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Abstract. Brachytherapy, a type of radiotherapy, may be used to place radioactive sources into or in close proximity to tumors, providing a method for conformally escalating dose in the tumor and the local area surrounding the malignancy. High-dose-rate interstitial brachytherapy of vaginal tumors requires precise placement of multiple needles through holes in a plastic perineal template to deliver treatment while optimizing dose and avoiding overexposure of nearby organs at risk (OARs). Despite the importance of needle placement, image guidance for adaptive, intraoperative needle visualization, allowing misdirected needles to be identified and corrected during insertion, is not standard practice. We have developed a 360-deg three-dimensional (3-D) transvaginal ultrasound (TVUS) system using a conventional probe with a template-compatible custom sonolucent vaginal cylinder and propose its use for intraoperative needle guidance during interstitial gynecologic brachytherapy. We describe the 3-D TVUS mechanism and geometric validation, present mock phantom procedure results, and report on needle localization accuracy in patients. For the six patients imaged, landmark anatomical features and all needles were clearly visible. The implementation of 360-deg 3-D TVUS through a sonolucent vaginal cylinder provides a technique for visualizing needles and OARs intraoperatively during interstitial gynecologic brachytherapy, enabling implants to be assessed and providing the potential for image guidance.

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1 Introduction

Vaginal tumors represent a major surgical challenge, and aggressive radiation is favored to prevent more morbid surgery. Standard-of-care treatment commonly includes external beam radiation followed by brachytherapy, a method of radiotherapy that brings radiation sources into or in close proximity to tumors, conformally irradiating the tumor and the surrounding local tissues.^{1,2} This approach allows the dose delivered to the tumor to be escalated in comparison to the nearby healthy tissues.² Brachytherapy for vaginal tumors may be delivered through a high-dose-rate (HDR) transperineal interstitial approach in which hollow needles are inserted directly into the tumor and the surrounding area. Subsequently, a single high-activity radiation source, typically Iridium-192, is temporarily placed at planned positions via these needles with planned dwell times at each position to deliver the dose.² HDR transperineal interstitial brachytherapy requires precise needle placement to optimize dose distributions, achieve local control, and avoid overexposure of nearby organs at risk (OARs), including bladder and rectum.¹ Typically, an ideal implant has needles distributed in 10-mm increments throughout the target region;

however, due to the radiative effects from multiple needles, a clinically acceptable implant may be achieved with 10 ± 5 mm spacing between adjacent needles.^{3–6} Despite the need for precise placement to optimize the implant, currently there is no standard image guidance approach for adaptive, intraoperative needle visualization during interstitial gynecologic brachytherapy of vaginal tumors. Current proposed methods of intraoperative visualization suffer from limitations, including restricted fields of view, operator dependence associated with two-dimensional (2-D) imaging, and limited accessibility of three-dimensional (3-D) systems. This lack of image guidance causes clinicians to rely on clinical examination, experience, and preoperative images.¹ The implementation of an image guidance system may allow misdirected needles to be identified and corrected immediately, whereas misplaced needles discovered in postinsertion imaging may not be usable for treatment.^{1,2}

During the procedure, the patient's legs are raised in stirrups and a plastic plate (template) with needle holes is sutured between their legs onto the perineum to secure the needles and aid needle distribution. Commonly, a Syed–Neblett⁴ or a Martinez Universal Perineal Interstitial Template (MUPIT),⁵ shown in Fig. 1(a), is used.⁶ These templates consist of either concentric

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Fig. 1 (a) Drawing of the stepper with placement of perineal needle template, vaginal cylinder, and example needles shown and (b) a broader view of the system design, including stabilizer, stepper, and US probe relative to the end of the patient bed.

circles or a linear grid of needle holes surrounding a larger central hole, which allows a cylinder to be inserted vaginally, providing stability and separating the vaginal walls.^{7,8} During procedures at our center, typically about 14 needles are manually placed by the radiation oncologist using a MUPIT-style template (Varian Medical Systems Inc., Palo Alto, California), such that the needles are approximately parallel to the vaginal cylinder, to create the implant; however, due to the variability in presentation and challenging anatomical locations of gynecologic malignancies, the distribution, depth, and number of needles used varies greatly. Source positions beyond the target region are necessary to achieve acceptable dose coverage. This may cause the needles to impinge on OARs, potentially leading to major side effects or undesired toxicities.² Postinsertion imaging is typically performed using x-ray computed tomography (CT) to verify needle positions prior to the radiation source being placed at planned positions using an afterloader,⁹ but the lack of intraoperative needle visualization can contribute to inaccurate needle placement, leading to a suboptimal implant and treatment.^{10,11}

Intraoperative guidance using laparoscopy or laparotomy,^{12–14} fluoroscopy,¹⁵ ultrasound (US),^{16–20} electromagnetic (EM) tracking,²¹ CT,²² and magnetic resonance (MR)^{23–25} approaches have been previously proposed. Fluoroscopy, laparoscopy, and laparotomy are not commonly used as they provide limited visibility of the structures of interest and the surgical approaches are associated with an increased risk of complications.^{15,16,26} A 2-D transabdominal US approach may be used to visualize anterior needles and facilitate avoidance of the bladder,¹⁹ but the pubic symphysis impedes the visualization of needles near

the vagina. Alternatively, the 2-D nature of the transrectal ultrasound (TRUS) approach proposed by Stock et al.¹⁶ causes clinicians to mentally collate images to create an impression in 3-D space, which can be an inefficient and difficult process.²⁷ The use of 3-D image guidance may mitigate the operator dependence associated with 2-D US. Further, a more comprehensive view of needle, target, and OAR positions intraoperatively may allow for fewer needles to be inserted to achieve dose coverage.^{1,2} One approach to 3-D guidance is the use of EM tracking; however, this approach may be susceptible to inaccuracies in clinical environments,²⁸ and to date, this approach has been limited to phantom studies.²¹ Lee et al.²² and Kapur et al.²⁴ have proposed 3-D image guidance using an iterative approach with CT and 3T MR imaging, respectively, to verify needle positions. Viswanathan et al.²³ have also proposed MR 3-D image guidance for needle insertion using specialized interventional 0.5T MR imaging. These techniques are limited by the additional length of the procedure under anesthesia and the necessity for specialized equipment and costly intervention suites, which restricts accessibility to only a few institutions worldwide.²

Transvaginal ultrasound (TVUS) is occasionally used during interstitial gynecologic brachytherapy to visualize anterior needles prior to the insertion of the vaginal cylinder.²⁹ A 360-deg 3-D image is necessary to visualize all needles transvaginally in one acquisition. A method for 360-deg 3-D US imaging has been investigated for pelvic floor examination and for anorectal ultrasonography, using a specialized transducer.^{30–32} Petric et al.³³ proposed the use of a rotating transcervical US transducer prior to cervical brachytherapy, generating a 2-D 360-deg image to visualize the tumor and assist in implant guidance and investigated its use in a single-patient feasibility study. Although this technique shows the potential to assist in gynecologic brachytherapy procedures, further investigation would be required to determine its potential role in interstitial implants and this method has not been used to visualize interstitial needles. We have previously proposed the use of a 3-D TRUS system for intraoperative verification of needle placement.²⁰ Although this system may be suitable for some patient cases, 6 of the 73 needles imaged were not visible due to a shadowing artifact caused by the vaginal cylinder.²⁰ The use of TVUS would eliminate this shadowing artifact, bring the US probe in closer proximity to needles, and allow needles to be imaged parallel to the US probe, potentially improving the clarity of visualization.

We have developed a 360-deg 3-D side-fire TVUS system and propose its use for intraoperative needle guidance during HDR transperineal interstitial gynecologic brachytherapy of vaginal tumors. The preliminary development and validation of this system have been presented by Rodgers et al.,³⁴ and the initial results from a mock phantom procedure, preliminary qualitative findings from the first patient scan, and initial needle localization results from three patients are described in Rodgers et al.³⁵ The objective of this study was to extend the preliminary work with a more detailed description of the 360-deg 3-D side-fire TVUS acquisition system, more extensive validation of the system and technique, and evaluation of its potential use for intraoperative visualization and localization of interstitial needles by increasing the number of patients from the previous preliminary report. In this paper, we describe the details of the mechanism and validation of the geometric accuracy of the 3-D image, present the results of the mock phantom procedure in further detail, and report on needle localization accuracy during

a patient study, involving six patients imaged intraoperatively using the system.

2 Materials and Methods

2.1 Three-Dimensional Transvaginal Ultrasound System

The 3-D TVUS system uses a conventional 2-D side-fire endocavity US probe, which is placed into a cradle and rotated through 360 deg. The acquired 2-D US images are reconstructed into a 3-D US image following the tilt scanning approach described by Fenster et al.,²⁷ modified for 360-deg rotation. To support the scanning mechanism and allow clinicians to easily position the US probe, we have developed a counterbalancing stabilizer³⁶ and a rotational/translational stepper, as shown in Fig. 1(b). The stabilizer clamps securely to the patient bed and is used for the gross motions, allowing the clinician to position the US probe appropriately and lock it in place with a trigger-activated locking mechanism to minimize motion during scanning. The unique stabilizer design is simpler and more compact than any other available counterbalancing systems^{37–39} and is easily adaptable to many linkage systems. The stepper is used to rotate the US probe cradle to create the 3-D TVUS image and for fine adjustments (Fig. 1).

2.1.1 Stepper and probe cradle

The motorized stepper [Fig. 1(a)] allows precise rotation and 7-cm translation of the cradle along the longitudinal probe axis, using two Faulhaber 1717T012SR DC motors (MicroMo Electronics, Clearwater, Florida) mounted to the base of the stepper and mechanically linked to the cradle via a gear train that decouples the linear and rotational movements. Mechanically decoupling the movements simplifies the closed loop motor control system, as the computer does not have to coordinate both motors simultaneously to create a 3-D image. The translational motion allows the clinician to fine-tune the probe insertion depth to ensure that the features of interest are visualized, while the rotational motion is used to generate the 3-D US image and align the probe to the trajectory associated with the desired template hole for real-time monitoring of needle insertion.

The cradle [Fig. 1(a)] was designed to hold the clinical US probe securely and provide a mechanical link to the stepper. As the body of the probe is not concentric with the axis of rotation, needles in close proximity to the probe have the potential to interfere with the cradle. A bearing mounted on the front end of the cradle provides a frictionless support for needles during probe rotation, mitigating any potential interference between the probe motion and the needles.

2.1.2 Three-dimensional ultrasound image acquisition

To accommodate the US probe transvaginally, a custom sonolucent vaginal cylinder with a hollow core and closed end was created to temporarily replace the clinical vaginal cylinder, providing the same geometry for needle insertion. The hollow sonolucent cylinder was designed with the same outer dimensions as the solid clinical cylinder, making it fully compatible with the central vaginal cylinder hole in the current perineal template [Fig. 1(a)], with a 1.3-mm-thick wall of sonolucent TPX™ polymethylpentene plastic (Mitsui Chemicals America, Inc., Rye Brook, New York) to create a hollow center to accommodate

the US probe. The probe was not fixed within the sonolucent cylinder and the sonolucent cylinder was not coupled to the template, allowing for free rotation. The biocompatibility of the material was verified by Geneva Laboratories (Elkhorn, Wisconsin).

For phantom imaging, a BK Falcon 2101 EXL US system with an 8658 endocavity biplane US probe (BK Medical, Boston, Massachusetts) at 7.5 MHz was used and for patient imaging, a BK Profocus 2202 diagnostic US system with an 8848 endocavity biplane US probe (BK Medical, Boston, Massachusetts) at 9 MHz was used, with image intensities digitized to 0 to 255. This system was selected as it is currently used in the procedure room at our institution; however, the probe cradle for the system can be simply adapted to accommodate other clinical US probes. During image acquisition, the US probe inside the sonolucent cylinder is rotated through 360 deg and 420 2-D US frames at angular intervals of 0.86 deg are obtained via an Epiphan digital VGA2USB video frame grabber (Epiphan Systems, Inc., Ottawa, Ontario, Canada), which connects the video output of the clinical US machine to a desktop computer. These 2-D frames are reconstructed using software developed in our laboratory^{27,40–43} to generate a 3-D 360-deg ring-shaped image [Fig. 2(a)] with $488 \times 1034 \times 1034$ voxels and a voxel size of $0.126 \times 0.126 \times 0.126$ mm³. The acquired 2-D US frames are placed into their proper location in the 3-D TVUS image as they are acquired with the final 3-D image available immediately after the 360-deg sweep is completed. The original 2-D frames are also stored, allowing clinicians to view these alongside the patient's 3-D TVUS image, with the position of the 2-D frame indicated (Fig. 2), facilitating assessment of the needle positions relative to each other and the OARs. The needles appear distinctly in both the 2-D and 3-D images, as they are imaged approximately parallel to the US probe, easing interpretation of the images by the clinicians. A complete scan takes 20 s to acquire; however, the system includes an option for the operator to pause and resume the scan as desired. This can also be used to image an angular subvolume of the 360-deg ring to examine or update particular needles or features.

2.2 Geometric Reconstruction Validation

The calibration of the 3-D TVUS image reconstruction was verified by making linear measurements in each of the image coordinate directions using a 3-D grid phantom, described in Rodgers et al.,²⁰ with a hole in the center added to accommodate the US probe. This grid phantom was embedded in a solidified mixture of 35-g agar powder (Sigma Aldrich, Co., St. Louis, Missouri) and 80-mL glycerol (Sigma Aldrich, Co., St. Louis, Missouri) per 1-L distilled water to approximate the speed of sound in soft tissue (1540 m/s).⁴⁴ The phantom was scanned using the 3-D TVUS system without and with the sonolucent cylinder surrounding the probe to assess if the introduction of the sonolucent cylinder affected the geometric measurements in the resulting image. Linear measurements [nominal values indicated in Fig. 3(a)] were obtained using software developed in our laboratory for visualization of 3-D US images.²⁷ A total of 64 measurements were made in each of the x and y directions, and 32 measurements were made in each of the two z directions for each image.

The geometric reconstruction was further validated using a phantom with an embedded sphere to evaluate the volumetric accuracy of the reconstructed 3-D TVUS image. The sphere had

Fig. 2 (a) A patient 3-D TVUS image, showing a reconstructed axial view and needles (indicated by outlined black arrows), with the position of a 2-D US frame indicated and (b) the corresponding, original frame used in 3-D US generation.

Fig. 3 Sections of 360-deg 3-D US images of a geometric grid phantom acquired (a) without the sonolucent cylinder (with nominal values indicated) and (b) with the sonolucent cylinder.

a nominal volume of 22.45 cm^3 and was made from the previously described agar mixture. The background agar had 10-g SigmaCell cellulose powder (Sigma Aldrich, Co., St. Louis, Missouri) added per 1-L distilled water to create contrast relative to the sphere. Four images of the phantom were acquired using the system: (1) without the sonolucent cylinder, (2) without the sonolucent cylinder with a 90-deg rotation in initial probe orientation, (3) with the sonolucent cylinder, and (4) with the sonolucent cylinder with a 90-deg rotation in initial probe orientation. The sphere was manually segmented three times in each image by picking points on the boundary and fitting a 3-D mesh to the points. The volume measurements from the segmentations were compared to the nominal volume and surface area-to-volume ratios (SA/V) were calculated to assess the sphericity of the segmentation.

2.3 Pelvic Phantom Study

The female pelvic phantom, as previously described in Rodgers et al.,²⁰ was used to evaluate the visualization of needles in the 3-D TVUS images under idealized conditions. Twelve stainless steel needles were inserted through the template, representing a common clinical pattern. Rubber stoppers were placed on the needles at predefined depths such that each needle was inserted a known depth into the phantom, ensuring that all needle tips

were visible within the field of view of the 3-D TVUS image. An image was acquired using the 3-D TVUS system with the sonolucent cylinder in place after all needles had been positioned. The sonolucent cylinder was then removed and replaced with a replica of the clinical vaginal cylinder. Mimicking the clinical procedure, a postinsertion CT scan was performed using a Revolution CT (GE Healthcare, Milwaukee, Wisconsin) with a helical acquisition (325 mA, 120 kVp, 0.625-mm slice thickness).

The 3-D TVUS and CT images were manually, rigidly registered based on the position of the replica clinical vaginal cylinder, rectal canal, and phantom box walls. In each image, the tip and the point on the needle path where the needle entered the image field of view were identified for each needle and a vector representing the needle trajectory was calculated using the two points selected. The angular difference between the vectors and the 3-D Euclidean distance separating needle tips were calculated for the needles in 3-D TVUS and compared to the expected positions based on the known insertion depth and template geometry and the positions determined in the CT image. As the second point along the needle path may not correspond between the 3-D TVUS and CT images, a corresponding point was established by projecting the point chosen in the US image onto the line generated by the two points selected in CT, as shown in Fig. 4.

Fig. 4 Illustration indicating how the corresponding entrance [most inferior (I)] and exit (most superior (S)) points are established by projecting the needle points in US onto the axis line created by the points in CT, which are used to calculate the point differences between the modalities. The needle insertion direction is oriented superiorly.

2.4 Patient Study

Six patients receiving HDR transperineal interstitial brachytherapy for vaginal tumors at the London Health Sciences Centre supplied informed, written consent in accordance with the protocols established by The University of Western Ontario (London, Ontario, Canada) Research Ethics Board. Patients requiring intrauterine tandem insertion were excluded from this study. Prior to insertion, US coupling gel was applied inside the sonolucent cylinder and the probe was inserted slowly to remove as many air bubbles as possible, with a visual inspection performed to ensure that there were no large air pockets. During the implant procedure, the sonolucent cylinder and US probe were inserted together into the vagina following template positioning, with the sonolucent cylinder inserted to the largest depth the vaginal canal would reasonably allow, when possible. Stainless steel needles [1.65-mm diameter (Varian Medical Systems Inc., Palo Alto, California)] were then inserted, and once most of the needles had been placed, a 3-D TVUS image was acquired while the patient remained in the lithotomy position. The needle internal mandrins were removed prior to image acquisition, when possible, to avoid interference of the large mandrin head with the cradle and to allow the needles to relax into their treatment shape. The 3-D TVUS images were obtained by a single radiation oncologist with an US depth setting of 5.6 cm for four patients and 6.4 cm for two patients. Following acquisition, the probe and custom sonolucent cylinder were removed together and were replaced by the conventional clinical cylinder for the remainder of the procedure, inserted to approximately the same depth as the sonolucent cylinder. Any remaining needles, including four needles that can be placed via the clinical cylinder, were then positioned.

Following the insertion of all needles and with the clinical cylinder in place, the patient underwent the standard, clinical postinsertion CT scan acquired with a helical acquisition (325 mA, 120 kVp, 3.0-mm slice thickness) using a Philips Brilliance CT Big Bore Scanner (Philips Healthcare, Andover,

Massachusetts). This scan was acquired with the patient in the supine position, potentially introducing some positional differences from the time of US acquisition but reflecting the current clinical practice. The geometry of the US probe and sonolucent cylinder were used to rigidly register the 3-D TVUS and CT images under the initial assumption that the sonolucent and clinical cylinders were inserted to the same depth. Another point, including the Foley balloon catheter in the urethra/bladder, pubis, and pubic symphysis, was identified in the images from the two modalities to rotationally orient the registration about the cylinders and refine the depth.

For each inserted needle, the entrance point was defined to be the most inferior (I) visible point along the path in each modality, and the exit point was defined to be the most superior (S) point. As the edge of the needle closest to the probe is most prominent in US, points were selected with an offset corresponding to the radius of the needle to represent the center of the needle shaft for comparison. Over the 6-cm width of the US image, there was assumed to be minimal needle deflection and thus needles were assumed to be linear within the images. Corresponding points between the modalities were established, as described in Sec. 2.3., for the phantom, such that the point identified in 3-D TVUS was projected onto the needle path established in CT (Fig. 4).

The angular differences between needle paths identified in each modality were calculated using the vectors formed between the calculated, corresponding entrance and exit points. These angular differences were decomposed into image planes, which approximately correspond to the anterior/posterior (A/P), left/right (L/R), and superior/inferior (S/I) planes. The S/I plane was excluded from analyses as the needles were inserted approximately perpendicular to this plane, appearing point-like. A positive angular difference indicates that the path identified in 3-D US is angled anteriorly and to the left relative to the path in CT, in the A/P and L/R planes, respectively.

The 3-D Euclidean distances between corresponding entrance points and corresponding exit points were calculated to assess point differences between the modalities. Based on the assumption of linearity within the images, either the entrance point pair or exit point pair with the greater difference was selected and used to calculate a maximum point difference between the needles in the two modalities. Given the differing spatial resolution of the US transducer in each direction, the corresponding points were transformed^{20,45} into radial (r), tangential (t), and insertion (z) coordinates to assess the impact of the spatial resolution differences. Principal component analysis (PCA) was performed to generate a 95% prediction interval ellipse in the (r, t) plane to evaluate the primary direction of point differences; however, the process of establishing corresponding points results in small differences in the insertion (z) direction, as shown in Fig. 4, thus, differences in the z direction were excluded from the analysis.

2.5 Statistical Analysis

Analyses were performed using GraphPad Prism 7 (GraphPad Software, La Jolla, California), with the exception of PCA, which was performed in MATLAB R2017a (MathWorks, Natick, Massachusetts). The normality of distributions was assessed using the Shapiro–Wilk test with a significance level of $p < 0.05$. Volumetric measurements and SA/V measurements were compared across the four images using an analysis of variance (ANOVA).

3 Results

3.1 Geometric Reconstruction Validation

A 360-deg 3-D US image of the grid phantom acquired without the sonolucent cylinder in place is shown in Fig. 3(a) with the expected measurements and coordinate directions indicated. The measurements in each of the coordinate directions had a mean difference ranging from 1.4% to 2.0% of the nominal values, with mean differences [lower 95% confidence interval (CI) limit, upper 95% CI limit] of 0.20 [0.14, 0.26], 0.14 [0.10, 0.19], 0.16 [0.10, 0.23], and 0.23 [0.16, 0.31] mm in the x , y , z_1 , and z_2 directions, respectively. Figure 3(b) shows a 3-D US image of the grid phantom acquired with the sonolucent cylinder in the same initial orientation as the no-cylinder scan. The mean differences in each of the coordinate directions ranged from -0.3% to 3.2% of the nominal values, with mean differences [95% CI limits] of 0.16 [0.09, 0.22], 0.17 [0.11, 0.22], 0.32 [0.25, 0.40], and -0.04 [-0.13 , 0.05] mm in the x , y , z_1 , and z_2 directions, respectively. Figure 5 summarizes the differences in the measurements from their nominal values without and with the sonolucent vaginal cylinder.

For the spherical volumetric phantom, the mean volume [95% CI limits] was 22.21 [21.91, 22.51] cm^3 without the presence of the sonolucent cylinder and 22.18 [21.48, 22.89] cm^3

Fig. 5 Mean differences with 95% CI from the nominal distance values for the linear measurements taken in each of the coordinate directions of a geometric grid phantom, without and with the sonolucent cylinder in place.

with the sonolucent cylinder, corresponding to mean errors of 1.2% and 2.7%, respectively (expected volume: 22.45 cm^3). The mean difference in SA/V ratios for the segmented volume relative to a perfect sphere was 0.57% and 0.99%, without and with the sonolucent cylinder, respectively. ANOVA failed to show a statistically significant difference between the volumes obtained from each of the four images ($p = 0.082$) or the SA/V ratios ($p = 0.106$), where the four volumes corresponded to images acquired without and with the sonolucent cylinder and following a 90-deg rotation from the initial probe orientation for each case.

3.2 Pelvic Phantom Study

The 360-deg 3-D TVUS image acquired from the pelvic phantom after 12 needles were inserted is shown in Figs. 6(a) and 6(b), with the rigidly registered CT image shown in Fig. 6(c). Table 1 summarizes the angular differences and point positional differences between the needles localized in 3-D US and CT, as well as relative to their expected positions based on the phantom geometry. The maximum point differences failed to pass the normality test ($p = 0.04$). The median [first quartile (Q1), third quartile (Q3)] angular difference between the 3-D US and CT for the 12 inserted needles was 1.60 [1.18, 2.11] deg and the median [Q1, Q3] maximum point difference was 0.84 [0.68, 1.33] mm.

3.3 Patient Study

Figure 7 shows an example of a patient 3-D TVUS image, with key features indicated. Needle cross sections were clearly distinguishable in the axial views of the images [Fig. 7(a)] and the needle paths were clearly visualized in both the sagittal [Fig. 7(b)] and coronal [Fig. 7(c)] views of all patient images. Other features were clearly visible, including the Foley catheter in the urethra, the rectum, pubis, and pubic symphysis in all images, bladder in four images, and vaginal wall in three images. Examples of entrance and exit points identified in both modalities are shown in Fig. 8, also demonstrating the alignment between the registered images.

All patient data distributions passed normality testing using the Shapiro–Wilk test (significance level: $p < 0.05$), with the exception of the overall L/R angular difference ($p = 0.0354$), entrance point difference ($p < 0.0001$), and maximum point

Fig. 6 (a) Axial and (b) oblique views of the 3-D US image of the pelvic phantom following the insertion of 12 needles and (c) the corresponding view in the registered CT image.

Table 1 Median [Q1, Q3] angular and point positional differences between the needles localized in a 3-D TVUS image, CT image, and the expected positions within the phantom.

Median [Q1, Q3] difference	3-D TVUS versus expected	CT versus expected	3-D TVUS versus CT
Angular (deg)	1.44 [0.87, 1.89]	0.73 [0.58, 0.89]	1.60 [1.18, 2.11]
Entrance point (mm)	—	—	0.76 [0.42, 1.33]
Tip (exit point) (mm)	0.35 [0.25, 0.52]	0.53 [0.24, 0.77]	0.52 [0.36, 0.66]
Maximum point (mm)	—	—	0.84 [0.68, 1.33]

Fig. 7 A patient 360-deg 3-D TVUS image with eight needles inserted (indicated with outlined black arrows), showing the US probe and hollow sonolucent vaginal cylinder, needles, bladder (shown with dotted outline), Foley balloon/catheter, and rectum (shown with dotted outline) in (a) axial, (b) sagittal, and (c) coronal views.

Fig. 8 Entrance and exit points with the rectum visible, shown in oblique views of Patient E, with outlier needles indicated, in (a) a 3-D TVUS image with the hollow sonolucent vaginal cylinder, (b) the corresponding, registered CT image with the clinical vaginal cylinder, and (c) an image with 3-D TVUS and CT aligned and overlaid.

difference ($p = 0.0284$) data. Table 2 summarizes the angular differences between corresponding needles identified in the 3-D TVUS and CT images and the median angular differences in the approximate A/P and L/R planes. Two needles localized for Patient E were identified as outliers (Fig. 8) based on the angular differences and were excluded from angular comparisons and all further analyses. Examination of these needles

showed additional migration in needle positions between the time of 3-D TVUS and CT image acquisition (2 h), likely due to changes in patient position and the needles' remote insertion position relative to the vaginal cylinder. For consistency, an additional two needles were excluded from Patient E as they were placed in the template holes on the other side of the template corresponding to the outliers. These needles had angular

Table 2 Median [Q1, Q3] angular differences in needles identified in 3-D TVUS and CT in 3-D space and the approximate A/P and L/R planes, such that an anterior and leftward shift in US relative to CT is indicated by a positive value in the approximate A/P and L/R planes, respectively.

	Number of needles	Median [Q1, Q3] angular difference (deg)	Median [Q1, Q3] angular difference in the A/P plane (deg)	Median [Q1, Q3] angular difference in the L/R plane (deg)
Patient A	8	1.72 [1.28, 2.05]	-1.32 [-1.97, -0.40]	-0.31 [-0.64, 0.64]
Patient B	10	1.65 [1.21, 2.28]	0.56 [-0.41, 1.45]	0.00 [-1.21, 0.93]
Patient C	10	1.58 [0.94, 2.07]	0.61 [-0.43, 1.05]	0.69 [-0.20, 1.84]
Patient D	10	2.00 [1.74, 2.72]	-1.05 [-1.40, -0.22]	0.68 [-1.32, 2.60]
Patient E	8	2.19 [1.88, 2.50]	1.32 [-0.53, 1.84]	-1.08 [-1.46, 1.91]
Patient F	8	2.30 [1.81, 2.84]	0.21 [-0.88, 2.30]	-1.07 [-1.54, 2.14]
Overall	54	1.87 [1.50, 2.48]	-0.12 [-1.07, 1.06]	0.10 [-1.15, 1.66]

Fig. 9 Histograms showing the distribution of (a) angular and (b) maximum point differences between the needles localized in the 3-D TVUS images and the corresponding CT images.

errors ranging between 2.60 deg and 8.63 deg. For the total of 54 needles included, the median [Q1, Q3] angular difference was 1.87 [1.50, 2.48] deg and 92.6% of needles had angular differences of <3 deg, as shown in Fig. 9(a). In the approximate A/P plane, the median [Q1, Q3] angular difference was -0.12 [-1.07, 1.06] deg, where a negative value indicates that the 3-D US needle path is angled posteriorly relative to the needle path localized in the CT image. The median [Q1, Q3] angular difference was 0.10 [-1.15, 1.66] deg in the approximate L/R plane, where the positive difference is associated with an angular shift left in 3-D US relative to CT. The angular differences in the

needle paths in the approximate A/P and L/R planes are shown in Fig. 10.

The median [Q1, Q3] entrance point difference between the 3-D TVUS and CT images was 1.40 [0.92, 2.17] mm and the median [Q1, Q3] exit point difference was 2.05 [1.34, 2.84] mm for the 54 needles included, with the point differences for each patient summarized in Table 3. The median [Q1, Q3] maximum difference between corresponding needles was 2.12 [1.65, 2.84] mm with 77.8% of needles having a maximum difference of <3 mm and 98.1% with a difference of <5 mm, as shown in Fig. 9(b). In the radial and tangential directions, the centroid

Fig. 10 Angular differences in needles identified in the 3-D TVUS images relative to the corresponding needle in registered CT images in the approximate (a) A/P and (b) L/R planes.

Table 3 Median [Q1, Q3] point positional differences between the entrance and the exit points determined in 3-D TVUS and CT. The maximum difference was taken to be the maximum of the entrance or exit difference for each needle.

	Number of needles	Median [Q1, Q3] entrance point difference (mm)	Median [Q1, Q3] exit point difference (mm)	Median [Q1, Q3] maximum difference (mm)
Patient A	8	1.67 [0.56, 1.67]	1.41 [0.97, 2.05]	1.91 [1.62, 2.10]
Patient B	10	3.12 [1.52, 4.27]	2.95 [1.61, 3.82]	3.58 [2.07, 4.39]
Patient C	10	1.25 [0.97, 1.74]	1.26 [0.98, 1.81]	1.50 [1.14, 2.26]
Patient D	10	1.28 [0.57, 2.17]	2.17 [1.82, 3.13]	2.17 [1.82, 3.13]
Patient E	8	1.16 [0.58, 1.67]	2.02 [0.89, 2.64]	2.26 [1.33, 2.65]
Patient F	8	1.05 [0.79, 1.83]	2.49 [2.03, 3.36]	2.49 [2.03, 3.36]
Overall	54	1.40 [0.92, 2.17]	2.05 [1.34, 2.84]	2.12 [1.65, 2.84]

Fig. 11 Point positional differences between the corresponding points determined in the patient 3-D TVUS images and the corresponding, registered CT images in the radial (r) and tangential (t) plane and the 95% prediction ellipse determined using PCA.

of the distribution was at $(r, t) = (-0.14 \text{ mm}, -0.65 \text{ mm})$, as shown in Fig. 11, with the 95% prediction ellipse.

4 Discussion

This study investigated the use of a 360-deg 3-D side-fire TVUS system through the evaluation of both phantom and patient images to localize needles and visualize nearby anatomy intraoperatively during HDR transperineal interstitial gynecologic brachytherapy of vaginal tumors. To the authors' knowledge, this is the first study evaluating 360-deg 3-D TVUS for brachytherapy of vaginal malignancies and visualization of interstitial needles. In the six-patient study, the images allowed for a clear visualization of key features, including a portion of the bladder for four patients and the rectum in all images, which is important for avoiding overexposure of OARs, though a further study with a larger patient cohort would be necessary to examine the impact of image guidance on OAR avoidance and dose optimization. In cases where the bladder was not visible, this was due to the

probe not being inserted deeply enough to capture this within the field of view. This may be rectified in the future by the examination of a preinsertion image prior to the insertion of the needles; however, the Foley catheter in the patient's urethra was clearly visualized in all patient images. Although all needles were clearly visualized in the images, in some patient images, small air gaps appeared when using the sonolucent cylinder at either the US probe-cylinder interface or the cylinder-vaginal wall interface, resulting in air artifacts in the images. These were typically at the inferior edge of the image due to the insertion depth of the vaginal cylinder and were never large enough to fully obscure any needle paths or other key features.

Registration of 3-D TVUS to clinical CT images as a reference standard may contribute to the differences observed in needle positions, as this introduces the potential for differences in bladder or rectal filling, as well as swelling or edema due to the needle insertions, which could lead to needle shifts.^{46–48} Further, 3-D TVUS images were acquired with the patient's legs raised in stirrups while the CT images were acquired with their legs lowered in supine position, which could introduce errors due to the different pelvic tilt. These potential effects are illustrated in the angular biases shown in Fig. 10, where needles in 3-D TVUS were tilted in the posterior direction relative to the needles in the CT for Patients A and C. Patients D and F showed needles split into two distinct groups [Fig. 10(b)], such that needles on the patient right were angled left in 3-D US relative to CT and, similarly, on the patient left needles were angled right. This indicates that the needles appear angled outward, away from the vaginal cylinder, in the CT image relative to the 3-D TVUS image, potentially due to patient position or edema. Patient B had the largest maximum point difference, and in the (r, t) directions there was a much larger error in the tangential (t) direction with a 95% prediction interval of $\pm 6.42 \text{ mm}$ relative to the radial (r) direction with a 95% prediction interval of $\pm 2.72 \text{ mm}$, and also relative to all other patients in the study. This indicates that one other possible cause of the point differences observed is a rotational misalignment during the registration process, which is supported by the low angular error observed for this patient. The overall median maximum difference was $<2.5 \text{ mm}$, which may be sufficient for implant assessment, as a clinically acceptable implant may allow for a tolerance of $\pm 5 \text{ mm}$ spacing between adjacent needles.^{3–6}

A broader patient study aimed at dosimetric evaluation of the differences between observed needle locations in 3-D TVUS and CT planning images is required to refine the target accuracy for needle localization, accounting for the effects of a multi-needle implant. Overall point differences in the (r, t) coordinate system (Fig. 11), demonstrated a slightly larger difference in the tangential (t) direction (95% prediction interval of ± 4.68) than radial (r) direction (95% prediction interval of ± 3.40) but with no notable bias in the position of the centroid. This may be due to the lower spatial resolution in the tangential (t) direction and tilt acquisition method, creating a smearing effect on points, as demonstrated in the (x, y) plane of Fig. 3, consequentially, making it more difficult to identify the point.

Although the effects of patient posture, movement of the patient, and time delays between insertion and CT acquisition on implant geometry require further investigation for gynecologic brachytherapy, the effect of pelvic tilt, patient relocations, time, and potential for edema have been reported for HDR transperineal prostate brachytherapy.^{49–55} These studies have reported needle shifts >2 mm in the first few hours following implantation, with Mullokandov and Gejerman⁵⁰ emphasizing the time-dependent nature of the displacements. Similar shifts may occur during transperineal interstitial gynecologic brachytherapy, as evidenced by studies of interfraction motion, where Mikami et al.⁴⁷ and Rey et al.⁵⁶ reported caudal displacements between the first two fractions, which may contribute to some of the differences observed in the interstitial gynecologic implants in this study. This is further supported by Shukla et al.⁴⁸ who reported needle displacements of 1.7, 2.1, 1.7, and 0.6 mm in the anterior, posterior, right, and left directions, respectively, over the course of treatment with the majority of migration occurring during the early fractions. They attributed this to the development of postprocedural edema during the first 24 h. Although changes from needle insertion to planning CT have not been documented in the literature, it is possible that these changes contribute to needle shifts between the 3-D TVUS and CT images. In particular, given their remote location relative to the vaginal cylinder and closer proximity to the patient hips, the outlier points observed in Patient E may have been affected by these factors. These needles passed through a greater amount of fatty tissue relative to those closer to the center, which may have led to differing needle migration, as evidenced by the large angles of these needles relative to the other needles in the CT image, which were not present at the time of 3-D TVUS imaging.

The current system has limited applicability for disease sites superior to the mid-vagina, such as cervical and upper vaginal tumors, as needle tips extend beyond the field of view of the 3-D TVUS images for these cases. To overcome this limitation, we are currently investigating combining the 3-D side-fire TVUS images with a 3-D end-fire TVUS image using the same system and acquired through the same sonolucent vaginal cylinder, capturing the tip information, as well as the trajectory provided by the side-fire image. This provides the potential for the system to be extended to a broader range of gynecologic malignancies treated with transperineal interstitial brachytherapy. In this study, a single 3-D TVUS image was acquired once the majority of needles had been placed, but clinically, the system may be used periodically throughout the insertion procedure. Ideally, once the probe and sonolucent cylinder have been positioned, a preinsertion 360-deg 3-D TVUS image can be acquired, and clinicians can use the system to align the probe to the needle

trajectory corresponding to a particular needle template hole for real-time insertion monitoring. A final 360-deg 3-D TVUS image can be acquired to visualize all of the needles in context and relative to the OARs prior to the replacement of the US probe and sonolucent cylinder with the clinical cylinder, allowing four additional needles to be placed and treatment to proceed. Future studies will include investigating the radiation dose distribution changes caused by the hollow sonolucent cylinder to determine if this cylinder could remain in place for the duration of treatment rather than be replaced by the clinical cylinder. A broader multicenter patient trial is also required to refine the clinical workflow using this system prior to routine clinical use. The current study has provided the basis for this, with the use of 3-D TVUS allowing accurate needle localization and OARs to be clearly visualized during interstitial needle insertion for HDR transperineal gynecologic brachytherapy of vaginal tumors, allowing for intraoperative assessment of the implant.

5 Conclusion

The use of 360-deg 3-D TVUS through a sonolucent vaginal cylinder provides a technique for visualizing and localizing needles, as well as visualizing OARs, intraoperatively during HDR transperineal interstitial gynecologic brachytherapy of vaginal tumors. This enables interstitial implants to be intraoperatively assessed during the needle insertion procedure and adjustments to be made, providing the potential for increased confidence in needle positions and improved implant quality.

Disclosures

The authors have no relevant conflicts of interest to disclose.

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