Clinical application and validation of an iterative forward projection matching algorithm for permanent brachytherapy seed localization from conebeam-CT x-ray projections

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Purpose: To experimentally validate a new algorithm for reconstructing the 3D positions of implanted brachytherapy seeds from postoperatively acquired 2D conebeam-CT (CBCT) projection images.

Methods: The iterative forward projection matching (IFPM) algorithm finds the 3D seed geometry that minimizes the sum of the squared intensity differences between computed projections of an initial estimate of the seed configuration and radiographic projections of the implant. In-house machined phantoms, containing arrays of 12 and 72 seeds, respectively, are used to validate this method. Also, four ¹⁰³Pd postimplant patients are scanned using an ACUTY digital simulator. Three to ten x-ray images are selected from the CBCT projection set and processed to create binary seed-only images. To quantify IFPM accuracy, the reconstructed seed positions are forward projected and overlaid on the measured seed images to find the nearest-neighbor distance between measured and computed seed positions for each image pair. Also, the estimated 3D seed coordinates are compared to known seed positions in the phantom and clinically obtained VariSeed planning coordinates for the patient data.

Results: For the phantom study, seed localization error is (0.58 ± 0.33) mm. For all four patient cases, the mean registration error is better than 1 mm while compared against the measured seed projections. IFPM converges in 20–28 iterations, with a computation time of about 1.9–2.8 min/iteration on a 1 GHz processor.

Conclusions: The IFPM algorithm avoids the need to match corresponding seeds in each projection as required by standard back-projection methods. The authors' results demonstrate ~ 1 mm accuracy in reconstructing the 3D positions of brachytherapy seeds from the measured 2D projections. This algorithm also successfully localizes overlapping clustered and highly migrated seeds in the implant. © 2010 American Association of Physicists in Medicine. [DOI: [10.1118/1.3480962](https://doi.org/10.1118/1.3480962)]

Key words: brachytherapy, localization, iterative forward projection matching, conebeam-CT, x-ray projections

I. INTRODUCTION

In the past decade, permanent implantation of radioactive ¹²⁵I or ¹⁰³Pd seeds into the prostate has become a common treatment option for patients with organ-confined prostate cancer.¹ Current clinical practice involves creating an ultrasound-based preimplant plan about a week before treatment. A postimplant dose evaluation is then performed using 3D CT images acquired at week four, following the implantation to document the delivered dose. However, as presently practiced, this process does not allow for intervention during the implant procedure to improve the actual treatment.

Recent advances in imaging and treatment delivery technology now provide the opportunity to perform intraoperative dose reconstruction to further optimize the implant. A key step in intraoperative planning is identifying the locations of all seeds with respect to the underlying anatomy. In principle, one can use in-room fan-beam CT (FBCT) for this purpose. Reconstruction of seed coordinates from postim-

plant 3D CT images is already routinely applied in clinical practice.^{2,3} However, in addition to poor soft-tissue contrast and large (up to 8 mm when compared to axial magnetic resonance images) prostate contouring errors,⁴ FBCT suffers from streaking artifacts arising from the implanted metal seeds, overlapping seed clustering, and resolution limited by the slice thickness. Also, intraoperative FBCT installations in brachytherapy suites are uncommon.

A more common approach to seed localization is back-projection of seed positions in 2D x-ray projections using two-film⁵ and three-film^{6–11} techniques. The reconstructed implant geometry is then fused to intraoperatively acquired ultrasound images, upon which dose planning can be performed. However, in back-projection methods, corresponding seeds in each projection must be identified and matched.^{12–19} This problem is not always soluble because of seed clustering and overlapping, resulting in inaccurate seed localization due to mismatched or missing seeds. Patient mo-

tion and uncertainty in imaging device positioning during image acquisition can further confound seed localization when using back-projection methods.

With the introduction of dedicated conebeam-CT (CBCT) imaging systems for seed placement, we can combine the advantages of a rigidly mounted intraoperative imaging system, seed reconstruction from 2D projection radiographs, and reconstruction of 3D anatomy in the same coordinate system from a full set of projections. However, even with the resulting improvements in the calibration and stability of the imaging geometry, reconstruction via back-projection remains problematic.

This study assesses the robustness and accuracy of a promising new reconstruction method, the “iterative forward projection matching” (IFPM) algorithm, which was introduced by Murphy and Todor²⁰ for reconstructing 3D coordinates of implanted seeds from 2D radiographic projections. The IFPM method was designed to avoid the problems of back-projection localization methods, such as the need to determine the seed correspondences between different projections, the ambiguities presented by clustered or missing seeds in the projections, and uncertainties in the projection geometry such as gantry angle inaccuracy and possible patient motion between image acquisitions. It accomplishes this by iteratively adapting an initial estimate of the 3D seed configuration until the agreement between the acquired projections of the implanted seeds and the computed projection images of the estimated seed configuration is maximized. By matching the projection of the full seed configuration rather than individual seed projections, IFPM intrinsically accommodates incomplete and ambiguous data by recreating the overlapping seeds in the matching computed images. The algorithm also allows the imaging viewpoints (projections) for the digitally reconstructed radiographs (DRRs) to be adjustable parameters to accommodate gantry angle uncertainties up to 8° with respect to the first projection. This is a particularly useful feature if the images have been acquired using a mobile C-arm. In this study, we experimentally validate IFPM using a dummy seed (nonradioactive) containing phantoms and demonstrate its ability to reconstruct clinical patient implants.

II. MATERIALS AND METHODS

II.A. IFPM algorithm

The IFPM algorithm²⁰ works with a set of M 2D projection images of the actual seed configuration in the patient. The imaging geometry for the M projections is measured to obtain the detector model.²⁰ The IFPM algorithm starts with an initial estimate of the seed configuration. The (x,y,z) coordinates of the center of each seed are free parameters. The initial estimate of the 3D seed configuration is forward projected onto each 2D detector plane via a detector model simulating that of the acquired projection to produce M computed projection images of the seeds that emulate the acquired images. The computed projections are compared to the actual projections by calculating the pixel-by-pixel squared intensity differences (SSQD) of the image intensi-

FIG. 1. The perspective projection geometry for the imaging system. The 3D seed configuration is in the world coordinate system, which is defined by three translational and three rotational coordinates relative to the CBCT isocenter. The image receptor plane is defined by the imaging viewpoint angles (α, β, γ) , where S and D denote the constant values between the source to isocenter and detector to isocenter distances, respectively. The imaging axis rotates by angle α around the x axis. The pixel index (i, j) denotes the projected seed in the 2D imaging plane (u, v) .

ties. The (x,y,z) coordinates of each seed are then independently adjusted in an iterative process until the computed projections optimally match the acquired images (i.e., when the total SSQD for the M image pairs has been minimized).

The world coordinate frame is defined by three translational variables (x,y,z) , where the x , y , and z axes are left/right lateral, anterior/posterior, and superior/inferior directions, respectively, relative to the CBCT isocenter for a supine patient with the head toward the gantry base. Figure 1 shows a schematic of the perspective projection geometry used to create each of the M projection images of the seed configuration. In the world frame, the 3D seed configuration of N total seeds is defined by $\{r_k\}, k=(1,N)$. In the extrinsic detector model, the orientation of each isocentric projection in the world coordinate frame is defined by the angles (α, β, γ) , which describe rotations of the detector image plane around the x , y , and z axes, respectively. In practice, $\alpha \approx 90^\circ$, $\beta \approx 0^\circ$, and γ is the gantry angle for each M image viewpoint. However, the complete extrinsic detector model allows for a precise calibration of the imaging plane orientation (α, β, γ) at each gantry angle to allow for tilting and/or twisting of the image plane due to gantry flex and other mechanical imperfections. The intrinsic detector model is parametrized by describing its magnification, image center, image size, and pixel resolution. S and D denote the constant values between the source to isocenter and detector to isocenter distances, respectively, and (u, v) is the 2D detector plane.

As mentioned earlier, IFPM not only adjusts the individual seed positions until the computed and measured projections match, but can also simultaneously adjust each x -ray projection, with six degrees of freedom relative to the first projection (i.e., the reference projection, which is fixed) to

FIG. 2. (a) The ACUITY imaging system in the brachytherapy imaging suite and a phantom setup. (b) Schematic of the geometrical configuration of a precision-machined phantom containing 72 dummy seeds arranged as four nine-seed slabs alternating with three 12-seed slabs in a rectangular grid. This phantom was used to test the IFPM seed localization accuracy. The centers of the seeds were coplanar and perpendicular to the plane of the slabs.

account for uncertainties in the detector model calibration (i.e., the uncertainties in the relative imaging viewpoints).

To avoid the time-consuming task of computing complete DRRs of the simulated seed configuration via attenuation ray-tracing through the patient's anatomy, it is sufficient for IFPM to project the centers of the seeds in the model configuration along the rays from x-ray source to the detector. This produces binary 2D images of the centers of the seeds. The center of each projected seed on the detector plane is dilated to represent a small disk of uniform brightness of thickness t , which is approximately equal to a Theragenics Model 200 ^{103}Pd seed (Theragenics Corporation, Buford, GA) radiographic marker, so that the unblurred projections of each binary seed image are approximately equal to the measured projections in shape and size. The acquired images are then filtered to highlight the seeds, also yielding a set of binary images. Both sets of binary images are then convolved with a Gaussian blurring function to produce grayscale images in which the seeds appear as fuzzy spots. The blurring process produces smoothly varying grayscale image gradients that facilitate gradient-driven minimization of the SSQD. The algorithm then computes the gradient of the SSQD with respect to each seed's three degrees of freedom to drive the iterative minimization process. It also computes the gradient of the SSQD with respect to the degrees of freedom, e.g., (α, β, γ) , in the detector model to adjust the imaging geometry for an optimal match.

II.B. Image acquisition details and autosegmentation of the seeds

Both the phantom and patient validation tests reported here use projection images obtained with the Varian ACUITY intraoperative imaging system (Varian Inc., Palo Alto, CA), which is used for image-guided brachytherapy procedures in our dedicated brachytherapy suite. This imaging system can be operated in CBCT, fluoroscopic, and/or radiographic modes. Figure 2(a) shows the phantom setup in the

ACUITY system and Fig. 2(b) shows the geometric configuration of the 72-seed phantom used in this study (see Sec. II D 1 for more details).

The projection images are acquired with the Varian 4030CB flat panel detector. This detector is $40 \times 30 \text{ cm}^2$ with a 1024×768 image size, pixel size of 0.388 mm/pixel , and 16-bit depth. The ACUITY imaging geometry has a 100 cm source to isocenter distance and a 150 cm source to detector distance, giving a magnification factor of $3/2$. Approximately 660 CBCT images are obtained for a complete 360° gantry rotation. Subsets of three to ten images each are used for the IFPM tests.

For the model 6711 ^{125}I dummy seeds (Medi-Physics Inc., Arlington Heights, IL) used in the phantom study, the radio-opaque components include $3 \times 0.5 \text{ mm}^2$ cylindrical silver markers that are represented by their center locations. This requires postprocessing of the acquired projection images to find and highlight the marker projections. The postprocessing involves (a) cropping the images to a 256×256 pixel square region of interest, (b) normalizing the image intensity by finding its maximum and minimum values in the image, (c) morphological top-hat filtering to suppress the background, and (d) automatic thresholding using the three standard deviation value of the pixel intensity histogram to create a binary marker for each seed in each projection in order to separate the seeds from the background. This produces binary bitmap images with intensity=0 in the background and intensity=1 over the area of each projected seed marker. The center locations of each seed projection image in the 2D detector plane are obtained by computing the center of mass for each radio-opaque marker. The binary images are then convolved with a 2D Gaussian blurring function to create diffuse seed spots with a known intensity distribution. This produces smoothly varying image gradients that can be computed analytically in the test projections to guide the objective function minimization and speed up the convergence of the matching process.

For the patient study (see Sec. II D 2 for more details), image processing is identical to that applied to the phantom implant projections, except that we retain the binary image of the entire radio-opaque marker ($1.09 \times 0.5 \text{ mm}^2$) in the model 200 ^{103}Pd seed, which avoids resolving seed clusters in the 2D measured projections.

II.C. Algorithm details

II.C.1. Initial seed configuration estimates and computed projection images

For the phantom study, the initial seed configuration $\{\mathbf{r}_k\}$ is chosen as follows, where $k=(1, N)$ is the seed number and N is the total number of seeds. For each seed k , the known 3D seed coordinates $\{\mathbf{r}_{k,0}\}$ are randomly perturbed by adding a displacement $\mathbf{d}_k$, such that $\mathbf{r}_k = \mathbf{r}_{k,0} + \mathbf{d}_k$, where $\mathbf{d}_k$ is randomly sampled from a uniform distribution $[-2 \text{ mm}, 2 \text{ mm}]$ in each of the three orthogonal directions, resulting in a mean displacement of 1.98 mm. To construct the computed projec-

tion images at each iteration, the initial configuration $\{r_k\}$ is rotated and translated to each imaging viewpoint and then projected on the (u, v) imaging plane.

For each patient case, $\{r_k\}$ is derived from the pretreatment transrectal ultrasound (TRUS) volume study, which gives x , y , and z coordinates of each seed centroid in an image coordinate system that is fixed to the TRUS planning target volume structure. Since the 2D measured projection images used by IFPM are taken in the CBCT reference frame, we transform the seed centroid TRUS coordinates to the CBCT coordinate system by using rotation, translation, and scaling. The reference frames of both imaging systems are orthogonal, right-handed coordinate systems. Therefore, the translation is performed by aligning the isocenters (centroids) of the two imaging systems and the rotation is obtained by finding the conventional x , y , and z coordinates of the ultrasound imaging system used in our clinic and transforming them to the known CBCT imaging coordinate system. As with the phantom study, the transformed 3D seed configuration (ultrasound-to-CBCT reference frame) is rotated and translated for each imaging viewpoint and then projected on the imaging plane.

For each imaging gantry position γ , each seed's position projected onto the imaging plane (u, v) , where it is represented by a small disk of uniform brightness of thickness t , which is approximately equal to a model 200 ^{103}Pd seed radiographic marker. This produces a binary bitmap image of the seed projections. These images are then convolved with the same 2D Gaussian blurring filter (with standard deviation σ) that is used for the measured projections to produce grayscale images and denoted by $I_c(u, v | \{r_k\}, \sigma, \gamma)$, where u and v are pixel indices along the 2D imaging plane.

The purpose of blurring the projected seed disks with a Gaussian is to create grayscale images with smoothly varying gradients that extend beyond the seed's projected cross section. This facilitates the use of a gradient-driven iterative solution. If the binary bitmap images were used directly, there would be large areas with no gradient to guide the iterative search. The blurring can be thought of as creating a potential well around each seed that attracts neighboring seeds and accelerates convergence. Increasing the width of the Gaussian increases the capture range (i.e., the maximum distance over which seeds in the two images can be drawn together).

II.C.2. Similarity measure and gradient search

The metric used to assess the overall similarity of the images is computed by combining the pixel-by-pixel SSQD for all computed $I_c(u, v | \{r_k\}, \sigma, \gamma)$ and measured $I_m(u, v | \sigma, \gamma)$ seed image pairs.

$$\text{SSQD}(\{r_k\} | \sigma, \gamma) = \sum_{\gamma} \sum_{u, v} [I_c(u, v | \{r_k\}, \sigma, \gamma) - I_m(u, v | \sigma, \gamma)]^2, \quad (1)$$

where (u, v) are pixel indices in the 2D image plane and γ is the gantry angle. The seed positions $\{r_k\}$ and the initial imaging viewpoint parameters except for the first projection

(i.e., the reference viewpoint) are iterated simultaneously by a steepest descent search algorithm. Unlike the reference viewpoint, which is not allowed to vary, other imaging viewpoints are defined relative to the first projection in terms of rotation and translation. Because the image grayscale intensities are described entirely by the Gaussian blurring function, the gradients of SSQD with respect to all of the free parameters can be calculated analytically.²⁰ Since the brachytherapy seed marker represented by a small disk in this study has rotational symmetry, we use seed center coordinates to calculate one derivative per seed per degree of freedom.

After computing the analytical gradients to adjust all free parameters, the process iteratively refines the 3D seed positions and projection orientations (α, β, γ) , until the agreement between the computed and measured seed projections is maximized. To iteratively adjust the free parameters that minimize SSQD, we use a nonlinear gradient search method that combines the steepest descent gradient search with a parabolic approximation of the SSQD surface around the global minimum.²⁰ The computed and measured projections must have the same imaging geometry, image size, and pixel resolution. At least two, but preferably three or more, pairs of computed and measured projection image data sets with corresponding imaging geometry are required for one reconstruction process. The $3N$ seed positions plus six $(M-1)$ degrees of freedom of the imaging viewpoints are the freely moveable parameters in each iteration, where M is the total number of projections.

II.C.3. Two-step adaptive Gaussian blurring

From the phantom studies, it is observed that the computed seed locations at convergence vary somewhat (i.e., trapping in local minima). That means if the initial estimate of the seed configuration is far apart from the measured configuration, there is a chance of less than optimal matching. To improve the accuracy of the patient study, we apply a two-step adaptive blurring scheme: We use a larger 2D Gaussian spreading (i.e., σ_1) to achieve initial convergence and then recompute the images using a smaller Gaussian blurring filter (i.e., σ_2), using the optimal σ_1 seed configuration as initial conditions for the σ_2 search. The two-step Gaussian blurring strategy uses more diffuse seed spots (i.e., increases the capture range) in the configuration at the beginning to draw the computed and measured seeds into close proximity and then increases the sharpness of the seed spots to get the optimal match near convergence. The optimal values of two-step blurring, σ_1 and σ_2 , are obtained from trial and error for each patient seed configuration and are between 3.8 and 3.0 mm, and 2.6 and 2.0 mm, respectively.

II.D. Algorithm validation

II.D.1. Brachytherapy phantom design

Two different in-house brachytherapy phantoms were designed and fabricated using acrylic plates with dummy seeds in known configurations. In the acrylic plates, a matrix of parallel holes was drilled such that each hole is of 0.9 mm diameter so that seeds can be placed in the holes. The model

6711 ^{125}I seeds are each 4.5 mm long and 0.8 mm in diameter. The seeds were arranged in rectilinear layers separated by 6 mm, with 8–12 mm interseed spacing within a plate. After loading the seeds, the plates were mounted tightly together with screws. Both phantoms were $10 \times 10 \times 7 \text{ cm}^3$. The first phantom contains 12 seeds. The second phantom contains 72 seeds, a more clinically realistic brachytherapy phantom. For the 72-seed phantom, the seeds were arranged by four nine-seed slabs alternating with three 12-seed slabs in a rectangular grid as shown in Fig. 2(b).

To evaluate the positional accuracy, the known 3D seed centroids obtained from the machined phantoms were compared to the corresponding reconstructed IFPM seed centroids. Accurate comparisons of the seed positions can be made since the absolute positions of the seeds in the phantom are known within the machining precision of 0.2 mm.

II.D.2. Patient data acquisition

Following the phantom tests, the IFPM algorithm was applied to the more difficult problem of brachytherapy seed reconstruction for actual patients, using images acquired 1 month after the permanent seed implants. The four selected patients (I–IV) all had been treated for low risk stage I prostate adenocarcinoma and were imaged postoperatively, i.e., approximately 4 weeks postimplant using a Varian ACUITY digital simulator equipped with a CBCT imaging system. The preloaded permanent seed implants consisted of 67, 62, 81, and 60 model 200 ^{103}Pd interstitial sources, respectively. The 660 CBCT projections were acquired in a 360° gantry rotation using the Varian 4030CB imager in full-fan/half-fan mode. The images were acquired at 125 kVp, 80 mA, and 25 ms per projection. For those postoperative scans, the patients were positioned head first and supine with legs down.

To make up the measured projection data set, we selected three to ten x-ray images from the CBCT projection data sets acquired from the ACUITY digital simulator. The choice of perspectives was based on visibility of the large number of seeds on the projection images and also to avoid imprecision caused by excessively small parallaxes. For the patients I, III, and IV, the images were selected at 8° – 12° angular intervals over a $\pm 40^\circ$ range of gantry angles. Since patient II was scanned in half-fan mode, the images were selected at the same angular interval as the other patients but over $\pm 160^\circ$ (i.e., posterior/anterior view) range of gantry angles. The images were postprocessed as described in Sec. II B. One example case of the image postprocessing and seed detection for a patient is presented in Fig. 3. The binary seed images are then convolved with a 2D Gaussian blurring function. Three to six pairs of selected gantry angle projection images were used in each seed reconstruction process.

II.D.3. Assessment of seed registration/reconstruction error

For the phantom study, the seed reconstruction error was computed by directly comparing the computed seed coordinates with the physically measured (with machined uncertainty of $\pm 0.2 \text{ mm}$) seed coordinates. For the patient data

FIG. 3. An example case of the image postprocessing of the projection images obtained from the Varian 4030CB digital simulator. (a) Raw projection image, (b) filtered image, (c) seed-only image, and (d) blurred image using the IFPM algorithm for patient III (81 implanted Theragenics model 200 ^{103}Pd seeds).

sets, there are no ground truth seed coordinates. Assessment of seed reconstruction error was performed in two ways. First, seed registration error is calculated by reprojecting the IFPM seed coordinates at convergence onto the 2D image planes, overlaying the computed and measured seed projection and calculating the nearest-neighbor distance between the measured and computed seed positions in each image plane, making sure that no measured seed projection was matched to more than one computed image. In the second approach, we compared the IFPM 3D coordinates from the reconstructed CBCT image sets to those obtained by the VariSeed planning system. For each candidate IFPM seed position, we find the VariSeed source position that minimized the 3D distance between the IFPM and VariSeed coordinates. The seed reconstruction error was quantified by computing the vector and scalar displacement between the IFPM and VariSeed coordinates. In the VariSeed planning system, the resultant seed centroids have limited accuracy because of slice thickness limitations, metal streaking artifacts, and problems of resolving seed clusters. These uncertainties are included in our estimation of the accuracy of the IFPM solution for the seed positions.

III. RESULTS

III.A. Validation test with phantoms

The phantom study is the best way to test the accuracy of the IFPM algorithm since the reconstructed seed positions can be compared to the measured precision-machined seed positions. Figure 4 shows the convergence of the objective function Eq. (1) as defined in Sec. II C 2, for the 12-seed and 72-seed phantom data sets. In these cases, we used a one-step ($\sigma = 2.4 \text{ mm}$) convergence process. For the 72-seed phantom case, the root-mean-square (RMS) error, in terms of 3D distance between IFPM and benchmark coordinates, was found

FIG. 4. The convergence rate of the IFPM algorithm for the two example cases: 12-seed and 72-seed phantom data sets.

to be (0.58 ± 0.33) mm. For the 12-seed phantom case, the RMS error was even smaller (0.43 ± 0.24) mm. The distribution of seed reconstruction errors is shown in Fig. 5 where we show that greater than 96% of the reconstructed seed positions are within 1 mm from the measured seed positions (72-seed phantom). The reconstructed values of relative (α, β, γ) deviated from their nominal values with respect to 0° gantry angle (i.e., reference viewpoint) by 0.08° , 0.06° , and 0.7° for -20° gantry angle and 0.09° , 0.03° , and 0.6° for $+20^\circ$ gantry angle. Experiments showed that relative viewpoints uncertainties as large as $\pm 8^\circ$ could be accommodated.

All test trials for 12-seed phantom data sets converge in four to six iterations with a total computation time of 2.8–4 min and for 72-seed phantom data sets the objective function converges on eight to ten iterations with a total computation time of 30–53 min on a 1 GHz processor (running time depends on number of seeds used in the implants, i.e., the number of free parameters to optimize). Several experiments

FIG. 5. Histograms of the seed positional error for the 12-seed and 72-seed phantom study.

FIG. 6. An illustration of the iterative sequence morphing of the convergence process. (a) Initial estimate of the seed configuration, (b) computed images after first step of convergence, (c) computed images after second step of convergence, and (d) the measured images at different gantry angle for patient III. Despite large differences between the preplanned seed geometry (based on a TRUS volume study acquired about a week before the implant) and that observed 4 weeks after the implant, IFPM was able to accurately reproduce the desired seed configuration.

were performed using different gantry angle combinations as well as different initial starting configurations in the course of this study. Theoretically, one should expect $SSQD=0$ at the convergence, i.e., all computed seed images exactly match with those measured. However, from Fig. 4, for the 72-seed phantom data sets, it is evident that the $SSQD$ does not exactly converge to zero (i.e., less than 3% difference between measured and computed seed images), showing less than optimal convergence. To improve the accuracy of the reconstructed seed positions in the patient study, we used a two-step blurring scheme as described earlier.

III.B. Patient study

For each of the four postimplant prostate patient data sets, we followed the two-stage iterative process as described in Sec. II C 3. Figure 6 illustrates the convergence process for the 81-seed implant performed on patient III. Three projections, at 0° and $\pm 20^\circ$ gantry angle, were used. Column (a) shows the initial seed configuration estimate derived from the TRUS-based preplan while column (d) shows the projections acquired four weeks after the procedure. Columns (b) and (c) show projections of the converged seed configurations for the initial (σ_1) and final (σ_2) Gaussian blurring models. Comparison of (c) and (d) shows good agreement, including successful replication of overlapping seed clusters, which appear as brighter or elongated seed features in the images. For this case, the first stage (Gaussian width $\sigma_1=3.6$ mm) required 23 iterations with a computation time of about 2.4 min/iteration and five iterations in the second stage ($\sigma_2=2.4$ mm), with a computation time of about 2.8 min/iteration on a 1 GHz processor. Figure 7 shows the two-stage convergence rate of the objective function for the four example patient cases. An example of the reconstructed seed

FIG. 7. The similarity metric convergence for the two-step IFPM algorithm for the four patient cases. The arrow in the bottom of the figure indicates the transition from larger to smaller Gaussian spread for patient III. The one-dimensional image-intensity profiles in the inset illustrate the capture ranges of the two-step filtering operations.

positions projected on the digital simulator images is presented in Figs. 8(a)–8(c). The distribution of nearest-neighbor distances between the computed and measured projected seed centroids is presented in Fig. 9. The RMS errors are (0.78 ± 0.56) (0°), (0.89 ± 0.49) ($+20^\circ$), and (0.82 ± 0.54) mm (-20°), respectively. We see that most seed positions agree to within 1.5 mm and no error exceeds 2.5 mm in the detector plane.

For patient III, Fig. 10 shows the seed-by-seed vector displacement between IFPM and VariSeed seed coordinates. The mean values along the x, y, and z directions were found to be (0.22 ± 0.96) , (-0.24 ± 0.97) , and (0.23 ± 0.92) mm, respectively. The 3D RMS error was (1.58 ± 0.56) mm. The comparison is summarized for all four patients in Table I. Since we do not know the ground truth for the patient study, this seed localization error includes not only the error from the IFPM algorithm but also the error contributed by the

FIG. 8. Superposition of measured seed images (white seeds) with automatically detected seed positions (black markers) projected on the detector planes. (a) 0° gantry angle, (b) -20° gantry angle, and (c) $+20^\circ$ gantry angle for patient III. While many seeds coincided exactly, a few still exhibit significant discrepancies.

FIG. 9. Seed registration error calculated from the nearest-neighbor distance between measured and computed seed position on each detector plane for patient III. The RMS error was found to be (0.78 ± 0.56) (0°), (0.89 ± 0.49) ($+20^\circ$), and (0.82 ± 0.54) mm (-20°) gantry angles, respectively.

VariSeed planning system. Table I also shows the residual 2D registration error between the measured and computed seed projections in each image plane. In all cases, the RMS value of the seed registration error is within 1 mm and the maximum seed displacement ($d_{\max}$) did not exceed 2.5 mm. Increasing the number of projections from three to six reduces this error by a factor of $\sqrt{2}$ at the cost of doubling computation time.

In Fig. 11, we overlay measured seed images (white seeds) with automatically detected seed positions (black markers) projected on the detector planes for patient IV, who presented an example of incomplete data due to more seeds existing in the preplan than observed on postimplant projections (i.e., missing seeds). In this case, the clinical records (and preplan) showed that 60 ^{103}Pd seeds were implanted, but only 59 seeds could be localized on the postimplant images acquired 4 weeks after the procedure. Thus the 3D model seed configuration had one more seed than was present in the computed images; gantry angle 0° is shown in Fig. 11(a), -20° is shown in Fig. 11(b), and $+18^\circ$ is shown in Fig. 11(c), respectively. The red circle indicates the projected position of the extra seed in the 3D preplan, which has

FIG. 10. Seed-by-seed vector difference between IFPM coordinates and those obtained from the VariSeed planning system for patient III data sets.

TABLE I. Summary of the comparisons of the seed positions deduced by the IFPM algorithm and by the VariSeed planning system for all example case patients. The mean value, standard deviation (sd) in each of the three directions, and overall 3D RMS error is reported. The seed registration error in the 2D image plane in terms of RMS value. The sd and the maximum displacement ($d_{\max}$) of the seed is also presented.

Patient no.	Image viewpoint used (deg)	Total no. of iterations	IFPM vs VariSeed (mm)			3D RMS error	2D registration error in each image plane (mm)	
			$\bar{\delta}x \pm \text{sd}$	$\bar{\delta}y \pm \text{sd}$	$\bar{\delta}z \pm \text{sd}$		RMS error	$d_{\max}$
I	0	28	0.38 ± 0.97	0.20 ± 0.98	0.25 ± 0.87	1.64 ± 0.54	0.63 ± 0.86	1.96
	+15						0.74 ± 0.53	
	-16						0.78 ± 0.72	
II	180	25	0.35 ± 0.98	0.19 ± 1.08	0.26 ± 0.89	1.76 ± 0.59	0.82 ± 0.83	2.44
	-160						0.94 ± 0.74	
	+165						0.86 ± 0.92	
III	0	26	0.22 ± 0.96	-0.24 ± 0.97	0.23 ± 0.92	1.58 ± 0.56	0.78 ± 0.56	2.35
	-20						0.89 ± 0.49	
	+20						0.82 ± 0.54	
IV ^a	0	27	0.37 ± 1.16	-0.29 ± 1.04	0.28 ± 0.98	1.86 ± 0.68	0.83 ± 0.63	2.48
	-20						0.98 ± 1.22	
	+18						0.96 ± 0.82	

^aIncomplete data case.

no counterpart in the measured images. The IFPM algorithm converged robustly to an accurate estimate of the seed configuration that was only slightly perturbed in the vicinity of the extra seed. Comparing measured and computed seed images shows that the two-step iterative convergence process closely reproduces the desired seed distribution. In the same case of patient IV, the IFPM algorithm was able to account for seeds that had migrated as far as 5 mm from their pre-planned positions (which appear in the lower left corner of the postimplant images). Clusters of two to four overlapping seeds were also reproduced on the computed projections.

IV. DISCUSSION

We have experimentally validated a novel iterative forward projection matching method to reconstruct 3D brachytherapy seed coordinates from measured 2D projection images. The iterative process does not require one to establish seed correspondences between the projection images. Also, it

avoids the intraobserver and interobserver variability of seed finding that is often observed when using three-film methods.⁵⁻¹¹ It can correct for errors in the measured imaging geometry by iteratively adjusting the imaging gantry positions used in the iterative projection process.

Current clinical practice relies on reconstructed 3D CT images for reconstructing seed positions.^{21,22} As reported in the literature^{3,12} and found in our clinical experience with VariSeed planning, this method frequently finds more than the actual number of implanted seeds, as the same seed may appear in more than one slice. Also, the 3D CT method is hampered by metal streaking artifacts.

Because the spatial resolution of the seeds in the 2D image planes is superior to CT, IFPM has the potential to reconstruct 3D seed positions more accurately than the 3D CT method. By using CBCT projections, the IFPM method provides the potential for intraoperative brachytherapy planning. Several methods are available for reconstructing brachytherapy seeds from 2D projection images¹²⁻¹⁹ but they are limited by the requirement that all seeds must be accurately identified in each projection. It is a difficult problem because the large number of implanted seeds in a relatively small prostate volume often results in seed clustering and overlaps in the projections. Lee *et al.*²⁶ have proposed a fluoroscopy based algorithm to solve the overlapping seed problem using dimensionality reduction. A brachytherapy seed reconstruction method based on digital tomosynthesis has recently been applied in clinical practice.²⁷ In one clinical experience, nearly 20% of the implanted seeds overlapped with other seeds in at least one projection.¹⁹ Tubic *et al.*¹² have shown that their method can handle seed localization in small clusters of two or three overlapping seeds in the projection but fail to correctly reconstruct seeds in large clusters.

Our method reproduces overlapping seed clusters and highly migrated seeds in the postimplant data analysis by

FIG. 11. Overlay of the measured seed images (white seeds) with automatically detected seed positions (black markers) projected on the detector planes for patient IV, who presents with incomplete data: 60 seeds are thought to be implanted but only 59 seeds are found on the week four postimplant dosimetry study. Gantry angle 0° is shown in (a), -20° is shown in (b), and $+18^\circ$ is shown in part (c). The circle in part (b) indicates the extra seed found by IFPM at convergence. The IFPM algorithm converged accurately, recreating the identified 59 seed positions, including overlapping clustered and highly migrated seeds.

finding the best solution that accounts for the data available. In our approach, individual seed identities do not matter; the algorithm works with the images of the complete seed configuration so it can easily accommodate incomplete data as well. For the case of patient IV, which showed a missing seed on the measured projection images (i.e., incomplete data), the algorithm converged to an accurate solution that was only slightly perturbed near the extraneous seed. Identification of the extra seed(s) in this way allows one to modify the initial 3D seed configuration and to correct the preplan before rerunning the reconstruction.

To improve the accuracy of the seed localization validation study, we plan to design a more precise prostate seed implant phantom and test IFPM performance against a more accurate ground truth. Also, more extensive investigation of the initial estimate of the seed configurations as well as a more optimal search of the blurring parameter will be performed to further validate this algorithm. Other geometric uncertainties such as detector in/out of plane motion and inaccuracy in the magnification factor are also an area of future investigation.

For elongated seeds (such as the model 6711 ^{125}I seed, which has a 3 mm long by 0.5 mm diameter cylindrical marker), there are two additional degrees of freedom for each seed that describe their orientations in 3D space. The IFPM method described herein does not accurately localize seeds with highly elongated radiographic markers. This is because the disk-shaped binary seed image model assumed by the forward projector within the algorithm does not reproduce the binary images produced by cylindrical seeds in shape and size, which can vary from a small disk to highly elongated rectangles depending on seed orientation. The data presented here suggest that the IFPM algorithm works effectively for seeds with radio-opaque components having an aspect ratio no larger than the 2:1 ratio characteristic of the model 200 ^{103}Pd source. Other currently available brachytherapy seeds satisfying this constraint include the Prospera (North America Scientific Inc., Chatsworth, CA) model MED3631,²³ IsoAid (IsoAid LLC, Port Richey, FL) AdvantageTM model IAPd-103A,²⁴ and Best (Best Medical International, Inc., Springfield, VA) model 2335 sources.²⁵ Because sources with radio-opaque components with an aspect ratio larger than this dominate the market (i.e., model 6711 ^{125}I seed), our next developmental priority is to model entire elongated line seeds, allowing IFPM to estimate individual seed orientations as well as locations. IFPM is also being extended to localization of larger metal objects, e.g., surgical needles and brachytherapy applicators (i.e., tandem and colpostats).

V. CONCLUSIONS

In this paper, we described a clinically useful and refined implementation of the IFPM algorithm, which was described conceptually and tested on synthetic data sets by Murphy and Todor. Testing on phantoms demonstrates that seed localization error is ± 0.5 mm or better on average, which is less than the estimated uncertainty of the seed centroid coordi-

nates taken as the gold standard for validating accuracy. Application of the algorithm to four patient data sets demonstrates the potential for accurate implant reconstruction in clinical settings, with average 2D convergence errors less than 1 mm. The outcomes on these early test cases, while not comprehensive, suggest that IFPM performance is not negatively impacted by seed clusters or missing seeds. In its current form, clinical implementation of IFPM is limited to seed models containing internal radio-opaque markers with an aspect ratio of approximately 2:1 or less.

Postimplant imaging is currently done 4 weeks after implant but can potentially be done intraoperatively via CBCT to permit immediate postimplant dosimetry assessments. This requires a fast, automatic, and robust method to reconstruct the seed configuration at the time of implantation. The fully automatic IFPM algorithm is accurate, robust, and capable of completing a reconstruction in a few minutes using state-of-the-art workstations and is therefore a highly promising tool for implementing fusion-based intraoperative brachytherapy planning.

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