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Deformable registration of X-ray to MRI for post-implant dosimetry in prostate brachytherapy

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Abstract

Post-implant dosimetric assessment in prostate brachytherapy is typically performed using CT as the standard imaging modality. However, poor soft tissue contrast in CT causes significant variability in target contouring, resulting in incorrect dose calculations for organs of interest. CT-MR fusion-based approach has been advocated taking advantage of the complementary capabilities of CT (seed identification) and MRI (soft tissue visibility), and has proved to provide more accurate dosimetry calculations. However, seed segmentation in CT requires manual review, and the accuracy is limited by the reconstructed voxel resolution. In addition, CT deposits considerable amount of radiation to the patient. In this paper, we propose an X-ray and MRI based post-implant dosimetry approach. Implanted seeds are localized using three X-ray images by solving a combinatorial optimization problem, and the identified seeds are registered to MR images by an intensity-based points-to-volume registration. We pre-process the MR images using geometric and Gaussian filtering. To accommodate potential soft tissue deformation, our registration is performed in two steps, an initial affine transformation and local deformable registration. An evolutionary optimizer in conjunction with a points-to-volume similarity metric is used for the affine registration. Local prostate deformation and seed migration are then adjusted by the deformable registration step with external and internal force constraints. We tested our algorithm on six patient data sets, achieving registration error of (1.2 ± 0.8) mm in < 30 sec. Our proposed approach has the potential to be a fast and cost-effective solution for post-implant dosimetry with equivalent accuracy as the CT-MR fusion-based approach.

Keywords

Post-implant dosimetry; prostate brachytherapy; X-ray to MRI registration; deformable registration

1. INTRODUCTION

Permanent prostate brachytherapy (PPB) is one of standard treatment options for localized prostate cancer. PPB involves permanent implantation of 30–100 radioactive seeds in the prostate gland so that the seeds directly irradiate the target. The clinical outcome of PPB critically depends on the ability to treat the target with a sufficient amount of therapeutic

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dose while minimizing radiation toxicity to adjacent healthy tissues. To plan and guide the implantation, transrectal ultrasound (TRUS) is used as the intraoperative imaging modality in contemporary PPB. However, ultrasound images exhibit strong image intensities produced by multiple echoes from various sources including seeds, needles, and calcifications, which impedes accurate identification of seed locations and prostate boundary during the PPB procedure. To better predict the morbidity and assess the treatment quality of PPB, post-implant dosimetric assessment is therefore highly recommended.

Computed tomography (CT) has been generally considered as the standard imaging modality for post-implant dosimetry due to its wide availability in radiation oncology and the capability of seed identification. Unfortunately, there are considerable uncertainties in the contours of the prostate and organs at risk (OAR) due to poor soft tissue contrast in CT. This leads to large intra- and inter-observer variability in target contouring, thus critically impacting on the quality of CT-based dosimetry calculations. MRI shows excellent soft tissue contrast, and is therefore advantageous for contouring the prostate and OAR. The drawback of using MRI alone for post-implant dosimetry is the poor visualization of seeds as brachytherapy seeds generate no signal and appear as dark voids in MR images.

CT-MR fusion-based dosimetry has been advocated due to the complementary capabilities of CT and MRI. However, seed segmentation in CT still requires manual review and correction, and CT deposits considerable amount of radiation dose to the patient. In addition, CT and MR images are not acquired at the same imaging session, and there could be considerable tissue deformation between CT and MR images, which requires deformable registration. CT-MRI registration often fails as CT and MR images are highly uncorrelated, in which case, the fusion may be approximately done in a rigid way or may not be used.

To take advantages of CT-MR fusion-based approach while replacing the CT scan with fluoroscopy, Acher et al. [1] proposed to use a combined X-ray and MR imaging (XMR) system, which comprises a MRI scanner, a fluoroscopic C-arm, and a sliding table built in an interventional suite. The patient scan is carried out in the same room at the same position for both scans, and registration between fluoroscopy and MR images are given, which is the big advantage of the XMR-based dosimetry. This system has proven to produce post-implant dosimetry calculations that are similar to CT-MR fusion-based method. However, XMR system is a specially-designed system that requires a dedicated suite and is not widely available in most hospitals. Also, their seed reconstruction requires tedious manual seeds segmentation in X-rays.

In this paper, we propose to combine X-ray and MRI for post-implant dosimetry. The basic underlying idea is the same as Archer et al. [1], but instead of using a dedicated system, our method uses a mobile C-arm or on-board cone-beam imager equipped with a linear accelerator (LINAC) and MRI that are available in most hospitals.

2. METHODS

The proposed approach consists of two key components, 1) seed reconstruction from X-rays and 2) registration of the reconstructed seeds to MRI where the prostate and OAR are

contoured. To reconstruct seeds from X-rays, we will use our previously developed seed reconstruction algorithm, APC-REDMAPS (automatic pose correction – reduced dimensionality matching for prostate brachytherapy seed reconstruction) that simultaneously corrects X-ray image pose errors and reconstructs seeds as a point cloud [2, 3]. To reconstruct seeds, three X-ray images are first taken at different image pose using a mobile C-arm or an on-board cone-beam imager in LINAC. The collected images are processed for distortion correction and seed segmentation [4, 5]. APC-REDMAPS reconstructs seeds from the processed X-rays by solving a constrained combinatorial optimization problem. APC-REDMAPS has been extensively tested on simulations, phantom and clinical data sets, achieving superior performance to CT-based seed reconstruction with the seed localization error of $\sim 0.5\text{mm}$.

To register the reconstructed seeds to MR images, we first pre-process MR images and generate a smooth distance field from candidate seed regions by geometric filtering, distance transform, and Gaussian blurring. The pre-processed MR images are used to compute the similarity metric during registration. To initialize the registration, we align the centers of mass between the reconstructed seed cloud and the MR prostate volume. Affine registration is then performed between the initially aligned seeds and the pre-processed MR images to estimate the rigid transformation and scaling that accounts for the systematic prostate expansion/shrinkage caused by edema. Finally, deformable registration is performed to adjust local misalignment of individual seeds. Figure 1 shows the overall procedure of our approach. We now describe each step of our registration process in detail.

2.1 MRI pre-processing

In our study, we use T2-weighted MR images as they clearly show the prostate boundary. However, seeds do not generate any signal and are shown as dark voids in T2-weighted MR images as shown in figure 2(a). There are also a significant number of seed-like dark spots which make it difficult to reliably segment seeds solely based on MR image intensities. To reduce the number of false positives and extract potential candidate seeds, we pre-process MR images by circular and cylindrical filtering. To avoid directional bias when computing geometric properties, we resample MR images to have isotropic voxels with the finest resolution spacing among x , y , and z axes. We extract the prostate region of interest using the physician's contouring on MRI. We then apply a circular matched filter on each 2D axial slice to produce seed-highlighted images (see figure 2(c)) in which the image intensities are distributed as $I_C \in [0, 1]$.

Based on I_C , we find the voxels included in a cylindrical shape region with the implant dimension, $0.8 \times 5\text{mm}$ (diameter $\times$ height) in our experiments. Principal components analysis is performed in 3D at each connected candidate seed region whose $I_C > 0.5$ to find the shortest/longest direction and their lengths of the point distribution. Among the blobs whose height $\in (5 - \delta)\text{mm}$ and the ratio of the longest length to the shortest length $> r$, we search voxels within $(0.4 + e)\text{mm}$ around the longest centerline. $\delta = 1$, $r = 2$, and $e = 0.3$ are used in our experiments.

Next step is a distance map computation for the whole volume to determine how close an arbitrary point to the candidate seed regions. We segment the filtered images by thresholding to obtain binary candidate-seed-only images, I_T , and apply distance transform to the I_T as

$$I_D(x, y, z) = \min_{x_s, y_s} \sqrt{(x - x_s)^2 + (y - y_s)^2}, \text{ s.t. } I_T(x_s, y_s, z) = 1$$

Distance transform measures the distance between each pixel and the closest non-zero-pixel in the same slice. To achieve better convergence in our intensity-based registration, smoother seed-highlighted images are preferred. Finally, we blur the distance maps, I_D , by unit-height Gaussian function defined as $I_G(\mathbf{x}) = \exp(-I_D^2(\mathbf{x})/2\sigma^2)$, where σ determines the width of the blur. This binary seed generation and Gaussian smoothing approach was used for X-ray-based seed reconstruction [6] and ultrasound-fluoroscopy registration [7], improving the convergence of the associated optimization problem. Figure 2 shows the processed image at each step. The final image I_G is used as the input to successive affine and deformable registrations.

2.2 Affine registration

Similar to [7], we first perform a points-to-volume affine registration. For efficient computation, we move the seed point cloud rather than moving the processed MR images, and measure the similarity by computing the overlapping volume between the Gaussian-blurred images, I_G , and rectangular cuboids with dimensions $x \times y \times z$ (we use $2 \times 2 \times 6 \text{ mm}^3$ in our experiments considering the seed size) around the X-ray seeds in the MR coordinate as where and as

$$S = \sum_{n=1}^N \int_{-\frac{\Delta z}{2}}^{\frac{\Delta z}{2}} \int_{-\frac{\Delta y}{2}}^{\frac{\Delta y}{2}} \int_{-\frac{\Delta x}{2}}^{\frac{\Delta x}{2}} I_G \left(T(\mathbf{s}_n) + \begin{bmatrix} x \\ y \\ z \end{bmatrix} \right) dx dy dz$$

Where

$$T(\mathbf{x}) = \begin{bmatrix} \lambda_x^{-1} & 0 & 0 \\ 0 & \lambda_y^{-1} & 0 \\ 0 & 0 & \lambda_z^{-1} \end{bmatrix} \mathbf{R}(\boldsymbol{\theta})\mathbf{x} + \mathbf{t}$$

and $\mathbf{s}_n \in \mathbb{R}^3$ is the position vector of the n -th seed in the X-ray coordinates, and $\mathbf{R}(\boldsymbol{\theta})$ is a 3×3 rotation matrix and $\mathbf{t}$ is a 3×1 translation vector. Notice that we achieve the largest volume overlap, i.e., largest S value, when the seed cloud is aligned with I_G . We maximize the similarity using the Covariance Matrix Adaptation Evolutionary Strategy (CMA-ES) [8] which is a stochastic and gradient-free optimization method suitable for solving nonlinear and nonconvex problems. This optimizer samples the search region based on a normal distribution, while updating its covariance matrix, iteratively, based on the information from the sample points at the current and previous iterations. In this work, we find 9 affine

transformation parameters, three for translation, three rotation angles, and three scaling factors.

2.3 Deformable registration

Even though we consider global scaling in the affine registration, there are local deformations caused by the prostate edema and individual seed migration after treatment. The final deformable registration step corrects such local movement of each seed so that its position is aligned to the center of the closest seed region in I_G . To adjust local variations, we apply local forces to each seed point according to its position in I_G . First, we introduce external force to move each seed (in the affine-registered X-ray reconstruction) to the center of the closest seed region in I_G . To prevent unreliable and/or unrealistic deformation, we also add internal force to conserve the initial position and angular distributions relative to neighboring seeds. Combining both forces, we define a global energy function as

$$E = \sum_n \left\{ -\alpha |I_G(T(\mathbf{s}_n) + \mathbf{d}_n)|^2 + \beta |\mathbf{d}_n|^2 + \frac{\gamma}{2} \sum_{i \in N(\mathbf{s}_n)} \sum_{j \neq i \in N(\mathbf{s}_n)} \left| \theta(T(\mathbf{s}_i), T(\mathbf{s}_j), T(\mathbf{s}_n)) - \theta(T(\mathbf{s}_i) + \mathbf{d}_i, T(\mathbf{s}_j) + \mathbf{d}_j, T(\mathbf{s}_n) + \mathbf{d}_n) \right|^2 \right\} \quad (1)$$

where $\theta(\mathbf{x}_i, \mathbf{x}_j, \mathbf{o})$ is the angle between two vectors, $(\mathbf{x}_i - \mathbf{o})$ and $(\mathbf{x}_j - \mathbf{o})$, and α, β, γ are user-defined constants. $N(\mathbf{s}_n)$ is the nearest neighboring seeds of the n -th seed, and we used 15 nearest neighbors in our experiments. $\mathbf{d}_n$ is the displacement vector on the n -th seed position. We minimize (1) by using a quasi-Newton method to obtain the optimal deformation fields $\{\mathbf{d}_n\}$.

3. RESULTS

We tested our method on 6 prostate cancer patients who were treated by prostate brachytherapy with ^{103}P seeds at Johns Hopkins Hospital. Three X-rays were taken at the end of the implantation using an OEC 9800 mobile C-arm (GE Healthcare, Milwaukee, WI) under IRB-approved protocol for intra-operative dosimetry visualization. MRI scans were performed on day 1 after the implantation as a routine clinical procedure using a 1.5T Siemens MAGNETOM Espree scanner (Siemens AG, Erlangen, Germany). X-ray image has the pixel size of $0.4 \times 0.4 \text{ mm}^2$, and MR image has the pixel spacing of 0.70–0.94mm with the slice thickness of 3mm. Our registration algorithm was implemented using MATLAB and ran on a desktop PC with Intel Core i7 3.4GHz CPU and 16GB main memory.

Figure 3 shows an example of registration. Qualitatively, the seeds are well aligned to the dark void regions in MR images after registration. For quantitative evaluation, we obtained ground truth seed positions by fusing post-implant CT and MR images. Seeds were semi-automatically extracted from CT images and manually corrected by an expert brachytherapy physicist so that each seed detected in CT was aligned to the MR images. We carefully selected a subset of seeds as the ground truth seeds for which we can guarantee the seed

position from both CT and MR images. Target registration error (TRE) is obtained by computing the Euclidean distances between the registered X-ray seeds and the ground truth seeds. As shown in Table 1, the overall TREs (mean $\pm$ standard deviation in mm) are 1.5 ± 0.9 and 1.2 ± 0.8 for the affine and deformable registrations, respectively. Considering that it has been reported that seed localization uncertainty of 2mm results in less than 5% deviation of prostate D90 (minimum dose received by 90% of the prostate) [9], an overall error of 1.2mm is considered well within clinically acceptable limits. The computation time for the whole image processing steps of the seed reconstruction is approximately 1 minute [5] and registration takes less than 30 seconds.

4. CONCLUSIONS

We proposed a novel X-ray and MRI registration method for post-implant dosimetry in PPB. The implanted seeds are accurately reconstructed and localized by using only three X-ray images taken by any cone-beam imaging system. The proposed intensity-based deformable registration allows us to align the reconstructed seeds to MR images where prostate and OAR boundaries can be accurately defined, thus enabling an accurate estimation of post-implant dosimetric parameters. Our points-to-volume registration can be computed in very efficient way and takes less than 30 seconds for the initial affine registration and local adjustment by deformable registration. Considering the overall registration accuracy, fast computation and cost-effectiveness, hospitals may easily adopt the proposed method for post-implant dosimetry assessment. In addition, by replacing the CT scan with a few X-rays, unnecessary radiation dose to the patient can be significantly reduced.

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REFERENCES

- [1]. Acher P, Rhode K, Morris S, Gaya A, Miquel M, Popert R, Tham I, Nichol J, McLeish K, Deehan C, Dasgupta R, Beaney R, Keevil SF, "Comparison of combined X-ray radiography and magnetic resonance (XMR) imaging – versus computed tomography-based dosimetry for the evaluation of permanent prostate brachytherapy implants," *International Journal of Radiation Oncology, Biology, Physics* 71(5), 1518–1525 (2008).
- [2]. Lee J, Labat C, Jain AK, Song DY, Burdette EC, Fichtinger G, Prince JL, "REDMAPS: Reduced-dimensionality matching for prostate brachytherapy seed reconstruction," *IEEE Transactions on Medical Imaging* 30(1), 38–51 (2011). [PubMed: 20643600]
- [3]. Lee J, Kuo N, Deguet A, Dehghan E, Song DY, Burdette EC, Prince JL, "Intraoperative 3-D reconstruction of prostate brachytherapy implants with automatic pose correction," *Physics in Medicine and Biology* 56(15), 5011–5027 (2011). [PubMed: 21772077]
- [4]. Kuo N, Deguet A, Song DY, Burdette EC, Prince JL, Lee J, "Automatic segmentation of radiographic fiducial and seeds from x-ray images in prostate brachytherapy," *Medical Engineering & Physics* 34(1), 64–77 (2012). [PubMed: 21802975]
- [5]. Kuo N, Dehghan E, Deguet A, Mian OY, Le Y, Burdette EC, Fichtinger G, Prince JL, Song DY, Lee J, "An image-guided system for dynamic dose calculation in prostate brachytherapy using ultrasound and fluoroscopy," *Medical Physics* 41(9), 091712 (2014). [PubMed: 25186387]
- [6]. Lee J, Liu X, Jain AK, Song DY, Burdette EC, Prince JL, Fichtinger G, "Prostate brachytherapy seed reconstruction with Gaussian blurring and optimal coverage cost," *IEEE Transactions on Medical Imaging* 28(12), 1955–1968 (2009). [PubMed: 19605321]

- [7]. Dehghan E, Lee J, Fallavollita P, Kuo N, Deguet A, Le Y, Burdette EC, Song DY, Prince JL, Fichtinger G, “Ultrasound-fluoroscopy registration for prostate brachytherapy dosimetry,” *Medical Image Analysis* 16(7), 1347–1358 (2012). [PubMed: 22784870]
- [8]. Hansen N, “Towards a New Evolutionary Computation. Advances on Estimation of Distribution Algorithms, Studies in Fuzziness and Soft Computing,” in *The CMA evolution strategy: a comparing review*, Lozano JA, Larranaga P, Inza I, Bengoetxea E (Eds.), Springer, Berlin/Heidelberg, 75–102 (2006).
- [9]. Su Y, Davis BJ, Furutani KM, Herman MG, and Robb RA, “Dosimetry accuracy as a function of seed localization uncertainty in permanent prostate brachytherapy: Increased seed number correlates with less variability in prostate dosimetry,” *Physics in Medicine and Biology* 52(11), 3105–3119 (2007). [PubMed: 17505092]

Figure 1.
X-ray to MRI registration procedure.

Figure 2.
MRI pre-processing. (a) Original MR image. (b) Prostate extraction. (c) Matched (circular) filtering. (d) Cylindrical filtering. (e) Gaussian blurring.

Figure 3.
Input MRI (left) and seed registration (right). Red dots show the registered seeds overlaid with the MRI.

Table 1.

Registration results.

Case	Number of seeds		Registration error (mm)	
	Total implanted	Selected as ground truth	Affine	Deformation
1	86	40	1.5 ± 0.9	1.2 ± 0.8
2	87	35	1.6 ± 0.9	1.2 ± 0.8
3	110	45	1.4 ± 1.0	1.1 ± 0.9
4	75	40	1.3 ± 0.8	1.1 ± 0.7
5	61	35	1.5 ± 0.9	1.4 ± 0.7
6	77	35	1.5 ± 0.8	1.3 ± 0.8