
| Double-scattered protons | Prostate PTV (expanded CTV) | 4.3 | 12 | 51.6 | 80.2 | 95 | Max (0.03 cm ³) | 53.2 | < 54.2 | Max (0.03 cm ³) | 52.8 | < 54.2 |
| | | | | | | | 90 | 33.8 | < 46.4 | 90 | 43.0 | < 46.4 |
| | | | | | | | 80 | 12.6 | < 41.3 | 50 | 8.8 | < 25.8 |
| | | | | | | | 50 | 0.3 | < 25.8 | — | — | — |

Abbreviations: RTOG, Radiation Therapy Oncology Group; Fx, fractions; PTV, planned target volume; CTV, clinical target volume; Max, maximum.

Table 4. Comparison of CI for HT versus proton plans using RTOG 0815 guidelines and for CK versus proton plans using RTOG 0938 guidelines, averaged data.

| Protocol | Modality | RTOG CI ± SD | Inverse Paddock index ± SD |
|----------------------|--------------|--------------|----------------------------|
| RTOG 0815 | HT | — | 1.34 ± 0.12 |
| | Proton | 1.45 ± 0.24 | 1.57 ± 0.22 |
| RTOG 0938, 5-Fx arm | CK 5 Fx | 1.28 ± 0.03 | 1.3 ± 0.04 |
| | Proton 5 Fx | 1.42 ± 0.17 | 1.57 ± 0.19 |
| RTOG 0938, 12-Fx arm | CK 12 Fx | 1.17 ± 0.11 | 1.22 ± 0.11 |
| | Proton 12 Fx | 1.29 ± 0.06 | 1.39 ± 0.05 |

Abbreviations: CI, conformality index; HT, helical tomotherapy; RTOG, Radiation Therapy Oncology Group; CK, Cyberknife.

and bladder with a marked reduction at the 50% volume, as would be expected for proton irradiation. Femoral head dose for both HT and CK plans as well the corresponding dose from PT plans met all RTOG planning criteria (data not included).

Discussion

The pre-510(k) version of Pinnacle treatment planning software for a PT beam model was compared with HT and CK plans and showed comparable targeting, sparing of normal tissues, and conformality of dose distribution. In addition, 14 of 15 of the selected HT and CK patients eligible for the comparison study (93%) complied with the well-known RTOG clinical trials for treating prostate cancer in both a standard and a hypofractionated setting. These results were consistent with results reported by Schwarz et al [5], where a similar comparison with HT versus IMPT in 8 patients with prostate cancer was successfully benchmarked with a European clinical trials group. As described by Rana et al [17], the low- and medium-dose regions surrounding the prostate that anterior and oblique field techniques show decreased dose for proton planning. However, in the important high-dose regions surrounding critical OARs, the sculpting power of the HT and CK irradiation methods often produce plans that have superior conformality compared with DS PT techniques. The abstracted data using stereotactic body radiation therapy CK according to RTOG 0938 presented by Kole et al [21] similarly showed superiority of the DS PT in the low- and mid-dose regions but mixed efficacy in the high-dose regions surrounding the OAR for a small cohort of patients.

In attempts to expand treatment beyond just the prostate (ie, seminal vesicles, nodal chain, etc), the compliance with RTOG OAR criteria frequently failed for target volumes that wrap around critical structures (eg, PTV wrapping around portions of rectum or bladder). This is an inherent limitation of the DS PT approach regarding covering concave target volumes where noncoplanar VMAT, HT, or IMRT methods and scanning proton beam technology have been shown to have some advantage.

Summary findings indicated that, for the patients selected, RTOG benchmark for inclusion was met for most patients treated through all 3 modalities. The CIs for the prescription dose and target volume calculated using the inverse Paddick for HT and CK were marginally, but consistently, superior compared with parallel-opposed PS PT plans ($P < 0.05$). The use of CIs as an indicator of plan robustness has been shown to be most useful when the PTV is surrounded in all directions by sensitive tissues at risk (eg, brain parenchyma [25]). However, it can be argued that CIs used for targets in the lung or prostate may not be as useful if an excess dose can be safely deposited in atelectatic sites in the lung or low-risk regions just medial to the femoral heads for prostate irradiation. Comparison of biologically effective corrected-total dose to organs at risk and the volume of irradiation in the local region with maximum coverage at therapeutic doses to the target remain the hallmark for determining plan superiority.

To our knowledge, this is the first study using the Pinnacle TPS PT module for prostate planning. Our study using RTOG protocols as benchmarks for plan comparison is particularly significant in that clinical outcomes from the RTOG trials have significant clinical impact on cancer management.

Conclusion

Plan comparisons show that all 3 modalities (HT, CK, and DS PT) substantially met the dose-volume criteria in RTOG 0815 and 0938. The CI for the prescription dose and target volume calculated using the inverse Paddick for HT and CK were marginally, but consistently, superior compared with parallel-opposed PS PT plans, whereas PT was superior in the sparing dose to the patient in the low- and mid-dose regions of the DVH.

ADDITIONAL INFORMATION AND DECLARATIONS

Conflicts of Interest: Barry W. Wessels has a master contact agreement with Philips in treatment planning equipment only. All other authors have no direct conflicts of interest to disclose.

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