Reconstruction of brachytherapy seed positions and orientations from cone-beam CT x-ray projections via a novel iterative forward projection matching method

Damodar Pokhrel, Martin J. Murphy, Dorin A. Todor, Elisabeth Weiss, and Jeffrey F. Williamson^{a)}

Department of Radiation Oncology, School of Medicine, Virginia Commonwealth University, Richmond, Virginia 23298

(Received 8 June 2010; revised 15 November 2010; accepted for publication 16 November 2010; published 29 December 2010)

Purpose: To generalize and experimentally validate a novel algorithm for reconstructing the 3D pose (position and orientation) of implanted brachytherapy seeds from a set of a few measured 2D cone-beam CT (CBCT) x-ray projections.

Methods: The iterative forward projection matching (IFPM) algorithm was generalized to reconstruct the 3D pose, as well as the centroid, of brachytherapy seeds from three to ten measured 2D projections. The gIFPM algorithm finds the set of seed poses that minimizes the sum-of-squared-difference of the pixel-by-pixel intensities between computed and measured autosegmented radiographic projections of the implant. Numerical simulations of clinically realistic brachytherapy seed configurations were performed to demonstrate the proof of principle. An in-house machined brachytherapy phantom, which supports precise specification of seed position and orientation at known values for simulated implant geometries, was used to experimentally validate this algorithm. The phantom was scanned on an ACUITY CBCT digital simulator over a full 660 sinogram projections. Three to ten x-ray images were selected from the full set of CBCT sinogram projections and postprocessed to create binary seed-only images.

Results: In the numerical simulations, seed reconstruction position and orientation errors were approximately 0.6 mm and 5°, respectively. The physical phantom measurements demonstrated an absolute positional accuracy of (0.78 ± 0.57) mm or less. The θ and φ angle errors were found to be $(5.7 \pm 4.9)^\circ$ and $(6.0 \pm 4.1)^\circ$, respectively, or less when using three projections; with six projections, results were slightly better. The mean registration error was better than 1 mm/6° compared to the measured seed projections. Each test trial converged in 10–20 iterations with computation time of 12–18 min/iteration on a 1 GHz processor.

Conclusions: This work describes a novel, accurate, and completely automatic method for reconstructing seed orientations, as well as centroids, from a small number of radiographic projections, in support of intraoperative planning and adaptive replanning. Unlike standard back-projection methods, gIFPM avoids the need to match corresponding seed images on the projections. This algorithm also successfully reconstructs overlapping clustered and highly migrated seeds in the implant. The accuracy of better than 1 mm and 6° demonstrates that gIFPM has the potential to support 2D Task Group 43 calculations in clinical practice. © 2011 American Association of Physicists in Medicine. [DOI: [10.1118/1.3528220](https://doi.org/10.1118/1.3528220)]

Key words: brachytherapy seed orientation, localization, gIFPM, cone-beam CT, x-ray projections

I. INTRODUCTION

Postimplant localization of brachytherapy seeds implanted in the prostate allows for validation against the planned seed poses (positions and orientations) as well as the opportunity to recalculate the actual delivered dose. Transrectal ultrasound (TRUS) guidance implantation provides adequate imaging of the soft-tissue anatomy but is not able to accurately reconstruct individual seed poses relative to the prostate during or after the implantation.¹ Currently, postimplant CT is the standard of practice for evaluating and reporting dose;^{2–7} however, it does not allow for altering and optimizing the treatment plan intraoperatively. The 3D CT method is ham-

pered by metal streaking artifacts and limited spatial resolution due to slice thickness effects, as well as lack of intraoperative CT imaging capability.

With the introduction of dedicated ACUITY (Varian Medical System, Palo Alto, CA) cone-beam CT (CBCT) digital simulator for seed placement, we can combine the advantages of a rigidly mounted intraoperative imaging system for the both seed reconstruction and reconstruction of 3D anatomy of the patient, which could be used for contouring.⁸ However, the ACUITY CBCT imaging system in our procedure room requires about 4 min to acquire CT images and cannot provide useful images with the TRUS

probe and metal stirrups that are located within or occlude the field of view. Reconstructing seeds from a few sinogram projections can overcome some of the problems associated with the CT-based method, such as limited spatial resolution due to slice thickness effect, ambiguities created by the metal streaking artifacts, and reduced imaging time since neither a full sinogram nor a reconstructed 3D image are necessary. By fusing the seed coordinates reconstructed from radiographs with TRUS images,^{9–17} rapid intraoperative seed reconstruction can be combined with the higher soft-tissue contrast characteristic of TRUS.¹⁸ However, widely used conventional back-projection (BP) methods^{19–25} for localizing seeds from projection images require corresponding seed images in each projection to be matched. When a large number of elongated seeds are projected into a small area in each projection, it can be very difficult to completely resolve seed clusters and isolate each seed centroid.

As currently practiced, conventional seed localization techniques only attempt to find the center of the elongated line seeds (i.e., point-source approximation) for dose calculation. By directly measuring the individual 3D pose of each implanted brachytherapy seed, more accurate Monte Carlo-based dose calculations (or 2D TG-43 dose calculations²⁶) can be employed to include the effect of 2D anisotropy and interseed attenuation on the resultant dose distribution. Corbett *et al.*²⁷ found that incorporating 2D anisotropy functions into the dose calculation slightly improved ($\sim 1\%$) the dose volume histogram (DVH) accuracy relative to the isotropic point-seed model, but they did not report on local dose differences. However, for ¹²⁵I and ¹⁰³Pd implants, Lindsay *et al.*²⁸ showed that omitting 2D anisotropy corrections introduced large local dose variations that collectively exceeded 10% in 20%–40% of the target volume. Monte Carlo-based dose evaluations demonstrate that interseed attenuation^{29,30} may reduce D_{90} doses by as much as 5% and dose-calculation models that account for the local seed anisotropy³¹ may deviate by as much as 7.5% from one-dimensional point-source dose computations. While a few investigators have developed generalized BP^{32,33} and CT-based algorithms³⁴ for estimating seed orientation as well as position, they suffer from the same limitations as their more widely used centroid localization counterparts.

In a companion paper, we have introduced³⁵ and experimentally validated on both phantom and patient data sets a novel algorithm,³⁶ iterative forward projection matching (IFPM), which overcomes many of the disadvantages of CT-based and BP methods for localizing seed centroids from radiographic images. In this paper, we introduce a generalized IFPM (gIFPM) algorithm that allows reconstruction of seed orientations as well as positions. gIFPM uses a model of the projection geometry and preplan seed positions and then iteratively adjusts the imaging system model parameters and the 3D seed poses to maximize agreement between the computed forward projections and measured (acquired) projections. Our method eliminates the need to match corresponding seed images, resolves overlapping seed clusters, and has the potential to accommodate incomplete data due to missing

FIG. 1. Elongated line seed of length L is characterized by the seed center (black dot) positions (x, y, z) and orientation coordinates (θ, ϕ) angle pair in the world coordinates frame, where z is the axis of implantation.

seeds. We demonstrate the accuracy and robustness of five degrees of freedom gIFPM using both synthetic data sets and experimentally measured projections of an in-house precision-machined prostate seed implant phantom.

II. MATERIALS AND METHODS

II.A. Generalized IFPM algorithm

The IFPM algorithm³⁶ was adapted from Murphy and Todor³⁵ and generalized to reconstruct seed orientations as well as positions. This expanded line-seed model requires five free pose parameters $(x, y, z, \theta, \phi)_k$ for each of the seeds $k=1, \dots, N$ in the world coordinate system where, $\mathbf{r}_k = (x, y, z)_k$ denotes the coordinates of the k th seed center and $(\theta, \phi)_k$ describes its orientation. The length of the radiographically visible seed components is denoted by L as shown in Fig. 1. A model of the CBCT projection geometry is made and positioned at M different locations and orientations specified by translation and rotation matrices $T_{x,y,z}$ and $[R]_{\alpha,\beta,\gamma}$ for each image viewpoint. The origin of the world coordinate is at the CBCT isocenter; the x axis is left-right, the y axis is anterior-posterior, and the z axis is superior-inferior direction for a patient in supine position with feet pointing away from the gantry stand. The three angles (α, β, γ) describe the orientation of CBCT central ray and detector panel relative to the three world coordinate system axes for each image viewpoint. In practice, $\alpha=90^\circ$, $\beta=0^\circ$, and γ is the gantry angle for each M image viewpoint. The detector model is parametrized by describing its magnification, image center, image size, and pixel resolution. The source-to-isocenter and isocenter-to-detector distances are denoted by S and D , respectively.

Each of the N seeds is characterized by its centroid location $\mathbf{r}_k$, direction cosines $\boldsymbol{\Omega}_k$ describing the k th seed axis orientation, and radiographically visible length L . The direction cosine vector is related to the original pose variables $(\theta, \phi)_k$ in the world coordinate system by

$$\boldsymbol{\Omega}_k = (\sin \theta \cos \phi, \sin \theta \sin \phi, \cos \theta)_k. \quad (1)$$

The end point coordinates of the seed marker are denoted by $\mathbf{r}_{2,k}$ and $\mathbf{r}_{1,k}$, where $|\mathbf{r}_{2,k} - \mathbf{r}_{1,k}| = L$, so that $\mathbf{r}_{2,k} = (L/2) \cdot \mathbf{\Omega}_k + \mathbf{r}_k$ and $\mathbf{r}_{1,k} = -(L/2) \cdot \mathbf{\Omega}_k + \mathbf{r}_k$. In this study, we used either the Model 6711 ^{125}I seed (Medi-Physics Inc., Arlington Heights, IL) which has a 3.0 mm $\times$ 0.5 mm cylindrical radio-opaque marker for 6711, giving an $L=3$ mm or machined stainless steel cylinders of 0.8 mm $\times$ 4.5 mm having an $L=4.5$ mm. In general, each seed can be represented by a locus of points in the CBCT rotated and translated projection frame, such that $\{\mathbf{r}'\}_k = \{\mathbf{r}' | \mathbf{r}' = \mathbf{r}_k + \eta \mathbf{\Omega}_k, \eta \in [-L/2, L/2]\}$. In practice, the Bresenham line drawing algorithm³⁷ is used to represent each seed by a finite set of Q equally spaced points to represent the seed in the world coordinate frame, such that

$$\{\mathbf{r}'\}_k = \{\mathbf{r}'_{jk} | \mathbf{r}'_{jk} = \mathbf{r}_k + ((j-1) \cdot \delta l_k - L/2) \cdot \mathbf{\Omega}_k,$$

$$j = 1, \dots, Q, \quad (2)$$

where, $\delta l_k = L/(Q-1)$ is the interval between two adjacent points and $((j-1) \cdot \delta l_k - L/2) = L_k$ represents the total length of the k th seed.

Each member of $\{\mathbf{r}'\}_k$ projects onto the detector plane defined by gantry angle γ with coordinates $(u'_{jk}, v'_{jk})_\gamma$ in each rotated and translated image plane. Then, we obtained the initial estimate of the computed binary image intensity $I_0(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \gamma)$, which is set to unity for all detector pixels (u, v) containing a projected point from the set $\{\mathbf{r}'\}_k$ and zero elsewhere. More explicitly, the digitized line-seed image pixels intensity is given by

$$I_0(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \gamma) = \begin{cases} 1 & \text{if } \exists j, k \text{ such that } P_\gamma(\mathbf{r}_{j,k}) \in (u, v), 1 \leq j \leq Q, 1 \leq k \leq N \\ 0 & \text{if not.} \end{cases}, \quad (3)$$

where $P_\gamma(\mathbf{r}) = (u'_k, v'_k)_\gamma$ are the coordinates of the point $\mathbf{r}$ in the detector plane for a gantry angle of γ and $\{\mathbf{r}_k, \mathbf{\Omega}_k\}$ denotes the set of N seed centroids and direction cosines.

The projected seeds on the detector plane were dilated 1 pixel along each direction, yielding a line segment of uniform brightness and thickness t , which is approximately equal to the width of the shadow cast by a Model 6711 ^{125}I 0.5 mm diameter radiographic marker. This ensured that each computed binary seed projection had approximately the same shape and size as binary seed images segmented from experimentally acquired projections. In our notation, the index j is dropped because after projecting the points corresponding to a line seed, it was represented by a line segment of uniform intensity on the 2D detector plane. The binary mask representation of the projected line seed was then blurred by convolving it with a 2D Gaussian blurring function with a standard deviation σ . For a set of N line seeds projected from the world frame then the total computed image is

$$I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) = \sum_k \sum_{u'_k, v'_k} I_0(u'_k, v'_k | \mathbf{r}_k, \mathbf{\Omega}_k, \gamma) \times \exp[-(u - u'_k)^2 / 2\sigma^2 - (v - v'_k)^2 / 2\sigma^2], \quad (4)$$

where $(u - u'_k)$ and $(v - v'_k)$ denote the distances between the corresponding pixel centers. The main purpose of the Gaussian blurring is to create a continuous-value grayscale image to which a gradient-driven iterative search process can be applied. In the absence of any blurring on the images, large areas of the intensity map would have zero intensity, providing no gradient to guide the similarity minimization search. The blurring creates a “source attractive” potential well around each seed, with tails extending beyond the seed foot-

print, causing computed seed images to be pulled toward measured seed images and accelerating the convergence of the iterative minimization search.

The metric sum-of-squared-difference (SSQD), which describes the “similarity” between all grayscale images $I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma)$ of a candidate set of the seed poses $\{\mathbf{r}_k, \mathbf{\Omega}_k\}$ and the corresponding experimentally acquired or “measured” images $I_m(u, v | \sigma, \gamma)$ at nominal gantry angle γ , is given by

$$\text{SSQD}(\{\mathbf{r}_k, \mathbf{\Omega}_k\} | \sigma, \gamma) = \sum_\gamma \sum_{u, v} [I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) - I_m(u, v | \sigma, \gamma)]^2. \quad (5)$$

The seed pose parameters $\{\mathbf{r}_k, \mathbf{\Omega}_k\}$ were iteratively adjusted by simultaneously adjusting the seed poses and the imaging viewpoint parameters relative to the first projection^{35,36} (i.e., 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) and then computing updated $I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma)$. By allowing the projection viewpoints to vary, we were able to correct for imprecision in the measured gantry positions and thereby obtain a more precise projection match. The parameter adjustments were calculated from the first derivatives of SSQD with respect to each degree of freedom. For example, the derivative with respect to the x -coordinate of the k th seed was computed as follows:

$$\partial(\text{SSQD}) / \partial x_k = 2 \sum_\gamma \left(\sum_{u, v} [I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) - I_m(u, v | \sigma, \gamma)] \partial I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) / \partial x_k \right). \quad (6)$$

Because the image grayscale intensities are represented entirely by the Gaussian blurring function, the grayscale image gradient $\partial I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) / \partial x_k$ for each seed was calculated analytically from Eq. (4) for that degree of freedom. Similarly, we computed the first derivatives of SSQD with respect to the other spatial and angular coordinates. Detailed derivations of the gradient calculation can be found in the Appendix.

After computing the analytical gradients to adjust all free parameters, the process iteratively refined the 3D seed's pose and each imaging viewpoint parameter (except first projection) until the computed projections optimally matched the measured projections of the seed geometry. 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 projections with corresponding imaging geometry are required for a stable reconstruction process. The $5N$ seed pose plus six $(M-1)$ degrees of freedom for the relative viewpoints (i.e., excluding the first fixed projection) are the freely moveable parameters in each iteration, where M is the total number of projections.

To iteratively adjust the free parameters leading to the minimization of SSQD, we used a nonlinear gradient search method^{35,36} that combined a steepest descent gradient search with a parabolic approximation of the SSQD surface around the global minimum.

For overlapping clusters and highly migrated seeds, it was observed that the computed seed pose at convergence varied somewhat with initial starting configuration. This indicated less than optimal convergence matching. For example, if the initial seed position estimates are far from the measured configuration, the gIFPM algorithm may not converge to an optimal configuration. To improve the accuracy in such settings, we applied a two-step adaptive blurring scheme in which a larger 2D Gaussian blurring (i.e., σ_1) was used for the initial iterations. The output of the first-step convergence was taken and used as an initial estimate with a reduced Gaussian spreading (i.e., σ_2) for the remaining iterations. The two-step blurring strategy used a more diffuse computed image with a larger capture range in the beginning to draw the computed seeds closer to the measured ones and then increased the sharpness of the computed image to improve accuracy at the final convergence. The optimal values of two-step blurring σ_1 and σ_2 were obtained from trial and error for each seed configuration and were between (3.0–2.2) mm and (2.0–1.4) mm, respectively.

II.B. Validation via simulated implant geometries

The numerical simulation studies used computational models of configurations of 56–70 elongated line-seed sources in 3D space. Clinically realistic initial estimates of the seed configuration and synthetically produced projections were obtained from patient preplans based on a pretreatment ultrasound volume study, which give the centroid coordinates $\{\mathbf{r}_k\}$ relative to the planning target volume for each patient. Since our gIFPM algorithm used the CBCT reference frame,

the TRUS-based preplan coordinates were transformed to the CBCT coordinate system by using rotation, translation, and scaling.

Then line seeds of length L (3.0 mm $\times$ 0.5 mm cylindrical radio-opaque marker of Model 6711 ¹²⁵I seed) were centered at the transformed $\{\mathbf{r}_k\}$ centroid coordinates and aligned with the axis of implantation (i.e., $\theta=0$, $\varphi=0$) which we called the “straight seed” implant. This was our initial estimate of the implant seed configuration. The 3D position of each seed in the configuration was shifted by a displacement, $\mathbf{d}_k$ randomly sampled from the uniform distribution $[-2$ mm, 2 mm] in each of the three directions, resulting in a mean displacement of 1.98 mm. The θ and φ values were randomly sampled from the uniform $[-\pi/6, \pi/6]$ and $[-\pi/2, \pi/2]$ distributions, respectively. To simulate migrated seeds in the implant, we manually adjusted the 3D pose of a few seeds after perturbing the configuration. These configurations were used to compute three “synthetic measured” projection images, i.e., projections of the configuration that we wished to determine. The source-to-isocenter distance was 100 cm and source-to-detector distance was 150 cm. The images were 288×288 pixels square and had a resolution of 0.388 mm/pixel.

The accuracy of each trial was quantified by calculating the root-mean-square (RMS) difference and the standard deviation between the estimated and known 3D seed poses.

II.C. Validation via physical phantoms

A validation phantom (see Fig. 2) was designed and fabricated from eight interchangeable 9.5 cm $\times$ 9.5 cm $\times$ 0.6 cm acrylic slabs, allowing up to 100 decayed Model 6711 ¹²⁵I seeds to be placed at known locations and orientations. Each slab, which represents a single plane of seeds, contains 10 mm diameter removable cylindrical plugs, each of which can contain a single dummy seed. The position and polar orientation θ of each seed are determined by the location and angle (with respect to plug rotational axis) of the seed cavity created by a digital milling machine. The azimuthal angle φ can be controlled by rotating the plug within its slab and is quantified by means of an angular scale [see Fig. 2(a)]. Because plugs and planes are interchangeable, one can realize many different seed configurations. The seeds were arranged in rectilinear layers separated by 6 mm, with 6–10 mm interseed (center-to-center) spacing within each slab. Up to ten clusters of as many as five seeds were physically modeled in the implants (for example, see Fig. 3) in order to test the robustness of gIFPM in the presence of both clustered and nonoverlapping seeds. The slabs are held in rigid configuration by placing them inside a hollow acrylic rectangular box designed for this purpose [see Fig. 2(b)] prior to scanning. The positional accuracy of the known 3D seed centroids of the precision-machined phantom was ± 0.1 mm in each of the three directions and about 1° angular accuracy for the θ and φ angle pair.

Initial estimates of each seed configuration were obtained by randomly perturbing the known 3D seed configuration as described earlier. The initial estimates of θ and φ values were

FIG. 2. Close-up photographs of (a) an acrylic slab of the phantom containing Model 6711 ^{125}I seeds, where the polar angle θ was defined as the angle between the implant axis and the major axis of the seed. It was assigned across the slab at different orientation for each seed (see inset). The azimuthal angle φ was assigned by using the adjustable reference grid drawn for each seed in known orientation. (b) Multiconfiguration precision-machined phantom assembly with all eight replaceable slabs. This phantom was used to create different seed configurations to test the gIFPM algorithm seed localization accuracy in the clinical setting.

also randomly sampled from the uniform $[-\pi/6, \pi/6]$ and $[-\pi/2, \pi/2]$ distributions, respectively. To make the computed projection images, the perturbed seeds configuration was rotated and translated to each imaging viewpoint and then projected on the (u, v) detector planes. The seed centroids were transformed to obtain extended line seeds before making projections as described in Sec. II A.

In this study, three clinically realistic brachytherapy seed configurations containing totals of 50, 72 and 76 seed data sets were realized on the phantom. For the 50 seed case, decayed Model 6711 ^{125}I seeds obtained from Oncura Inc. (Arlington Heights, IL) were used. In that case, we modeled only 3 mm radiographically visible radio-opaque marker. For the remaining cases, machined stainless steel cylinders (4.5 mm long by 0.8 mm in diameter) were used.

II.D. Acquisition and processing of radiographic projections

To experimentally validate this algorithm, the phantom was imaged on a Varian ACUITY CBCT imaging system

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) binary seed-only bitmap image, and (d) blurred grayscale image using the gIFPM algorithm for 76 seed phantom data sets.

which is used for performing image-guided brachytherapy insertions in our dedicated brachytherapy suite. The ACUITY system can be operated in CBCT, fluoroscopic, or radiographic mode. CBCT images of the phantom were acquired for a complete gantry rotation around the phantom capturing approximately 660 projections through 360° using a Varian 4030CB flat panel detector. The detector is $40\text{ cm} \times 30\text{ cm}$ with a 1024×768 image size and resolution of 0.388 mm/pixel and a 16-bit depth. The ACUITY imaging geometry consists of a 100 cm source-to-isocenter distance and a 150 cm source-to-detector distance. Three to ten radiographic projections at 5° – 10° angular intervals were selected from the full set CBCT x-ray projections between $\pm 30^\circ$ gantry angles. The choice of perspectives was based on maximizing visibility of the implanted seeds in the projections and avoiding excessively small parallaxes.

The postprocessing involved (a) cropping the images to 288×288 pixels square; (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 binary line-seed images in each projection in order to separate the seeds from the background. This process resulted in binary bitmap images with zero intensity in the background and intensity one over the area of each projected line seed.

The gIFPM method does not require transforming cylindrical seed images into pointlike landmarks. Instead we match elongated line-seed features in the 2D images including overlapping seed clusters. This avoids a major difficulty encountered by back-projection methods: Resolving seed clusters and isolating each seed centroid before reconstruction. The binary images were then convolved with the same 2D Gaussian blurring function that is used for the computed projection to create diffuse elongated seed lines with a known intensity distribution. This produces smoothly vary-

ing grayscale image gradients that can be calculated analytically in the computed projections to guide toward minimization of the objective function, SSQD, and speed up the convergence of the matching process. An example case of image postprocessing is shown in Fig. 3. Our previous work³⁶ included four patient cases in which IFPM was used to reconstruct the centroids of the Model 200 ¹⁰³Pd seed radiographic markers. In that experience, our segmentation and image postprocessing algorithms encountered no difficulties.

II.E. Assessment of the seed reconstruction/registration error

In the simulated implant study, the accuracy of each trial was quantified by calculating the RMS difference and the standard deviation between all estimated and true/synthetic measured 3D pose parameters.

For the phantom studies, the seed reconstruction error was quantified in three ways. First, the seed reconstruction error was computed by directly comparing the computed seed coordinates with the known seed poses obtained from the precision-machined phantoms. In the second approach, the seed registration error was evaluated by reprojecting the gIFPM line-seed pose at convergence onto the 2D image planes, overlaying the computed and measured seed projection, and calculating the nearest-neighbor difference between the measured and computed seed poses in each image plane. In this approach, for all nonclustered computed seed images, we empirically calculated the seed centroids (center of mass of each seed region) and orientation angles (angle between the x -axis and the major axis of each seed) in each 2D image plane and compared to those obtained from the measured seed images at convergence.

In the third approach, we compared the gIFPM positional coordinates to those obtained by the VARISEED planning 8.0 software (Varian Medical System, Palo Alto, CA) operating on the CBCT data set reconstructed from the same set of projections, from which the gIFPM measured projections were selected. The VARISEED automatic seed finder tool was used. Since VARISEED frequently detected more seeds than were actually implanted, manual corrections were performed to estimate the approximate seeds locations. As VARISEED does not provide the individual seed orientations coordinate, we compared only the seed centroids. Accuracy was quantified in terms of the minimum 3D distance between each gIFPM seed centroid position and the nearest VARISEED seed location. The seed reconstruction error was quantified by computing the vector and scalar displacement between the gIFPM and VARISEED positions. VARISEED seed centroids have limited accuracy due to the CT partial volume artifacts, metal streaking artifacts, and difficulty in resolving overlapping seed clusters. These uncertainties were included in our estimation of the accuracy of the gIFPM solution for the seed positions.

FIG. 4. An illustration of the convergence process for a 60 seed simulated implant. (a) Initial estimated seed configuration with straight seeds derived from a patient preplan, (b) computed images after convergence with $\sigma_1 = 2.8$ mm, (c) computed images after convergence with $\sigma_2 = 1.8$ mm and using poses (b) as the initial configuration, and (d) the true/synthetic measured images, where the rows represent different gantry angles. The gIFPM algorithm was able to reproduce orientation of each individual seed including overlapping clustered and highly migrated seeds.

III. RESULTS

III.A. Simulated implants

In Fig. 4 we illustrate an example of the iterative matching process for a simulated implant consisting of 60 seeds. The three projections have gantry angles of 0° and $\pm 30^\circ$. The initial seed configuration was obtained from a patient's preprocedure planned implant geometry assuming the seed axes to be parallel to the gantry axis. Comparison of the final computed images [Fig. 4(c)] to the measured images [Fig. 4(d)] shows excellent agreement, including reproducing overlapping seed clusters which appear as brighter and/or extended seed group image features. The gIFPM algorithm successfully found seeds that were placed as far as 5 mm from their preplanned positions. This case required 11 iterations in the first step (Gaussian width, $\sigma_1 = 2.8$ mm) with computation time of about 12 min/iteration and four iterations in the second step ($\sigma_2 = 1.8$ mm), with computation time of about 16 min/iteration on a 1 GHz processor (computation time depended on number of seeds used in the implants, i.e., the number of free parameters to optimize in each iteration).

Figure 5 shows the convergence of the objective function score for the four simulated patient implants, where the black arrow indicates the plateau regions of the similarity when switching from first step to second step iterations. Similar transitions can be seen for the other patient cases convergence histories. For the 60 seed test case, from one-to-one correspondence between the true/synthetic measured and computed sets of seed coordinates, the gIFPM absolute accuracy was (0.53 ± 0.43) mm for position and $(3.9 \pm 2.7)^\circ$ and $(4.4 \pm 3.8)^\circ$ for polar and azimuthal angles, respectively. Figure 6 shows the histograms of the seed localization errors. More than 98% of the reconstructed seed positions are within

FIG. 5. The similarity metric score vs iteration number for the two-step gIFPM algorithm for the four simulated patient cases: 56, 60, 66, and 70 seed configurations. The transition from larger to smaller blurring for the 66 seed configuration is shown by the black arrow. The one-dimensional image-intensity profiles in the inset illustrate the difference in capture range for the two blurring levels.

1 mm of their true positions and more than 95% of the reconstructed seed orientations are within 5° of their true orientations.

Several experiments were performed to test the accuracy and robustness of the gIFPM algorithm, including arranging the seed geometry to simulate seed clusters and overlaps of increasing complexity in more than one or more projections, e.g., two or three seeds overlapping in one or more than one projection, etc. Figure 4 illustrates successful resolution of more than four seed clusters consisting of up to five seeds in the cluster on more than one projection. We found that gIFPM could accurately determine seed poses with clusters

FIG. 6. Histograms of the seed localization error for the 60 seed simulated patient configuration. (a) Positional error in terms of 3D distance between reconstructed and true location and (b) orientation error. The gIFPM absolute accuracy was (0.53 ± 0.43) mm for position and $(3.7 \pm 2.7)^\circ$ and $(4.5 \pm 3.8)^\circ$ for θ and φ angles, respectively.

consisting of as many as five seeds. Table I summarizes the accuracy of gIFPM reconstructions for four simulated implants derived from patient cases. In all cases, the RMS seed position error was less than 0.7 mm and the maximum error did not exceed 1.5 mm. The RMS orientation errors were found to be about 5° for the both angular coordinates.

TABLE I. Accuracy of gIFPM reconstructed poses for four simulated implants derived from patient preplans. The RMS value and standard deviation for the positional and orientation coordinates are reported. The maximum displacement (Max. error) of the seed position is also reported.

Patient no. (no. of seeds)	Gantry angles (deg)	Total no. of iterations	gIFPM vs true seed pose			
			RMS error in seed position (mm)	Max. error (mm)	RMS error in seed orientation (deg)	
					θ	φ
I (56)	0	15	0.63 ± 0.45	1.32	4.4 ± 3.2	5.3 ± 3.1
	+20					
	-20					
II (60)	0	14	0.53 ± 0.43	1.19	3.9 ± 2.7	4.4 ± 3.8
	-30					
	+30					
III (66) ^a	0	11	0.68 ± 0.54	1.46	5.2 ± 5.7	5.8 ± 5.3
	-20					
	+20					
IV (70)	0	16	0.65 ± 0.52	1.38	6.0 ± 2.8	6.2 ± 3.2
	+30					
	-30					

^aTwo extra seeds in the preplan.

FIG. 7. Illustration of gIFPM seed reconstruction for simulated case III in Table I for a single projection. In the first row (+20°), 66 seeds are present in the simulated implant derived from the preplan but 68 are assumed in the initial seed configuration (a) with seed axes parallel to the gantry axis. In the second row (+20°), 66 seeds are present both in the initial estimated configuration and in the simulated implant, along with an additional seedlike artifact which is present in the measured images. (a) Initial estimate of the seed configuration, (b) computed images at final convergence, (c) the synthetic measured images corresponding to the “true” seed configuration, and (d) difference between images (b) and (c). The ellipse and arrow in part (d) indicates the extra seed(s) found by gIFPM at convergence.

Figure 7 illustrates the convergence process for Table I, case III, in which ambiguities are created by incomplete (two seeds missing from the true implant but present in estimate) and excessive (one additional seedlike artifact in the measured projections with no counterpart in the computed images) data. Figure 7(d) shows in both cases that the two-step iterative convergence process closely reproduces the measured seed projections. However, the gIFPM algorithm converged robustly to an optimal solution of the seed configuration that was only slightly perturbed in the region adjacent to the additional or missing seed images. Since difference images readily identify the additional and/or missing seeds, gIFPM could be rerun with a modified initial configuration having the correct number seeds and/or seedlike objects, which would slightly improve reconstruction accuracy.

FIG. 8. The similarity metric score vs iteration number for the two-step gIFPM algorithm for the three example physical phantom seed configurations. The transition from larger to smaller blurring filter for the 50 seed configuration is highlighted by the black arrow.

III.B. Validation test with phantoms

Physical phantoms with different seed configurations were imaged in order to evaluate the gIFPM algorithm in a more clinically realistic setting. Figure 8 shows the convergence of the objective function for the three example seed configurations derived from the same phantom, where the black arrow indicates the plateau region where the algorithm transition from the larger to smaller Gaussian width.

As shown in Table II and Fig. 9, the phantom study shows good agreement between the generalized IFPM and the known seed coordinates realized by the phantom. Table II shows RMS reconstruction errors ranging from 0.56 to 0.78 mm with angular coordinate RMS errors ranging from 3° to 6°. These errors are only slightly larger than those of the idealized simulated implant study, indicating that the additional errors associated with determination of the seed poses in the phantom and ACUTY forward projection modeling errors are not significant. Increasing the number of projec-

TABLE II. Accuracy of seed poses deduced by the gIFPM algorithm for three seed configurations realized by our physical phantom and imaged on the VCU ACUTY system. The RMS value and standard deviation for the positional and orientation coordinates are reported while using three vs six experimentally acquired projections. The maximum displacement (Max. error) of the seed position is also reported.

No. of seeds	No. of projections	Total no. of iterations	gIFPM vs true seed pose			
			RMS error in seed position (mm)	Max. error (mm)	RMS error in orientation (deg)	
					θ	φ
76 ^a	3	19	0.78 ± 0.57	1.88	5.7 ± 4.9	6.0 ± 4.1
	6	21	0.67 ± 0.47	1.56	4.6 ± 3.6	4.5 ± 3.3
72 ^a	3	17	0.72 ± 0.48	1.74	5.0 ± 3.8	5.7 ± 3.3
	6	18	0.56 ± 0.52	1.37	3.8 ± 2.9	4.2 ± 3.7
50 ^b	3	15	0.75 ± 0.46	1.78	4.9 ± 3.3	5.3 ± 3.8
	6	16	0.59 ± 0.42	1.44	3.2 ± 2.8	4.3 ± 2.9

^aLine seed made up of stainless steel (4.5 mm long and 0.8 mm in diameter)

^bActual Model 6711 ¹²⁵I dummy seed (3.0 mm × 0.5 mm radio-opaque marker)

FIG. 9. Histograms of the seed localization error in 3D space between reconstructed and true pose for the 76 seed phantom configuration for three projection images. (a) Positional error and (b) orientation error. The RMS error was found to be (0.78 ± 0.57) mm for position. The θ and φ angle distributions were found to be $(5.7 \pm 4.9)^\circ$ and $(6.0 \pm 4.1)^\circ$, respectively.

tions from three to six reduced these errors by approximately a factor of $\sqrt{2}$ at the cost of doubling computation time. For the 76 seed phantom case, from one-to-one correspondence between the two sets of seed coordinates, the RMS error was (0.78 ± 0.57) mm. The θ and φ angle distributions were found to be $(5.7 \pm 4.9)^\circ$ and $(6.0 \pm 4.1)^\circ$, respectively, when using three projections. The seed reconstruction error is reported in the histograms of Fig. 9(a) show that 97% of the reconstructed seed positions are within 1.5 mm from the measured seed locations and [Fig. 9(b)] 95% of the reconstructed seed orientations are within 8° of their known orientations.

An example of the reconstructed seed configurations projected onto the imaging planes is presented in Fig. 10. For the subset of seed images that do not overlap, the residual 2D RMS error in computed vs. measured seed images were 0.69 ± 0.55 ($+5^\circ$), 0.83 ± 0.56 (-20°), and 0.79 ± 0.58 mm ($+20^\circ$) for nearest-neighbor displacement and $5.4 \pm 3.7^\circ$ ($+5^\circ$), $6.9 \pm 6.2^\circ$ (-20°), and $6.7 \pm 5.1^\circ$ ($+20^\circ$), respectively, for polar angle. This indicated very good agreement between measured and computed seed images.

Figure 11 shows the seed-by-seed vector displacement between gIFPM and VARISEED coordinates. The mean (and RMS) values along the x , y , and z directions were found to be 0.39 ± 1.02 (0.87 ± 0.54 mm), -0.27 ± 1.06 (0.90 ± 0.52 mm), and 0.35 ± 0.98 mm (0.72 ± 0.48 mm), respectively. The 3D RMS error was 1.69 ± 0.63 mm. This

FIG. 10. Superposition of measured (white) and computed (black) line-seed images projected on the detector planes for gantry angles of (a) $+5^\circ$, (b) -20° , and (c) $+20^\circ$ for 76 seed phantom configuration. While many computed seeds coincided exactly with the measured ones, a few still reveal small discrepancies.

level of agreement seems reasonable given uncertainties in VARISEED centroid localization due to metal streaking artifacts, partial volume averaging, and finite CT slice width.

IV. DISCUSSION

A novel IFPM algorithm has been successfully extended to the more complex five degrees of freedom problem of reconstructing the 3D pose, as well as centroid, of radio-opaque cylindrically symmetric implanted objects such as implanted brachytherapy seeds from a limited number of radiographic projections. The IFPM approach does not require a solution of the challenging NP3 seed image matching problems unlike standard BP methods. It avoids the intraobserver and interobserver variability in localizing seeds that is frequently observed on three-film methods.^{9–16} This method also allows the imaging viewpoints for the digitally reconstructed radiographs to be free parameters to adjust gantry angle uncertainties relative to the first projection. In addition, a novel precision-machined prostate seed implant phantom, capable of realizing multiple seed configurations with an accuracy of 0.1 mm, was developed for rigorously testing the new algorithm.

Several algorithms are available for reconstructing 3D seed pose, including seed orientation, from measured 2D projections.^{19,20,32,33} The algorithms presented by Tubic *et al.*^{19,20} use mathematical morphology to detect the center of

FIG. 11. Seed-by-seed vector difference between gIFPM positions and those obtained from the VARISEED planning system for 76 seed phantom data sets. The 3D RMS error was (1.69 ± 0.63) mm.

the seeds as well as their orientation on the 2D image plane. This information (seed center and orientation in 2D) was then used to perform 3D reconstruction of each individual seed including orientation.³⁸ However, their method fails to correctly reconstruct seeds in large clusters of more than three seeds. Another approach, proposed by Siebert *et al.*,³² separately back-projects the tip and end positions of each seed image and uses a heuristic search algorithm to efficiently solve the NP3 matching problem. While in principle this method identifies seed orientation, no quantitative data are shown. A promising brachytherapy seed reconstruction method using seven digital tomosynthesis projections has recently been applied to clinical data sets.³³ In their method, seed-only 3D binary images were obtained by back-projecting each detector pixel shadowed by an elongated seed based on prereconstruction binarization of each projection. They were then able to estimate orientation by finding the major and minor axes of the each reconstructed 3D binary voxel cluster. However, their method cannot distinguish between orientations of seed clusters and individual seeds. The methods discussed above all have the disadvantages of BP, including intolerance to incomplete and inconsistent data, as well as difficulty of resolving overlapping clusters. By accurately modeling each elongated line seed in 3D space and iteratively finding the best solution that accounts for the measured projections, our method explicitly detects the orientation of each individual seed and is capable of reproducing overlapping seed clusters and highly migrated seeds in the implants. By using a few CBCT projections, the gIFPM has the potential for fusion-based intraoperative brachytherapy planning.

Tubic and Beaulieu³⁴ have proposed a new brachytherapy seed reconstruction technique that seeks to extract seed pose by analyzing the seed projections in the raw CT sinograms rather than reconstructed CT images. Essentially, their method involves segmenting the sinusoidal trace produced by each seed and fitting a mathematical model to each trace from which the centroid (derived from centerline of trace) and orientation (modulation of trace width as a function of gantry angle) can be derived. By working with higher resolution sinograms, their method avoids the major difficulties of CT-based localization, such as limited spatial resolution due to slice thickness limitation and uncertainties created by metal streaking artifacts. Excellent results were obtained for an idealized 16 seed phantom. However, automatically segmenting the sinusoidal seed projections, especially in the presence of realistic anatomic structure and image noise, remains a significant and unsolved technical challenge. Similarly, detecting variable width traces, quantifying trace width, dealing with seeds normal to the scanner axis, and resolving tightly bunched seed clusters also challenge this algorithm. While we have not yet applied our five degrees of freedom gIFPM algorithm to actual clinical data, in our previous study,³⁶ our relatively simple filtering and segmentation algorithms were successfully applied to anterior and oblique x-ray images of four Model 200 ¹⁰³Pd seed implants.

The ¹²⁵I and ¹⁰³Pd seeds exhibit considerable anisotropy in their dose distributions due to their internal geometry. The

“self-attenuation” by the material along the seed major axis is the main cause for the seed anisotropy. However, identification of the seed orientations on CT images is difficult primarily because of the slice thickness and voxel size limitations. To avoid this difficulty, the AAPM TG-43 (Ref. 26) one-dimensional point-source approximation, employing an average distance-dependent anisotropy correction, the 1D anisotropy function, is used almost universally in clinical treatment planning. This approach is valid for a multiseed implant if all seed orientations are equally probable. However, Corbett *et al.*²⁷ demonstrated that the seeds are preferentially orientated along the needle directions based on the distribution of the polar angle θ , derived from analysis of seed projection angles on 1 month postimplant anterior-posterior radiographs of ten patients. By averaging the dose over an ensemble of ¹²⁵I implants with identical centroids but randomly sampled orientations from the above distributions, Corbett *et al.*²⁷ demonstrated that seed orientation had little effect on DVH parameters, e.g., D_{90} , commonly used for clinical dose specification.

However, the theoretical study presented by Prasad *et al.*³⁹ concluded that the actual dose rate may differ from the expected dose rate by a factor of 2 when taking account of the anisotropy of the individual seeds. In the postimplants geometry using ¹²⁵I and ¹⁰³Pd seed, Lindsay *et al.*²⁸ showed that the 1D TG-43 treatment of anisotropy resulted in significant local dose computation errors ($\pm 10\%$ for CTV and $\pm 5\%$ for the rectum) compared to the more accurate 2D line-seed model which requires specification of the seed orientation. However, none of these studies had available actual seed orientations for their studies nor did they present a practical method for measuring orientation. Our five parameter model allows the individual seed position and orientation distribution to be determined for each implant. By directly measuring the individual 3D pose of each implanted brachytherapy seed, our method allows the 3D dose distribution to be more rigorously computed using the full 2D TG-43 line-seed formalism.²⁶

As reported in the literature⁴⁰ and found in our clinical experience, metallic ¹⁰³Pd or ¹²⁵I seeds cause moderate to severe streaking artifacts on CBCT images which introduce errors in soft-tissue segmentation, deformable image registration, and CT-based dose calculation. Accurate identification of the metal seed boundary and its orientation in the sinogram projections is very useful for suppressing such artifacts by projecting each metal seed boundary onto the sinogram so that the missing soft-tissue information can be recovered by interpolation from the surrounding soft-tissue image texture. Reconstruction of CBCT images with corrected sinogram projections can then be performed. Thus, another application of gIFPM is aiding in the accurate identification of seed traces in support of interpolative sinogram corrections. By reducing streak and associated noise propagation artifacts, significant clinical value can be added to CBCT imaging for image-guided brachytherapy.

By subtracting the measured images from the computed images at convergence, in the current version of gIFPM, one can locate extra seed(s) in the implant. Future versions of

gIFPM will automatically correct for overcounted and undercounted seed(s) in the implant and rerun the reconstruction process to obtain a more optimal match. More extensive investigation of the initial estimate of the seed configurations using TRUS preimplant geometry of the actual patient will be performed to further validate this algorithm. This iterative pose search method has not been optimized for speed. Improving the computation efficiency is also an area of future development.

The data presented in this paper demonstrate that the gIFPM algorithm works effectively for seeds with radioopaque markers having aspect ratios of 6:1 or larger. Besides the Model 6711 ^{125}I seed, other seed models satisfying this constraint include the selectSeed,⁴¹ (Amersham 6733 seed, IsoAid Advantage, DraxImage LS-1, Source Tech Medical STM1251),⁴² symmetra,⁴³ Model 9011,⁴⁴ and Best Model 2301 (Ref. 45) sources. Our previous work³⁶ demonstrated that the three degrees of freedom IFPM algorithm cannot accurately estimate the centroids of such elongated seeds because of the requirement that computed projections produce seed shadows that closely approximate the shape and size of the actual seed binary images. The centroid-only IFPM localization algorithm was shown to accurately reconstruct the positions of Model 200 ^{103}Pd seeds, which contain cylindrical lead markers with a 2:1 aspect ratio. Thus, to apply IFPM reconstruction to Model 6711 ^{125}I implants, the gIFPM is essential. The gIFPM method is further being generalized to reconstruct larger and noncylindrically symmetric metal objects in brachytherapy treatment, e.g., intracavitary applicators (i.e., colpostats and tandem) of known but arbitrary shape from a small set of 2D x-ray projections.

V. CONCLUSION

We have presented a new approach to brachytherapy seed localization, gIFPM able to accurately recover the orientation as well as location of individual seeds within a densely implanted volume from a limited set of measured 2D x-ray projections. By knowing the full 3D pose of each implanted seed, more rigorous Monte Carlo-based or 2D TG-43 dose calculations can be performed. Based on both physical and simulated implants, seed reconstruction errors were about 0.7 mm and 6° for θ and φ angles. The algorithm exhibits robust performance in the presence of overlapping seed clusters, highly migrated seeds, erroneous seed count, and errors in specifying the radiographic projection geometry. By incorporating a five degrees of freedom search capability, the IFPM approach, which does not require matching of corresponding images on each projection, can be extended to localization of cylindrically symmetric objects, e.g., implanted fiducial markers, whose aspect ratios are 6:1 or larger. This algorithm is more robust and tolerant of incomplete data than back-projection and has the potential to make intraoperative dose reconstruction and adaptive replanning from fused TRUS images and a few quick radiographic projections feasible.

ACKNOWLEDGMENTS

This work was supported in part by grants from Varian Medical System and the National Institutes of Health (Grant No. P01 CA 116602). The authors would like to thank Virginia Gilbert of Virginia Commonwealth University (VCU) for her continuous support of collecting data. The authors are grateful to Dr. John Ford of VCU for proof reading the manuscript.

APPENDIX: ANALYTIC GRADIENT OF THE SIMILARITY, SSQD WITH RESPECT TO FIVE DEGREES OF FREEDOM OF EACH SEED

Recalling Eq. (2), for each line seed k in the rotated and translated CT frame,

$$\{\mathbf{r}'\}_k = \{\mathbf{r}'_{jk}\} \mathbf{r}'_{jk} = \mathbf{r}_k + ((j-1) \cdot \delta l_k - L/2) \cdot \boldsymbol{\Omega}_k, \quad j = 1, \dots, Q, \quad (\text{A1})$$

where $j=1, \dots, Q$ is a finite set of Q points spaced at interval $\delta l_k = L/(Q-1)$ that represents the k th seed.

Now, rotate and translate the CT frame to the each projection coordinate system (in which z axis corresponds with its central axis), rewriting Eq. (A1) more explicitly,

$$\begin{aligned} \begin{Bmatrix} x' \\ y' \\ z' \end{Bmatrix}_k &= [R]_{\alpha,\beta,\gamma} \begin{Bmatrix} x_j \\ y_j \\ z_j \end{Bmatrix}_k + ((j-1) \cdot \delta l_k - L/2) \\ &\quad \times \begin{Bmatrix} \sin \theta \cos \varphi \\ \sin \theta \sin \varphi \\ \cos \theta \end{Bmatrix} - T_{x,y,z}, \end{aligned} \quad (\text{A2})$$

where

$$[R]_{\alpha,\beta,\gamma} = \begin{bmatrix} R_{11} & R_{12} & R_{13} \\ R_{21} & R_{22} & R_{23} \\ R_{31} & R_{32} & R_{33} \end{bmatrix}_{\alpha,\beta,\gamma}$$

is the complete rotation matrix for each image viewpoint and $((j-1) \cdot \delta l_k - L/2) = L_k$ represents the total length of the k th seed. No translation is applied, i.e., $T_{x,y,z}=0$. The complete rotation matrix was obtained by taking the product of the three rotation matrices defined in the world coordinate system, for each image viewpoint. The line seeds in the CT frame project to the detector plane (u, v) are given by

$$(u'_k, v'_k) = M(z'_k)(x'_k, y'_k), \quad (\text{A3})$$

where $M_k = (S+D/S+z'_k)$ is the magnification factor, which is different for each end points; S and D are the source-to-isocenter and isocenter-to-detector distances, respectively. Since, the brachytherapy line seed has rotational symmetry around the axis of rotation, we computed one derivative per seed per degree of freedom with respect to the each seed center coordinates (note that the index j has been dropped). From Eq. (4), the image grayscale gradient for x degree of freedom was calculated as follows:

$$I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) / \partial x_k \\ = \sum_k \sum_{u'_k, v'_k} (I_0(u'_k, v'_k | \mathbf{r}_k, \mathbf{\Omega}_k, \gamma) / \sigma^2) [(u - u'_k) \partial u'_k / \partial x_k \\ + (v - v'_k) \partial v'_k / \partial x_k] \cdot g(u - u'_k, v - v'_k | \sigma), \quad (\text{A4})$$

where, $g(u - u'_k, v - v'_k | \sigma) = \exp[-(u - u'_k)^2 / 2\sigma^2 - (v - v'_k)^2 / 2\sigma^2]$ and γ is the gantry angle estimate of the imaging view-point.

Finally, from Eqs. (A2) and (A3), using chain rule, we get

$$\left. \begin{aligned} \partial u'_k / \partial x &= M_k [R11 - (R31)x'_k / (S + z'_k)] \\ \partial v'_k / \partial x &= M_k [R21 - (R31)y'_k / (S + z'_k)] \end{aligned} \right\} \quad (\text{A5})$$

and similarly for the y and z coordinates of each seed. The analytical gradient of the similarity SSQD with respect to θ -angle coordinate for each seed was calculated from Eq. (5) as follows:

$$\left. \begin{aligned} \partial u'_k / \partial \theta_k &= M_k L_k [(R11 \cos \theta \cos \varphi + R12 \cos \theta \sin \varphi - R13 \sin \theta) - (R31 \cos \theta \cos \varphi + R32 \cos \theta \sin \varphi - R33 \sin \theta) x'_k / (S + z'_k)] \\ \partial v'_k / \partial \theta_k &= M_k L_k [(R21 \cos \theta \cos \varphi + R22 \cos \theta \sin \varphi - R23 \sin \theta) - (R31 \cos \theta \cos \varphi + R32 \cos \theta \sin \varphi - R33 \sin \theta) y'_k / (S + z'_k)] \end{aligned} \right\} \quad (\text{A8})$$

Similarly, we have computed analytical gradient of SSQD with respect to φ -angle coordinate of each seed.

- ^{a)} Author to whom correspondence should be addressed. Electronic mail: jwilliamson@mcvh-vcu.edu; Telephone: 804-828-8451.
- ¹ B. H. Han, K. Wallner, G. Merrick, W. Butler, S. Sutlief, and J. Sylvester, "Prostate brachytherapy seed identification on post-implant TRUS images," *Med. Phys.* **30**, 898–900 (2003).
- ² W. S. Bice, D. F. Dubois, J. J. Prete, and B. R. Prestidge, "Source localization from axial image sets by iterative relaxation of nearest neighbor criterion," *Med. Phys.* **26**, 1919–1924 (1999).
- ³ J. N. Roy, K. E. Wallner, P. J. Harrington, C. C. Line, and L. L. Anderson, "A CT-based evaluation method for permanent implants: Applications to prostate," *Int. J. Radiat. Oncol., Biol., Phys.* **26**, 163–169 (1993).
- ⁴ Z. Li, I. A. Nalcacioglu, S. Ranka, S. K. Sahini, J. R. Palta, W. Tome, and S. Kim, "An algorithm for automatic, computed-tomography-based source localization after prostate implant," *Med. Phys.* **28**, 1410–1415 (2001).
- ⁵ D. H. Brinkmann and R. W. Kline, "Automated seed localization from CT datasets of the prostate," *Med. Phys.* **25**, 1667–1672 (1998).
- ⁶ H. Liu, G. Cheng, Y. Yu, R. Brasacchio, D. Rubens, J. Strang, L. Liao, and E. Messing, "Automatic localization of implanted seeds from post-implant CT images," *Phys. Med. Biol.* **48**, 1191–1203 (2003).
- ⁷ Y. Yu, L. L. Anderson, Z. Li, D. E. Mellenberg, R. Nath, M. C. Schell, F. M. Waterman, A. Wu, and J. C. Blasko, "Permanent prostate seed implant brachytherapy: Report of American Association of Physicists in Medicine Task Group Vol. 64," *Med. Phys.* **26**, 2054–2076 (1999).
- ⁸ H. Westendorp, C. J. Hoekstra, A. van't Riet, A. W. Minken, and J. J. Immerzeel, "Intraoperative adaptive brachytherapy of iodine-125 prostate implants guided by C-arm cone-beam computed tomography-based dosimetry," *Brachytherapy* **6**, 231–237 (2007).
- ⁹ A. Y. C. Fung, "C-Arm imaging for brachytherapy source reconstruction: Geometrical accuracy," *Med. Phys.* **29**, 724–726 (2002).
- ¹⁰ R. L. Siddon and L. M. Chin, "Two-film brachytherapy reconstruction algorithm," *Med. Phys.* **12**, 77–83 (1985).
- ¹¹ H. I. Amols and I. I. Rosen, "A three-film technique for reconstruction of radioactive seed implants," *Med. Phys.* **8**, 210–214 (1981).

$$\partial(SSQD) / \partial \theta_k = 2 \sum_{\gamma} \left(\sum_{u, v} [I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) - I_m(u, v | \sigma, \gamma)] \partial I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) / \partial \theta_k \right). \quad (\text{A6})$$

Again, from Eq. (4), we computed the image grayscale gradient with respect to θ degree of freedom

$$\partial I_c(u, v | \{\mathbf{r}_k, \mathbf{\Omega}_k\}, \sigma, \gamma) / \partial \theta_k \\ = \sum_k \sum_{u'_k, v'_k} (I_0(u'_k, v'_k | \mathbf{r}_k, \mathbf{\Omega}_k, \gamma) / \sigma^2) [(u - u'_k) \partial u'_k / \partial \theta_k \\ + (v - v'_k) \partial v'_k / \partial \theta_k] \cdot g(u - u'_k, v - v'_k | \sigma). \quad (\text{A7})$$

Finally, from Eqs. (A2) and (A3), using chain rule, we get,

- ¹² D. D. Jackson, "An automated method for localizing radioactive seeds in implant dosimetry," *Med. Phys.* **10**, 370–372 (1983).
- ¹³ P. J. Biggs and M. D. Kelley, "Geometric reconstruction of seed implants using a three-film technique," *Med. Phys.* **10**, 701–704 (1983).
- ¹⁴ M. D. Altschuler, P. A. Findlay, and R. D. Epperson, "Rapid accurate, three-dimensional location of multiple seeds in implant radiotherapy treatment planning," *Phys. Med. Biol.* **28**, 1305–1318 (1983).
- ¹⁵ M. S. Rosenthal and R. Nath, "An automatic seed identification technique for interstitial implants using three isocentric radiographs," *Med. Phys.* **10**, 475–479 (1983).
- ¹⁶ M. D. Altschuler and A. Kassaei, "Automated matching of corresponding seed images of three simulator radiographs to allow 3D triangulation of implanted seeds," *Phys. Med. Biol.* **42**, 293–302 (1997).
- ¹⁷ L. Gong, P. S. Cho, B. H. Han, K. E. Waller, S. G. Sutlief, S. D. Pathak, D. R. Haynor, and Y. Kim, "Ultrasoundography and fluoroscopic fusion for prostate brachytherapy dosimetry," *Int. J. Radiat. Oncol., Biol., Phys.* **54**, 1322–1330 (2002).
- ¹⁸ W. L. Smith, C. Lewis, G. Bauman, G. Rodrigues, D. D'Souza, R. Ash, D. Ho, V. Venkatesan, D. Downey, and A. Fenster, "Prostate volume contouring: A 3D analysis of segmentation using 3DTRUS, CT, and MR," *Int. J. Radiat. Oncol., Biol., Phys.* **67**, 1238–1247 (2007).
- ¹⁹ D. Tubic, A. Zaccarin, J. Pouliot, and L. Beaulieu, "Automated seed detection and three-dimensional reconstruction: I. Seed localization from fluoroscopic images or radiographs," *Med. Phys.* **28**, 2265–2271 (2001).
- ²⁰ D. Tubic, A. Zaccarin, L. Beaulieu, and J. Pouliot, "Automated seed detection and three-dimensional reconstruction: II. Reconstruction of permanent prostate implants using simulated annealing," *Med. Phys.* **28**, 2272–2279 (2001).
- ²¹ D. A. Todor, G. N. Cohen, H. I. Amols, and M. Zaider, "Operator-free, film-based 3D seed reconstruction in brachytherapy," *Phys. Med. Biol.* **47**, 2031–2048 (2002).
- ²² D. A. Todor, M. Zaider, G. N. Cohen, M. F. Worman, and M. J. Zelefsky, "Intraoperative dynamic dosimetry for prostate implants," *Phys. Med. Biol.* **48**, 1153–1171 (2003).
- ²³ S. Narayanan, P. S. Cho, and R. J. Marks II, "Fast cross-projection algorithm for reconstruction of seeds in prostate brachytherapy," *Med. Phys.* **29**, 1572–1579 (2002).

- ²⁴Y. Su, B. J. Davis, M. G. Herman, and R. A. Robb, "Prostate brachytherapy seed localization by analysis of multiple projections: Identifying and addressing the seed overlap problem," *Med. Phys.* **31**, 1277–1287 (2004).
- ²⁵S. Narayanan, P. S. Cho, and R. J. Marks II, "Three-dimensional seed reconstruction from an incomplete data set for prostate brachytherapy," *Phys. Med. Biol.* **49**, 3483–3494 (2004).
- ²⁶M. J. Rivard, B. M. Coursey, L. A. DeWerd, W. F. Hanson, M. S. Huq, G. S. Ibbott, M. G. Mitch, R. Nath, and J. F. Williamson, "Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations Dose distributions," *Med. Phys.* **31**, 633–674 (2004).
- ²⁷J. F. Corbett, J. J. Jezioranski, J. Crook, T. Tran, and I. W. T. Yeung, "The effect of seed orientation deviations on the quality of ¹²⁵I prostate implants," *Phys. Med. Biol.* **46**, 2785–2800 (2001).
- ²⁸P. Lindsay, J. Battista, and J. V. Dyk, "The effect of seed anisotropy on brachytherapy dose calculations using ¹²⁵I and ¹⁰³Pd," *Med. Phys.* **28**, 336–345 (2001).
- ²⁹H. Afsharpour, M. D'Amours, B. Cote, J.-F. Carrier, F. Verhaegen, and L. Beaulieu, "A Monte Carlo study on the effect of seed design on the interseed attenuation in permanent prostate implants," *Med. Phys.* **35**, 3671–3681 (2008).
- ³⁰J.-F. Carrier, L. Beaulieu, F. Therriault-Proulx, and R. Roy, "Impact of interseed attenuation and tissue composition for permanent prostate implants," *Med. Phys.* **33**, 595–604 (2006).
- ³¹O. Chibani, J. F. Williamson, and D. Todor, "Dosimetric effects of seed anisotropy and interseed attenuation for ¹⁰³Pd and ¹²⁵I prostate implants," *Med. Phys.* **32**, 2557–2566 (2005).
- ³²F.-A. Siebert, A. Srivastav, L. Kliemann, H. Fohlin, and G. Kovacs, "Three-dimensional reconstruction of seed implants by randomized rounding and visual evaluation," *Med. Phys.* **34**, 967–975 (2007).
- ³³M. Brunet-Benkhoucha, F. Verhaegen, S. Lassalle, D. B. Nadeau, B. Reniers, D. Donath, D. Taussky, and J.-F. Carrier, "Clinical implementation of a digital tomosynthesis-based seed reconstruction algorithm for intra-operative postimplant dose evaluation in low dose rate prostate brachytherapy," *Med. Phys.* **36**, 5235–5244 (2009).
- ³⁴D. Tubic and L. Beaulieu, "Sliding slice: A novel approach for high accuracy and automatic 3D localization of seeds from CT scans," *Med. Phys.* **32**, 163–174 (2004).
- ³⁵M. J. Murphy and D. A. Todor, "Demonstration of a forward iterative method to reconstruct brachytherapy seed configurations from x-ray projections," *Phys. Med. Biol.* **50**, 2715–2737 (2005).
- ³⁶D. Pokhrel, M. J. Murphy, D. A. Todor, E. Weiss, and J. F. Williamson, "Clinical application and validation of an iterative forward projection matching algorithm for permanent brachytherapy seed localization from cone beam-CT x-ray projections," *Med. Phys.* **37**, 5092–5101 (2010).
- ³⁷A. S. Glassner, *Graphics Gems* (Academic, London, 1990).
- ³⁸G. Leclerc, M.-C. Lavalée, D. Tubic, J. Metivier, E. Vigneault, and L. Beaulieu, "Idealized line source configuration for permanent ¹²⁵I prostate implants," *Radiother. Oncol.* **72**, 213–220 (2004).
- ³⁹S. C. Prasad, D. A. Bassano, and P. I. Fear, "Dose distributions for ¹²⁵I implants due to anisotropic radiation emission and unknown seed orientation," *Med. Phys.* **14**, 296–298 (1987).
- ⁴⁰D. J. Moseley, J. H. Siewerdsen, and D. A. Jaffary, "High-contrast object localization and removal in cone-beam CT," *Proc. SPIE* **5745**, 40–50 (2005).
- ⁴¹P. Karaiskos, P. Papagiannis, L. Sakellidou, G. Anagnostopoulos, and D. Baltas, "Monte Carlo dosimetry of the selectSeed ¹²⁵I interstitial brachytherapy seed," *Med. Phys.* **28**, 1753–60 (2001).
- ⁴²M. J. Rivard, W. M. Butler, L. A. DeWerd, M. S. Huq, G. S. Ibbott, A. S. Meigooni, C. S. Melhus, M. G. Mitch, R. Nath, and J. F. Williamson, "Supplement to the 2004 update of the AAPM Task Group No. 43 Report," *Med. Phys.* **34**, 2187–2205 (2007).
- ⁴³H. Hedtjärn, G. A. Carlsson, and J. F. Williamson, "Monte Carlo-aided dosimetry of the symmetra model I25.S06 ¹²⁵I, intestinal brachytherapy seed," *Med. Phys.* **27**, 1076–1085 (2000).
- ⁴⁴M. J. Rivard, "Monte Carlo radiation dose simulations and dosimetric comparison of the model 6711 and 9011 ¹²⁵I brachytherapy sources," *Med. Phys.* **36**, 486–491 (2009).
- ⁴⁵K. T. Sowards and A. S. Meigooni, "A Monte Carlo evaluation of the dosimetric characteristics of the Best Model 2301 ¹²⁵I brachytherapy source," *Appl. Radiat. Isot.* **57**, 327–333 (2002).