Published in final edited form as:

IEEE Nucl Sci Symp Conf Rec (1997). 2013 ; 2013: . doi:10.1109/NSSMIC.2013.6829037.

Experimental Evaluation of a Deformable Registration Algorithm for Motion Correction in PET-CT Guided Biopsy

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Abstract

Positron emission tomography computed tomography (PET-CT) images are increasingly being used for guidance during percutaneous biopsy. However, due to the physics of image acquisition, PET-CT images are susceptible to problems due to respiratory and cardiac motion, leading to inaccurate tumor localization, shape distortion, and attenuation correction. To address these problems, we present a method for motion correction that relies on respiratory gated CT images aligned using a deformable registration algorithm. In this work, we use two deformable registration algorithms and two optimization approaches for registering the CT images obtained over the respiratory cycle. The two algorithms are the BSpline and the symmetric forces Demons registration. In the first optimization approach, CT images at each time point are registered to a single reference time point. In the second approach, deformation maps are obtained to align each CT time point with its adjacent time point. These deformations are then composed to find the deformation with respect to a reference time point. We evaluate these two algorithms and optimization approaches using respiratory gated CT images obtained from 7 patients. Our results show that overall the BSpline registration algorithm with the reference optimization approach gives the best results.

Index Terms

PET-CT; deformable registration; image-guided surgery; motion correction

I. Introduction

Percutaneous biopsy is a commonly performed procedure to distinguish between benign and malignant tissue. In this procedure, a biopsy needle is inserted through the skin to the target, typically using computed tomography (CT) images or ultrasound for guidance. Percutaneous biopsy subjects patients to a much lower risk than open surgical procedures.

However, CT guided percutaneous biopsy faces many challenges. CT imaging is unable to distinguish between benign and malignant tissue. Hence, CT imaging uses size criteria to predict cancer involvement in lymph nodes. Thus, use of CT imaging is associated with serial procedures and a corresponding increased radiation exposure for the patients. These serial procedures are needed to convincingly identify malignant lesions (defined by lesion growth) and effective tumor treatment response (defined as tumor size reduction or stability). Moreover, tumors are often heterogeneous in composition and so need multiple sampling attempts at different locations to obtain sufficient tissue for pathological evaluation. With advanced imaging and increased screening practices, tumors are being detected at an early stage and smaller size. Smaller lesion sizes lead to higher false negative biopsy results. Some lesions can be hard to see under CT and thus difficult to target by CT alone. Many of these challenges can be addressed by using a functionally active imaging modality like positron emission tomography (PET) [1], [2]. By combining CT and PET, the strengths of anatomical and functional imaging can be combined to enable more effective biopsies.

PET/CT diagnostic and operational benefits can be gravely affected by respiratory motion artifacts. Unlike CT images, that are obtained within a breath-hold, PET images are acquired over 1–10 minutes for each table gantry position. Thus, PET images include imaging artifacts due to involuntary respiratory and cardiac motion. These motions lead to a discrepancy between the CT and PET data leading to errors in attenuation corrections needed for accurate PET imaging. Moreover, the blurred PET images can lead to inaccurate tumor localization, shape distortion, or poor biopsy guidance, potentially resulting in incorrect staging of the tumor [6], [7], [8]. In this paper, we describe an approach for PET/CT motion correction that relies on a deformable registration algorithm to sharpen the images which could enable more precise biopsies [3].

Section II describes the details of our proposed approach for PET/CT motion correction relying on a deformable registration algorithm. In Section III, we present evaluation results of the registration algorithms using respiratory gated CT data obtained from consented patients. Finally, in Section IV, we discuss the results.

II. Method

Our proposed clinical workflow for PET/CT guided biopsy is shown in Fig. 1. In this workflow, we first obtain the pre-operative images in the PET-CT suite. A respiratory motion correction algorithm is then applied to these pre-operative PET/CT images. During the biopsy procedure, the intra-operative CT images are registered to the pre-operative CT images and the resulting deformation maps are then applied to the motion-corrected PET images. These deformed PET images are then fused with the intra-operative CT images to provide tumor localization during biopsy.

In this paper, we present a respiratory motion-correction algorithm using respiratory gated CT images. This is an essential component of the workflow described in Fig. 1. The motion correction algorithm proceeds as follows:

1. Apply a deformable registration algorithm to compute deformation maps for each 3D CT volume with respect to a reference in the 4D series.
2. Use the deformation maps computed in Step 1 to register each CT volume to the reference CT volume. This step will generate registered CT volumes.
3. Average the registered CT volumes to generate a single motion-free, high-quality (low noise) CT volume.

In the above algorithm, we use two optimization approaches and two registration algorithms for generating the deformation maps required in step 2. In the first optimization approach, hereon referred as the reference approach, each CT image is directly registered to the reference image to obtain the deformation map. In the second approach, hereon referred as the consecutive approach, we first find deformation maps by registering each CT image with an image from the adjacent time point. We use the B-spline and the demons algorithms for deformable registration. The deformation maps obtained by these methods are then composed to obtain the deformation with respect to the reference CT image. We now describe the formulation of the deformable registration algorithm.

Consider two images, the fixed image $I_F(x)$ and the moving image $I_M(x)$ each defined in their own spatial domain, $\Omega_F \subset R^d$ and $\Omega_M \subset R^d$, respectively. During registration, we try to find a transformation $T(x)$ that will align the moving image to the fixed image. The transformation is a mapping $T : \Omega_M \subset R^d \rightarrow \Omega_F \subset R^d$, that maps from the moving image to the fixed image. In order to align the two images, similarity metrics such as sum-of-square-distance and mutual information are used to evaluate the quality of the registration.

Registration is formulated as an optimization problem in which the cost function C is minimized with respect to the transformation T and is given by,

$$\hat{T} = \underset{T}{\operatorname{argmin}} C(T; I_F, I_M) \quad (1)$$

where $\hat{T}$ is the optimum transformation, I_F and I_M are the fixed and moving images, respectively, and C is the cost function given by

$$C(T; I_F, I_M) = -S(T; I_F, I_M) + \gamma P(T) \quad (2)$$

where $S(\cdot)$ is the similarity metric, and $P(T)$ is a penalty term for the transformation T . γ is a weighing factor that weighs similarity against penalty. In B-spline deformable registration, the transformation T is parameterized and the optimization in (1) becomes

$$\hat{\mu} = \underset{\mu}{\operatorname{argmin}} C(T(\mu); I_F, I_M) \quad (3)$$

where $(\hat{\mu})$ are the optimum B-spline parameters. The B-spline parameterization of the transformation $T(x)$ is given by

$$T(\mu)(x) = x + \sum_{x_k \in N_x} p_k \beta^3 \frac{x - x_k}{\sigma} \quad (4)$$

with x_k the control points, $\beta^3(x)$ the cubic multidimensional B-spline polynomial, p_k the B-spline co-efficient vectors, σ the control point spacing, and N_x the set of all control points within the compact support of the B-spline at x .

Unlike the B-spline optimization, the symmetric forces Demons algorithm is a non-parametric deformable registration algorithm that tries to optimize the global energy given by

$$E(s) = \frac{1}{\sigma_i^2} \operatorname{Sim}(I_F, I_M \circ s) + \frac{1}{\sigma_T^2} \operatorname{Reg}(s) \quad (5)$$

where s is a non-parametric transformation that maps points p to $s(p)$, $\operatorname{Sim}(I_F, I_M \circ s)$ is a similarity function giving the similarity between the fixed image I_F and the moving image I_M after undergoing through the transformation s , and $\operatorname{Reg}(s)$ is a regularization function for the transformation s . To pose the demons algorithm as a well-posed optimization, the above equation is rewritten by using a hidden variable c given by

$$E(c, s) = \left\| \frac{1}{\sigma_i^2} (I_F - I_M \circ s) \right\|^2 + \frac{1}{\sigma_x^2} \operatorname{dist}(s, c)^2 + \frac{1}{\sigma_T^2} \operatorname{Reg}(s) \quad (6)$$

where we allow for a non-parametric transformation c which has some errors from the spatial transformation s . σ_x allows for spatial uncertainty in the correspondences, $\operatorname{dist}(s, c) = \|s - c\|$, and $\operatorname{Reg}(s) = \|\nabla s\|^2$. This optimization problem can be solved very efficiently in two steps. In the first step, the first two terms of (6) are optimized with respect to c by assuming s is given, by starting from $c=s$. The second and third term can then be optimized with respect to s by assuming c is given. The second optimization is a closed form solution and can be shown to be a convolution by a Gaussian kernel when the regularization is quadratic and uniform. For symmetric registration framework the first two terms of (6) are rewritten as the following optimization

$$s_{opt} = \underset{s}{\operatorname{argmin}} (E(I_F, I_M, s) + E(I_F, I_M, s^{-1})) \quad (7)$$

where s^{-1} is an inverse transformation. In the symmetric demons algorithm a forward and inverse update is computed at every iteration. The interested reader can refer to [12], [11], [13] for more details.

III. Results

In this section, we present evaluation results of the two optimization approaches and two registration algorithms using the data described in Table I. Each dataset consisted of ten CT images obtained over the respiratory cycle. The 003 and 008 dataset also included five PET images obtained over the respiratory cycle that was phase-matched to five of the CT images.

For these experiments we used the open-source Elastic library implementation of the B-spline registration algorithm and the itk implementation of the multi-resolution symmetric forces demons algorithm [4], [10]. For the B-spline algorithm, we used the following parameters: a) image comparison metric: Advanced Mattes Mutual Information; b) number of resolutions: 4; and c) interpolation order: 1. For the multi-resolution symmetric demons registration algorithm, we used the following registration parameters: a) number of levels: 4; b) iterations per level: 40,40,32,32; c) standard deviation: 1.0; and d) interpolation type: linear.

As described earlier, we used two optimization approaches to obtain the deformation maps: a) reference and; b) consecutive. For both these approaches, we used a reference time point mid-way between the two end-exhale points (T40). Fig. 2 shows a color blending of CT image at time point 0 with the reference time point before and after registration. The figure depicts a large mismatch between the two images before registration with the bulk of the mismatch at the outer edges of the lung. After registration, we see a significant reduction in the mismatch within the lungs and at its periphery. Registration also reduces the mismatch resulting from motion artifacts. When using the symmetric forces algorithm, the misregistration artifacts are almost completely absent. Fig. 3 shows PET/CT fusion in the absence and presence of motion correction. We see from the images that both registration algorithms and approaches give sharper CT images compared to the one obtained by averaging the unregistered images. However, at the bottom of the right lung the image is sharper in the images obtained by the reference approach as compared to the consecutive approach.

To quantitatively evaluate the registration results for each method, we used two approaches. In the first approach, for cases 003 and 008, we semi-automatically segmented the lung masks for each time point of the CT data. For cases P0–P4, the liver region was segmented. We then computed surface errors between the transformed lung and liver masks at each time point with the reference time point masks. We used the MeshValmet tool to compute these distances [9]. The surface errors were computed for the two registration algorithms and approaches and is presented in Table II. From the results, we see that the surface errors are lower for the reference approach as compared to the consecutive approach. This is because the multiple composition of transformations in the consecutive approach leads to aggregated surface errors at the lung and liver boundaries. The surface errors for the two registration algorithms for the reference approach are almost identical to each other. We also used the

Dice coefficient metric to compare the transformed and reference point lung and liver masks and found that in 4 out of the 7 datasets, use of the BSpline algorithm with the reference approach improved performance as shown in Table III.

In the second quantitative evaluation, 10 landmarks, as described in Table IV, were manually marked in the CT data from each time point. Of these landmarks, the main carina and the bifurcation of the pulmonary artery could not be marked in the datasets P1 and P3. We then tabulated the errors in the landmark position at the reference time point and the corresponding transformed landmark point from another time point after undergoing the appropriate transformation. Fig. 4 shows the tabulated results in the form of a bar plot. In this figure, we see that in 6 out of the 10 landmarks, BSpline registered images using the reference approach gave the best results. Equivalent results are also obtained using the BSpline algorithm with the consecutive approach. However, the symmetric forces Demons algorithm gave the worst results.

IV. Conclusions

We have presented our initial results from an experimental evaluation of two algorithms and registration approaches to combine gated CT data to obtain motion-free CT data. This is an essential component of the PET-CT guided biopsy workflow. By combining CT data from different time points by using deformable registration, we are able to successfully obtain motion-free CT data. Our results using segmented liver and lung surfaces and 10 landmark points show that using the BSpline algorithm with the reference approach gives the best overall results. In the future, we also plan to evaluate groupwise registration approach for generating the deformation maps [5].

Acknowledgment

Research reported in this publication was supported by the NCI of the NIH under award number R42CA153488. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

1. Suh, J.; Kwon, O-K.; Scheinost, D.; Sinusas, A.; Cline, G.; Papademetris, X. Whole body nonrigid CT-PET registration using weighted demons; IEEE International Symposium on Biomedical Imaging: From Nano to Macro; 2011. p. 1223-1226.
2. Baluwala H, Risser L, Schnabel J, Saddi K. Toward physiologically motivated registration of diagnostic CT and PET/CT of lung volumes. Medical Physics. 2013; 40(2)
3. Grgic A, Nestle U, Schaefer-Schuler A, Kremp S, Ballek E, Fleckenstein J, Rbe C, Kirsch C-M, Hellwig D. Nonrigid Versus Rigid Registration of Thoracic 18 FFDG PET and CT in Patients with Lung Cancer: An Intraindividual Comparison of Different Breathing Maneuvers. Journal of Nuclear Medicine. 2009; 50(12):1921–1926. [PubMed: 19910420]
4. Klein S, Staring M, Murphy K, Viergever M, Pluim J. Elastix: a toolbox for intensity based medical image registration. IEEE Transactions on Medical Imaging. 2010 Jan; 29(1):196–205. [PubMed: 19923044]
5. Metz C, Klein S, Schaap M, van Walsum T, Niessen W. Nonrigid registration of dynamic medical imaging data using nD+t B-splines and a groupwise optimization approach. Medical Image Analysis. 2011; 15(2):238–249. [PubMed: 21075672]

6. Allen-Auerbach M, Yeom K, Park J, Phelps M, Czernin J. Standard PET/CT of the chest during shallow breathing is inadequate for comprehensive staging of lung cancer. *J. Nucl. Med.* 2006; 47(2):298–301. [PubMed: 16455636]
7. Beyer T, Rosenbaum S, Veit P, Statta J, Miller SP, Difilippo FP, Schder H, Mawlawi O, Roberts F, Bockisch A, Khl H. Respiration artifacts in whole-body (18)F-FDG PET/CT studies with combined PET/CT tomographs employing spiral CT technology with 1 to 16 detector rows. *Eur J. Nucl. Med. Mol. Imaging.* 2005; 32(12):1429–1439. [PubMed: 16133383]
8. Bettinardi V, Picchio M, Di Muzio N, Gianolli L, Messa C, Gilardi MC. PET/CT for radiotherapy: image acquisition and data processing. *Q. J. Nucl. Med. Mol. Imaging.* 2010; 54(5):455–475. [PubMed: 20927014]
9. Aspert N, Santa-Cruz D, Ebrahimi T. MESH: measuring errors between surfaces using the Hausdorff distance. *IEEE International Conference on Multimedia and Expo.* 2002; 1:705–708. vol. 1.
10. Ibanez L, Schroeder W. *The ITK Software Guide.* 2005
11. Vercauteren T, Pennec X, Perchant A, Ayache N. Diffeomorphic Demons: Efficient Non-parametric Image Registration. *NeuroImage.* 2009; 45(1S1):S61S72.
12. Vercauteren T, Pennec X, Perchant A, Ayache N. Symmetric Log-Domain Diffeomorphic Registration: A Demons-based Approach. *Proc. Medical Image Computing and Computer Assisted Intervention.* 2008; 5241:754761.
13. Dru F, Vercauteren T. An ITK Implementation of the Symmetric Log-Domain Diffeomorphic Demons Algorithm. *Insight Journal.* 2009

Fig. 1.
Clinical workflow for PET/CT-guided biopsy.

Fig. 2.

Blending using complementary colors. (a) shows blending of the CT image at time point 0 with the CT image at time point 40 for case 003 without registration. (b) shows blending of the CT image at time point 0 after registration with the CT image at time point 40 for case 003 by using the BSpline algorithm with the reference approach. (c) shows blending of the CT image at time point 0 after registration with the CT image at time point 40 for case 003 by using the symmetric forces Demons algorithm with the reference approach.

Fig. 3.

Comparison of PET/CT fusion using different registration algorithms and approaches. (a) shows a PET/CT fusion using unregistered CT data. The coronal slice of the CT data is obtained by averaging all the respiratory gated CT data for all the time points for case 003. (b) shows PET/CT fusion for a coronal slice of the CT data obtained after motion correction using the BSpline algorithm with the reference approach. (c) shows PET/CT fusion for a coronal slice of the CT data obtained after motion correction using the BSpline algorithm with the consecutive approach. (d) shows PET/CT fusion for a coronal slice of the CT data obtained after motion correction using the symmetric forces Demons algorithm with the reference approach.

Fig. 4.
Landmark errors with and without registration.

TABLE I

Data specifications

Cases	Scanner	Image dimensions ($X \times Y \times Z$)	Image resolution (x, y, z)
003,008	GE Discovery STE	(512,512,120)	(0.98,0.98,2.5)
P0–P4	GE Discovery ST	(512,512,168)	(0.98,0.98,2.5)

TABLE II

The surface errors in mm for unregistered, reference and consecutive type of registration

Case	B-spline		Demons	
	Unregistered	Reference	Consecutive	Reference
003	1.18±5.66	0.51±3.0	0.51±2.67	-0.70±1.77
008	0.89±2.83	0.02±1.09	0.05±1.38	-0.75±1.03
P0	-0.23±2.93	-0.13±1.61	-0.05±1.55	-1.10±1.65
P1	0.38±2.46	0.48±1.55	0.56±1.66	-0.63±1.58
P2	0.50±2.33	0.27±2.32	0.41±2.57	-0.73±2.31
P3	0.20±2.14	0.23±1.95	0.31±1.92	-0.88±1.67
P4	0.06±2.25	0.31±1.91	0.47±2.01	-0.81±2.01
				-3.32±2.99

TABLE III
Dice coefficients for unregistered and reference and consecutive registration approaches

Case	B-spline		Demons	
	Unregistered	Reference	Consecutive	Reference
003	0.94	0.97	0.97	0.97
008	0.96	0.98	0.98	0.97
P0	0.95	0.97	0.97	0.94
P1	0.94	0.96	0.95	0.95
P2	0.96	0.94	0.94	0.93
P3	0.95	0.95	0.95	0.94
P4	0.95	0.95	0.95	0.94
				0.85

TABLE IV

Landmarks for quantitative evaluation

Landmark #	Name
1	Main carina
2	Anterior-superior margin of L1
3	Bifurcation of pulmonary artery
4	Xyphoid
5	Top of liver
6	Top of spleen
7	Top of left kidney
8	Top of right kidney
9	Origin of left renal vein
10	Origin of left renal artery