Accuracy of Post-brachytherapy Dosimetric Data Derived from Computed Tomography (CT) versus Prostate Magnetic Resonance Imaging (MRI)

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Purpose

Transperineal permanent prostate brachytherapy is one of the definitive treatment options for localized prostate cancer\(^1\,\)\(^{-2}\). Postimplantation dosimetry calculations are a crucial component for treatment as it enables assessment of the delivered dose to the prostate and peri-prostatic structures, assesses the quality of the prostate implants, and gives feedback to the radiation oncologist regarding quality of the implantation technique\(^1\,\)\(^{-3}\).

Conventionally, postbrachytherapy data was performed using CT imaging largely because of its widespread availability, low cost, and convenience\(^1\). Soft-tissue structures including the prostate gland and peri-prostatic structures are contoured on sequential transaxial images\(^1\,\)\(^{-2}\). Dose-volume histograms (DVHs) are subsequently generated with visual representations of the isodose contours. Dosimetry measures are typically expressed as the parameter D90, defined as the minimum dose covering 90% of the prostate volume. The D90 value has been described as one of the most important predictive parameters for biochemical control in prostate cancer which may not be apparent for years after brachytherapy, unlike surgical treatment\(^1,\)\(^4\). Therefore, early assessment and analysis of postbrachytherapy implant quality and dosimetry is vital to physicians. Potential areas of underdosing may be addressed with further implantation as appropriate\(^1,\)\(^5\,\)\(^{-7}\).

There are many well-known challenges to defining the contours of the prostate and peri-prostatic structures on CT images given the poor tissue contrast\(^1,\)\(^4\,\)\(^{-8}\). Prior studies have demonstrated increased interobserver variations and associated variations in dosimetry results with increased dosimetric data derived from CT images\(^4,\)\(^9\,\)\(^{-14}\). Postbrachytherapy estimates for prostate dosimetry are traditionally derived from CT, however, multiple prior studies have demonstrated superior delineation of clinically relevant prostatic and peri-prostatic soft tissue structures on MRI compared to CT\(^4\,\)\(^{-8}\). T2-weighted MRI offers superior organ and tissue definition compared to CT. Prior studies have demonstrated that contouring the prostate on a T2-weighted MR image has greater reproducibility compared to contouring by CT imaging\(^8,\)\(^14\). Additionally, prior studies have demonstrated that the prostate volume on T2-weighted MRI more closely approximates the volume assessed by transrectal ultrasound and volume assessed at surgical resection\(^15\,\)\(^{-18}\). Treatment regimens derived from MRI based dosimetry data may reduce the complication probability to other organs including the rectum, penile bulb, and neurovascular bundles\(^15\).
The purpose of this study was to evaluate prostatic and periprostatic dosimetry data from postbrachytherapy CT compared to MRI. We hypothesized that MRI will enable more accurate dosimetry data based on its superior ability to discriminate prostatic margins and peri-prostatic structures compared to CT. To our knowledge there have been no prior studies simultaneously comparing postbrachytherapy dosimetry data derived from CT and MRI for the prostate, urethra, penile bulb, anterior rectal wall, and bilateral neurovascular bundles.
Methods and Materials

Patients:

Between June 2002 and April 2003, 15 patients were being treated for prostate cancer with brachytherapy who met the institutional inclusion criteria for prostate brachytherapy: (1) Stage ≤ T2; (2) positive findings in < 50% of biopsy cores; (3) prostate-specific antigen < 10 ng/ml; (4) Gleason-Score < 7; and (5) prostate gland volume < 50 cc. All patients were treated with palladium-103 implants (InterSource\textsuperscript{103}, IBT InterSource, Mallinckrodt Medical B.V., Petten, The Netherlands).

Exclusion criteria for this study included the following: general contraindications for MRI (e.g. pacemaker, orbital shrapnel) and disorders interfering with an endorectal coil examination (e.g., diagnosed proctitis, extreme hemorrhoids, and active inflammatory bowel disease with rectal involvement).

Of the 15 patients, 11 patients were eligible to participate in this study under an Institutional Review Board approved protocol, after informed consent was obtained. The 11 enrolled patients received postplanning CT evaluations (the standard of care) at 3-5 weeks following seed placement. A post-treatment MRI was also obtained at 3-5 weeks post-treatment. The CT and MRI were performed within 10 days of one another (mean interval between CT and MRI, 2 days; range, 9 days). All enrolled patients completed the study.

MR imaging preparations:

The patients had undergone rectal enema (Relaxyl Clyster, Nycomed-Amersham, Linz, Austria) 1 to 3 hours before MRI examinations were performed. Local anesthesia of the anal region with topical lidocaine gel application was performed just before the MRI examinations (Xylocain 2% Gel, Astra Zeneca, Wedel, Germany). To reduce bowel peristalsis, 0.5 mg Glucagon (Glucagen, Novo Nordisc, Bagsvaerd, Denmark) was administered i.v. just before the MRI examinations and 0.5 mg during the examinations (added to saline syringe of the automated injection system). MR imaging protocol All of the examinations were performed on a 1.5T scanner with a pelvic phased-array surface coil (Magnetom Vision, Siemens, Erlangen, Germany) combined with a disposable endorectal prostate coil (MRinnervu, Medrad, Pittsburgh, PA). The endorectal coil was connected to the pelvic phased-array surface coil, and combined images were obtained. All images were analytically corrected for the reception profile of the endorectal and pelvic phased-array coils. Sagittal and transverse half-Fourier single-shot turbo spin-echo sequences were first obtained to check the coil position. Highresolution T1- and T2-weighted images were then obtained in the transverse plane with a 16-cm field of
view (FOV), a matrix with 256 frequency-encoding steps, and 192 phase-encoding steps yielding in-plane spatial resolution of 0.63 x 0.93 mm, phase direction right-left, 100% phase over sampling. The T2-weighted sequence was a dual echo turbo spin-echo sequence that was acquired from below the apex of the prostate to above the seminal vesicles with the following parameters: repetition time msec/first effective echo time msec/second effective echo time msec = 4000/83/165, echo train length of 8.3, slice thickness (ST) 3 mm, no intersection gap, 28 slices, three signals averaged (acquisition time: 10 min 48 s). The T1-weighted images were acquired before and after contrast media administration. Contrast-enhanced (CE) MR imaging was performed after the bolus injection of contrast media using a fast 3D gradient echo sequence with a temporal resolution of 1 min 35 s. The imaging parameters included the following: repetition time msec/echo time msec of 8.1/4; flip angle of 18 degrees; FOV 160 cm; matrix of 256 x 192; and ST 3 mm, with no gap. Two precontrast and five postcontrast acquisitions were obtained in succession with no delay between acquisitions. Gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) was injected as a bolus at a dose of 0.1 mmol per kilogram of body weight by an automated injection system (Spectris MR Injection System, Medrad, Pittsburgh, PA) at a rate of 4 mL/s during the last seconds of the second precontrast acquisition. This standardized time protocol assured that the injection of the contrast media was completed exactly before the first postcontrast acquisition started. For this study, the last time point data set was used to determine the number and locations of brachytherapy seeds. All examinations were supervised by one of two investigators, thereby ensuring consistency of the imaging protocol.

**CT protocol:**

Non-contrast-enhanced CT was performed with transverse section of 5-mm thickness with a pitch factor of 1.5 on a single-row spiral CT scanner (Somatom Emotion, Siemens, Erlangen, Germany), according to the routine clinical protocol of our institution. Because we intended to compare the routine "standard of care" CT protocol with the HR-CERMRI, we did not match the slice thickness; postimplantation dosimetric studies are routinely performed with 5-mm CT images.

**MR and CT Dosimetric Analysis:**

The Software used in this study for prostate and per-prostatic tissue contouring was performed with MIM Symphony: LDR Brachytherapy Treatment Planning software which is a downloadable medical image computing platform for brachytherapy treatment planning (MIM Symphony, available: http://www.mimsoftware.com/markets/symphony/, accessed: 2007 Nov 13). Transaxial CT and MR images were transferred to 3D Slicer and each reader outlined the contours of the prostate gland, penile bulb, rectum, urethra, and bilateral neurovascular bundles for all 11 patients (Figures 1 & 2). The readers were comprised of a radiology attending and a radiation oncologist trained by a radiologist for prostate contours. To prevent MR information from influencing the CT analyses, the CT
and MRI images from all 11 patients were randomized so that the readers were blinded to the patient data. Subsequently, from these independent CT and MRI contours, dosimetry data was reported in terms of the following parameters: D90, D100, V100, V120, and V150. D90 is defined as the minimum dose covering 90% of the prostate volume and D100 is defined as the minimum dose covering 100% of the prostate volume. V100, V120, and V250 are defined as the percentage volume of the prostate receiving at least 100%, 120%, and 150% of the prescribed minimal peripheral dose (mPD), respectively. These parameters were calculated for the prostate, urethra, penile bulb, anterior rectum wall, and left and right neurovascular bundles.

**Statistical Analysis:**

Statistical analysis were performed assessing differences in the dosimetric data derived from CT versus MRI based prostate and the additional peri-prostatic clinically relevant structures using a Pearson's correlation, and mixed t-test. P values less than 0.05 were determined to be statistically significant.
**Fig. 1**: Axial, sagittal and coronal CT images showing CT contours for dosimetric calculations. Blue = prostate, yellow circle within the blue contour = urethra, orange = right neurovascular bundle, yellow = left neurovascular bundle, green = rectum, light purple = seminal vesicles.

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**Fig. 2**: Axial, sagittal, and coronal MR images showing MRI contours for dosimetric calculations. Blue = prostate, yellow circle within the blue contour = urethra, orange = right neurovascular bundle, yellow = left neurovascular bundle, green = rectum.

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Results

Prostate Doses:

Figure 3 gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the prostate gland determined by CT-derived prostate contours compared to MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 98.5% (1.54) compared to 96.2% (3.64) for MRI contours (p = 0.003). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the prostate between CT derived contours at 96.75% (2.7) compared to 93.7% (4.8) on MRI (p = 0.002). The mean V150 and standard deviation derived from CT and MR contours for the prostate gland demonstrated statistically significant differences at 92.6% (4.6) on CT compared to 88.7% (6.6) on MRI (p = 0.002). Additionally, strong statistically significant differences were noted between D90 and D100 values for the prostate gland derived from CT versus MRI contours. The mean D90 and standard deviation for the prostate gland 167.6% (27.7) on CT compared to 150.3% (35.5) on MRI (p = 0.012) whereas the mean D100 and standard deviation was 72.05% (18.3) on CT compared to 53.8% (20.2) on MRI (p = 0.006).

Urethra Doses:

Figure 4 gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the urethra determined by CT-derived prostate contours compared to MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 81% (6.55) compared to 88.7% (7.84) for MRI contours (p = 0.027). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the urethra between CT derived contours at 74.42% (7.7) compared to 84% (9.06) on MRI (p = 0.012). The mean V150 and standard deviation derived from CT and MR contours for the urethra demonstrated statistically significant differences at 65.6% (10.3) on CT compared to to 76.4% (11.1) on MRI (p = 0.008). Additionally, strong statistically significant differences were noted between D90 and D100 values for the urethra derived from CT versus MRI contours. The mean D90 and standard deviation for the urethra was 81.6% (19.3) on CT compared to 109.4% (31.5) on MRI (p = 0.04), whereas the mean D100 and standard deviation was 48.6% (15.7) on CT compared to 65.6% (19.3) on MRI (p = 0.031).

Penile Bulb Doses:

Figure 5 gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the penile bulb as determined by CT-derived prostate contours compared to
MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 0.09% (0.3) compared to 11.36% (17.22) for MRI contours (p = 0.005). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the penile bulb between CT derived contours at 0.06% (0.21) compared to 7.17% (12.1) on MRI (p = 0.017). The mean V150 and standard deviation derived from CT and MR contours demonstrated statistically significant differences at 0.09% (0.09) on CT compared to 5.2% (3.2) on MRI (p = 0.005). No statistically significant difference was noted between D90 and D100 values for the penile bulb derived from CT versus MRI contours. The mean D90 and standard deviation for the penile bulb was 11.2% (4.9) on CT compared to 12.4% (9.2) on MRI (p = 0.554). A statistically significant difference was noted between the mean D100 and standard deviation was 4.9% (3.14) on CT compared to 2.56% (2.6) on MRI (p = 0.03).

**Anterior Rectal Wall Doses:**

Figure 6 gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the anterior rectal wall as determined by CT-derived prostate contours compared to MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 8.9% (5.78) compared to 2.8% (1.71) for MRI contours (p < 0.0001). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the anterior rectal wall between CT derived contours at 6.5% (4.7) compared to 1.65% (1.21) for MR (p < 0.0001). The mean V150 and standard deviation values derived from CT and MR contours of the anterior rectal wall demonstrated statistically significant differences at 4.1% (3.5) for CT compared to 0.68% (0.68) for MR (p =0.0002). Statistically significant differences were noted between D90 values for the anterior rectal wall derived from CT versus MRI contours with the mean D90 and standard deviation for the anterior rectal wall was 2.5% (3.44) for CT compared to 0.12% (0.05) for MR (p < 0.003). There was no statistically significant difference between the mean D100 and standard deviation was 0.21% (0.28) for CT compared to 0.1% (0.0) for MR (p = 0.099).

**Left Neurovascular Bundle Doses:**

Figure 7 gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the left neurovascular bundle as determined by CT-derived prostate contours compared to MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 77.9% (21.9) compared to 51.5.8% (17.9) for MRI contours (p = 0.002). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the left neurovascular bundle between CT derived contours at 66.7% (25.7) compared to 37.9% (17.88) on MR (p = 0.002). The mean V150 and
standard deviation derived from CT and MR contours of the left neurovascular bundle demonstrated statistically significant differences at 49.9% (27.5) on CT compared to 23.8% (17.2) on MR (p = 0.006). Additionally, strong statistically significant differences were noted between D90 and D100 values for the prostate gland derived from CT versus MRI contours. The mean D90 and standard deviation for the prostate gland 167.6% (27.7) was 98.2% (33.9) on CT compared to 58.6% (12.9) on MR (p = 0.001), whereas the mean D100 and standard deviation was 64.7% (24.6%) on CT compared to 35.5% (9.8) on MR (p = 0.002).

**Right Neurovascular Bundle Doses:**

*Figure 8* gives the mean, minimum, and maximum D90, D100, V100, V120, and V150 doses for the right neurovascular bundle as determined by CT-derived prostate contours compared to MRI-derived prostate contours. There was a statistically significant difference between the mean V100 value and standard deviation derived from CT contours was 69.2% (17.9) compared to 43.1% (22.2) for MRI contours (p = 0.001). Strong, statistically significant differences were observed between the mean V120 value and standard deviation for the right neurovascular bundle between CT derived contours at 54.3% (22.4) compared to 29.4% (19.8) on MR (p = 0.001). The mean V150 and standard deviation derived from CT and MR contours of the right neurovascular bundle demonstrated statistically significant differences at 35.3% (25.9) on CT compared to 16.2% (14.3) on MR (p = 0.005). Additionally, strong statistically significant differences were noted between D90 and D100 values for the prostate gland derived from CT versus MRI contours. The mean D90 and standard deviation for the prostate gland 167.6% (27.7) was 87.5% (32.5) on CT compared to 55.5% (20.3) on MR (p = 0.001), whereas the mean D100 and standard deviation was 60.6% (25.7) on CT compared to 34.5% (15.1) on MR (p = 0.001).

The level of statistical significance between CT and MRI-derived contours for V100, V120, and V150 data increases for assessment of the prostate and anterior rectal wall contours. This observed phenomena is likely secondary to the improved structure delineation on MR images with its superior tissue contrast compared to CT imaging where structural outlines between the prostate and anterior rectal wall cannot be delineated. These findings are detailed in *Figure 9.*
Fig. 3: Prostate Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the whole prostate gland for CT and MRI-derived contours. Note that the mean CT contours are larger than the mean MRI contours and the D90 and D100 values are greater for CT-derived contours.

Fig. 4: Urethra Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the urethra based on CT and MRI-derived contours. Note that the mean MRI contours are larger than CT-derived contours. An associated increase in the D90 and D100 values are noted for the MRI-derived contours.
**Fig. 5:** Penile Bulb Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the penile bulb based on CT and MRI-derived contours. Note that the mean MRI contours are larger than MRI-derived contours. The small values for the CT contoured derived V100, V120, and V150 values are very small secondary to reader inability to visualize and delineate this structure on CT images.

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**Fig. 6:** Anterior Rectal Wall Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the anterior rectal wall based on CT and MRI-derived contours. Note that the mean CT contours are larger than MRI-derived contours. An associated increase in the D90 and D100 values are noted for the CT-derived contours.

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Fig. 7: Left Neurovascular Bundle Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the left neurovascular bundle based on CT and MRI-derived contours. Note that the mean CT contours are larger than MRI-derived contours. An associated increase in the D90 and D100 values are noted for the CT-derived contours.

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Fig. 8: Right Neurovascular Bundle Dosimetric Data Parameters. Mean V100, V120, V150, D90, and D100 values are depicted for the right neurovascular bundle based on CT and MRI-derived contours. Note that the mean CT contours are larger than MRI-derived contours. An associated increase in the D90 and D100 values are noted for the CT-derived contours.

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Fig. 9: Dosimetric Data for Prostate Gland and Clinically Relevant Peri-Prostatic Structures. The mean, minimum, and maximum V100, V120, V150, D90, and D100 values are depicted for the prostate gland in addition to the urethra, anterior rectal wall (rectum), left and right neurovascular bundles (L and R NVB respectively), and penile bulb (PB). The D90 and D100 values were calculated in reference to 110mGy exposures. Levels of statistical significance were measured using both a two-tailed t-test in addition to a Pearson's correlation coefficient. P values < 0.05 were considered statistically significant.

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Conclusion

Topographic knowledge and radiation dosages to the prostate and clinically relevant structures has implications in the diagnosis, prognosis, and treatment of prostate cancer; therefore, accurate contouring for dosimetric assessment is vital to understanding potential complications of dose delivery to these structures. Damage to the penile bulb and adjacent erectile structures has been correlated with erectile dysfunction. Damage to the neurovascular bundles are also correlated with erectile dysfunction after radiation therapy. It has been well documented that the approximation of the rectum and prostate at the prostate apex is very poorly defined on CT imaging. Multiple prior studies cite an overestimation of the prostate volume given impaired delineation from the rectum ultimately leading to increased dose delivery to the rectum and increased potential for post-radiation toxicity. Dose limitation to these clinically and functionally relevant structures is important for reduces overall patient morbidity, ultimately making accurate dosimetric evaluations vital for understanding dose delivery to these structures.

Commonly used cross-sectional imaging with CT has well-described deficiencies, mainly very low soft tissue contrast, for the evaluation of patients after brachytherapy seed placement to determine prostate and peri-prostate structure contours. Despite these known limitations, CT remains the conventional modality for the postbrachytherapy evaluation in most practices.

The findings in this study are congruent and reflective of prior findings in the literature evaluating the dosimetry of the prostate and peri-prostatic structures derived from CT versus MRI imaging. Given the superior soft tissue contrast on MRI localization and contours of these clinically relevant structures is better distinguished on MRI compared to CT imaging (Figure 10). This study demonstrates strong, statistically significant differences in calculated prostate dosimetric data based on CT compared to MRI based contouring of these structures. Dosimetry data including V100, V120, V150, D90, and D100 values are greater for CT-derived calculations of the prostate, rectum, and neurovascular bundles compared to MRI-derived calculations. We believe that these results reflect an over-estimation of prostatic dosimetry due to the impaired delineation of these structures on CT imaging compared to MRI. Additionally, because of the superior tissue contrast afforded by MRI the contours of the urethra and penile bulb were more accurately assessed on MRI compared to CT resulting in the low percentile volumes of the urethra and penile bulb on CT.

Multiple prior studies have compared contoured prostate volume on CT and MRI and found statistically significant differences whereby the CT-delineated prostate volume was 1.3 times larger than the MRI-delineated prostate volume. Specifically, the MRI-
delineated volume was smaller as visibility of the prostate apex was superior on MRI compared to CT and therefore there was improved differentiation of the prostate from the base of the seminal vesicles\textsuperscript{18-19}. Because the MRI-delineated prostate was smaller than the CT-delineated prostate, an associated decrease is noted on MRI-derived dosimetry data delivered to these clinically relevant structures as compared with a treatment plan based on CT\textsuperscript{19-24}. Debois et al. investigated differences in dosimetric data derived from CT and MRI noting that the volume of the rectum receiving 80\% of the prescribed dose was smaller for the treatment plans based on MRI compared to treatment plans based on CT delineation\textsuperscript{22}. Sannazzari et al. investigated differences in dosimetric data derived from CT versus MRI noting that approximately 10\% of the rectal volume could be spared with MRI prostate delineation\textsuperscript{23}. Krempien et al. showed in their report that the mean dose received by the rectum could be reduced from 74.9\% to 64.2\% of the prescribed dose using MRI delineation compared with CT delineation of the prostate\textsuperscript{24}.

Critical functional anatomy has implications in the diagnosis, prognosis, and treatment of prostate cancer; therefore, accurate contouring for dosimetric assessment is vital to understanding potential complications of dose delivered to these clinically relevant peri-prostatic structures\textsuperscript{25}. Damage to the penile bulb, adjacent to erectile structures, has been correlated with erectile dysfunction even though this structure is not directly involved in erectile function. This observed finding has been attributed to its close proximity to the corpus cavernosum and internal pudendal artery\textsuperscript{25-29}. Damage to the neurovascular bundles are also correlated with erectile dysfunction after radiation therapy. It has been well documented that the approximation of the rectum and prostate at the prostate apex is very poorly defined on CT imaging. Multiple prior studies cite an overestimation of the prostate volume given impaired delineation from the rectum ultimately leading to increased dose delivery to the rectum and increased potential for post-radiation toxicity\textsuperscript{26-29}. Dose limitation to these clinically and functionally relevant structures is important as it reduces the overall patient morbidity, making accurate dosimetric evaluations vital for understanding dose delivery to these structures. Ultimately, the improved accuracy of the dosimetric derived from MRI contours may translate to improved clinical outcomes.

In summary, it has been well documented in the literature that MRI enables superior distinction and delineation of prostatic and clinically relevant soft tissue structures due to its improved tissue contrast over conventional CT. These findings were demonstrated in our study. This study ultimately demonstrates proof of concept that MRI is superior to CT for the calculation of postbrachytherapy dosimetry data for the prostate and clinically relevant soft tissue structures.
Fig. 10: Contours of the prostate and clinically relevant structures on CT (left image) and MRI (right image) at similar levels. Orange = prostate, red = right neurovascular bundle, yellow = left neurovascular bundle, green = rectum.

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