First clinical release of an online, adaptive, aperture based IGRT strategy in IMRT to correct for inter- and intra-fractional rotations of the prostate

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Introduction

In image guided, intensity modulated radiotherapy (IGIMRT) of prostate cancer, inter- and intra-fractional movements of the organ are the main reason for safety margins between the clinical target volume (CTV) and the planning target volume (PTV). Implanted gold markers allow pre- and intra-treatment assessment of prostate movements in kV and MV projections. In addition to translations, significant rotations of the prostate (15° or more) have to be expected. While couch shifts can be applied for vector corrections, it is simply impractical to rotate patients in that magnitude. Therefore, we make use of the multi leaf collimator to adapt beam apertures instead

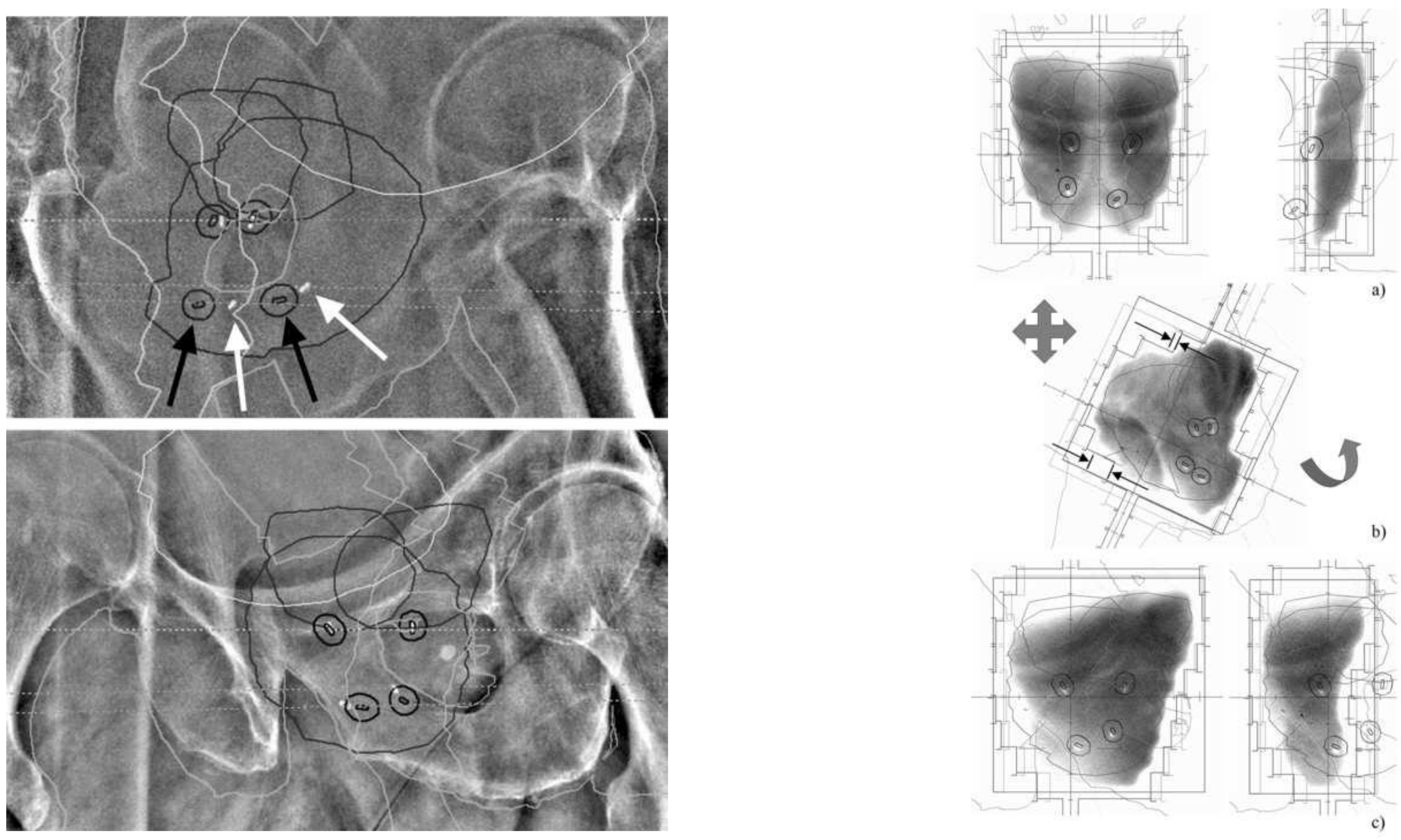

Figure 1: Left: Pre-treatment kV radiographs from two orthogonal views. Initially planned (untransformed) position of bony anatomy, markers and PTVs (prostate, SVs) are automatically overlaid to visualize inter-fractional changes before registration. Right: Correction of rotations and translations: 15 MV portal images of a sample of IMRT segments from different gantry angles: a) 0°, b) 103°, c) 254°. Initially planned beam aperture (leave positions in light grey) and real-time adapted field (bold) are blended in. Smaller discrepancies between gold marker projections of patient at actual fraction and augmentation of accordingly transformed structures from planning CT indicate intra-fractional movements.

Methods

We present the first clinical release of an online, adaptive, aperture based IGRT protocol for IMRT of the prostate that works without re-positioning of the patient on a standard linear accelerator equipped with an integrated multi leaf collimator (MLC 80 leaves 1 cm). 4 cylindrical gold markers are auto-detected in planar projection images captured on-the-fly, no initial cone beam acquisition is required (Fig. 2). Translations, rotations and organ swelling/shrinkage are immediately reconstructed. MLC leave positions for all IMRT segments are adapted to the transformed PTV and organs at risk (OARs) within seconds. For that purpose, a new record and verify system *open-radART* was developed to integrate real-time 3D treatment planning features and to control conventional linear accelerators (Elekta Synergy / RTD 7). Direct interfaces to the panels (kV and MV imaging) were embedded in the application to enable fast image feedback loops.

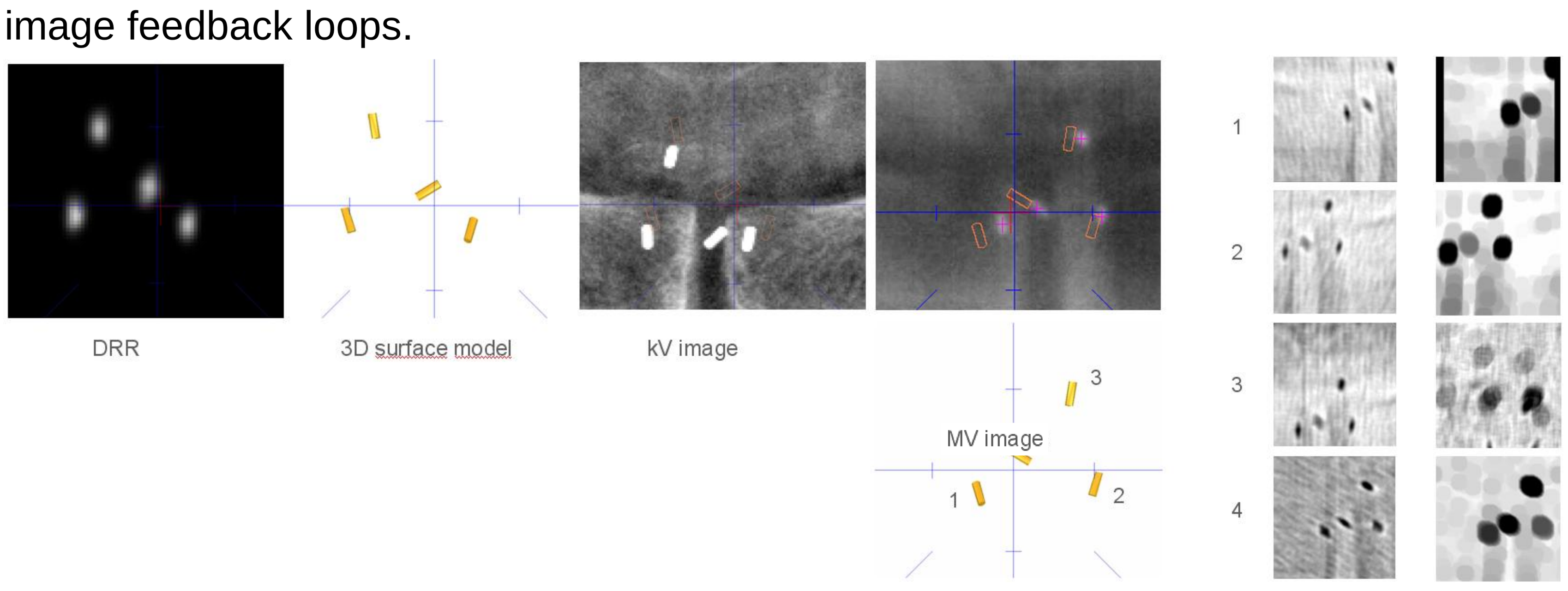

Figure 2: Segmentation and sub-voxel modelling of cylindrical gold markers (1.2 mm diameter, 3 mm length) is required to robustly auto-detect their positions in 2D projection images. Left: DRR, marker model, ventral kV and dorsal MV images - rotations! Right: Marker kernel convolution: Minimizing a cost function taking into account neighborhood constellations improves reliability and accuracy of auto-registration.

Results

Since 9/2009 we have treated >100 patients in this adaptive protocol (ongoing). 1013 fractions (9117 kV and MV images) of first 39 patients were analyzed and are presented here. In 7/1013 fractions, movements exceeded pre-defined limits (>30°/>2.0 cm). 833/1013 fractions showed marker migrations ≤2 mm; rigid transformations were analyzed from these fractions: Absolute daily L-R rotations were found to be 5.3°±4.9° (max. 30.7°) (numbers represent mean of means ± standard deviation of means per patient – the mean value over the whole population was 0°). 3D vector translations $\sqrt{(\Delta x^2+\Delta y^2+\Delta z^2)}$ of gold markers relative to skin tatoos were 9.3±4.4 mm (max. 23.6 mm). Intra-fractional movements in 7.7±1.5 minutes (max. 15.1 min) between first pre-treatment radiograph and last beam's EPI showed further L-R rotations of 2.5°±2.3° (max. 26.9°) and 3D vector translations of 3.0±3.7 mm (max. 10.2 mm) (Fig. 3). From analysis of 5831 MV portal images we conclude, that addressing intra-fractional errors by just-in-time adaptation of leaf positions for a following beam, based on recent kV and MV images captured on-the-fly, could further reduce margins down to 3 mm for the prostate (95% probability of 95% isodose coverage of the CTV); seminal vesicles to be discussed separately because of their non-rigid movements / shape changes.

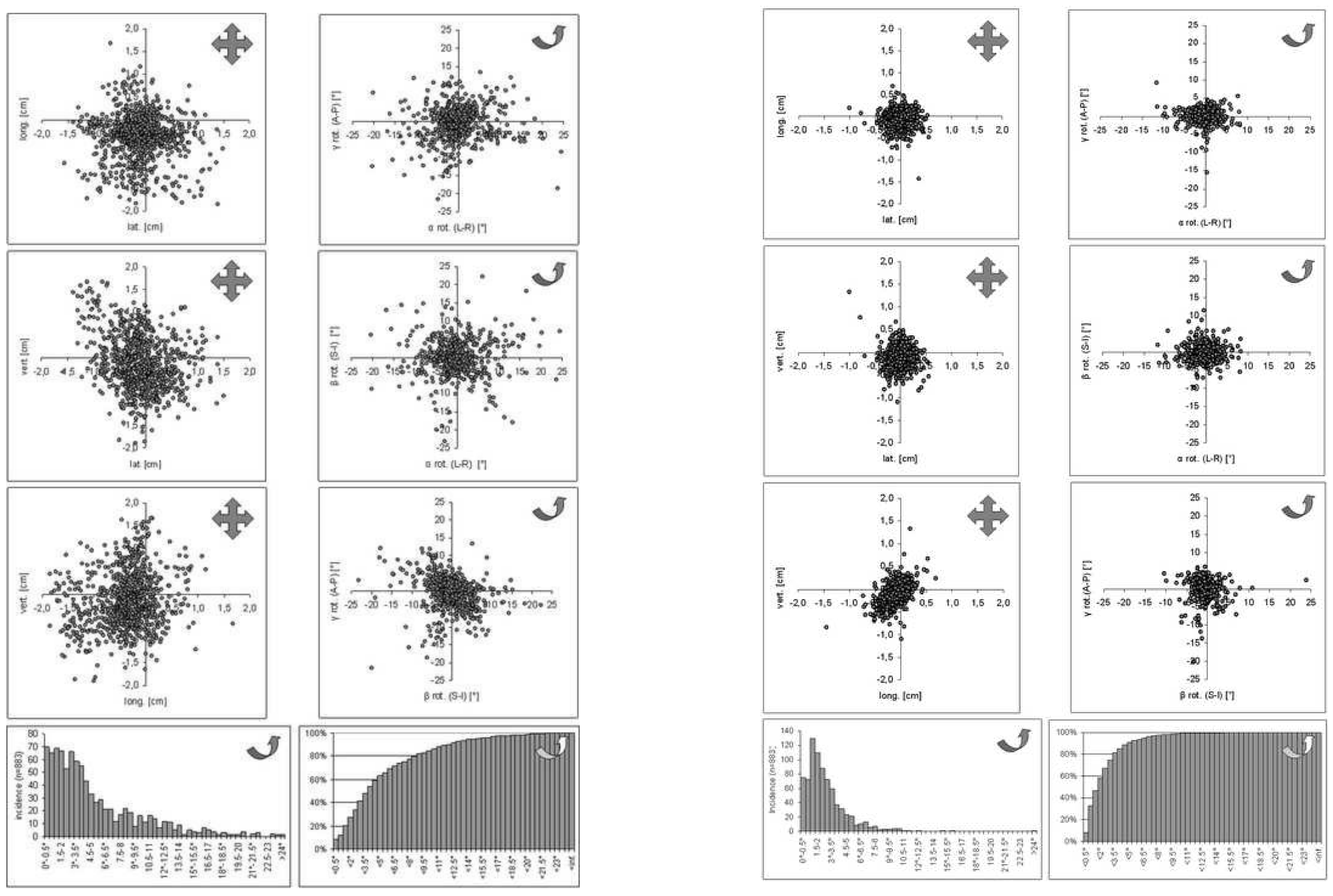

Figure 3: Left: Inter-fractional movements of prostate relative to skin markings. Translations, rotations, distribution of absolute rotational angles and cumulative histogram for rotational errors. Right: Intra-fractional movements within 7.7±1.5 minutes treatment time between 1st kV image and last beam off (7 field step and shoot IMRT).

There is a chance of 10% to see a >12° rotation of the prostate in the planning CT/MR, 5% for >15°. We assessed the influence of rotations on the overall PTV volume: For the average CTV of 80 ml, a composite margin M=T+R can be applied, where T covers potential translational errors and R reflects a margin component accounting for possible eccentric rotations of a non-spherical organ expressed as an additional shift. We derived R and T to ensure a 95% probability of 95% isodose coverage of the CTV. The volume of the resultant average PTV is 375 ml (T=10 mm, R=8 mm equivalent to 15° L-R rotation, 4.7 CTV) for the case of no IGRT. Inter-fractional IGRT focusing on the organ with daily x/y/z correction by means of couch translations can reduce the PTV volume to 258 ml (T=5 mm, R=8 mm, 3.2 CTV). However, if rotations are corrected, the PTV shrinks to 135 ml (T=5 mm, R≈0, 1.7 CTV). Intra-fractionally corrected, the PTV minimizes to 112 ml (T=3 mm, R=0, 1.4 CTV) (Fig. 4).

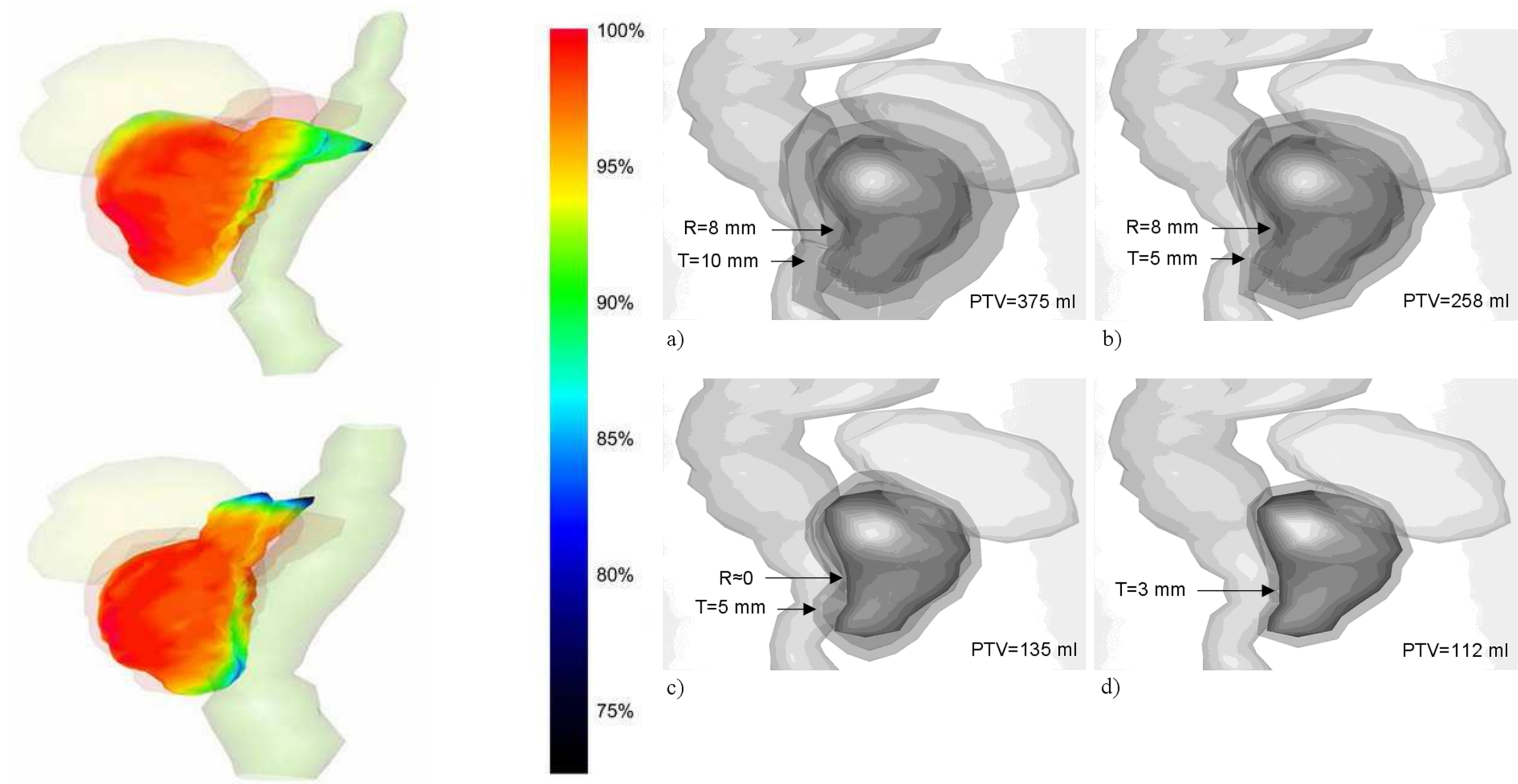

Figure 4: Left: Simulation of a ±15° L-R rotation of a prostate. Center of rotation is the center of gravity of 4 gold markers, translations were corrected to that point: Distal apex and (rigidly transformed) seminal vesicles would receive only 80% of prescribed dose if 6 mm margins CTV-PTV were applied. Right: Reduction of PTV volumes in different treatment protocols (CTV 80 ml): a) no IGRT 375 ml, b) inter-fractional correction of translations 258 ml, c) inter-fractional correction of translations and rotations 135 ml, d) intra-fractional correction in 6 DOF 112 ml (CTV 80 ml).

Conclusion

Having successfully integrated real-time imaging, real-time treatment plan adaptation and treatment delivery in one clinically released application, we are happy to announce that interested researchers and clinical investigators can download our software from ftp://192.168.141.15/radART/openSource for free (please contact the authors for access, www.open-radART.org). Further developments and contributions from other research institutions welcome! (The in-house development of the software *open-radART* is CE-certified, conform with the regulations of the European standard EN/ISO 13485:2003 + AC 2007, CE 0408. As a record and verify system, it is classified as a medical device class IIb and can be used clinically elsewhere.)

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