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Real-Time Intraoperative CT Assessment of Quality of Permanent Interstitial Seed Implantation for Prostate Cancer

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Abstract

Objectives—Evaluate real-time kilovoltage cone-beam computed tomography (CBCT) during prostate brachytherapy for intraoperative dosimetric assessment and correcting deficient dose regions.

Methods—Twenty patients were evaluated intraoperatively with a mobile CBCT unit immediately after implantation while still anesthetized. The source-detector system is enclosed into a circular CT-like geometry with a bore that accommodates patients in the lithotomy position. After seed deposition, CBCT scans were obtained, Dosimetry was evaluated and compared to standard postimplantation CT-based assessment. In eight patients deposited seeds were localized in the intraoperative CBCT frame of reference and registered to the intraoperative transrectal ultrasound (TRUS) images. With this information, a second intraoperative plan was generated to ascertain if additional seeds were needed to achieve the planned prescription dose. Final dosimetry was compared with postimplantation scan assessment.

Results—Mean differences between dosimetric parameters from the intraoperative CBCT and post-implant CT scans were <0.5% for V100, D90, and V150 target values. Mean percentage differences for average urethral doses were not significantly different. Differences for D5 (maximum dose) of the urethra were <4%. The dose to 2 cc of the rectum differed by 10% on average. After fusion of implanted seed coordinates from the intraoperative CBCT scans onto the intraoperative TRUS images, dosimetric outcomes were similar to postimplantation CT dosimetric results.

Conclusions—Intraoperative CT-based dosimetric evaluation of prostate permanent seed implantation prior to anesthesia reversal is feasible and may avert misadministration of dose

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delivery. Dosimetric measurements based on the intraoperative CBCT scans are dependable and correlate well with postimplant diagnostic CT evaluation.

Keywords

Prostate; brachytherapy; dosimetry; image-guidance

Accuracy of seed placement and the targeting of the appropriate radiation dose to the prostate have been shown to be critical elements for achieving long-term tumor control for prostate-cancer patients treated with brachytherapy.¹⁻² Intra-operative planning for prostate brachytherapy has been associated with more accurate dose delivery to the prostate as well as reduced normal tissue exposure and, as a result, a decreased rate of acute and late toxicities.³⁻⁴ Real-time planning takes into account changes observed during the operative procedure such as prostate edema and distortion of the glandular geometry due to needle placement, factors which cannot be easily accounted for using pre-planned techniques. With the availability of sophisticated algorithms, seed distributions can be optimized within seconds in the operating room to consistently achieve prescription doses to the prostate with concomitant minimization of dose to the rectum and urethra.

While in experienced hands significant under-dosage of the target and over-dosage of normal tissue structures are rarities, there is still room for improvement. For instance, approximately 10% or more of seed-implantation procedures will not achieve simultaneously optimal target coverage (V100 >90%) and urethral dose levels of <150% of the prescription dose.⁵⁻⁹ Less than optimal implants can be related to several factors including error in seed placement, migration of the seed from the needle tip, and difficulty visualizing the deposited seed location on ultrasound (US) images. As the quality of the procedure is evaluated only using postimplantation computed tomography (CT) scans, less than optimal dosimetric outcomes only become apparent to a physician when making amends for a flawed implant requires an additional surgical procedure.

We report on a novel approach using a portable CT-fluoroscopic unit with which we obtain real-time kilovoltage cone-beam CT (KV-CBCT) images in extended lithotomy position for treatment planning. We have used this device to obtain post-implantation scan assessments at the conclusion of the procedure prior to the reversal of anesthesia. We also demonstrate that scans and the deposited seed coordinates can be downloaded back into the treatment-planning system to allow for intra-operative correction of suboptimal regions of dose distribution.

Material and Methods

Twenty consecutive patients with localized prostate cancer treated with interstitial seed implantation were evaluated intra-operatively with a mobile fluoroscopy/CBCT unit (O-Arm™, Medtronic Navigation, Littleton, MA) at the conclusion of the implantation while the patient remained under anesthesia. Routinely, implantation is performed in our institution with intraoperative ultrasound and fluoroscopic x-ray guidance; and informed consent is obtained for the use of intraoperative x-ray imaging and in these patients for the CBCT scanning. The device employs an X-ray source and a Varian flat panel detector for

both stationary fluoroscopy/X-ray and CBCT. The device has been used as a tool for the use of computer-assisted surgical navigation and image guidance and navigation for orthopedic and vascular procedures. With its high fixed signal to noise ratio and relative slow scintillator speeds, the device is well suited for the visualization of heavy hardware such as pedicle screws. For this study, although the soft tissue resolution for delineation of the rectum and prostate is visualized but not optimized, the seeds in their titanium casings are well seen and easily amenable for image fusion. The source-detector system is enclosed into a circular CT-like geometry with a bore large enough (approximately 96 cm) to accommodate the patient in the lithotomy position (Figure 1).

Seed-implantation procedure was conducted as previously described using an intraoperative real-time treatment-planning technique.³ After seeds were deposited within the gland, US images were acquired and the initial CBCT scan was obtained in the lithotomy position, with the US probe still in place. Subsequently, a second CBCT was acquired with the TRUS probe removed, and the legs off the stirrups in the supine position on the operating table. Finally, after the patient returned from the recovery room, a routine diagnostic postimplantation CT scan was obtained approximately 3 hours after the brachytherapy procedure for routine quality assurance and dosimetric analysis. To verify the applicability of these image data sets, our analysis included assessments of dose volume histogram parameters for target coverage (V100, D90, V150) and dose to the urethra and rectum (D30 and Dmax). Dosimetric parameters based upon the CBCT images in the operating room were compared with those obtained with the postimplantation diagnostic CT scans that served for this study as the gold standard.

The central aim of our analysis was to determine the feasibility of fusing the extracted seed coordinate data obtained from the intraoperative CBCT images to the intraoperative transrectal US (TRUS) images. The application of CT and US fusion to combine volumetric data from US and the dosimetric information from CT has been previously suggested.¹⁰ Our aim was to devise a process that would function in a rapid and robust fashion which could be used intraoperatively. To accomplish this, six radio-opaque markers were embedded in the wall of the US probe in a non-coplanar configuration. The latter would allow the marker coordinates to be fixed in the US coordinate system. Thus when identified in CT space, the markers provided the basis for the registration of the two image sets. While in theory, four non-coplanar markers would be sufficient to define the registration, we observed that increasing the number of markers reduced the error associated with digitization of the markers in CT. A software program was written to transform the CT coordinates from CBCT space to US space. The program accepted as input the marker coordinates and seed coordinates as exported from the VariSeed™ (Varian Medical Systems, Charlottesville VA) seed-export function, and outputs the seed coordinates in the corresponding US space. The intra-operative real-time treatment-planning software used at our hospital was modified to accept previously implanted seeds and, if deemed necessary, generate a new treatment plan based on these previously implanted seeds.

CT/US evaluation: US images of the prostate from its base to the apex, and a KV CBCT of the patient in the lithotomy position with the TRUS probe still in place were acquired. KV CBCT images were loaded into VariSeed and US-probe markers and seeds were identified,

digitized, and exported. The CT-based seed coordinates were registered back on to the US images using the program described above, and the prostate and normal tissue contours were redrawn on the TRUS images. The treatment plan was then regenerated to determine areas of suboptimal dosimetry. The average added time in the operating room required for CT image acquisition and estimated time for regeneration for the treatment plan was 15 minutes.

To test whether the operating-room measurements differ from the postimplantation CT measurements taken after the procedure, two-sided Wilcoxon signed-rank tests were used. Three sets of analyses were done. Due to multiple testing, the Bonferroni correction was applied, resulting in the alpha level of $0.05/8 = 0.00675$. Thus differences were considered significant when the p value of the test was smaller than 0.00675.

Results

Table 1 includes a comparison of the dosimetric parameters for achieved target coverage based upon the intraoperative CBCT obtained at the completion of the procedure and the postoperative diagnostic CT scans. There was a remarkable correlation between the dosimetric parameters obtained from these two scans with mean percentage differences of less than 0.5% observed for V100, D90, and V150 values. The mean percentage differences for the average urethral doses were not significantly different between the two sets of scans. The mean percentage differences for the dose to 5% of the urethral volume (D5 used as the surrogate for maximum dose) between the intraoperative and postoperative scans were significant but less than 4%. The differences and greater variability observed for the maximal urethral dose measurements are likely related to several factors, including the small volume of the urethra, inherent inaccuracies in contouring, and the relatively poor resolution of the urethra on CBCT. The dose to 2 cc of the rectum differed between the intraoperative and postoperative scans by an average of 10%, likely explained by the presence of the US probe and differences in leg positioning between the scans.

To demonstrate whether the dosimetric parameters for the target and normal tissue structures were different if obtained in the lithotomy position with the TRUS probe in place and in the flat supine position without the TRUS probe, an additional analysis was performed in six patients. Table 1 demonstrates once again excellent correlation between the lithotomy and supine scans without significant differences observed for the target, urethral, and rectal dosimetric parameters evaluated.

We then determined the feasibility and accuracy of fusing all of the implanted seed coordinates from the intraoperative CBCT scans obtained in the lithotomy position with the intraoperative TRUS images. This exercise was performed in six patients, and once the actual seed coordinates were fused on the intraoperative TRUS images, the treatment plan and dosimetric parameters were regenerated based upon the US frame of reference. The dosimetric outcomes from the intraoperative TRUS images were compared in turn with the postimplantation CT dosimetric results. No significant differences were observed between these evaluations, as demonstrated in Table 1. These data indicate that intraoperative TRUS-generated dosimetric evaluation is an accurate reflection of the standard postimplantation

CT evaluation and can be reliably used for correction of suboptimal regions of implantation prior to reversal of anesthesia.

Comment

These data indicate that accurate intraoperative assessments can be accomplished to confirm the adequacy of dose coverage to the prostate with seed implantation. Using the O-arm device described in this report we demonstrated that intraoperative evaluations derived from the CBCT at the conclusion of the procedure prior to anesthesia reversal yielded similar dosimetric results compared with the routine dosimetric assessment based on the standard postoperative CT scan. Implicitly, we demonstrate the feasibility of extracting the seed coordinate positions from the CBCT with subsequent fusion on to the US frame of reference to allow for potential corrections of suboptimal dosimetry while the patients remains anesthetized. These findings have immediate and far-reaching potential ramifications for reducing the rate of poor-quality implantation outcomes and cases of misadministration of the radiation dose for prostate brachytherapy.

Others have explored intraoperative CB imaging at the end of the implant procedure to compare its accuracy to the postimplantation CT scan or use it as a tool to correct suboptimal areas of dose coverage at the conclusion of an implant. Westendorp and colleagues¹¹ reported on the use of C-arm-based CB imaging during the implantation procedure where seed coordinates were registered to TRUS images and areas of deficient target coverage were mended. That study supports the notion that seed locations obtained from CT datasets can be registered with the TRUS images. Nevertheless, in that report two problems that affected the quality of seed registration (and consequent dosimetry) have remained unaddressed. Firstly, because of the nature of the C-arm configuration, patients could not be imaged in the extended lithotomy position; this makes the C-arm approach less applicable for patients who are routinely implanted in such a position to reduce pubic arch interference issues. In addition, as the CBCT was not performed with the TRUS probe in place, this raises questions about the possible variability related to deformation of the prostate with and without the probe. These limitations also raise uncertainties as to whether the remedial corrections of added seeds to suboptimal dosimetric regions in the prostate would be accurate for correcting or evaluating a seed implant in a patient in the standard lithotomy position. In contrast, the O-arm we used has a bore size of 96 cm and was able to accommodate the patient in the extended lithotomy position to reduce the likelihood of pubic arch interference. In addition all intraoperative CT acquisition and quality assurance dosimetric assessments were compared with the gold standard of assessment (postimplantation CT) to determine the reliability and accuracy of these intraoperative measurements.

In yet another study, Steggerda et al¹⁰ demonstrated the feasibility of fusion of three-dimensional TRUS with standard CT acquired with the TRUS probe in situ. Similarly to the method used in our study, the registration was performed on the US probe with good results. However, the procedure was done for the purpose of postimplant evaluation, and not as an integral part of the implant procedure. While image quality of a standard CT is indisputably better than that of a CBCT, as with the C-arm, most patients cannot be scanned in the

extended lithotomy position using currently available CT scanners. Indeed, the current standard of care is to use a postoperative evaluation of the implant (a quality assurance procedure) to make decisions about the need of further intervention for that particular patient, and as a learning process to help improve future implants. In our study, the hardware used and the software developed were chosen specifically to make the CT/CBCT scans an integral quality-control tool that can be used several times during the implant process. In doing so we argue that not only can coverage of the gland be assured, but also that organs at risk can be potentially more effectively spared.

One of the prominent limitations of current brachytherapy techniques precluding intraoperative quality-assurance assessment is related to the US's relatively poor resolution of individual implanted seed coordinates. This is primarily due to intraoperative prostate edema, hemorrhage secondary to needle placement, and the relatively poor resolution of US images. While commercially available software programs can tag a seed coordinate making the assumption that the seed is deposited at the needle tip, it is not infrequent that the seed can migrate a few millimeters from the tip, the gland often changes shape as the implant progresses, and often not all seeds can be discriminated on the US during the process of implantation within the gland. For adequate quality assurance and, more importantly, correction or "fine tuning" of the implant, it would be imperative to use a system where all seeds can be consistently identified; a system which could only reliably track the coordinates of 90% of the seeds position or less could lead to mistaken assumptions regarding the quality of the procedure. The current approach relies on CT for seed identification, which is considered the standard imaging assessment for this purpose. Using CBCT images we successfully fused the identified seeds on to the intraoperative US images to allow for intraoperative correction of potential dosimetric inadequacies.

There are obvious advantages to accurate intraoperative assessment of implant adequacy compared with standard approaches that rely on postoperative measurements. Not only do such approaches obviate the need for postimplantation CT scan assessments, but more importantly provide an opportunity for corrections or refinements of the implant before the procedure is completed. Equally important is the ability to use a single imaging modality (US) for both planning and dosimetric verification of the implant. We are in the process of applying our CBCT-TRUS fusion technique to a large number of patients to provide opportunities for fine-tuning the implant quality. We are exploring as well the feasibility of multiple intraoperative CBCT assessments as the case progresses to achieve continuous monitoring and optimization of target coverage with concomitant reduction in dose exposures to both the rectum and the urethra.

There are several limitations to this study including its preliminary nature, the relatively small number of patients included and the fact that such an intraoperative assessment necessitate the addition of time in the operating room. In addition we note that there are recognized limitations of the current image quality of the O-arm in terms of soft-tissue resolution, which does not provide optimal discrimination of the anatomic interfaces such as the prostate and rectum as can be seen with diagnostic quality CT scans. Nevertheless we expect with software and hardware enhancements that this will improve with time. In

addition we are currently using CT-compatible table and stirrups to minimize artifact, which has also enhanced image quality.

Conclusions

The data presented in this report demonstrate that intraoperative CT-based dosimetric evaluation of prostate permanent seed implantation prior to anesthesia reversal is feasible. Dosimetric measurements of the prostate based on the intraoperative CBCT scans correlated well with measurements taken from the standard postimplant diagnostic CT evaluation. With ability to evaluate the adequacy of the implant procedure prior to reversal of anesthesia, correction of suboptimal regions of dose coverage can be performed. We also argue that, with multiple CBCT assessments made during the case, the intraoperative plan can be regenerated to modify the seed-loading plan to further restrict dose to the urethra and rectum based upon the coordinates of the deposited seeds on an ongoing real-time basis. Based on the feasibility of this approach we believe that such intraoperative assessments may be helpful in clinical practice for evaluating the quality of prostate implantation providing an opportunity for correction of the suboptimal dose coverage in regions of the prostate before the completion of the brachytherapy procedure.

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Figure 1. Patient with implanted needles in the extended lithotomy position with the CBCT imager in place.

Figure 2.
Axial CBCT image obtained during the implantation procedure with seeds in place.

Table 1
Dosimetric Outcomes and Differences Based on Assessments from Various Intraoperative Imaging Modalities

Prostate										Urethra						Rectum			
Volume (cc)		V100 % (%)		D90% (%)		V150% (%)		D5% (%)		Dave (%)		D2cc (%)		V100% (cc)					
Mean	%	Mean	%	Mean	%	Mean	%	Mean	%	Mean	%	Mean	%	Mean	%				
O-Arm Supine vs Postimplantation CT (n=20) ^a																			
Differences	-1.68	-3.1%	0.48	0.5%	0.29	0.5%	-0.20	0.1%	-6.04	-4.0%	3.54	3.9%	-10.52	-11.9%	-0.12	-0.49 ~ 0.19			
Standard error	0.73	1.8%	0.42	0.4%	1.38	1.1%	0.87	1.3%	1.96	1.3%	2.31	2.2%	4.63	7.3%	0.04	NA			
P value	0.036		0.277		0.388		0.825		0.004		0.114		0.027		0.016				
O-Arm Supine vs O-Arm Lithotomy (n=6) ^b																			
Differences	0.22	-0.6%	-0.40	-0.4%	-1.30	%	-1.04	%	-1.5	-1.3%	-0.7	-0.5%	-46.0	-25.0%	-0.1	NA			
Standard error	1.57	3.7%	0.76	0.8%	1.59	1.4%	0.71	1.1%	3.0	2.3%	5.7	5.7%	NA	NA	NA	NA			
P Value	0.844		1.000		NA		NA		0.844		1.000		NA		NA				
End of Case TRUS vs Postimplantation CT (n=8) ^c																			
Differences	-1.51	-0.1%	1.32	1.4%	4.02	3.8%	0.94	1.6%	2.34	1.7%	17.97	18.0%	0.92	-10.5%	-0.10	-0.5 ~ 0.19			
Standard error	2.80	6.9%	0.83	0.9%	3.98	3.7%	2.24	3.4%	2.31	1.7%	6.04	6.4%	4.26	14.3%	0.09	NA			
P value	0.742		0.250		0.547		1.000		0.742		0.023		1.000		0.402				

^a For rectum fields there are only 18 patients' data.

^b For rectum fields there is only 1 patient's data.

^c Since there is only 1 patient with rectum O-arm lithotomy data, the range is not applicable here (the rectum V100% difference for this patient is -0.25).

^c For rectum fields there are only 7 patients' data.