Intra-operative Multimodal Non-rigid Registration of the Liver for Navigated Tumor Ablation

Haytham Elhawary¹, Sota Oguro¹, Kemal Tuncali², Paul R. Morrison², Paul B. Shyn², Servet Tatli², Stuart G. Silverman², and Nobuhiko Hata¹

¹ Surgical Planning Laboratory, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA, USA
{elhawary,sota,hata}@bwh.harvard.edu

² Abdominal Imaging and Intervention Group, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA, USA
{ktuncali,pmorrison,pshyn,statli,sgsilverman}@partners.org

Abstract. CT guided tumor ablation of the liver often suffers from a lack of visualization of the target tumor and surrounding critical structures. This information is available on pre-operative contrast enhanced MR images and a non-rigid registration technique is desirable. However while registration methods have been successfully tested retrospectively on patient data, very few have been incorporated into clinical procedures. A non-rigid registration technique has been evaluated, optimized and validated to be able to perform registration of the liver between MR to CT images, and between intra-operative CT images. The method requires pre-processing and segmentation of the liver, and presents an accuracy of approximately 2mm. A clinical feasibility study has been conducted in 5 liver ablation cases. The method helps clinicians enhance interventional planning, confirm ablation probe location with respect to the tumor, and in the case of cryotherapy, evaluate tumor coverage by the ice ball.

1 Introduction

Liver cancer, namely hepatocellular carcinoma (HCC), is one of the most common cancers in the world, with an estimated 711,000 new cases reported worldwide in 2007 and 680,000 deaths [1]. Local tissue ablation has become a promising method of minimally invasive curative therapy that preserves uninvolved liver parenchyma with fewer systematic complications and side effects than major hepatic surgery [2]. Imaging technologies such as computed tomography (CT) can provide the guidance needed for the percutaneous placement of needle-like applicators for tumor ablation using chemical or thermal methods.

For procedure *planning*, an initial CT image of the liver is used to decide on an adequate entry point and probe tip location. The lack of soft tissue contrast of the CT image impedes a clear visualization of the tumor which is either barely distinguished or totally invisible. Most liver tumors are visible on pre-procedure contrast enhanced MRI and a visual correspondence of tumor location between the pre-procedure MRI and intra-operative CT images is performed by the physician using anatomical structures as landmarks. Once the position of the tumor is estimated and a plan devised, CT images are then taken to *guide* the probes into the planned location. Once the

probes are positioned, CT images are taken to *monitor* the effects of the ablation, for example observing the extent of the ice ball in cryotherapy. The lack of proper visualization of the tumor can lead to sub-optimal ablation applicator placement and inadequate coverage of tumor margins. Clinically, this can increase complications and rates of recurrence [2].

Registration between the pre-procedure MR images and the acquired CT intra-operative images would allow mapping tumor location and size as well as any surrounding critical structures onto the CT images. Carrillo et al. [3] compared several semiautomatic voxel-based registration algorithms to perform rigid registration between pre-procedure MRI and interventional MRI of the liver. Niculescu et al. [4] registered pre- and post-treatment CT images by using a surface based non-rigid method with a finite element model to simulate volumetric deformation. Archip et al. [5] compared several non-rigid registration techniques to match pre-procedure contrast enhanced MR images of the liver to intra-operative CT, including a finite element based method they had previously developed for neurosurgery. However, while these registration methods have been successfully tested retrospectively on patient data, very few of these solutions have been incorporated into the clinical setting. In this paper we describe the optimization of a multimodal non-rigid registration technique which will be used to register pre-procedure contrast enhanced MR images to intra-operative CT images, and to register CT images obtained during different stages of the intervention. The technique is then incorporated in the clinical workflow of CT-guided liver tumor ablation, with a clinical feasibility study performed in 5 cases. This work will form part of a fully integrated liver ablation navigation suite we are currently developing.

2 Intra-operative Non-rigid Registration Method

Although rigid registration has been used before in CT guided liver ablation, the accuracy is not sufficient for guidance of therapy [6]. Several non-rigid registration techniques are reported in the literature and reviews of available methods have been extensively published [7]. Considering the trade off between computation requirements and accuracy [5] we decided to use a 3D volumetric non-rigid registration method which uses an affine transformation to model the global motion of the liver, and which describes local motion by a free-form deformation based on B-splines as described in [8] using the mutual information similarity metric. Three important factors must be considered for the adequate translation of a registration technique into the clinical setting: it must be (i) accurate for the clinical application at hand, (ii) fast enough to be performed within the time frame of a clinical intervention and (iii) robust so that it almost never fails. This section describes the optimization of the registration method and several pre-processing steps in order for it to fulfill these three conditions. The registration method along with all processing steps were made available in the open source software 3D Slicer [9].

Image Acquisition. The T1 weighted MR images were obtained using a 1.5T GE SIGNA scanner, 3D image acquisition (TR/TE=4.1/2ms, 5mm slice thickness, 2.5mm slice spacing, 512 x 512 matrix size, 400mm field of view) with an 8 channel torso

surface coil. The intra-operative CT images were obtained from a 40 channel Siemens Sensation Open, with a matrix size of 512 x 512.

Cropping, Segmentation and Slice Thickness. To eliminate irrelevant voxels in the registration process and to reduce the number of voxels in the computations, the image volumes can be cropped. The cropping could occur in plane or in the slice thickness direction. To improve registration accuracy the liver can be segmented from the images to produce masked data in order to include only the relevant pixels in the similarity measurement. All segmentation was performed by a qualified radiologist with 7 years experience. The CT images acquired during the interventional procedure could also be reconstructed at different slice thickness.

Registration Algorithm. Once all the pre-processing steps have been performed on the images, they are subject to the registration algorithm, which involves two steps. The first is to use an affine transformation to describe the global motion of the liver. The second step enforces local deformation by modeling the displacement field using a free-form deformation model based on B-spline interpolation, in order to maximize mutual information between the images. The efficiency of the registration algorithm depends on variables such as spatial samples, iterations and grid size, which will be modified to evaluate their effect on the registration.

2.1 Procedure Optimization

In order to study the influence of the various pre-processing steps and algorithmic variables on both the accuracy and the speed of registration, several experiments were performed to register 9 patient datasets. Table 1 shows the range of parameters that were considered. In total 9 different parameter values were evaluated over 9 patient datasets, giving a total of 81 registrations.

The first three parameter values consist of changing the slice thickness of the CT images to 3mm, 5mm and 7.5mm. Thinner slices provide increased detail although make the segmentation process longer. The next three set of parameter values considered were related with in-plane cropping. The in-plane field of view (FOV) was varied from being 100% of the acquired image, 66% of the image and then just a region surrounding the liver. The next parameter was manual segmentation of the liver, with the registration being performed with segmentation and then without to see its influence on accuracy. The following parameter was cropping in the slice thickness direction, with registration being done with over 75% of the liver volume included and then with between 50-75%. Finally the algorithm variables were modified in three categories, the first being high resolution (50,000 spatial samples for affine registration and 500,000 for B-spline), medium resolution (25,000 and 250,000) and low resolution (5,000 and 50,000). All the registration steps were performed on a PC with 4 Dual Core AMD Opteron 2.2GHz processors, 16GB of RAM with Fedore Core 10 Linux operating system.

For each set of parameters the time for the entire registration process including the pre-processing steps was measured. Following previous studies [5], quantifying registration accuracy was done by extracting the edges of the segmented livers from the registered datasets using a Canny Edge detector and the 95% Hausdorff distance (HD) calculated between the sets of points comprising the edges. Perfect alignment will produce a 95% Hausdorff distance of 0mm.

Table 1. Experiments performed to evaluate the effect of the different parameters on the registration process. Set 1 corresponds to a reference set of parameters, and each consecutive set involves modifying one parameter from the reference set.

Parameter Set	Slice Thickness (mm)	FOV Size	Segmentation	Liver Volume	Resolution
1 (Ref)	5	66%	Yes	>75%	High
2	3	66%	Yes	>75%	High
3	7.5	66%	Yes	>75%	High
4	5	100%	Yes	>75%	High
5	5	Liver	Yes	>75%	High
6	5	66%	No	>75%	High
7	5	66%	Yes	50-75%	High
8	5	66%	Yes	>75%	Med
9	5	66%	Yes	>75%	Low

2.2 Results

Fig. 1 shows the results of the registrations performed on the 9 patient datasets with the different parameters specified in Table 1. Regarding *accuracy* it can be seen that except for the case where the pre-processing has not included manual segmentation and masking of the data, average accuracy ranged from 1.9 - 3.4mm. This is a satisfactory result for liver tumor ablation, given that most treated tumors are large in size, ranging from 1-20cm. Without segmentation of the liver, registration showed large errors which average 10.6mm with a large standard deviation. Segmentation is therefore essential to the method. Regarding *time*, the entire registration process can take anything from 28-52 minutes when manual segmentation and masking is performed. Segmentation is by far the most time consuming step in the process taking between 10-15 minutes for each image. One way of reducing segmentation time is to increment slice thickness, as this means that there are fewer slices per volume. However at 7.5mm slice thickness the registration error starts to increase as does the standard deviation, and image resolution visibly decreases. Regarding *robustness*, the mutual information algorithm proves to be extraordinarily robust over the entire spectrum of parameter sets, except for the case with no segmentation. Small standard deviations mean that the accuracy of each individual registered dataset is close to the average, giving an indirect measure of robustness. For cropping both in-plane and in the slice direction the algorithm performed extremely well, hence incomplete image acquisitions of the liver should have little effect. After a thorough analysis of these results parameter set 1 was selected as the best protocol for use in the clinical procedure. All the pre-processing (cropping and segmentation) of the MR images can be done previous to the intervention, reducing the actual time needed during the clinical procedure to perform the registration.

With the parameters of the registration method defined, two further measures of accuracy were used to ensure validation before applying the protocol in the clinical procedure. The first was the Dice Similarity Coefficient (DSC) which gives a measure of the spatial overlap between the segmented liver from the registered MRI and

Fig. 1. Registration results for the experiments with different parameters. For each parameter set the average time and accuracy are presented, along with a standard deviation.

the CT image [10]. The DSC can range from [0,1], where 1 is perfect alignment. The second consists of asking an experienced radiologist to identify well defined corresponding features on the intra-operative CT image of the liver and on the registered MR image and to measure the 3D distance between them. Three anatomical points were selected in each dataset and the error for each of the three points was averaged. Table 2 shows the results obtained by performing both non-rigid and rigid registration on the 9 patient datasets with all three evaluation metrics. Using the non-rigid registration, an obtained improvement of four fold in the 95% HD, 13% in the DSC metric and 3.3 fold anatomical landmarks is presented.

3 Registration during CT Guided Tumor Ablation Procedure

The registration method was then integrated into the workflow of a CT guided liver tumor ablation procedure for a clinical feasibility study. It was applied in parallel during 5 cases of liver ablation, although no clinical decisions were made based on the information obtained from the registration, in accordance to approval by our Institutional Review Board. Table 3 shows the patients that underwent the intervention with non-rigid registration. Before the intervention, the pre-procedure MR images were cropped and manually segmented. Once the patient is located on the table of the CT scanner, usually in a different position than the supine in which the MRI is taken, a CT image is acquired to plan the intervention and sent to our workstation outside the scanner room for registration. The results of the registration are presented in the last two columns of Table 3, where both accuracy and time taken for the registration procedure during the intervention are displayed.

Table 2. Validation results for both rigid and non-rigid registration on 9 patient datasets using registration parameters set 1

Dataset	95% Hausdorff Distance (mm)		DSC		Anatomical Landmarks (mm)	
	Rigid	Non-rigid	Rigid	Non-rigid	Rigid	Non-rigid
1	9.00	1.41	0.86	0.97	8.15	1.21
2	4.58	1.41	0.83	0.96	11.30	3.19
3	15.94	2.24	0.79	0.96	23.01	3.77
4	8.60	2.02	0.85	0.96	10.51	6.11
5	6.48	2.23	0.84	0.96	8.81	5.05
6	3.74	1.73	0.92	0.96	4.04	2.73
7	6.16	1.97	0.87	0.97	5.33	2.24
8	9.00	2.01	0.84	0.97	15.67	2.57
9	8.12	1.96	0.90	0.98	12.55	3.28
Avg	7.96	1.89	0.86	0.97	11.04	3.35

Table 3. Patients receiving liver ablation procedure with registration, along with accuracy and total time of registration during procedure (not including the pre-processing of the MR images before the procedure)

Case	Sex	Age	Therapy	Pathology	Liver Segment	Accuracy (95% HD)	Time (min)
1	M	63	Cryotherapy	Metastasis	7	1.9	22
2	M	63	Cryotherapy	Metastasis	6/5	2.3	21
3	M	49	RF ablation	HCC	5	2	20
4	M	53	RF ablation	HCC	5	2.2	17
5	M	82	Cryotherapy	Metastasis	5	2.4	18

The registration takes approximately 17-22 minutes to complete, and during this time the surgeons plan the interventional procedure in their usual manner. When the registration is complete, the registered MR image is superimposed on the CT image and shown to the practitioners. The tumor is segmented from the MR image and overlaid on the CT image to delineate the exact target location (Fig. 2(a-c)).

Registration was also performed between the CT images obtained during the procedure. This process was done between the planning CT image taken at the beginning of the procedure, the CT image which displayed the ablation probes once positioned (before ablation started), and in the case of cryotherapy, the CT image showing the maximum sized ice ball. These images were registered to the original pre-procedural CT images using the registration method (segmentation was not required). Fig. 2(d)-(f) show the CT image after probe placement and the CT image after the maximum ice ball is performed, both overlaid with the segmented liver tumor taken from the MR image. Fig. 2(f) shows a 3D model of the liver, cryoablation probes, ice ball (all segmented from the CT image) and the tumor (segmented from the registered MR image). This type of model will allow a 3D evaluation of the tumor coverage and margins.

Fig. 2. (a) Pre-procedure contrast enhanced MR image, (b) CT image for interventional planning, (c) registered and fused image showing liver from MR image overlaid on CT image, (d) CT image showing ablation probes overlaid with segmented tumor from the registered MR image, (e) CT image showing iceball (hypointense area around lesion) overlaid with segmented lesion (green) from registered MR image, and (f) 3D representation of liver (red), tumor (green), iceball (blue) and cryoprobes to evaluate tumor coverage and margins

4 Discussion and Conclusion

The objective of this study was to provide an adequate registration algorithm for use during CT guided liver tumor ablation. This involves registering pre-procedure MRI images with intra-procedure CT images, and to register CT images taken at different phases of the procedure. Many of the registration methods described in literature are not applicable directly to this clinical problem because they require registration times that are unfeasibly long for their implementation during the clinical ablation procedure, and hence need optimization to find a compromise between accuracy and registration time. In this paper we have optimized and evaluated the accuracy, speed and robustness of a non-rigid voxel-based registration technique, which required pre-processing of the images including manual segmentation. Segmentation is the most time-consuming process of the whole registration method, and any gains would directly impact on the overall process and its acceptance in the clinic. Future work is directed in evaluating semi-automatic segmentation algorithms, such as intensity based thresholding to produce an initial guess of the liver shape and an Estimation Maximization method [11]. We are also looking into computationally efficient implementations of Mutual Information [12]. The registration has been performed during 5 clinical cases, and with further shortening of registration times, will then be

applied in a prospective clinical study to evaluate the impact the registration has on clinical outcomes.

References

1. Garcia, M., Ward, E.M., Center, M.M., Hao, Y., Siegel, R.L., Thun, M.: Global Cancer Facts & Figures 2007. American Cancer Society, Atlanta (2007)
2. Tuncali, K., Morrison, P.R., Winalski, C.S., Carrino, J.A., Shankar, S., Ready, J.E., van Sonnenberg, E., Silverman, S.G.: MRI-guided percutaneous cryotherapy for soft-tissue and bone metastases: initial experience. *AJR Am. J. Roentgenol.* 189(1), 232–239 (2007)
3. Carrillo, A., Duerk, J.L., Lewin, J.S., Wilson, D.L.: Semiautomatic 3-D image registration as applied to interventional MRI liver cancer treatment. *IEEE Transactions on Medical Imaging* 19(3), 175–185 (2000)
4. Niculescu, G., Forand, D.J., Noshier, J.: Non-rigid Registration of the Liver in Consecutive CT Studies for Assessment of Tumor Response to Radiofrequency Ablation. In: Niculescu, G., Forand, D.J., Noshier, J. (eds.) 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2007. EMBS (2007)
5. Archip, N., Tatli, S., Morrison, P., Jolesz, F., Warfield, S., Silverman, S.: Non-rigid Registration of Pre-procedural MR Images with Intra-procedural Unenhanced CT Images for Improved Targeting of Tumors During Liver Radiofrequency Ablations. In: Ayache, N., Ourselin, S., Maeder, A. (eds.) MICCAI 2007, Part II. LNCS, vol. 4792, pp. 969–977. Springer, Heidelberg (2007)
6. Wilson, D.L., Carrillo, A., Zheng, L., Genc, A., Duerk, J.L., Lewin, J.S.: Evaluation of 3D image registration as applied to MR-guided thermal treatment of liver cancer. *Journal of Magnetic Resonance Imaging* 8(1), 77–84 (1998)
7. Hill, D.L.G., Batchelor, P.G., Holden, M., Hawkes, D.J.: Medical image registration. *Physics in Medicine and Biology* 46(3), R1–R45 (2001)
8. Rueckert, D., Sonoda, L.I., Hayes, C., Hill, D.L.G., Leach, M.O., Hawkes, D.J.: Nonrigid registration using free-form deformations: application to breast MR images. *IEEE Transactions on Medical Imaging* 18(8), 712–721 (1999)
9. Gering, D.T., Nabavi, A., Kikinis, R., Hata, N., O'Donnell, J., Grimson, W.E.L., Jolesz, F.A., Black, P.M., W. III, W.M.: An Integrated Visualization System for Surgical Planning and Guidance Using Image Fusion and an Open MR. *J. Magn. Reson. Imag.* 13(6), 967–975 (2001)
10. Bharatha, A., Hirose, M., Hata, N., Warfield, S.K., Ferrant, M., Zou, K.H., Suarez-Santana, E., Ruiz-Alzola, J., D'Amico, A., Cormack, R.A., Kikinis, R., Jolesz, F.A., Tempany, C.M.: Evaluation of three-dimensional finite element-based deformable registration of pre- and intraoperative prostate imaging. *Med. Phys.* 28(12), 2551–2560 (2001)
11. Wells III, W.M., Grimson, W.E.L., Kikinis, R., Jolesz, F.A.: Adaptive segmentation of MRI data. *IEEE Transactions on Medical Imaging* 15(4), 429–442 (1996)
12. Gholipour, A., Kehtarnavaz, N.D.: Computationally efficient mutual information estimation for non-rigid image registration. In: IEEE International Conference of Image Processing (2008)