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A frequency-based approach to locate common structure for 2D-3D intensity-based registration of setup images in prostate radiotherapy

Reshma Munbodh^{a)},

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

Zhe Chen,

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

David A. Jaffray,

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

Douglas J. Moseley,

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

Jonathan P. S. Knisely, and

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

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

In many radiotherapy clinics, geometric uncertainties in the delivery of 3D conformal radiation therapy and intensity modulated radiation therapy of the prostate are reduced by aligning the patient's bony anatomy in the planning 3D CT to corresponding bony anatomy in 2D portal images acquired before every treatment fraction. In this paper, we seek to determine if there is a frequency band within the portal images and the digitally reconstructed radiographs (DRRs) of the planning CT in which bony anatomy predominates over non-bony anatomy such that portal images and DRRs can be suitably filtered to achieve high registration accuracy in an automated 2D-3D single portal intensity-based registration framework. Two similarity measures, mutual information and the Pearson correlation coefficient were tested on carefully collected gold-standard data consisting of a kilovoltage cone-beam CT (CBCT) and megavoltage portal images in the anterior-posterior (AP) view of an anthropomorphic phantom acquired under clinical conditions at known poses, and on patient data. It was found that filtering the portal images and DRRs during the registration considerably improved registration performance. Without filtering, the registration did not always converge while with filtering it always converged to an accurate solution. For the pose-determination experiments conducted on the anthropomorphic phantom with the correlation coefficient, the mean (and standard deviation) of the absolute errors in recovering each of the six transformation parameters were $\theta_x: 0.18(0.19)^\circ$, $\theta_y: 0.04(0.04)^\circ$, $\theta_z: 0.04(0.02)^\circ$, $t_x: 0.14(0.15)$ mm, $t_y: 0.09(0.05)$ mm, and $t_z: 0.49(0.40)$ mm. The mutual information-based registration with filtered images also resulted in similarly small errors. For the patient data, visual inspection of the superimposed registered images showed

a) Author to whom correspondence should be addressed: Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., NY, NY 10021. munbodhr@mskcc.org.

that they were correctly aligned in all instances. The results presented in this paper suggest that robust and accurate registration can be achieved with intensity-based methods by focusing on rigid bony structures in the images while diminishing the influence of artifacts with similar frequencies as soft tissue.

Keywords

2D-3D image registration; spectral analysis; prostate radiotherapy; cone beam CT; setup verification; portal image

I. Introduction

Technological advances in external beam radiation therapy, such as 3D conformal radiation therapy and intensity modulated radiation therapy, allow accurate specification of a target volume from a 3D planning CT and the design of highly conformal treatment plans. These methods incrementally spare normal tissues relative to the target thereby allowing an escalation in radiation dose with improved local tumor control and reduced complications. However, geometric uncertainties in the daily treatment delivery arising from setup errors and organ motion and deformation are a limiting factor. In prostate radiotherapy, setup errors are defined as deviations in the position of the patient's pelvic bony anatomy with respect to the planned orientation of the treatment beams. Portal images, which are planar radiographs obtained at megavoltage energies during treatment, have been employed to improve the reproducibility of patient positioning between treatment fractions and reduce geometric uncertainties from setup errors.^{1,2} The 3D displacement in the patient's treatment setup relative to the planned setup can be estimated by calculating the geometric transformation that aligns the 2D megavoltage portal images and the 3D kilovoltage planning CT. In the last few years, 3D imaging capabilities have been added to linear accelerator treatment machines such that the 3D displacement in patient setup and internal organ motion may be determined by registering the 3D planning CT to a cone-beam CT acquired during treatment. At present, though, a majority of radiotherapy clinics still rely on 2D portal images for setup verification. In this paper, we discuss limitations in 2D-3D intensity-based registration of portal images to kV CT data and suggest a general approach to considerably improve registration accuracy with intensity-based methods.

2D-3D intensity-based registration of portal images and a CT is usually achieved by iteratively shifting and rotating the CT until a similarity measure computed on gray level values in radiographs, obtained by computing perspective projections of the CT, and portal images is maximized. In setup verification for prostate radiotherapy, because the prostate is not visible in the portal images, the bony anatomy of the pelvis may be used as a surrogate for the prostate. The bony anatomy of the pelvis is common to both modalities, non-deformable, and more stable relative to the prostate than other soft tissue structures (granted it may not correlate directly to the true position of the prostate in which case any anticipated relative motion should be accounted for by addition of an internal margin to the clinical target volume). Pelvic bony anatomy is also structurally more sensitive to position and orientation of the patient than soft tissue. Thus, setup errors may be estimated from the rigid transformation that aligns bony anatomy in CT and portal images. A number of factors result in reduced structural similarity between the two images. These factors include structure noise due to the superposition of deformable structures on bony anatomy in the projection images, additive intensity inhomogeneities from x-ray scatter associated with patient thickness, reduced contrast-to-noise ratio in portal images due to the reduced differential absorption between soft tissue and bone at megavoltage energies, shading artifacts from the heel effect and other imaging artifacts associated with x-ray scatter such as cupping artifacts in cone-beam CT images.²⁻⁶

In this study, we seek to determine, using spectral methods, if there are parts of the spatial spectrum of digitally reconstructed radiographs (DRRs) and portal images where the representation of bony anatomy is favorable with respect to the representation of non-bony anatomy. We subsequently investigate whether portal images and DRRs can be filtered to emphasize such spatial frequencies and if working with filtered images can result in higher registration accuracy. If the conclusion to these questions is positive, we wish to establish a generally applicable procedure. Towards this end, we performed registration tests using two similarity measures, mutual information and the Pearson correlation coefficient. The similarity measures were used within an automated 2D-3D intensity-based registration framework utilizing a single portal image in the AP view. Validation of the proposed techniques was performed on a set of accurately collected gold standard data consisting of portal images and cone beam CT data of an anthropomorphic phantom, as well as portal images and a CT scan of a patient acquired with a helical CT scanner.

II. Methods and Materials

A. Coordinate system

An orthogonal, right-handed coordinate system that is fixed with respect to the subject and with the origin at the isocenter was employed throughout this study. The x axis (medio-lateral) is directed across the subject from right to left, the y axis (inferior-superior) is directed along the subject from toe to head and the z axis (posterior-anterior) is directed upward, through the subject toward the x-ray source.

B. Phantom images

Pose determination experiments were conducted on an anthropomorphic phantom of the pelvic region. The aim of the experiments was to determine the capability of the proposed methods in automatically estimating deviations of the phantom from its ideal setup position using a kV CBCT image of the phantom at its ideal position and megavoltage AP portal images of the phantom acquired after it was displaced by a known amount. The anthropomorphic phantom consisted of a pelvis, lumbar spine and synthetic soft tissue structures enclosed in plexiglass. Three radio-opaque ball bearings of diameter 2 mm were affixed to the surface of the phantom for consistent setup by alignment to lateral and vertical lasers. A fourth ball bearing of diameter 5 mm was embedded inside the phantom and used with the other three ball bearings for ground truth validation.

The imaging system employed had both kilovoltage and megavoltage imaging capabilities. The system was based on an Elekta SL 20 linear accelerator with two flat panel imagers. Prior to data collection, the imaging equipment was calibrated to ensure the isocenter of the MV imaging system and that of the kV imaging system were coincident. Projection images were obtained at a pixel pitch of 0.4 mm and digitized to 16 bits.

Megavoltage AP portal images and matching kilovoltage CBCT scans of the phantom in a supine position were acquired at each of 15 known poses. The matching CBCT scans were acquired for 3D ground truth determination. The imaging system had 5 degrees of freedom. Absolute translational displacements of the phantom along each of the three axes ranged up to 10 mm and absolute rotational displacements around the AP and SI axes varied between 0° and 5° .

All CBCT scans were obtained at 120 kV. The first of the 15 CBCT images, obtained with the phantom at its ideal position (identity transformation), was used as the reference CBCT. The reference CBCT image used for alignment to the portal images was reconstructed on a $400 \times 400 \times 250$ matrix with a voxel size of $1.04 \text{ mm} \times 1.04 \text{ mm} \times 1.04 \text{ mm}$. When used for ground

truth determination, all 15 CBCT images were reconstructed at twice that resolution (half the voxel size). The ground truth, that is the exact 3D displacement of the phantom relative to its reference position, for every pose was calculated by registering the centroids of the ball bearings in each of the CBCT scans to those from the reference CBCT data set using a singular value decomposition method.⁷

The 15 AP portal images were acquired under conditions similar to clinical settings with a 6 MV beam at a dose of 6 MU. The source-to-axis distance (SAD) was 1003.1 mm and the source-to-detector distance (SDD) was 1601.8 mm. To reduce noise in the portal images, repeated projections were averaged at each pose. The portal images were down-sampled to 1 mm $\times$ 1 mm and only a subregion, of size 12 cm $\times$ 12 cm at the isocenter, of the original 20 cm $\times$ 20 cm portal fields was used for registration to the reference CBCT. This was done to exclude the femoral heads from the registration as these may move independently from the pelvis during patient treatment. The piercing point was not at the geometrical center of the images and this was taken into consideration in the registration.

The portal images contained bright horizontal lines due to defective detector elements in the top half of the image. The kV CBCT contained slight shading artifacts.

C. Patient images

A planning kV CT image and seven AP and LR portal images were acquired during treatment of a patient over 7 consecutive weeks. The CT was acquired on a GE CT scanner and the portal images were obtained with a Varian amorphous silicon electronic portal imager. The portal images were obtained at 6 MV. The SAD was 1000 mm and the SDD, calculated from the graticule spacing on the portal images, was 1454 mm. The planning CT isocenter was assumed to be at the location provided in the CT header file. The piercing point of the radiographs was assumed to be at the center of the image. Prior to registration, the CT and portal images were downsampled from an original isotropic voxel/pixel size of 0.78 mm to an isotropic resolution of 1 mm. A subregion of the original 15 cm $\times$ 15 cm AP portal images of size 13 cm $\times$ 12 cm and excluding the femurs was registered to the CT. The LR images were not used in the registration. The registration performance was assessed by visual comparison of the AP and LR portal images to AP and LR DRRs computed from the CT at the estimated optimal transformation. LR images were used in addition to the AP image to verify that the images were correctly registered since displacements such as r_x and t_z are difficult to visualize in the AP view where they appear as out-of-plane displacements. These show up as in-plane displacements in the LR view and can be better visualized allowing a better assessment of registration accuracy.

D. Spectral analysis

Central to the method employed here is an examination of the spectral content of projection images to determine if there are spatial frequencies where bony anatomy is favorably represented with respect to non-bony anatomy (soft tissue, muscle, fat, and air). Toward this end, we find it instructive to compare the sample spectrum of bone to the sample spectrum of other tissues. Two projection images, one each of bony and non-bony matter, were computed from a kV CT of the pelvic region of a male patient who was not part of the data set employed for the pose determination experiments. The CT was free of reconstruction artifacts and was considered to provide an accurate representation of the relevant anatomy. The tissue class to which a particular voxel belongs was deduced from the linear attenuation coefficient at that voxel. Examples of the bone and non-bone images computed from the CT are illustrated in Fig. 1. The power spectral densities (PSDs) for the bone and non-bone projection images was computed by estimating the sample spectrum along the rows and averaging over all sample spectra. Subsequently, the ratio of power of bony and non-bony anatomy as a function of spatial

frequency was determined by forming the ratio of the two PSDs. We term this measure the bone to no-bone spectral ratio (BNBSR). A construction of this nature is useful in that it can reveal spatial frequencies where bony anatomy is better represented than non-bony anatomy. Graphs of the PSDs and BNBSR are shown in Fig. 2. These are described further in Section III.

After identification of a relevant frequency band the portal images and DRRs computed from the CT were filtered to emphasize bony anatomy during the registration process. In this study, a finite impulse response (FIR) filter was designed to filter the DRRs and portal images. An FIR filter was chosen as it allows precise manipulation of the cutoff frequency and roll-off rate of the filter.

E. Similarity measures

The proposed filtering technique was validated with two intensity-based similarity measures, the correlation coefficient and mutual information. Both similarity measures have been employed for 2D-2D and 2D-3D registration in radiotherapy.

Let $G = \{G(x, y, z)\}$ be a homogeneous random field representing the CT in 3D space where (x, y, z) are the coordinates of points in the CT. Let $U = \{U(i, j)\}$ be a homogeneous random field from which the portal image is sampled, with (i, j) being the coordinates of points in the portal image on the 2D imaging plane. We shall denote the observed values of the random fields with lowercase letters. Let $g = \{g(x, y, z)\}$ be a realization of G with $g(x, y, z)$ being the intensity of a point in the CT at location (x, y, z) . Similarly, $u = \{u(i, j)\}$ is a realization of U and $u(i, j)$ is the intensity of a point at location (i, j) in the portal image. The position and orientation of the CT volume with respect to the portal image is described by the six transformation parameters $\psi = [\theta_x, \theta_y, \theta_z, t_x, t_y, t_z]$. The DRR, $V_\psi = \{V_\psi(i, j)\}$, is a homogeneous random field in 2D space obtained by summing the CT numbers in the spatially transformed CT along the rays from the x-ray source to locations (i, j) on the 2D image plane using projective geometry. That is, $V_\psi(i, j) = \int G(T_\psi(x, y, z))dr$, where T is the 3D spatial mapping defined by ψ . The gray level values observed at pixels (i, j) in the DRR are denoted by $v_\psi = \{v_\psi(i, j)\}$. The range of possible gray level values in U and V are denoted by $\mathcal{U}$ and $\mathcal{V}$, respectively.

Our task is to estimate ψ by maximizing some similarity, S , between U and V_ψ :

$$\hat{\psi} = \arg \max_{\psi} S(U, V_\psi).$$

1. Pearson correlation coefficient—The correlation coefficient, defined as the ratio of the co-variance of two random variables to the product of their standard deviations, measures both the magnitude and direction of the linear relationship between two variables. The Pearson estimator is commonly employed to estimate the correlation coefficient. The Pearson correlation coefficient, $\rho(U, V_\psi)$, between the portal image and the DRR is defined by Eq. 2.5.1.

$$\rho(U, V_\psi) = \frac{\sum_{i,j} (u(i, j) - \bar{u})(v_\psi(i, j) - \bar{v}_\psi)}{\sqrt{\sum_{i,j} (u(i, j) - \bar{u})^2} \sqrt{\sum_{i,j} (v_\psi(i, j) - \bar{v}_\psi)^2}}, \quad (1)$$

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

The Pearson correlation coefficient ranges from 1 and -1 depending on whether the two variables are directly or inversely correlated. The closer the absolute value of the estimated correlation is to 1, the stronger the linear relationship. The two random variables, in this case the pixel intensity values in the DRRs and portal images, are assumed to have a normal distribution. Deviations from the underlying assumption of normality may result in a less accurate estimate of the correlation coefficient although for large samples the assumption of normality may be less important.

2. Mutual information—Mutual information (MI) measures the general level of dependence between a pair of random variables although it does not indicate the nature of the relationship; MI “is a measure of the amount of information that one random variable contains about another random variable or the reduction in the uncertainty of one random variable due to the knowledge of the other.”⁸ The use of MI as a similarity measure in image registration was proposed by Refs. 9 and ¹⁰. It is expected that the MI between two images is maximized when they are aligned. MI varies as a function of the marginal entropy and joint entropy of the random variables. It is computed from the probability mass functions of the image intensities rather than directly from the intensity values. MI is more robust to nonlinearities in the intensity relationship between the images.

Let U and V_ψ have joint probability mass function $p(u, v_\psi)$ and marginal probability mass functions $p(u)$ and $p(v_\psi)$. The MI, $I(U; V_\psi)$, is the relative entropy or Kullback-Leibler distance between the joint distribution $p(u, v_\psi)$ and the product distribution $p(u)p(v_\psi)$:⁸

$$I(U; V_\psi) = \sum_{u \in \mathcal{U}} \sum_{v_\psi \in \mathcal{V}} p(u, v_\psi) \frac{\log p(u, v_\psi)}{p(u)p(v_\psi)}. \quad (2)$$

The definition of MI can be rewritten in term of the entropies of U and V_ψ as

$$I(U; V_\psi) = H(U) + H(U|V_\psi), \quad (3)$$

$$I(U; V_\psi) = H(U) + H(V_\psi) - H(U, V_\psi). \quad (4)$$

In this study, histogram-based MI was employed whereby the marginal and joint probability mass functions were estimated from the marginal and joint histograms of pixel intensities in the overlapping region of the images. Thirty two bins were used to compute the histograms. The implementation was nonparametric in that no prior shape was assumed about the density functions.

F. Optimization strategy

The similarity between the DRRs and portal image computed over all possible translations and rotations gives an objective function in 6D. The global peak of this objective function should be at the optimal transformation which aligns the CT to the portal image. A local search optimization technique similar to the technique proposed by Ref. 11 was employed. At every step of the optimization each of the six transformation parameters was perturbed in turn by a known small fixed quantity and the similarity between the DRR at this new transformation and the portal image computed. The optimization then proceeded in the direction of the perturbation that produced the largest increase in similarity between the two images. This process was

reiterated until the increase in similarity due to a small change in the transformation parameters was less than a predefined tolerance value.

A multiresolution optimization strategy was employed to accelerate convergence to the global maximum and increase the capture range of the algorithm. Multiresolution optimization involves performing the optimization over a number of levels, whereby the images to be registered are smoothed and downsampled to a greater extent at the higher levels. The transformation parameters obtained at the current level are used as the starting parameters to the next level until the final level is reached. At any given level n , the images were blurred with a Gaussian kernel of standard deviation $0.5 \times n$ and downsampled by a factor of n . Smoothing prior to downsampling prevents aliasing. Four optimization levels were employed when optimizing over mutual information and three levels were employed for the correlation coefficient. More levels were required for mutual information than for the correlation coefficient because the objective function was narrower.

G. Quantification of registration errors

Registration errors in estimating displacements applied to the phantom were quantified as the maximum distance moved by points on a virtual sphere centered about the simulated isocenter from their intended position.^{12,13} In this study, the isocenter was assumed to be at the geometrical center of the CBCT. The points can be considered to be contour points on the boundary of the treatment field. The maximum distance, $\mathcal{E}$, of points on the sphere from their desired position after registration was calculated as

$$\mathcal{E} = \max_{x \in S} \| (T_{\hat{\psi}}(x) - T_{\psi}(x)) \|, \quad (5)$$

where $T_{\hat{\psi}}$ and T_{ψ} are the transformation matrices at the estimated and actual transformation parameters, respectively, and x represents the coordinates of the points on the surface of a sphere with a radius of 30 mm and at an angular separation of 5° .

Similarly, the maximum distance, $\mathcal{D}$, of points on the sphere from the isocenter after a transformation T_{ψ} was computed from

$$\mathcal{D} = \max_{x \in S} \| T_{\psi}(x) \|. \quad (6)$$

III. Results

Projection images of bony and non-bony structure (soft tissue, muscle and air) of a kV CT of the pelvic region of a patient at the identity pose are shown in Fig. 1. As indicated above, this patient was not part of the datasets employed in the pose experiments. The power spectral density for these bone and non-bone projection images is shown in Fig. 2(a). The BNBSR, estimated from the sample spectra of the projected radiographs, is shown in Fig. 2(b). The BNBSR was computed as the ratio of the PSD of the projection of bony structure to PSD of a projection of non-bone regions. We note the following three features of the BNBSR. First, the BNBSR values are lowest at the lowest part of the spatial spectrum; that is, the signal due to bone is considerably lower than non-bone at very low spatial frequencies. Second, there is a steep transition to much higher BNBSR at approximately 0.3 cm^{-1} . Third, after rising to higher values the BNBSR falls off to a plateau, which extends into higher frequencies. A frequency band of interest was identified from the BNBSR as that part of the image spectrum where the power from bony anatomy is larger than power from non-bony anatomy. Since the power of

both bony and non-bony anatomy decreases as a function of frequency, it was deemed reasonable to use a high-pass filter rather than a bandpass filter.

The BNBSR was computed for a number of poses. These evaluations all showed the same characteristics and the cutoff frequency, selected as 0.1 cm^{-1} (slightly less than the transition frequency identified above) from plots of the BNBSR, was found to be invariant to pose. A high-pass FIR filter with a cutoff frequency of 0.1 cm^{-1} was used to filter the DRRs and portal images. Large bony structures, which typically have a spatial frequency of at least 0.25 cm^{-1} and bony ridges, which generally have a spatial frequency of about $3\text{--}6 \text{ cm}^{-1}$ were preserved. Figures 3(a) and 3(d) illustrate a kV CBCT DRR of the phantom, at the identity pose, and a sample MV portal image obtained at the reference position. The images obtained by high-pass filtering the above are shown in Figs. 3(b) and 3(e), respectively. The difference images, or the residual of the filtering operation are shown in Figs. 3(c) and 3(f). It is apparent, on visual inspection, that the pixel intensities that form the residual images removed by the filtering operation do not match. These residual images do not share common anatomical structure at the correct pose. Filtering improves the structural similarity of the images.

Full 3D validation of the two selected similarity measures, the Pearson correlation coefficient and mutual information, was performed on: (1) gold standard data comprising a 3D kV reference CBCT of an anthropomorphic phantom of the pelvis and corresponding MV electronic portal images in the AP view acquired at 15 different poses; the ground truth was determined in 3D by registering the kV reference 3D CBCT to 3D CBCT images acquired at each of 15 poses; (2) a 3D kV planning CT of a patient acquired on a conventional CT scanner and AP portal images of the same patient acquired during treatment on a weekly basis over 7 weeks. Experiments to assess registration performance were performed on both filtered and unfiltered images.

For tests on the phantom, both the mutual information and the correlation coefficient-based algorithms failed to converge to within 5 mm of the ground truth, for all poses, when unfiltered images were used for the registration. Translations along the y and z axes and rotations around the x and y axes were particularly erroneous. In contrast, an accurate registration solution was obtained, as described below, for every pose with both similarity measures on the filtered images.

Table I shows the ground truth and estimates of the poses with the correlation coefficient and mutual information on the filtered images. The mean, standard deviation, minimum, and maximum of the absolute registration errors for each of the six transformation parameters over all 15 poses for the correlation coefficient are shown in Table II. The mean (and standard deviation) of the absolute errors for each of the six transformation parameters were θ_x : $0.18 (0.19)^\circ$, θ_y : $0.04(0.04)^\circ$, θ_z : $0.04(0.02)^\circ$, t_x : $0.14(0.15) \text{ mm}$, t_y : $0.09(0.05) \text{ mm}$ and t_z : $0.49(0.40) \text{ mm}$. The mean (and standard deviation) of the overall error from Eq. (5) were $0.64(0.43) \text{ mm}$, respectively. For all the poses the correlation coefficient at the optimal transformation was greater than or equal to 0.8 indicating a strong linear relationship between the filtered DRR and filtered portal image.

The results obtained with mutual information on the filtered images were similar to those obtained with the correlation coefficient. The corresponding mean absolute error (and standard deviation) for each of the six transformation parameters with mutual information, as presented in Table III were θ_x : $0.20(0.17)^\circ$, θ_y : $0.08(0.07)^\circ$, θ_z : $0.04(0.03)^\circ$, t_x : $0.17(0.13) \text{ mm}$, t_y : $0.08 (0.05) \text{ mm}$ and t_z : $0.57(0.48) \text{ mm}$. The mean (and standard deviation) of the overall error were $0.74(0.48) \text{ mm}$. It should be noted that the small errors for θ_x with both the correlation and mutual information are simply an indication that the algorithm did not drift from its initial value since θ_x was not varied in the simulated poses.

As an example, the 2D objective functions obtained by plotting the correlation coefficient and MI between the unfiltered kV CBCT DRR and MV portal image from Figs. 3(a) and 3(d) as a function of translations along the x and y axes for the identity pose are shown in Figs. 4(a) and 4(c), respectively. The peak of the objective functions, in this instance, should be at (0, 0). For this data set, prior to filtering, the correlation coefficient increased monotonically as a function of translation along the y axis. For the unfiltered images the global maximum of the objective function occurred when there was no displacement along the x axis and at the end-point of the translation range tested for t_y , that is at (0, 15 mm). In the case of mutual information, a global maximum was obtained at the correct pose. The mutual information, however, also increased along the y axis giving another maximum at (0, 15 mm), i.e., the objective function had multiple maxima. Optimization on the unfiltered data resulted in the algorithm getting trapped in local maxima and not converging to the true pose.

Figures 4(b) and 4(d) show the objective functions obtained with both measures when the high-pass filtered images of Figs. 3(b) and 3(e) were used. Registration after filtering gave rise to a well-behaved objective function with a sharper peak at the correct transformation which aligns the portal image to the CT.

Considerable improvements with filtering were observed with both similarity measures with patient images. A sample kV DRR computed from the planning CT of the patient and a sample portal image before and after filtering are shown in Fig. 5. For the patient images visual inspection, as described for the following example, was performed to determine registration accuracy. Figures 6(a) and 6(d) illustrate fused AP and LR images of the patient prior to registration. In these images, red denotes a line-enhanced DRR while green denotes a line-enhanced portal image.^{12,13} At alignment, the two sets of features, and hence the red and green, should overlap so that the amount of yellow is maximized. This can be seen in Figs. 6(b), 6(c), 6(e), and 6(f). It should be noted that although the registration was performed with the AP portal image only, both LR and AP images were employed for visual validation of the results to ensure that the out-of-plane parameters had been correctly estimated. When unfiltered images were used for the registration, visual inspection of the fused images indicated registration errors of several millimeters, with errors of more than 5 mm along the z axis and about 3–5 mm along the x and y axes; that is, errors in the registration were of the same magnitude as or larger than the setup errors being quantified. When filtered images were employed errors in the registration could not be detected upon visual inspection of all seven sets of images. With the filtered images, estimated shifts in the patient setup were less than 4 mm and 4° . Table IV lists the estimated shifts in the patient position relative to the treatment field for the correlation and mutual information-based registration algorithms over the 7 weeks. The estimated setup errors were similar with both similarity measures.

IV. Discussion

Two similarity measures, the Pearson correlation coefficient and mutual information were tested within a completely automated 2D-3D image registration framework to align DRRs from a 3D kV CT image to a single MV portal image of the pelvis in the AP view. A spatial frequency band of interest was identified from the BNBSR as the part of the spectrum of the projection images where bony anatomy has more power than non-bony anatomy. Very high registration accuracy was achieved once the phantom and patient images were high-pass filtered suggesting that using the identified frequency band in the DRRs and portal image can reduce the bias and variance inherent to intensity-based registration algorithms. No other preprocessing of the images was necessary. While care was taken to exclude the femoral bones from the DRRs and portal images during the registration, it was not necessary to identify specific subregions of interest in these images.

CT and portal images are both formed by the interaction of x rays with matter suggesting that they can be treated as related modalities. As indicated before, there are a number of differences in the image formation process which result in differences in intensity variations between DRRs and portal images and reduced structural similarity. It may be inferred that factors that reduce structural similarity between the two images would adversely affect their coregistration. We hypothesize that the key to successful registration is to focus on anatomical structure common to the two images, that is bony anatomy, while diminishing the influence of confounding factors which diminish structural similarity between the images.

The approach employed in this study was to consider a spectral ratio, called the BNBSR, of image intensity for bone and non-bone regions of the planning CT of a patient. The BNBSR aids in determining which segments of the image spectrum have greater power from bone relative to non-bone, and serves as the basis for determining the cutoff of a filter designed to reduce intensity variations from non-bony anatomy. Other intensity variations which are present at very low frequencies, such as scatter radiation and the heel effect, were also removed because of the nature of the filter selected.

The effect of high-pass filtering has been presented in three manners: (1) through figures of filtered images, (2) through examples of objective functions, and (3) through the estimates of errors obtained after registration. The effect of filtering on the objective functions is illustrated in Fig. 4. It was observed that filtering the projection images produces a well-behaved objective function with a global peak at the correct position. Filtering also appeared to increase the peakedness of the objective functions. A downside was that increased peakedness of the objective function came at the cost of a narrower base and thus a smaller capture range. In this study, this was addressed by employing a multiresolution optimization strategy.

It would be informative to try to understand why the performance of the correlation coefficient or mutual information is poor when unfiltered images are used for the registration. The intensity differences present at low frequencies can have high energy. They are present in a majority of pixels resulting in regions of gradually varying intensities, which are similar, but may not match exactly or at the correct position, as can be seen in Figs. 3 and 5 and indicated by the objective functions in Fig. 4. Since the correlation coefficient is computed directly from the pixel intensity values, the low frequency intensity variations can dominate the value of the correlation coefficient. The high value of the correlation coefficient in Fig. 4(a), for example, shows that there is a strong linear relationship between intensities in the unfiltered images before filtering. Unfortunately, this correlation is driven by regions that do not necessarily correspond anatomically.

Mutual information varies as a function of the marginal entropy of the DRR and the joint entropy between the DRR and portal image. Mutual information is maximized for the combination of marginal and joint entropies which yields the largest difference. It can reasonably be assumed, that at alignment the marginal entropy is large while the joint entropy is low indicating a joint histogram which is highly focused (compact). Registration with mutual information may be guided by structures in the image that have high entropy and which contribute most to the decrease in joint entropy at alignment. As mentioned before, low-frequency artifacts have high energy and are present in a majority of the pixel intensity values, which are used to estimate the probability density functions. They also have a wide intensity range and therefore high entropy. We believe, for example, that the joint entropy may be lower for transformations where the larger high-entropy regions containing the shading artifacts match. That is, not only is the dispersion of the marginal histogram large for the low-frequency regions, but the dispersion of the joint histogram is least when the low-frequency regions are aligned giving rise to either a local or global maximum at the wrong pose. In this case, a more accurate estimate of the density functions or the use of a larger number of pixels to estimate

the probability density functions might not necessarily improve the registration. By avoiding the low frequency band, we are reducing the amount of soft tissue structure and other low frequency artifacts present in the image, and thus, their influence on the registration.

A number of 2D-2D^{14–25} and 2D-3D^{12,13,26–35} registration methods have been proposed for the determination of setup errors in pelvic sites. Other 2D-3D registration methods developed for sites other than the pelvis but which use the correlation coefficient or mutual information include the work by Refs. 11 and ^{36–41}. Of the 2D-3D registration methods proposed, Refs. 15, ^{25, 38}, and ³⁴ studied the effect of image preprocessing on intensity-based registration accuracy. It should be noted that most of the proposed 2D-3D registration methods require at least two portal images to determine the 3D setup error.

The method proposed here is similar thematically to procedures described by Kreuder *et al.*,¹⁵ Munbodh *et al.*,^{12,13,26} Dekker *et al.*,²⁵ and Bansal *et al.*,^{29–31} though with differences as indicated. Kreuder *et al.*¹⁵ presented a Fourier implementation of the normalized cross-correlation for the quantification of in-plane translational setup errors. Their method has been used mostly for portal-to-portal matching with additional testing on kV DRR and portal images. The portal images were first contrast enhanced and then bandpass filtered by convolving the images with a combination of a block filter and Gaussian kernel. The width of the convolution kernel was chosen to be about 0.3 cm^{-1} . After filtering, nonridge pixels were set to zero. The authors bandpass filtered the portal images prior to registration to enhance bony ridges and reduce low frequency artifacts such as scatter radiation and high frequency noise such as air bubbles. The correlation function was found to have a steep and distinct maximum which made reliable matching using the Fourier implementation of the correlation possible.

In a previous study,^{12,13,26} which strongly influenced the current study, we developed an automated 2D-3D registration algorithm to align a 3D CT and 2D kV AP radiographs and 2D AP portal images through correlation of enhanced linear image features mainly representing bony ridges. Feature enhancement was performed by filtering the images with line operators, that is, short line segments varied in orientation, to achieve the maximum projected value at each pixel in the image. This also served to diminish the influence of slowly varying background intensities. No other image preprocessing was performed. The objective function defined by correlating the line-enhanced images had a wide attraction basin and a sharp peak at the correct pose allowing full 3D quantification of setup errors. The accuracy achieved was similar to the accuracy reported here.

Dekker *et al.*²⁵ conducted an interesting study where they evaluated the performance of six intensity-based measures with and without pre-processing in the 2D registration of DRRs to portal images. Preprocessing involving unsharp masking followed by gray level histogram equalization was applied to both the reference and portal images. Unsharp masking enhances local changes in the images by subtracting a blurred version of the image from itself. It may also entail adding this difference image back to the original. The width of the blurring kernel was chosen to enhance bony ridges and edges. Although image preprocessing improved registration accuracy, the objective functions for a few of the similarity measures had a large number of local minima. This was mainly a problem with mutual information which had the most number of local minima. The success of mutual information was also found to be sensitive to the number of bins used to compute the histogram. Mutual information (and other measures) performed better if the images were histogram equalized after being unsharp masked.

Finally, Bansal *et al.*^{29–31} reported an integrated information theoretic segmentation/registration framework to register a 3D CT to dual portal images using Parzen windows as the density estimator. This work is based on the assumption that the probability density function of the transmission images is a mixture density consisting of the probability density function

of bone and non-bone regions in the images. The authors argue that by decomposing the mixture density into its individual component densities a better estimate of the mutual information between the images being aligned can be computed. The method requires segmenting the portal image into distinct bone and non-bone regions, which is achieved through an iterative segmentation/registration approach. As part of their study, they compared the performance of the integrated information theoretic segmentation/registration framework to Parzen windows-based mutual information. The authors reported an improvement in registration accuracy with their method over mutual information in tests on large field of view portal images simulated from a phantom and patient data. The solutions were found to be dependent on preprocessing such as histogram equalization.

The method developed here is different in that it does not rely on image segmentation, feature enhancement or on nonlinear contrast enhancement in the form of histogram equalization or thresholding. There are no subjective steps in the procedure presented. The methods presented here also enable full 3D quantification of setup errors using a 3D kV CT and a single AP portal image. We present filtering as a single general step which results in a considerable improvement in registration accuracy. A procedure is outlined to detect spatial frequencies where the representation of bone is favorable. The procedure allows the use of the large and well-developed literature on filters to design specific filters to capitalize on identified spatial frequencies. We employed a general frequency band where as much bony structure as possible was preserved rather than just ridges and edges. Filtering resulted in a well-behaved objective function. A higher cutoff frequency than the one employed in this study might result in an objective function that has a narrower capture range with multiple local maxima making optimization difficult and extension to 3D computationally prohibitive. Our strategy of avoiding the low frequencies differs from unsharp masking in instances where the difference image is added back to the original image. In the latter case, although the bony ridges are enhanced, the low frequency variations are still present. Such preprocessing may well improve registration, but it may not guarantee consistently accurate registration if low frequency artifacts are pronounced. With respect to the study of Bansal *et al.* we note de-emphasizing low frequency artifacts with filtering is fundamentally different from the segmentation of the radiographs into bone and non-bone regions, particularly in the case of low-contrast projection images, where the bony regions actually consist of bone buried in soft tissue and other low frequency artifacts with the signal from the bone being weak relative to the artifacts. Since there is no clear delineation between bone and non-bone anatomy, the artifacts, in this case, are still present in the pixel intensities from which the densities are estimated. Contrast enhancement of the unfiltered images through adaptive histogram equalization also does not eliminate low frequency artifacts.

Though demonstrated with the correlation coefficient and mutual information on images of the pelvis, we wish to suggest that the procedure developed in this study is generally applicable to other intensity-based registration methods and possibly to other treatment sites where the position of bony anatomy correlates with the tumor position.

V. Conclusion

We have presented a procedure to identify spatial frequencies favorable for intensity-based registration of a diagnostic 3D CT image to treatment portal images for setup verification in prostate radiotherapy. A spatial frequency band was identified from the bone-to-no-bone spectral ratio as the part of the projection images spectrum where bony anatomy has more power than non-bony anatomy. Validation was performed on portal images and a cone beam CT of an anthropomorphic phantom, and portal images and a conventional CT of a patient. Accurate registration was achieved with two similarity measures, the Pearson correlation coefficient and mutual information, when the identified spatial frequency band was employed.

Our results also indicate that the three rotations and three translations that constitute the registration transformation parameters can be estimated accurately with a fully automated procedure using a 3D CT and a single portal image in the AP view.

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Fig. 1. Projection images of bone and non-bony anatomy. The images were computed from a kV CT of the pelvic region of a patient under an identity transformation. The CT was not part of the data set employed for the subsequent pose determination experiments. The CT was free of reconstruction artifacts and was considered to provide an accurate representation of the patient anatomy.

Fig. 2.

Power spectral density and bone-to-bone spectral ratio (BNBSR). (a) The power in the bone and no-bone images illustrated in Fig. 1 as a function of spatial frequency. In both images, power decreases with frequency. (b) The BNBSR, expressed in dB, for different spatial frequencies. The BNBSR was computed as the ratio of the power spectral density of the bone image to the power spectral density of the no-bone region. We note the following three features of the BNBSR. First, the signal due to bone is considerably lower than no-bone at very low spatial frequencies. Second, there is a steep transition to much higher BNBSR at approximately 0.3 cm⁻¹. Third, BNBSR falls off to a plateau from the transition frequency to higher frequencies.

Fig. 3.

Effect of high-pass filtering the DRR and portal image of the phantom. (a), (b), and (c) show a kV DRR at the identity pose, the DRR obtained after filtering with a high-pass FIR filter at a cutoff of 0.1 cm^{-1} , and the residual of the filtering operation, respectively. (d), (e), and (f) show the effect of the filtering operation on the corresponding portal image. There was no displacement between the two images. After filtering, bony anatomy in the DRR and portal image becomes clearer. (c), (f) Visual inspection of the residual DRR and portal image shows that the pixel intensity variations do not match exactly, and there is but a low degree of structural similarity between the two residual images.

Fig. 4.

Effect of high-pass filtering on the objective functions. (a), (c) The 2D objective functions defined obtained by calculating correlation coefficient and mutual information between a kV DRR and the reference portal image over translations ranging from -15 to 15 mm along the x and y axes. The correlation coefficient (a) did not peak at the correct pose of $t_x = 0$ mm and $t_y = 0$ mm, but was maximum at $t_x = 0$ mm and $t_y = 15$ mm. That is, the maximum was obtained when the DRR was shifted by 15 mm along the positive y axis with respect to the portal image. For the mutual information measure (c), although the global peak was at $t_x = 0$ mm and $t_y = 0$ mm, another maximum was observed at $t_x = 0$ mm and $t_y = 15$ mm. The objective functions defined by the correlation coefficient and mutual information were recomputed on the filtered DRR and portal image and are shown in (b) and (d), respectively. For both measures, filtering gave rise to well-behaved objective functions with the global peak at the correct position. This suggests that the bias and variance in registration accuracy can be reduced by improving bony anatomy contrast and reducing dissimilar intensity variations in the images being registered.

Fig. 5.

Effect of high-pass filtering the patient images. The original kV DRR of a patient, computed at the identity pose, and an MV portal image of the same patient are shown in (a) and (d), respectively. The corresponding high-pass filtered images (cutoff of 0.1 cm^{-1}) are given in (b) and (e) and the residuals of the filtering operation in (c) and (f). As with the phantom images, filtering improves the contrast of bony anatomy while removing dissimilar intensity variations in the DRR and portal image.

Fig. 6.

Example of overlaid line-enhanced DRR and line-enhanced portal image prior to registration in the AP and LR view (a), (d) and after registration of the high-pass filtered AP images shown in Fig. 5 with the correlation coefficient (b), (e) and mutual information (c), (f). In these images, red represents linear features in the DRR and green represents linear features in the portal images. At alignment red and green features overlap to maximize the amount of yellow present in the fused images. It should be noted that although the registration was performed with the AP portal image only, both the LR and AP images were employed for visual validation of the results to ensure that the out-of-plane parameters had been correctly estimated.

1 through 15 denote the poses tested for with the pelvic phantom. The true transformation parameters ψ , estimated transformation $\hat{\psi}$, magnitude of the displacement $\mathcal{D}$ corresponding to ψ , and overall error ε in estimating ψ are shown for the correlation coefficient and mutual information. The overall registration ε was not correlated to the distance $\mathcal{D}$. Filtered images were employed in the registration.

Table 1

		θ_x (°)	θ_y (°)	θ_z (°)	t_x (mm)	t_y (mm)	t_z (mm)	$\mathcal{D}$ (mm)	
								ε	(mm)
1.	ψ	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	CC	$\hat{\psi}$	0.008	-0.015	-0.009	0.006	-0.004	-0.064	0.074
	MI	$\hat{\psi}$	0.032	0.029	0.037	-0.039	0.027	-0.002	0.077
2.	ψ	0.027	0.018	1.059	-11.427	-8.966	-10.701	18.480	0.665
	CC	$\hat{\psi}$	-0.023	0.016	1.093	-11.455	-8.973	-11.338	0.276
	MI	$\hat{\psi}$	-0.077	0.013	1.088	-11.492	-8.883	-10.502	8.933
3.	ψ	0.113	0.007	1.081	-5.757	-4.401	-4.380	0.667	0.348
	CC	$\hat{\psi}$	-0.007	0.126	1.062	-5.752	-4.544	-4.939	4.106
	MI	$\hat{\psi}$	-0.062	0.201	1.119	-5.805	-4.527	-4.549	1.529
4.	ψ	0.085	4.999	1.035	-1.415	0.022	-0.232	1.830	5.740
	CC	$\hat{\psi}$	-0.086	5.110	1.077	-1.752	-0.036	1.154	0.524
	MI	$\hat{\psi}$	-0.140	4.888	1.002	-1.695	0.012	1.443	0.139
5.	ψ	0.000	-0.005	6.466	-1.496	1.817	-0.196	6.486	0.967
	CC	$\hat{\psi}$	0.000	-0.031	6.429	-1.494	1.699	-0.697	0.818
	MI	$\hat{\psi}$	0.063	0.013	6.447	-1.523	1.723	-0.151	9.202
6.	ψ	0.000	4.995	6.466	-1.496	1.817	-0.196	0.332	0.425
	CC	$\hat{\psi}$	-0.578	5.079	6.554	-1.814	1.675	0.404	11.237
	MI	$\hat{\psi}$	-0.507	5.068	6.564	-1.781	1.621	0.271	0.904
7.	ψ	0.140	-0.001	1.128	8.570	-0.150	-0.786	0.519	3.379
	CC	$\hat{\psi}$	-0.047	0.047	1.140	8.545	-0.278	-0.596	0.437
	MI	$\hat{\psi}$	-0.023	0.013	1.135	8.523	-0.270	-0.471	1.350
8.	ψ	0.004	0.009	1.082	-1.057	10.591	-0.778	0.084	
	CC	$\hat{\psi}$	0.063	-0.031	1.101	-1.135	10.613	0.084	
	MI	$\hat{\psi}$	0.118	0.091	1.135	-1.117	10.527	-0.346	
9.	ψ	0.081	0.024	1.130	-0.724	-2.586	-0.846	3.379	
	CC	$\hat{\psi}$	0.000	0.032	1.077	-0.807	-2.661	-1.228	
	MI	$\hat{\psi}$	-0.030	0.076	1.072	-0.867	-2.645	0.427	

	$\theta_x (^{\circ})$	$\theta_y (^{\circ})$	$\theta_z (^{\circ})$	t_x (mm)	t_y (mm)	t_z (mm)	$\mathcal{D}$ (mm)	ε (mm)
10.	ψ	0.068	-0.007	1.130	-0.833	0.735	9.724	9.902
CC	$\hat{\psi}$	0.008	0.001	1.062	-0.939	0.613	9.670	0.212
MI	$\hat{\psi}$	-0.038	0.185	1.158	-1.023	0.707	10.115	0.548
11.	ψ	0.094	-0.022	1.105	-0.809	0.777	-4.121	4.421
CC	$\hat{\psi}$	-0.047	-0.078	1.054	-0.861	0.613	-3.955	0.322
MI	$\hat{\psi}$	-0.023	0.013	1.119	-0.945	0.668	-3.190	1.010
12.	ψ	-0.052	0.004	1.129	-0.861	1.081	-10.631	10.833
CC	$\hat{\psi}$	-0.015	-0.007	1.069	-0.885	1.113	-10.557	0.102
MM	$\hat{\psi}$	-0.069	0.060	1.119	-0.945	1.137	-9.604	1.063
13.	ψ	0.124	5.022	5.328	9.647	1.607	0.061	13.593
CC	$\hat{\psi}$	-0.359	5.141	5.359	9.271	1.496	0.092	0.571
MI	$\hat{\psi}$	-0.335	5.185	5.392	9.266	1.504	-0.338	0.797
14.	ψ	-0.095	5.013	5.328	-1.769	9.774	0.165	12.967
CC	$\hat{\psi}$	-0.320	5.001	5.296	-2.065	9.831	-0.728	1.051
MI	$\hat{\psi}$	-0.382	5.169	5.408	-2.133	9.855	-0.706	1.121
15.	ψ	0.152	5.032	5.283	-1.877	0.997	10.304	13.262
CC	$\hat{\psi}$	-0.382	5.040	5.304	-2.252	0.910	9.350	1.297
MI	$\hat{\psi}$	-0.382	5.068	5.338	-2.258	0.926	9.916	0.790

Correlation coefficient and filtered images experiment results on phantom data. The table shows the mean, standard deviation, maximum and minimum value of the absolute value of the registration errors for each of the six transformation parameters and the overall registration error, ε , for poses 1 through 15.

Table II

	θ_x°	θ_y°	θ_z°	t_x mm	t_y mm	t_z mm	ε
Mean absolute error	0.182	0.044	0.038	0.141	0.085	0.490	0.644
Std absolute error	0.193	0.043	0.022	0.150	0.053	0.407	0.432
Max absolute error	0.578	0.119	0.088	0.375	0.165	1.386	1.529
Min absolute error	0.000	0.002	0.009	0.002	0.005	0.031	0.074

Mutual information and filtered images experiment results on phantom data. The table shows the mean, standard deviation, maximum, and minimum values of the absolute value of the registration errors for each of the six transformation parameters and the overall registration error, ε , for poses 1 through 15.

Table III

	θ_x°	θ_y°	θ_z°	t_x mm	t_y mm	t_z mm	ε
Mean absolute error	0.201	0.081	0.041	0.169	0.082	0.572	0.741
Std absolute error	0.170	0.066	0.026	0.134	0.047	0.480	0.482
Max absolute error	0.534	0.193	0.098	0.381	0.196	1.675	1.830
Min absolute error	0.018	0.005	0.006	0.027	0.011	0.002	0.077

Estimated shifts in a patient's position relative to the treatment field for correlation and mutual information-based registration over seven weeks. Only portal images in the AP view were used for the registration although images in both the AP and LR views were employed for visual verification of registration performance as illustrated in Fig. 6.

Table IV

		θ_x°	θ_y°	θ_z°	t_x mm	t_y mm	t_z mm
1.	CC	2.01	-1.19	-1.19	-1.15	-1.97	0.25
	MI	2.00	-1.13	-1.21	-1.17	-1.98	0.44
2.	CC	2.50	-1.02	-0.78	-0.06	-2.57	1.18
	MI	2.44	-1.06	-0.76	-0.01	-2.53	2.57
3.	CC	2.98	-0.44	-1.37	-2.56	-3.31	1.52
	MI	3.13	-0.56	-1.41	-2.68	-3.42	1.21
4.	CC	1.89	-0.01	-0.30	-3.47	-2.96	3.67
	MI	1.88	0.00	-0.30	-3.47	-2.98	3.59
5.	CC	3.03	-0.59	-1.05	0.33	1.30	-0.66
	MI	3.03	-0.63	-1.00	0.39	1.36	0.41
6.	CC	3.78	-1.28	-1.20	2.20	-2.60	-1.26
	MI	3.91	-1.28	-1.13	2.29	-2.57	-1.30
7.	CC	2.16	0.64	-0.93	-0.85	-1.82	2.67
	MI	2.13	0.63	-0.89	-0.82	-1.73	3.66