3D geometric gel dosimetry verification of intraprostatic fiducial guided hypofractionated radiotherapy of prostate cancer

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Abstract. This pre-study is aimed to investigate the feasibility of a normoxic polyacrylamide gel (nPAG) dosimeter with implanted gold fiducials to evaluate the geometric precision, including setup correction strategies, in the delivery of hypofractionated treatments. For this purpose a phantom consisting of three parts was constructed: (1) the patient simulating volume, providing realistic scatter conditions and weight, (2) a bottle containing the active dosimetric volume and (3) the gold fiducials and the fiducial support structure. A 6.1 Gy prostate IMRT treatment was delivered to the phantom using the sliding-window technique. The phantom was positioned prior to the treatment using the implanted fiducials and kV on-board imaging. An overlay of the 95% isosurface of the TPS calculated dose distribution and the measured dose distribution using gel showed good agreement. The clinical target volume (CTV) was well centred inside the 95% isodose surface of the measured volume. It was shown for the evaluated case that the use of on-board imaging and integrated setup correction tools could be used to compensate for a deliberately introduced offset in CTV position. The study showed that MRI based nPAG gel dosimetry can be used to verify setup correction procedures using implanted gold fiducials.

1. Introduction
Several studies have suggested that dose-escalated external radiotherapy could prolong the freedom from failure time, measured as a rising prostate-specific antigen (PSA) [1-3]. On the other hand, preliminary results from a randomized MD Anderson study reported an increase of rectal toxicity in the dose-escalation arm by a factor of two [4]. If the prostate is localized prior to treatment and by adjusting the patient position to account for the inter-fraction prostate movement, the planning target volume (PTV) could be reduced [5]. This would reduce the dose to the surrounding normal tissue,
including rectum, and potentially reduce side-effects of the treatment. Image guided radiotherapy (IGRT) has been widely adopted to minimize the effects of inter-fractional motion. Intraprostatic gold fiducials are the most wide-spread approach for IGRT of the prostate in clinical practice [6]. The importance of prostate localization is undoubtedly higher when increasing the fraction dose.

A randomized multicenter phase III study (HYPO-RT-PC) of patients with intermediate risk prostate cancer has been initiated [7]. Conventional fractionation (2.0 Gy in 39 fractions) to a total absorbed dose of 78.0 Gy is compared with hypofractionation (6.1 Gy in 7 fractions) to a total absorbed dose of 42.7 Gy. All fractions are delivered with either conventional (3D-CRT) or intensity modulated radiotherapy (IMRT). The position of the prostate, as determined by the implanted gold fiducials, is verified prior to each fraction with kV/MV portal imaging or cone beam CT.

Polymer gel dosimetry can be used to measure absorbed dose distributions in a complete volume with high spatial resolution [8, 9]. The use of gel dosimetry has also been found feasible for verification of dynamic delivery [10, 11].

This pre-study aims to investigate the feasibility of a normoxic polyacrylamide gel (nPAG) dosimeter with implanted gold fiducials to evaluate the dosimetric consequences of the setup correction strategies used at the centers participating in the HYPO-RT-PC study.

2. Material and methods

2.1. Gel preparation

In this study a single batch of normoxic polyacrylamide gel (nPAG) was used, based on 3% w/w acrylamide (electrophoresis grade, ≥99%, powder, Sigma Aldrich) and 3% w/w N,N’-methylenebisacrylamide (electrophoresis grade, ≥98%, powder, Sigma Aldrich). Gelatine (300 bloom, Sigma Aldrich) was used as the matrix substance and tetrakis(hydroxymethyl)–phosphonium chloride (techn. ~80% in water, Sigma Aldrich) was used as an oxygen scavenger. The remaining constituent was ultra-pure deionized water (resistivity > 18.2 MΩ cm). The method used for gel preparation has been described elsewhere [12]. Vials containing the gel were irradiated with an absorbed dose ranging from 1 to 7 Gy in order to assure the linearity of the gel dose response for this batch of gel.

2.2. Phantom

The phantom consists of three parts: the patient simulating volume, providing realistic scatter conditions and weight, a bottle containing the active dosimetric volume and the fiducials and the fiducial support structure (figure 1). The outer part of the phantom was created using polystyrene slabs of 5 mm thickness that were glued together and modified to an oval shape to simulate the body outline in the pelvic region. A hole was drilled in the center of the polystyrene that fits an oxygen resistant glass bottle, containing the nPAG gel. The fiducials (1 mm diameter, 5 mm length) were fixated at the ends of three 5 mm thick polymethyl methacrylate (PMMA) rods attached to the lid of the bottle.

2.3. CT scanning and treatment planning

Treatment planning was performed on planar CT images of the phantom with a slice thickness of 3 mm, in accordance with the HYPO-RT-PC study protocol. Structures from a dummy patient was imported onto the phantom and a six field, 6 MV, sliding-window IMRT treatment plan was created with a fractional dose of 6.1 Gy (figure 1). The planning target volume (PTV) included the prostate (CTV) with a margin of 7 mm in all directions. All DVH constraints and technical aspects of the study protocol were fulfilled. The TPS calculated dose matrix was interpolated from 2.5 × 2.5 × 3 mm to 1 × 1 × 3 mm using cubic spline.
2.4. Treatment delivery
A Clinac 2100C/D (Varian medical systems) equipped with an x-ray on-board imager (OBI) was used for treatment delivery. The phantom was intentionally placed at an offset position from iso-center, with a rotation of the glass bottle around the longitudinal axis. Planar imaging at 0° and 270° using the OBI was performed and the integrated automatic correction possibilities (longitudinal, lateral and vertical couch movement) in the Aria verification system (Varian medical systems) were used to correct for the simulated misplacement. The dose-rate was 400 monitor units per minute and Portal Dosimetry (Varian medical systems) was performed prior to the gel dosimetry in order to exclude possible machine-dependent errors.

2.5. Magnetic resonance imaging
Magnetic resonance imaging (MRI) of the gels was carried out 24 hours after the irradiation, using a 1.5 T MRI unit (Siemens Medical Systems) and a circularly polarized receive-only head coil. The images were acquired using a 32-echo multi spin echo sequence with an inter-echo spacing of 25 ms and a repetition time of 4000 ms. The voxel size was $1 \times 1 \times 3$ mm. To obtain an accurate background signal, an unirradiated gel bottle of the same dimensions was also scanned. An in-house developed software was used for calculation of the transversal relaxation rate ($R_2 = 1 / T_2$) [13].

3. Results and discussion
The $\gamma$ pass-ratio between the measured and calculated EPID dose distribution agreed within 96 % using a 3% / 3 mm criterion, confirming that there was no machine dependent delivery errors.

The planar images obtained with the OBI at 0° and 270° were matched with the DRRs generated in the TPS using the Aria (Varian medical systems) verification system, and the resulting geometrical corrections were used to account for the present offset (figure 2, table 1).

Figure 1. The six field, 6MV, sliding-window IMRT treatment plan with structures from a dummy patient (left). The fiducials are clearly visible in the digital reconstructed radiographs (DRR) generated in 0° and 270°, respectively (middle and right).
Figure 2. kV images of the phantom taken with the OBI at 0° (left) and 270° (right). The images were matched against the DRR generated in the TPS and used to correct for the offset.

Table 1. Position of the phantom relative to the isocenter determined using an external laser system (LAP Laser Applications).

| Initial position | Position after correction |
|------------------|---------------------------|
| Longitudinal     | -7 mm                     | +2 mm |
| Lateral          | +3 mm                     | -1 mm |
| Vertical         | +5 mm                     | +2 mm |
| Rotation         | 6.3° CCW                  | 6.3° CCW |

The gel results were normalized to a TPS calculated dose using a region of homogenous dose in a slice without the presence of the fiducials or the fiducial support structure. Evaluation of the irradiated vials confirmed the linearity of the gel dose response for this batch of gel ($R^2 = 0.98$). An overlay of the 95% isosurface of the TPS calculated dose distribution and the measured dose distribution using gel showed good agreement (figure 3, left). The numbers of voxels inside the 95% dose level were 46586 and 45303 for the calculated and measured dose distribution, respectively. Further, the CTV volume was well centred inside the 95% isodose surface of the measured volume (figure 3, right). An increase of the R2 value was apparent in the region surrounding the fiducial support structure. This MRI readout artefact typically corresponded to a relative dose increase of 25% in a radius of 1 cm around the structure compared to the TPS calculated dose distribution. However, this effect did not compromise the determination of the location of the 95% isodose surface as the fiducials were located centrally in the volume of interest.

Figure 3. An overlay of the TPS calculated dose distribution (red) and the measured dose distribution (green) using alpha blending (left). Only the 95% isodose are shown. A 2D slice with both the measured and calculated 95% isodoses (black), as well as the CTV and PTV structures (white) are shown to the right.
4. Conclusions
This study showed that MRI based nPAG gel dosimetry can be used to verify setup correction procedures using implanted gold fiducials. For the case used in this pre-study, it was shown that the use of on-board imaging and integrated setup correction tools could be used to compensate for a deliberately introduced offset in CTV position. By expanding this study to include more patient cases, it should be possible to draw more general conclusions about the IGRT setup correction capabilities. This would be of value in order to determine the part of the PTV margin magnitude intended to account for inter-fractional movement of the prostate.

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