Published in final edited form as:

Med Phys. 2006 May ; 33(5): 1398–1411.

Automated 2D-3D registration of a radiograph and a cone beam CT using line-segment enhancement^{a)}

Reshma Munbodh^{b)},

Department of Electrical Engineering, Yale University, New Haven, Connecticut 06520

David A. Jaffray,

Radiation Physics, Princess Margaret Hospital, University Health Network, Princess Margaret Hospital, Toronto, ON M5G-2M9, Canada

Douglas J. Moseley,

Radiation Physics, Princess Margaret Hospital, University Health Network, Princess Margaret Hospital, Toronto, ON M5G-2M9, Canada

Zhe Chen,

Department of Therapeutic Radiology, Yale University, New Haven, Connecticut 06520

Jonathan P. S. Knisely,

Department of Therapeutic Radiology, Yale University, New Haven, Connecticut 06520

Pascal Cathier, and

INRIA, Sophia-Antipolis, France

James S. Duncan

Department of Electrical Engineering, Yale University, New Haven, Connecticut 06520 and
Department of Diagnostic Radiology, Yale University, New Haven, Connecticut 06520

Abstract

The objective of this study was to develop a fully automated two-dimensional (2D)–three-dimensional (3D) registration framework to quantify setup deviations in prostate radiation therapy from cone beam CT (CBCT) data and a single AP radiograph. A kilovoltage CBCT image and kilovoltage AP radiograph of an anthropomorphic phantom of the pelvis were acquired at 14 accurately known positions. The shifts in the phantom position were subsequently estimated by registering digitally reconstructed radiographs (DRRs) from the 3D CBCT scan to the AP radiographs through the correlation of enhanced linear image features mainly representing bony ridges. Linear features were enhanced by filtering the images with “sticks,” short line segments which are varied in orientation to achieve the maximum projection value at every pixel in the image. The mean (and standard deviations) of the absolute errors in estimating translations along the three orthogonal axes in millimeters were 0.134 (0.096) AP(out-of-plane), 0.021 (0.023) ML and 0.020 (0.020) SI. The corresponding errors for rotations in degrees were 0.011 (0.009) AP, 0.029 (0.016) ML (out-of-plane), and 0.030 (0.028) SI (out-of-plane). Preliminary results with megavoltage patient data have also been reported. The results suggest that it may be possible to enhance anatomic features that are common to DRRs from a CBCT image and a single AP radiography of the pelvis for use in a completely automated and accurate 2D-3D registration framework for setup verification in prostate

^{a)}This study was supported by NIH Grant Nos. 8R01EB002164 and EB002470.

^{b)}Address for correspondence: Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021. munbodhr@mskcc.org.

radiotherapy. This technique is theoretically applicable to other rigid bony structures such as the cranial vault or skull base and piecewise rigid structures such as the spine.

Keywords

image registration; prostate radiotherapy; cone beam CT; sticks; setup verification; portal; radiograph

I. Introduction

In external beam radiation therapy, the prostate is irradiated with high doses of ionizing radiation to eradicate tumors and cancerous cells. The radiation dose is administered in fractions, daily, over a five to seven week period rather than in a single treatment session. The treatment setup must be reproduced accurately during each treatment session to ensure adequate dosimetric and geometric coverage of the tumor and the exclusion of sensitive anatomy. Three-dimensional conformal radiation therapy techniques allow radiation dose escalation and improved local tumor control while sparing surrounding healthy tissue. These techniques, however, are susceptible to geometric (targeting) uncertainties in treatment delivery which arise from setup errors and organ motion. Setup errors refer to variations in the positioning of the patient's bony anatomy with respect to the planned orientation of the radiation beam. Patient setup errors can be estimated and corrected by matching pretherapy reference images (three-dimensional CT and two-dimensional DRRs) acquired for treatment planning purposes, and single or multiple two-dimensional intratherapy radiographs of the patient acquired in the treatment environment. The intratherapy radiographs can be portal images, or more recently with the integration of kilovoltage imaging onto the treatment machine, kilovoltage radiographs. The pretherapy reference images give the intended position and orientation of the patient, while the intratherapy images indicate the actual position and orientation during treatment delivery.

There has been active interest in setup verification during radiation therapy using automated image registration methods since the early 1990s. A number of two-dimensional (2D) registration methods were developed before the advent of three-dimensional (3D) conformal radiotherapy techniques. While there has been a shift towards the design and implementation of 3D methods more recently, 2D registration methods are still being proposed, sometimes to demonstrate proof of concept. In 2D registration a simulator image, a digitally reconstructed radiograph (DRR), or the portal image from the first treatment fraction is employed as the reference image. In the latter case, the reference portal image is subsequently matched interactively to the simulator image or DRR. Semiautomated methods that have been developed for prostate radiotherapy include the work by Balter *et al.*,¹ Berger *et al.*,^{2,3} and Cai *et al.*⁴ Automated two-dimensional methods for prostate radiotherapy include chamfer distance-based,^{5–8} ridge-based,⁹ edge-based,¹⁰ combined chamfer distance and edge-based,¹¹ gray level correlation-based,¹² and phase-based correlation¹³ methods as well as an evaluation study of intensity-based similarity measures.¹⁴ A serious limitation of two-dimensional methods is their inability to resolve out-of-plane deviations accurately. The presence of undetected out-of-plane deviations can also result in erroneous estimation of in-plane parameters.^{15,16} Relatively few three-dimensional registration solutions have been developed for setup verification in prostate radio-therapy. Bijhold *et al.*¹⁷ explored the feasibility of using a single portal image with a simulator image and CT scan in a semi-automated point matching procedure to determine all six transformation parameters of the 3D translation and rotation of the patient. More recently, there have been reports of automated three-dimensional methods for the registration of a 3D CT to two orthogonal portal images of the pelvis. The earliest of these is a chamfer matching procedure reported by Gilhuijs *et al.* in 1996.¹⁸ Bansal *et al.*^{19–23} have reported an integrated information theoretic segmentation/registration framework. Clippe *et*

*al.*²⁴ presented a comparison of four intensity-based similarity measures, namely the Pearson correlation coefficient, correlation ratio, mutual information and chi-square measure. Reported accuracies of 2D and 3D registration methods range from 1 mm to 7 mm. Three-dimensional solutions applied to treatment sites other than the prostate include the work by Weese *et al.*,²⁵ Penney *et al.*,^{26,27} and Kim *et al.*²⁸

The overall aim of our work is to develop a fully automated registration framework to estimate patient setup deviations between treatment planning and treatment delivery during radiation therapy of the prostate. The full 3D shift in the patient setup relative to the intended setup is estimated by calculating the shift that brings bony features in a single planer radiograph into alignment with bony features in a reference 3D cone-beam CT (CBCT) image. In the case of portal images, the task of determining setup errors is complicated by their inherently low anatomical contrast-to-noise ratio. Moreover, the 3D to 2D nature of the registration problem makes out-of-plane setup deviations difficult to quantify. Since the prostate is not visible in the radiographs organ motion is not studied.

The success of existing methods that seek to use bony features for the registration is governed by their ability to extract bony anatomy in portal images. We chose to enhance features in the DRRs and radiographs rather than extract features believing this approach to be more robust to the presence of noise in the images.^{29–31} The linear features enhanced correspond mainly to bony ridges since these are the most prominent type of anatomy present in the images employed. Feature enhancement is accomplished with an adapted version of an algorithm proposed by Lee *et al.*³² for the enhancement of linear features in noisy and low contrast imagery and by Czerwinski *et al.*^{33,34} for boundary enhancement in ultrasound images. The rotating kernel min-max transform (RKMT), proposed by Lee and Rhodes³² was developed for the enhancement of linear features, such as edges, ridges, and valleys. The image to be enhanced is convolved with a local line operator, a long, narrow 2D kernel, which is rotated incrementally over 180°. The kernel can have a rectangular, triangular or Gaussian profile. As the kernel rotates, the minimum and maximum values obtained by convolving the kernel with the local image neighborhood centered at each pixel are stored, along with the angles at which these extremum values are found. The output image is a function of the minimum and maximum values. Ridges can be enhanced using the maximum values, valleys can be enhanced using the minimum values, and both ridge and valley information can be enhanced from the difference of the maximum and minimum values. A particularly desirable property of the RKMT operator is that it is rotation invariant.

Czerwinski *et al.*^{33,34} proposed a method, based on that of Lee and Rhodes³² for boundary enhancement and detection in ultrasound speckle. Czerwinski *et al.* were the first to apply this idea to medical imaging. Using techniques from statistical decision theory they formulated several line detection rules based on various statistical models of image signal and noise. One of the detectors proposed was the “sticks” detector. The “sticks” detector consists of a filterbank of short line segments which are varied in orientation. Linear features are first enhanced by filtering the image with the “sticks” to achieve the maximum projected value at each pixel. The maximum value is then retained as the test statistic for the presence of a line. The sensitivity of the sticks detector to lines of varying scale and curvature can be altered by varying the size and shape of the sticks. Czerwinski *et al.* referred to the set of lines as “sticks” because although they are long compared with the correlation length of the ultrasound speckle field, they are short relative to features of interest; in a sense, large-scale linear features are “built up” of sticks at different locations and orientations. The “sticks” detector has the form of a matched filter, and was found to be optimal for the detection of a signal in additive white Gaussian noise. The detector was also shown to be extremely robust to deviations from such a model making it applicable to the detection of linear structures in images where the noise statistics are unknown or inexact modeled.

In this study, we propose a framework to automatically determine patient setup errors in 3D through the correlation of enhanced linear features in 2D DRRs, obtained by computing perspective projections through the 3D CBCT, and in 2D radiographs. The linear features correspond mainly to rigid bony anatomy that appears in the planar images. We sought to use bony ridges since these are most invariant to photon energy.¹⁸ Pelvic bony anatomy is nondeformable at the scales studied, so if there is no femur motion and no unaccounted geometric distortions in the imaging process, patient setup deviations can be described by a global rigid three-dimensional rotation and translation of the patient around the three principal axes (anterior-posterior, superior-inferior, and medio-lateral). We therefore sought to estimate the six transformation parameters, three rotations and three translations, which bring the two-dimensional radiograph into alignment with the three-dimensional CBCT. We also investigated the feasibility of using only a single radiograph to determine out-of-plane setup deviations. We report our results with kV CBCT data and kV radiographs of an anthropomorphic phantom of the pelvis. The results presented should help establish the upper limits of accuracy achievable with megavoltage portal images. These results should also help gauge the applicability of the algorithm in instances where kilovoltage intrathelary images are used for setup verification. The kV imaging system employed here allowed for very accurate acquisition of gold-standard data. The registration framework presented was designed and implemented to be fully transferable to megavoltage images. We also report preliminary results on two sets of megavoltage patient data.

II. Methods and Materials

A. Experimental design

Pose determination experiments were performed with diagnostic energy cone beam CT data of an anthropomorphic phantom and diagnostic energy electronic radiographs in the AP view collected at the Princess Margaret Hospital, Toronto. The phantom contained a pelvis, lumbosacral spine and soft tissue structures, which were fixed in position with respect to the pelvis, enclosed in plexiglass. The aim of the experiments was to determine the capability of the proposed algorithm to automatically recover known setup deviations.

Coordinate system—An orthogonal, right-handed coordinate system that is fixed with respect to the patient with the origin at the isocenter was used to quantify setup deviations. The x -axis (medio-lateral) is directed across the patient from right to left, the y -axis (superior-inferior) is directed along the patient from toe to head and the z -axis (anterior-posterior) is directed through the patient toward the x-ray source. Note, in the notations employed in this study: r_x corresponds to rotations around the ML axis, r_y corresponds to rotations around the SI axis, r_z corresponds to rotations around the AP axis, t_x corresponds to translations along the ML axis (positive t_x is from right to left), t_y corresponds to translations along the SI axis (positive t_y is in the inferior-superior direction), and t_z corresponds to translations along the AP axis (positive t_z is in the posterior-anterior direction). Out-of-plane parameters comprise r_x , r_y , and t_z , and in-plane parameters consist of r_z , t_x , and t_y . A schematic of the patient coordinate system is shown in Fig. 1.

Imaging system overview—The images were acquired on a bench-top system designed to have geometry similar to that of a tomographic imaging system on a linear accelerator. The kV CBCT imaging system allows for very precise manipulation of the phantom position including translations along the three principal axes and rotations around the SI axis, and was considered to be the ideal imaging system for benchmarking the performance of the algorithms developed in this study. The system comprises a kilovoltage x-ray tube, an object rotation stage, and a flat panel imager mounted rigidly on an optical bench with a source-to-axis distance (SAD) of 1000 mm and a source-to-detector (SDD) distance of 1550 mm. These distance

parameters were measured with an accuracy of ± 0.5 mm. The system has four degrees of freedom (three translations and one rotation) and the position of all components is computer controlled. The displacement of each component relative to its “home” position is reproducible to 0.02 ± 0.01 mm. The flat panel imager consists of an array of 1536×2048 photodiodes with a pixel pitch of 0.194 mm giving a sensitive area of 30×40 cm². Projection images were digitized to 16 bits. A beam of 140 kVp was used for all measurements.

Kilovoltage CBCT acquisition—The CBCT scan was obtained with the phantom at its ideal setup position. A total of 320 projections over an angle of 360° were acquired by rotating the phantom in 320 steps around the superior-inferior (SI) axis. Feldkamp's filtered backprojection algorithm was used to reconstruct the 3D CBCT from the projections. The projections can be reconstructed on a matrix of $2048 \times 2048 \times N$ voxels (where N is the number of slices) with an isotropic voxel size of $0.125 \times 0.125 \times 0.125$ mm³. For the purposes of our experiments, the CBCT was reconstructed on a grid of $512 \times 512 \times 384$ voxels with an isotropic voxel size of $0.5 \times 0.5 \times 0.5$ mm³ corresponding to a volume of $256 \times 256 \times 192$ mm³. The CBCT was subsequently downsampled to a voxel size of $1 \times 1 \times 1$ mm³ during validation of the registration algorithms for computational efficiency. The isocenter of the CBCT data set, which identifies the point (0,0,0) in the CT, was at the geometrical center of the reconstructed data set.

Kilovoltage radiograph acquisition—Acquisition of the kV CBCT scan was followed by the acquisition of 14 sets of radiographs of the phantom for known displacements. All displacements were relative to the position of the phantom after acquisition of the CBCT, absolute translations ranging from 0 to 10 mm along the anterior-posterior (AP), medio-lateral (ML) and superior-inferior (SI) axes, and out-of-plane rotations -5° around the SI axis. The 14 positions tested were labeled A to N and are given in Table I. The orientation of the axes is illustrated in Fig. 1. The images were acquired with both single and multiple transformation parameter variations. Five consecutive projections were acquired per view at the previously defined SAD and SDD and averaged to form a radiograph. The ray piercing point, which is the point on the imaging plane where the normal vector to the latter intersects the x-ray source, gives the location of the origin (0,0) in the radiographs. The piercing point was measured during data acquisition and found not to be at the center of the imaging plane. This difference was adjusted for when reporting the results of the registration.

The first two of the 14 poses, A and B , had no displacement. The radiographs for these two poses were acquired sequentially without moving the phantom from its final position after acquisition of the CBCT. Poses A and B were introduced as a calibration step to correct for offsets that may have been introduced by the phantom rotation during acquisition of the CBCT and other experimental errors. An offset of $r_x = -0.091^\circ$, $r_y = -1.103^\circ$, $r_z = 0.000^\circ$, $t_x = 0.080$ mm, $t_y = 0.003$ mm, $t_z = -1.268$ mm was found at the reference position, as computed from the average of the estimated pose for A and B . This offset was subtracted from the results returned for all poses when reporting estimates of the transformation parameters. The calibration step is discussed in more detail in the Discussion section.

The radiographs, which originally had dimensions 512×384 pixels and a resolution of 0.776×0.776 mm² on the imaging plane, were downsampled to 397×298 pixels and a resolution of 1.0×1.0 mm². This corresponds to a field of view of approximately 25×20 mm² at the isocenter. A sub-region of the downsampled radiographs which excluded the femurs was employed for the registration. This corresponded to a field of view of approximately 15×13 mm² at the isocenter.

Preprocessing of projections—As part of the data acquisition and reconstruction, the projections were preprocessed in order to correct for defective pixels, small variations in the

x-ray tube output, and detector response nonuniformity. These nonuniformities were corrected through “flat fielding,” a process where a set of flood and dark field images are acquired to provide correction values for each of the detector elements. No further preprocessing was performed on the acquired images.

Artifacts—The kV CBCT data set contained shading artifacts including cup, streak and ring artifacts. The cup and streak artifacts are attributable to the scattered radiation present in the projection images from which the CBCT was reconstructed. The ring artifact was due to the limited field of view of the projections used to reconstruct the CBCT. In addition, the pelvic structure in the CBCT could not be captured completely because of the limited field of view of the imager.

B. Algorithm design

Setup deviations were estimated by iteratively shifting the CT via a 3D rigid spatial transformation, computing a 2D DRR from the shifted CT, enhancing linear features in the DRR, and matching the feature-enhanced DRR to the feature-enhanced radiograph until the similarity between the feature-enhanced DRR and feature-enhanced radiograph was maximized. The feature enhancement procedure, similarity measure, optimization method, and procedure by which the registration errors were quantified are provided in the following sections.

To formalize the problem, let $g(x, y, z)$ denote the intensity of a voxel in the CT at the 3D spatial coordinates (x, y, z) , and $u(x, y)$ denote the intensity of a pixel in the kV radiograph on the 2D image plane at spatial location (x, y) . An estimate of the rigid transformation, T , that aligns the CT to the kV radiograph is found by iteratively rotating and shifting the CT and matching 2D feature-enhanced DRRs, computed from the CT under projective geometry, to the feature-enhanced kV radiograph. The vector of rotations and translations which define the spatial mapping, T , is given by $\psi = [r_x, r_y, r_z, t_x, t_y, t_z]$; r_x, r_y, r_z are the three unknown rotations around the ML, SI, AP axes and t_x, t_y, t_z are the three unknown translations along the same axes. In this study, the center of the rotational components is at the simulated treatment isocenter. This is at the geometrical center of the CT. The intensity of pixel $v_\psi(x, y)$ in a DRR is computed by summing the CT numbers in the spatially transformed CT, $g \circ T_\psi$, along the ray from the x-ray source to location (x, y) on the 2D image plane. That is, $v_\psi(x, y) = P(g \circ T_\psi)$, where P represents a ray-tracing operation under projective geometry. The line-enhanced radiograph and DRR, are represented by p and q_ψ , respectively; $p = Y(u)$ and $q_\psi = Y(v_\psi)$, where Y is the linear feature enhancing operator and is described in the next section.

Enhancement of linear features—Linear structures were enhanced by multiplying the raw gray-level values in the images by weights that correspond to the “likelihood” that a pixel lies on a ridge of a given orientation. The weights are computed by filtering the images with an adapted version of the “sticks” algorithm of Czerwinski *et al.*^{33,34} and the RKMT algorithm by Lee and Rhodes.³²

The line enhancement operator consists of a filterbank of short line segments, or sticks, of variable orientation with a rectangular profile and circular support. Gray level information in a circular neighborhood centered at each pixel in the image is used to compute the weights indicating the “likelihood” that a pixel lies on a ridge as follows. Let $f(x, y)$ denote a pixel in the original image. At each pixel (x, y) the output of the line enhancement operator is the maximum projection value, $l(x, y)$, of the line segments over all orientations, along with the projection value, $b(x, y)$, of the circular region surrounding the line segment which gave the maximum value,

$$\begin{aligned}
l(x, y) &= \max_{\theta} \frac{1}{M} \sum_{i,j} s_{\theta}(i, j) f(x - i, y - j), \quad 0 \leq \theta < \pi, \\
\alpha(x, y) &= \arg \max_{\theta} \frac{1}{M} \sum_{i,j} s_{\theta}(i, j) f(x - i, y - j), \quad 0 \leq \theta < \pi, \\
b(x, y) &= \frac{1}{N-M} \sum_{i,j} d_{\alpha}(i, j) f(x - i, y - j).
\end{aligned} \tag{1}$$

Here, $s_{\theta}(i, j)$ is a stick at orientation θ , $\alpha(x, y)$ is the orientation of the stick giving the maximum projection value at pixel (x, y) , $d_{\alpha}(i, j)$ is a mask which is unit valued in the union of support of the sticks excluding the stick at orientation α and zero elsewhere. M is the number of pixels on a stick and N is the size of the circular support of the sticks.

The test statistic for the presence of a linear feature is the difference between the largest stick projection and the projection of pixels in the circular neighborhood of the stick. The weight, $w(x, y)$, indicating the “likelihood” of pixel (x, y) lying on a line at orientation α is given as

$$w(x, y) = \max \left[0, 1 - \exp \left(- \frac{l(x, y) - b(x, y)}{C} \right) \right], \tag{2}$$

where C is a constant which affects the contrast of the resulting output image. The value of C was determined through empirical testing with a separate set of images. A value of 20 was used for all tests performed here. This value produced images which appeared to have better contrast visually than with the other constants tested. $w(x, y)$ is positive and lies between 0 and 1. Computing w from the difference of $l(x, y)$ and $b(x, y)$ accommodates additive variations in image brightness due, for example, to variations in overlying soft tissue or the presence of scattered radiation. The output, $f'(x, y)$, of the linear feature enhancement procedure at each pixel is obtained from the product of $f(x, y)$ and $w(x, y)$,

$$f'(x, y) = f(x, y) \times w(x, y). \tag{3}$$

Thus, we obtain a line-enhanced image, f' , where the gray level values are weighted by the “likelihood” that a pixel lies on a linear feature. The product of the weights and gray level values serves to emphasize linear structures which are present, in brighter regions while decreasing the presence of artifacts in darker regions. As mentioned earlier, the line-enhanced radiograph and DRR, are represented by p and q_{ψ} , respectively.

A filterbank of 15 line segments evenly oriented between 0° and 180° and of length 11 pixels and width 1 pixel was employed in both DRRs and kV radiographs. The scale at which linear features are detected can be adjusted by varying the width of the line segments. For this study, a fixed width of 1 pixel was found to be adequate for the filter bank of sticks and feature-enhancement was performed on the original unsmoothed image. Examples of line-enhanced images are shown in Fig. 2.

Similarity measure—The Pearson correlation coefficient, $\rho(p, q_{\psi})$, between the line-enhanced radiograph, p , and the line-enhanced DRR, q_{ψ} , was employed as the similarity measure,

$$\rho(p, q_\psi) = \frac{\sum_{x,y} (p(x, y) - \bar{p})(q_\psi(x, y) - \bar{q}_\psi)}{\sqrt{\sum_{x,y} (p(x, y) - \bar{p})^2} \sqrt{\sum_{x,y} (q_\psi(x, y) - \bar{q}_\psi)^2}}, \quad (4)$$

where $\bar{x}$ is the mean of the pixels in x .

Optimization—The optimal set of parameters that align the CT to the radiographs was found by maximizing the correlation coefficient between p and q_ψ ,

$$\hat{\psi} = \arg \max_{\psi} \rho(p, q_\psi). \quad (5)$$

For simplicity of notation, we denote $\rho(\mathbf{p}, \mathbf{q}_\psi)$ by $\rho(\psi)$. Steepest gradient ascent was used as the search strategy to reach the global maximum of the objective function defined by $\rho(\psi)$.

The gradient, $\nabla \rho(\psi)$, of $\rho(\psi)$ at every step of the optimization was computed as

$$\begin{aligned} \nabla \rho(\psi) &= \frac{d\rho}{d\psi} \\ &= \frac{1}{\sigma_p \sigma_q} \sum_{x,y} \left[p(x, y) - \bar{p} - \frac{\sigma_{pq}^2}{\sigma_q^2} (q_\psi(x, y)) - \bar{q}_\psi \right] \frac{dq_\psi(x, y)}{d\psi}, \end{aligned} \quad (6)$$

where σ_p and σ_q are the standard deviations and σ_{pq} is the covariance of the pixel intensities in p and q_ψ .

The optimal transformation parameters $\hat{\psi}$ were found by iteratively transforming the CT by an amount given by Eq. (6) and computing the correlation between the line-enhanced DRR and radiograph until the increase in the correlation coefficient due to a small change in the transformation parameters was less than a predefined tolerance value. For computational efficiency, optimization is first performed in 2D using a projection of the CT at its initial position and the radiograph. The in-plane transformation parameters computed by the 2D optimization procedure were then used as the initial parameters to the full 3D optimization algorithm which solves for all six transformation parameters (three rotations and three translations along the AP, ML, and SI axes). In-plane parameters returned by the 2D optimization procedure using AP images only comprise translations along the SI and ML axes and rotations around the AP axis.

A multiresolution optimization scheme was employed in both 2D and 3D to accelerate convergence to the global maximum and increase the capture range of the registration algorithm. Multiresolution optimization involves performing the optimization over a number of levels, whereby the images to be registered are convolved with a Gaussian kernel of a larger scale and subsampled by a greater factor at higher levels. The transformation parameters obtained at a given level are used as the starting parameters for the next level until the final level is reached. This coarse-to-fine optimization strategy blurs out fine structures in the images at the higher levels yielding an objective function with a broad capture range, but shallow peak, which is easy to optimize and enables the algorithm to approach the global maximum while avoiding becoming trapped at local maxima which might be present at a finer image scale. As the optimization progresses through the levels, the objective function increases in steepness

and the peak becomes sharper, thus improving the accuracy and precision of the estimates of the transformation parameters.

The 2D multiresolution optimization was performed over eight levels for 1 mm data. At level eight, the line-enhanced images, p and q_{lp} , obtained by filtering the radiograph and DRR with the sticks operator were blurred with a Gaussian kernel of width 7 mm and downsampled by a factor of 7 prior to being registered. The width of the Gaussian kernel and subsampling factor were decreased over subsequent levels to a final value of 0.5 mm and 1, respectively. Figure 3 shows the 2D objective function obtained by computing the correlation coefficient between the downsampled feature-enhanced DRR and radiograph as a function of translation along the SI (t_y) and ML axes (t_x) for pose H at optimization level 4. The DRR and portal image had an initial resolution of $1 \times 1 \text{ mm}^2$. A Gaussian kernel of width 3 mm and a subsampling factor of 3 were employed when downsampling the images. For these two translations, the objective function was smooth with a single peak at the global maximum.

The multiresolution optimization procedure illustrated in Fig. 4 shows the 2D contour plots of the correlation coefficient as a function of translation along the SI (t_y) and ML axes (t_x) for pose H for optimization levels 8, 6, 4, and 1. The contour plots show the isolines, or slices of constant correlation values, of the corresponding 2D objective functions for these four levels. The isolines are shown for correlation values of 0.1 to 0.9 at an interval of 0.1. The position of the peak of the objective function for each of the four levels presented is indicated with a dot and the value of the true displacement is indicated with a $\times$. The objective function becomes steeper and narrower as the optimization proceeds from level 8 to level 1, giving a more precise estimate of the transformation parameters. Optimization at the higher levels is faster since the images are downsampled by a larger factor. In all experiments, the initial estimates of the transformation parameters were set to zero. Figure 4 illustrates that if the registration were performed at the finest resolution (level 1) only, it would not be possible to reach the peak of the objective function with a hill-climbing optimization procedure since the starting point (0,0) lies in a flat region of the objective function. An optimization procedure using a global search strategy would be too computationally expensive.

The computational time for the registration is a function of the resolution of the images, the size of the DRR, the magnitude of the out-of-plane transformations, and the tolerance value used to end the optimization. On a 2.66 GHz Dell Precision 650 workstation, the 2D optimization for the in-plane parameters was of the order of a minute for 1 mm data. In the presence of out-of-plane displacements, the registration time for the full 3D solution varied from 8–12 minutes for a 198×149 DRR with a resolution of $2 \times 2 \text{ mm}^2$ computed from a CT of the same resolution, and 60–90 minutes for a 397×298 DRR with a pixel size of $1 \times 1 \text{ mm}^2$ computed from a CT with an isotropic voxel size of 1 mm. It should be noted our efforts were focused on establishing registration accuracy, and not on the speed with which this accuracy was obtained. We believe the registration algorithm is amenable to being improved for speed, especially by using new techniques for fast DRR computation to overcome the bottleneck of DRR computation.

All adjustable parameters for the proposed registration method were selected based on experiments conducted with a phantom data set which was not part of the data set reported in this paper. The values of these parameters were maintained during all testing of the algorithm.

Quantification of error with displacement—We chose to quantify setup displacements applied to the phantom and errors in recovering these displacements as the magnitude of the maximum distance moved by points on a sphere centered about the simulated isocenter from their intended position. In this study, the isocenter was assumed to be at the geometrical center of the CBCT. These points can be considered to be contour points defining the treatment field.

We quantified setup deviations in this manner as opposed to the root-mean-square value of the individual rotations and translations as the effect of a translation on an image is different from that of a rotation. Furthermore, the magnitude of the displacement due to a rotational setup error increases as we move away from the axis of rotation while the magnitude of translational displacements due to translational setup errors does not vary with distance.

We considered points on a surface of a sphere of radius 30 mm representing a treatment field of diameter 60 mm centered at the simulated treatment isocenter. The 3D location of the points on the sphere were obtained from their spherical coordinates. The points were positioned with an angular separation of 5° in the YZ and XY planes giving a total of 2664 points. A sphere larger than the size of the prostate was employed to allow appropriate weighting of rotational errors which cause a small displacement at a radius corresponding to that of the prostate.

The magnitude of the setup displacement, $\mathcal{D}$, for a particular set of transformation parameters, ψ , applied to points x was computed as

$$\mathcal{D} = \max_{x \in S} \|Tx\|, \quad (7)$$

where T is the transformation matrix representing the setup displacement and S is the set of points on the sphere. We used the maximum value since although we are working with rigid body motion, points on the sphere move by different amounts in the presence of rotations and translations.

Similarly, the displacement, $\mathcal{E}$, due to errors in estimating the setup deviation applied to the phantom is quantified as

$$\mathcal{E} = \max_{x \in S} \|\hat{T}x - Tx\|, \quad (8)$$

where $\hat{T}$ is the estimate of the transformation matrix T , and x are the coordinates of the points on the surface of a sphere with a radius of 30 mm. $\mathcal{E}$ is the maximum distance between a set of points transformed by $\hat{T}$ and T . That is, $\mathcal{E}$ is the maximum distance of the set of points from their desired position.

III. Results

Examples of linear-enhanced images are shown in Fig. 2. The sacroiliac joints and pelvic brim are clearly visible since they are present in bright regions of high contrast. The pubic symphysis, obturator foramina, and ischial tuberosities, which are located in a darker region of lower contrast are less clear. Figure 5 is an example of a feature-enhanced DRR superimposed on a feature-enhanced radiograph prior to registration (a) and after registration (b). In these images, red and green represent linear features in the DRR and kV radiograph, respectively. At alignment red and green features overlap to maximize the amount of yellow present in the image. In this experiment, the radiograph was obtained with the phantom rotated by -5° around the SI axis and shifted 10 mm along the SI axis (pose F).

Of the 14 poses, (labeled A through N), three had no displacement (A , B , and N), and two of them (G , H) had in-plane displacements only, the remaining nine all contained an out-of-plane displacement (see Table I). Of these nine poses, four had an out-of-plane rotation of -5° around the SI axis combined with translations ranging from -10 mm to 10 mm along the SI axis (C ,

D, E, F), another four had out-of-plane translations of -10 mm to 10 mm along the AP axis (*I, J, K, L*) and the last pose had a combined translation of 10 mm along the SI axis and -10 mm along the AP axis (*M*).

Table I shows the true pose, the estimated pose, the difference between the estimated and true pose, the displacement $\mathcal{D}$, and the error ε [see Eqs. (7) and (8)] and the correlation coefficient at the estimated pose for each of the fourteen positions tested. The estimated poses reported in Table I were obtained by subtracting the offset calculated from poses *A* and *B* from the estimates of transformation parameters returned by the registration algorithm. A high correlation coefficient value, mean 0.948 and standard deviation 0.005 , was obtained in all tests, indicating a strong linear relationship between the gray-level values in the images being matched.

Table II shows the mean and standard deviation of the absolute error in the estimated pose for poses *C* through *N*. Poses *A* and *B* were excluded since they were used to estimate the offset present at the reference position. The mean (and standard deviations) of the absolute errors in estimating translations along the three orthogonal axes in millimeters were 0.134 (0.0956) AP (out-of-plane), 0.021 (0.023) ML, and 0.020 (0.020) SI. The mean and (standard deviations) of the absolute errors for rotations in degrees were 0.011 (0.009) AP, 0.029 (0.016) ML (out-of-plane), and 0.030 (0.028) SI (out-of-plane). Table II also shows the minimum and maximum absolute errors observed for each of the six parameters. All errors, were less than 0.34 mm and 0.1° , with errors in the in-plane translations being less than 0.07 mm. Note that only a limited number of poses were available to compute the mean and standard deviation of the errors. Note also that only one of the data sets contained a translation along the ML axis and none of them contained rotations around the ML and AP axes. The small errors obtained for these parameters indicate simply that the algorithm did not drift from the reference value during registration.

Using a single radiograph would imply lack of sensitivity to out-of-plane parameters, particularly to translations along the AP axis. Figure 6 is a plot of the error, ε in recovering the true pose against magnitude of the displacement, $\mathcal{D}$ of the phantom from its reference position. In this figure, points that have in-plane displacements only are labeled with a diamond and points that contain an out-of-plane rotation or translation are labeled with a circle in order to gauge the effect of the presence of out-of-plane displacements on the accuracy of the registration algorithm. Tables I and II indicate that out-of-plane translations along the AP axis are the most difficult to estimate. Figure 7 illustrates the variation of the total registration error (diamonds) and the registration error excluding errors from translations along the AP axis (circles) as a function of total displacement. It illustrates the contribution of errors in estimating translations along the AP axis to the total error.

Although this study was focused on validation of the registration algorithm with kilovoltage data, we thought it valuable to include preliminary data to evaluate its performance on MV patient images. Towards this end, we have included examples of fused images obtained by registering a kV CT data set and 2 weekly AP portal. images of a patient. The CT was acquired on a GE CT scanner and the portal images were obtained with a Varian aSi electronic portal imager at 6 MV. All images had an isotropic voxel and pixel size of 1 mm. The registration field of view was 13×12 cm².²⁹ Validation of the registration results was performed by visual comparison of the superimposed feature-enhanced portal images and DRRs, as illustrated in Fig. 8. The images were generated in a like fashion to those in Fig. 5. Red represents linear features in the DRR, and green, linear features in the portal image. Only the AP images were employed for the registration. The lateral images were used to visually verify alignment along the AP axis and around the ML axis. Figure 8 shows examples of superimposed feature-enhanced DRRs and feature-enhanced portal images in the AP and lateral views prior to registration (a), (b) and after registration (c), (d) for the first week. Figures 8(e)–8(h) show similar examples for week 2. The estimated patient setup error was $r_x = 3.38^\circ$, $r_y = -0.63^\circ$,

$r_z = -1.37^\circ$, $t_x = -1.00$ mm, $t_y = -0.27$ mm, $t_z = 0.75$ mm for week 1 and $r_x = 3.88^\circ$, $r_y = -1.25^\circ$, $r_z = -1.17^\circ$, $t_x = 3.78$ mm, $t_y = 0.60$ mm, $t_z = -2.13$ mm for week 2. The correlation coefficients at alignment for weeks 1 and 2 were 0.83 and 0.85, respectively.

IV. Discussion

We have presented a completely automated 3D image registration algorithm to align digitally reconstructed radiographs (DRRs) from a 3D CBCT image to a single AP radiograph through correlation of line-enhanced images. Full 3D validation of the method was carried out on a kV CBCT and kV electronic radiographs of an anthropomorphic phantom of the pelvis containing both bony and soft tissue structures. Feature enhancement was performed by filtering the images with sticks, that is, short line segments varied in orientation, and determining the maximum projected value at each pixel in the image. To our knowledge, this is the first application of the line enhancement algorithm to setup verification in radiation therapy.

The data collection for this experiment was conducted in two stages: (1) acquisition of a CBCT and (2) acquisition of radiographs. In the first stage, the phantom was rotated in 320 steps. In the second stage, the phantom was moved to 13 unique positions. It is possible that systematic and random errors would be introduced during the experiment. Sources of error include (1) position errors during movement of the phantom, (2) inaccuracies in the measurement of the imaging geometry, and (3) errors introduced in the reconstruction of the CBCT. In addition, there may also be errors that are intrinsic to the registration algorithm. We sought to reduce the effect of all such errors from our analysis by adding two poses, *A* and *B*, with no displacement at the start of the second stage of this experiment. The average of the estimated poses for *A* and *B* was considered to be an offset present in the experiment. An offset of $r_x = -0.091^\circ$, $r_y = -1.103^\circ$, $r_z = 0.000^\circ$, $t_x = 0.080$ mm, $t_y = 0.003$ mm, $t_z = -1.268$ mm was found. The variance in the estimated poses for *A* and *B* was small. All offsets apart from those for r_y and t_z were minor. The offset estimated by the registration algorithm around r_y was due to the angular position of the phantom being 358.92° after acquisition of the CBCT and not 360° as assumed during computation of the DRRs. Since all subsequent displacements of the phantom were relative to the position of the phantom after the CBCT acquisition, this would cause an offset of -1.08 degrees in the estimate of r_y . The offset of -1.08° was estimated as -1.10° in the corrective step we introduced. The exact cause of the initial offset of -1.27 mm along the AP axis was not known and could be due to any of the four causes identified above. Addition of the extra poses at the reference position can be considered a calibration step to be performed once for every type of equipment where the algorithm is to be employed.

For each of the 14 poses, the test displacements and errors observed were quantified with the use of a sphere of radius 30 mm centered at the simulated isocenter as described above. From Table I, it can be seen that the maximum distance tested, as quantified by the maximum displacement of the sphere, was 14.14 mm. The maximum total error, computed with the same sphere was 0.4 mm (pose *F*). The mean of the total error, which gives the overall accuracy of the algorithm, was 0.17 mm. The overall precision is given by the standard deviation of the total error and was found to be 0.11 mm. These results demonstrate that submillimeter accuracy was achieved both in individual parameter estimation, and in the combined error estimate calculated from all parameters. The algorithm correctly estimated in-plane and out-of-plane translations as small as 1 mm and out-of-plane rotations as small as 1° . The registration algorithm was robust to shading artifacts (cup, streak, and ring artifacts) that were present in the CBCT data. No pre-processing of the images such as histogram equalization or contrast adjustment was required. Registration of the same images (without line enhancement) with the correlation coefficient as a similarity measure failed, particularly when estimating translations along the AP and SI axes and out-of-plane rotations.²⁹

The overall error in recovering setup deviations did not increase with the presence of out-of-plane rotational or translational displacements (see Fig. 6). Furthermore, there was no observable trend in the overall error with distance moved over the range of displacements tested. Figure 7 confirms that translations along the AP axis were the most difficult to estimate correctly. In the absence of errors from translations along the AP axis, an overall accuracy of at least 60 microns was achieved as opposed to an overall accuracy of 0.17 mm when the errors along the AP axis were included. It should be noted that a depth error of 1.0 mm corresponds to a scaling difference of approximately 1.001 in the projection images being matched. The relatively larger error observed in out-of-plane translations should not necessarily be considered a limitation of the algorithm, but rather should be viewed as resulting from a lack of sensitivity of the contents of the projection images to small translations of the CT along the AP axis.

A 2D multiresolution optimization procedure was employed over eight levels with image resolution ranging from 7 mm to 1 mm. An examination of the intermediate results of the multiresolution optimization procedure showed that the algorithm performs well at the data resolutions employed. This is illustrated in the multiresolution optimization plots in Fig. 4. These plots indicate that the results obtained in this study were not the outcome of a fortuitous selection of image resolution. Increasingly better accuracy is achieved with higher resolution and less blurring. However, the results at lower resolutions and higher blurring are reasonably accurate. For example, with data half the resolution of that used in this study, all parameters, except out-of-plane translations, were estimated with an accuracy which is reasonably close to the final results reported here. An examination of the intermediate results obtained with the multiscale optimization method suggested that most parameters converged relatively quickly to values which are very close to final values with out-of-plane translations benefiting most from successive iterations with increasingly higher resolution data.

Preliminary data indicating registration performance on MV patient data were also included and are illustrated in Fig. 8. Registration accuracy on patient data may be adversely affected by the presence of air cavities and soft tissue structures that are deformable and move relative to the prostate. For the two sets of patient data tested, visual comparison of the superimposed AP and lateral DRRs and portal images indicated that the bony anatomy was aligned correctly and the algorithm was insensitive to the presence of other non-rigid structures. It should be noted from the superimposed lateral images in Figs. 8(g) and 8(h), that even though the femoral bones were tilted with respect to the pelvic cage, the algorithm aligned the pelvic bony anatomy correctly since the femurs were excluded from the AP images used for the registration. Although promising, further testing of the algorithm on patient data is necessary to assess its clinical applicability.

Very few studies have reported registration algorithms that use a single radiograph to estimate setup deviations in radiotherapy. Lujan *et al.*³⁵ assessed the feasibility of using planar registration to determine out-of-plane setup deviations in images of the skull. They showed that AP skull radiographs contain anatomic features that are sensitive in position and orientation to out-of-plane rotations. As indicated previously, Bijhold *et al.*¹⁷ investigated the feasibility of using a single portal image and a 3D CT to estimate out-of-plane parameter variations. They proposed two methods, the plane and the volume methods, to estimate setup deviations in 3D from the positions of manually selected anatomical points. Testing was performed on an anthropomorphic phantom of the pelvis. The plane method, which assumes that all anatomical match points are in one single plane perpendicular to the beam axis, was found to be useful for the estimation of in-plane parameters only. The volume method matches points in the 3D CT to points in the portal images. For this method to work a sufficient number of points must be found which can be localized in 3D in the phantom and located in the portal image. Since it was difficult to identify a sufficient number of such points in the AP portal image fields, the

volume method could not be applied to AP fields. The volume method was, however, applied successfully to lateral fields. Out-of-plane rotations were estimated to within 1° of their true value by matching anatomical points on the acetabula.

The results achieved in this study indicate that, for the range of displacements tested, it is possible to determine out-of-plane deviations from a single AP radiograph of the pelvis which does not contain the femurs. These results are significant since, in practice, the presence of the femoral bone in the lateral images might restrict their use in the event of femur motion with respect to the pelvic girdle. In the event that the femurs can be immobilized completely or that a region of interest excluding the femurs could be selected from the lateral image, the latter could be used to determine out-of-plane translations along the AP axis with the high level of accuracy reported here for the other translations. It should be noted that algorithms using a single radiograph are particularly susceptible to errors arising from miscalibration of the source-to-axis distance, source-to-detector distance or voxel size of the CT. The presence of a translational shift along the AP axis could be attributable to any of the above factors or could be due to an actual shift of the patient. It is not, possible, though, to differentiate between these different sources of errors with a single radiograph. Studies with a single radiograph allow us to understand the information contained within a single image and thus assess the contribution of each additional radiograph employed to registration accuracy. Increasingly accurate solutions can thus be built in a programmatic manner.

We sought to develop an algorithm which works by enhancing, rather than extracting, linear structures representing tissue boundaries in the images being matched. This is because exact feature extraction and localization in megavoltage portal images is known to be difficult. Feature enhancement may be more robust to noise than feature detection where the decision process as to the presence of a ridge or an edge may result in either useful anatomical information being discarded in the presence of noise or in noise being erroneously retained as bony structure. The line-based feature enhancement algorithm was selected because it is known to be robust to noise. The results from the experiments performed in this study indicate promise as to the applicability of the lines enhancement method to the problem of setup verification in prostate radiotherapy.

V. Conclusion

This study indicates that it may be possible to enhance linear features that are common to DRRs from a 3D kV CBCT and radiographs for use in a completely automated 3D registration framework for setup error correction in prostate radiotherapy. For 14 displacements, the mean (and standard deviations) of the absolute errors in estimating translations along the three orthogonal axes in millimeters were 0.134 (0.096) AP (out-of- plane), 0.021 (0.023) ML, and 0.020 (0.020) SI. The mean and (standard deviations) of the absolute errors for rotations in degrees were 0.011 (0.009) AP, 0.029 (0.016) ML (out-of-plane), and 0.030 (0.028) SI (out-of-plane). The overall accuracy of the algorithm, as quantified by the mean of the maximum distance moved by points on a sphere centered at the simulated isocenter from their ideal position over all displacements, was 0.17 mm. The overall precision, as quantified by the standard deviation of the maximum distance moved, was 0.11 mm. Average overall accuracy was 0.06 mm when excluding errors in estimates of translations along the AP axis. Errors in estimating each of the six transformation parameters were all less than 0.4 mm and 0.1° , with errors in in-plane translations being less than 0.08 mm. This level of accuracy with kV images of a phantom study is very promising. Further, the accuracy achieved with a single radiograph suggests that the AP view of the pelvis contains features which can be used for the determination of out-of-plane rotations and translations, and for a single radiograph solution. Preliminary results with MV patient data have also been reported. The technique developed in this study is theoretically applicable to other rigid or piecewise-rigid bony structures such as

the cranial vault, skull base, and the spine. Further testing is necessary to determine its applicability for kV and MV clinical images where the presence of mobile soft tissue structures may affect accuracy.

References

1. Balter JM, Pelizzari CA, Chen GT. Correlation of projection radiographs in radiation therapy using open curve segments and points. *Med Phys* 1992;19:329–334. [PubMed: 1584126]
2. Berger, M.; Danuser, G. Deformable multi template matching with application to portal images. Proceedings 1997 IEEE Computer Society Conference on Computer Vision and Pattern Recognition; San Juan, Puerto Rico: IEEE Computer Soc Tech Committee on Pattern Anal and Machine Intelligence; 1997. p. 374-379.
3. Berger, M.; Gerig, G. Motion measurements in low contrast x-ray imagery. In: Wells, WM., editor. Medical image computing and computer assisted intervention—MICCAI'98; Proceedings Lecture Notes in Computer Science; 1998. p. 832-841.
4. Cai J, Chu JC, Saxena VA, Lanzl LH. A simple algorithm for planar image registration in radiation therapy. *Med Phys* 1998;25:824–829. [PubMed: 9650169]
5. Fritsch DS, Chaney EL, Boxwala A, McAuliffe MJ, Raghavan S, Thall A, Earnhart JR. Core-based portal image registration for automatic radiotherapy treatment verification. *Int J Radiat Oncol, Biol, Phys* 1995;33:1287–1300. [PubMed: 7493854]
6. Gilhuijs KG, el Gayed AA, van Herk M, Vijlbrief RE. An algorithm for automatic analysis of portal images: clinical evaluation for prostate treatments. *Radiother Oncol* 1993;29:261–268. [PubMed: 8310154]
7. Leszczynski KW, Loose S, Boyko S. An image registration scheme applied to verification of radiation therapy. *Br J Radiol* 1998;71:413–426. [PubMed: 9659135]
8. Petrascu O, Bel A, Linthout N, Verellen D, Soete G, Storme G. Automatic online electronic portal image analysis with a wavelet-based edge detector. *Med Phys* 2000;27:321–329. [PubMed: 10718135]
9. Eilertsen K, Skretting A, Tennvassas TL. Methods for fully automated verification of patient setup in external beam radiotherapy with polygon shaped fields. *Phys Med Biol* 1994;39:993–1012. [PubMed: 15551575]
10. Girouard LM, Pouliot J, Maldague X, Zaccarin A. Automatic setup deviation measurements with electronic portal images for pelvic fields. *Med Phys* 1998;25:1180–1185. [PubMed: 9682203]
11. Jobse M, Davelaar J, Hendrics E, Kattevilder R, Reiber H, Stoel B. A new algorithm for the registration of portal images to planning images in the verification of radiotherapy, as validated in prostate treatments. *Med Phys* 2003;30:2274–2281. [PubMed: 14528947]
12. Kreuder F, Schreiber B, Kausch C, Dossel O. A structure-based method for on-line matching of portal images for an optimal patient set-up in radiotherapy. *Philips J Res* 1998;51:317–337.
13. Wang JZ, Reinstein LE, Hanley J, Meek AG. Investigation of a phase-only correlation technique for anatomical alignment of portal images in radiation therapy. *Phys Med Biol* 1996;41:1045–1058. [PubMed: 8794484]
14. Dekker N, Ploeger LS, van Herk M. Evaluation of cost functions for gray value matching of two-dimensional images in radiotherapy. *Med Phys* 2003;30:778–784. [PubMed: 12772984]
15. Hanley J, Mageras GS, Sun J, Kutcher GJ. The effects of out-of-plane rotations on two dimensional portal image registration in conformal radiotherapy of the prostate. *Int J Radiat Oncol, Biol, Phys* 1995;33:1331–1343. [PubMed: 7493858]
16. Remeijer P, Geerlof E, Ploeger L, Gilhuijs K, van Herk M, Lebesque JV. 3D portal image analysis in clinical practice: an evaluation of 2D and 3D analysis techniques as applied to 30 prostate cancer patients. *Int J Radiat Oncol, Biol, Phys* 2000;46:1281–1290. [PubMed: 10725642]
17. Bijhold J. Three-dimensional verification of patient placement during radiotherapy using portal images. *Med Phys* 1993;20:347–356. [PubMed: 8497221]
18. Gilhuijs KG, van de Ven PJ, van Herk M. Automatic three-dimensional inspection of patient setup in radiation therapy using portal images simulator images, and computed tomography data. *Med Phys* 1996;23:389–399. [PubMed: 8815382]

19. Bansal, R.; Staib, L.H.; Chen, Zhe; Rangarajan, A.; Knisely, J.; Nath, R.; Duncan, JS. A novel approach for the registration of 2D portal and 3D CT images for treatment setup verification in radiotherapy. In: Wells, WM.; Colchester, A.; Delp, S., editors. *Medical Image Computing and Computer Assisted Intervention—MICCAI'98; Proceedings Lecture Notes in Computer Science*; Cambridge, MA: Cambridge University Press; 1998. p. 1075-1086.
20. Bansal, R.; Staib, L.H.; Chen, Zhe; Rangarajan, A.; Knisely, J.; Nath, R.; Duncan, JS. Entropy-based, multiple portal to 3D CT registration for prostate radiotherapy using iteratively estimated segmentation. In: Taylor, C.; Colchester, A., editors. *Medical Image Computing and Computer Assisted Intervention — MICCAI'99; Proceedings Lecture Notes in Computer Science*; United Kingdom: Cambridge University Press; 1999. p. 567-578.
21. Bansal R, Staib L, Chen Z, Rangarajan A, Knisely J, Nath R, Duncan J. A minimax entropy registration framework for patient setup verification in radiotherapy. *Comput Aided Surg* 1999;4:287–304. [PubMed: 10631372]
22. Bansal, R. PhD thesis. Yale University; 2000. Information theoretic integrated segmentation and registration of dual 2D portal image and 3D CT images.
23. Bansal R, Staib LH, Chen Z, Rangarajan A, Knisely J, Nath R, Duncan JS. Entropy based dual portal to 3D CT registration incorporating pixel correlation. *IEEE Trans Med Imaging* 2003;22:29–49. [PubMed: 12703758]
24. Clippe S, Sarrut D, Malet C, Miguët S, Ginestet C, Carrie C. Patient setup error measurement using 3D intensity-based image registration techniques. *Int J Radiat Oncol, Biol, Phys* 2003;56:259–265. [PubMed: 12694847]
25. Weese J, Penney GP, Desmedt P, Buzug TM, Hill DL, Hawkes DJ. Voxel-based 2D/3D registration of fluoroscopy images and ct scans for image-guided surgery. *IEEE Trans Inf Technol Biomed* 1997;1:284–293. [PubMed: 11020832]
26. Penney GP, Weese J, Little JA, Desmedt P, Hill DL, Hawkes DJ. A comparison of similarity measures for use in 2D-3D medical image registration. *IEEE Trans Med Imaging* 1998;17:586–595. [PubMed: 9845314]
27. Penney GP, Batchelor PG, Hill DL, Hawkes DJ, Weese J. Validation of a two- to three-dimensional registration algorithm for aligning preoperative CT images and intraoperative fluoroscopy images. *Med Phys* 2001;28:1024–1032. [PubMed: 11439472]
28. Kim J, Fessler JA, Lam KL, Balter JM, TenHaken RK. A feasibility study of mutual information based setup error estimation for radiotherapy. *Med Phys* 2001;28:2507–2517. [PubMed: 11797954]
29. Munbodh, R. PhD thesis. Yale University; 2004. Achieving accurate automated image registration for prostate radiotherapy.
30. Munbodh R, Jaffray DA, Moseley DJ, Chen Z, Knisely JP, Duncan JS. Automated three dimensional quantification of setup deviations in radiation therapy using a single radiograph and cone beam computed tomography data. *Int J Radiat Oncol, Biol, Phys, Suppl* 2004;60:S199–S200.
31. Munbodh R, Chen Z, Knisely JP, Nath R, Duncan JS. An automated image registration algorithm for quantifying three-dimensional setup variations in prostate radiotherapy. *Int J Radiat Oncol, Biol, Phys, Suppl* 2002;54:S183.
32. Lee, YK.; Rhodes, WT. Scale- and rotation-invariant pattern recognition by a rotating kernel min-max transformation. In: Luk, FT., editor. *Proceedings of SPIE—Optical information processing systems and architectures— Part II*. Vol. 1347. 1990. p. 146-155.
33. Czerwinski RN, Jones DL, O'Brien WD Jr. Line and boundary detection in speckle images. *IEEE Trans Image Process* 1998;7:1700–1714. [PubMed: 18276236]
34. Czerwinski RN, Jones DL, O'Brien WD Jr. Detection of lines and boundaries in speckle images— Application to medical ultrasound. *IEEE Trans Med Imaging* 1999;18:126–136. [PubMed: 10232669]
35. Lujan AE, Baiter JM, Ten Haken RK. Determination of rotations in three dimensions using two-dimensional portal image registration. *Med Phys* 1998;25:703–708. [PubMed: 9608481]

Fig. 1. This figure depicts the patient coordinate system employed. The three principal axes, ML, SI, and AP, and their orientation with respect to the X, Y, and Z axes are displayed.

Fig. 2.

(a) and (b) show a DRR obtained by taking a projection through the kV CBCT and a kV radiograph acquired with the phantom at its reference position, respectively. Shading artifacts in the CBCT gave rise to darker regions of lower contrast in the central part of the DRRs as compared to the kV radiographs. (c) and (d) show the line-enhanced DRR and kV radiograph obtained by filtering images (a) and (b) with “sticks,” short line segments varied in orientation, and which have the form of a matched filter. Filtering the images with the “sticks” operator improves the contrast of linear features to background.

Fig. 3.

2D objective function obtained by computing the correlation coefficient between the downsampled feature-enhanced DRR and radiograph as a function of translation along the SI (t_y) and ML axes (t_x) for pose H at optimization level 4. A Gaussian kernel of width 3 mm and a subsampling factor of 3 were employed when downsampling the images. The objective function is smooth with a single peak at the global maximum. Such an objective function allows easy optimization. The value of the correlation coefficient at alignment, as given by the global peak of the objective function, was 0.9572 indicating a strong linear relationship between the images being matched.

Fig. 4.

The multiresolution optimization strategy employed in 2D is illustrated by means of contour plots of the correlation coefficient as a function of translation along the SI (t_y) and ML (t_x) axes. The contour plots show slices of constant correlation coefficient values through the corresponding 2D objective functions. The optimization was performed over eight levels. Contour plots for levels 8, 6, 4, and 1 are shown here. The position of the peak of the objective function for each of the four levels is indicated with a dot and the value of the true displacement is indicated with an $\times$. The starting point was at (0, 0) and is also indicated with a dot. Note how the objective functions become narrower and steeper as the optimization proceeds from level 8 to level 1. Note also the stability of the global peak. The optimization algorithm reaches the peak at level 8 and moves only marginally after that at higher resolutions. Although the global peak was reached at level 8 in this instance, this is not necessarily the case for all poses and for all transformation parameters. The peak value of the objective function at level 1 was 0.9483.

Fig. 5.

Example of superimposed feature-enhanced DRRs and feature-enhanced radiographs prior to registration (a) and after registration (b). In these images, red and green represent linear features in the DRR and kV radiograph, respectively. At alignment red and green features overlap to maximize the amount of yellow present in the fused image. In this experiment, the radiograph was obtained with the phantom rotated by -5° around the SI axis and shifted 10 mm along the SI axis (pose F).

Fig. 6.

This figure illustrates the maximum total error in determining setup deviations against the magnitude of the setup deviations for poses A through N. The error and displacements were calculated for points on the surface of a sphere of radius 30 mm. Poses that have in-plane displacements only are labeled with a diamond. Poses that contain an out-of-plane rotation and/or an out-of-plane translation are labeled with a circle. For the displacements tested, the overall error in recovering setup deviations did not increase with the presence of out-of-plane rotational or translational displacements. Furthermore, there was no observable trend in the overall error.

Fig. 7.

Error in recovering setup deviation (with and without the error in determining translations along the AP axis) as a function of displacement. This figure illustrates the maximum error in determining setup deviations for poses A through N. The error and displacements were calculated for points on the surface of a sphere of radius 30 mm. Diamonds denote the total registration error and circles denote the registration error excluding errors in the estimation of out-of-plane translations along the AP axis. Note that registration inaccuracies stem mainly from errors in estimating translations along the AP axis.

Fig. 8.

Examples of superimposed feature-enhanced kV DRRs and portal images for two sets of patient data [week 1, (a)–(d) and week 2, (g)–(h)]. Red represents features in the DRRs and green, features in the portal images. The left column shows the unaligned AP and lateral images and the right column shows the corresponding images after registration of the AP portal images to the planning CT. The lateral images were used to visually verify alignment along the AP axis and around the ML axis. Both sets of data were correctly aligned despite the presence of air cavities and deformable soft tissue structures.

Table I

Table of displacements and residual errors. A through N denote the different poses tested. The true pose, estimated pose, and residual errors in estimating the true pose are presented for each of the six transformations parameters. The correlation coefficient, ρ , obtained at the estimated pose, total distance moved, $\mathcal{D}$, and total registration error, ε are also shown. The offset present at the start of the experiment, computed from the mean of the estimated pose for A and B, was subtracted from the estimated poses reported here.

Pose	r_x°	r_y°	r_z°	t_x mm	t_y mm	t_z mm	$\mathcal{D}$ mm	ε mm	ρ
A	True pose	0.000	0.000	0.000	0.000	0.000	0.0000		
	Estimated pose	0.011	0.002	-0.002	-0.005	0.002	0.123		0.950
	Error	0.011	0.002	-0.002	-0.005	0.002	0.123	0.129	
B	True pose	0.000	0.000	0.000	0.000	0.000	0.000		
	Estimated pose	-0.011	-0.002	0.002	0.005	-0.002	-0.123		0.952
	Error	-0.011	-0.002	0.002	0.005	-0.002	-0.123	0.129	
C	True pose	0.000	-5.000	0.000	0.000	-10.000	0.000	10.337	
	Estimated pose	-0.050	-4.977	-0.017	-0.023	-10.054	0.093		0.951
	Error	-0.050	0.023	-0.017	-0.023	-0.054	0.093	0.140	
D	True pose	0.000	-5.000	0.000	0.000	1.000	0.000	2.801	
	Estimated pose	-0.059	-5.032	0.000	0.020	0.984	0.092		0.957
	Error	-0.059	-0.032	0.000	0.020	-0.016	0.092	0.131	
E	True pose	0.000	-5.000	0.000	0.000	3.000	0.000	3.981	
	Estimated pose	0.028	-4.895	-0.028	-0.065	3.014	0.340		0.952
	Error	0.028	0.105	-0.028	-0.065	0.014	0.340	0.404	
F	True pose	0.000	-5.000	0.000	0.000	10.000	0.000	10.337	
	Estimated pose	-0.016	-5.007	-0.013	-0.007	10.045	-0.181		0.952
	Error	-0.016	-0.007	-0.013	-0.007	0.045	-0.181	0.196	
G	True pose	0.000	0.000	0.000	0.000	10.000	0.000	10.000	
	Estimated pose	-0.044	0.007	-0.009	0.009	10.015	-0.211		0.945
	Error	-0.044	0.007	-0.009	0.009	0.015	-0.211	0.235	
H	True pose	0.000	0.000	0.000	10.000	0.000	0.000	10.000	
	Estimated pose	-0.034	-0.026	0.018	10.072	-0.003	-0.121		0.948
	Error	-0.034	-0.026	0.018	0.072	-0.003	-0.121	0.159	
I	True pose	0.000	0.000	0.000	0.000	0.000	10.000	10.000	
	Estimated pose	0.018	0.059	-0.024	-0.005	-0.024	9.794		0.947

Pose	r_x°	r_y°	r_z°	t_x mm	t_y mm	t_z mm	$\mathcal{D}$ mm	ε mm	ρ
<i>J</i>	Error	0.018	0.059	-0.024	-0.005	-0.024	-0.206	0.241	0.947
	True pose	0.000	0.000	0.000	0.000	0.000	3.000	3.000	
	Estimated pose	0.019	0.013	0.005	0.005	0.014	2.999		
<i>K</i>	Error	0.019	0.013	0.005	0.005	0.014	-0.001	0.025	0.946
	True pose	0.000	0.000	0.000	0.000	0.000	1.000	1.000	
	Estimated pose	0.015	0.017	-0.005	0.013	0.002	0.851		
<i>L</i>	Error	0.015	0.017	-0.005	0.013	0.002	-0.149	0.161	0.947
	True pose	0.000	0.000	0.000	0.000	0.000	-10.000	10.000	
	Estimated pose	0.036	0.031	-0.002	0.004	0.001	-9.999		
<i>M</i>	Error	0.036	0.031	-0.002	0.004	0.001	0.001	0.027	0.936
	True pose	0.000	0.000	0.000	0.000	0.000	-10.000	14.142	
	Estimated pose	-0.033	-0.001	-0.003	0.020	10.053	-9.938		
<i>N</i>	Error	-0.033	-0.001	-0.003	0.020	0.053	0.062	0.101	0.951
	True pose	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	Estimated pose	-0.003	0.039	-0.007	0.005	0.002	-0.150		
	Error	-0.003	0.039	-0.007	0.005	0.002	-0.150	0.171	

Table of residual errors. The mean, standard deviation, minimum, and maximum value of the absolute value of the residual errors for poses C through N.

Table II

	r_x°	r_y°	r_z°	t_x mm	t_y mm	t_z mm
Mean absolute error	0.029	0.030	0.011	0.021	0.020	0.134
Std. absolute error	0.016	0.028	0.009	0.023	0.020	0.096
Min absolute error	0.003	0.001	0.000	0.004	0.001	0.001
Max absolute error	0.059	0.105	0.028	0.072	0.054	0.340
Median absolute error	0.030	0.025	0.008	0.011	0.015	0.135