

Copyright © 2003 IEEE. Reprinted from Engineering in Medicine and Biology Society, 2003. Proceedings of the 25th Annual International Conference of the IEEE, Vol. 1, No., pp. 592-594, September 17-21 2003

This material is posted here with permission of the IEEE. Internal or personal use of this material is permitted. However, permission to reprint/republish this material for advertising or promotional purposes or for creating new collective works for resale or redistribution must be obtained from the IEEE by writing to pubs-permissions@ieee.org. By choosing to view this document, you agree to all provisions of the copyright laws protecting it.

Automatic Registration and Fusion of High Resolution Micro-CT and Lung Perfusion SPECT Images of the Rat

Baowei Fei¹, Christian Wietholt², Anne V. Clough³,
Christopher A. Dawson^{2,4}, David L. Wilson^{1,5}

¹Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA

²Department of Biomedical Engineering, Marquette University, Milwaukee, WI, USA

³Department of Computer Science and Mathematics, Marquette University, Milwaukee, WI, USA

⁴Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, USA

⁵Department of Radiology, University Hospitals of Cleveland, Cleveland, OH, USA

Abstract — Small animal imaging can provide high-throughput phenotypic data for functional genomic studies and better mechanistic understanding of disease. Fusion of anatomical and functional images will aid interpretation of functional images having relatively little anatomical detail. In this study, we are investigating automatic registration and fusion visualization methods for micro-CT and SPECT images of rat lung. The immediate application is studies of pulmonary perfusion in a healthy rat and one with an occluded left pulmonary artery. Registration experiments were performed on images acquired from rats and a phantom. Fusion visualization showed excellent registration results. Quantitative measures such as distances and perimeters from phantom results show that the registration is quite accurate.

Keywords—Image registration and fusion, small animal imaging, SPECT, micro-CT, lung perfusion

I. INTRODUCTION

Small animal imaging is a fast growing field that has numerous applications in the studies of functional genomics, the biology of disease, and therapeutics [1][2]. Since commonly, functional imaging modalities such as single photon emission tomography (SPECT), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have little anatomic information, images acquired from computed tomography (CT) or MRI are used to provide structural identification and localization of organs/regions of interest and may also provide additional diagnostic information [5]. In this particular study, we investigate automatic image registration and fusion visualization methods applied to SPECT and micro-CT images for this new important application. The model application used to demonstrate the registration/fusion methods is the localization of a lung perfusion image obtained with SPECT within the anatomical lung field image obtained with micro-CT. We performed registration experiments using image volumes acquired both from rats and a gamma emitting, x-ray absorbing phantom.

II. MATERIALS AND METHODS

A. Registration Algorithm

Based on our previous experiences [6][7], we chose normalized mutual information (NMI) as the similarity measures in our registration because it is robust and suitable for multi-modality image registration [8]. We used rigid body transformation (three translations and three angles) and trilinear interpolation. For optimization, we used the downhill simplex method of Nelder and Mead [9]. Optimization of alignment ends either when the maximum number of NMI calculations is reached (typically 500) or the fractional change in NMI is smaller than a tolerance (typically 0.0001). Our very first initial guesses are all zeros for the three displacements and three angles. We use IDL (Interactive Data Language, Research System Inc., Boulder, CO) as the program language.

B. Image Acquisitions

We used the SPECT and micro-CT systems developed by Marquette University and Medical College of Wisconsin as described previously [4]. For SPECT data acquisition, a mobile gamma camera was positioned in front of the specimen stage and perpendicular to the x-ray beam. The center of the pinhole collimator was positioned at the height of the x-ray source focal spot. The SPECT data were acquired in a step-and-shoot fashion using 128 equiangular increments over a full 360° at 40 sec/view and reconstructed using ordered subset expectation maximization (OSEM) [4]. Subsequently, micro-CT images were acquired at 1° increments over 360°. Seven frames were averaged at each position. This data was reconstructed using Feldkamp [3] conebeam reconstruction.

We performed imaging experiments with a phantom consisting of three test tubes filled with technetium (Tc99m), which were embedded within a larger cylinder. The phantom was placed on the specimen stage and imaged as described above. After the SPECT acquisitions were completed, the phantom was imaged using micro-CT.

We acquired image sets from two rats that were anesthetized with 40mg per kg pentobarbital sodium [4]. One rat underwent surgery in which the left pulmonary

artery was occluded 8 days prior to the imaging. The other rat was untreated. A femoral venous catheter was used to inject 0.6 ml of Tc99m labeled macro-aggregated albumin with a total radioactivity of 2.0 mCi. After allowing the compound enough time to distribute and accumulate in the rat's lungs, the animals were sacrificed using an overdose of the anesthetic. The rats were then placed head down in a plastic tube with diameter of 52mm, and were positioned on the specimen stage. The center of rotation was set so that the right and left lungs were within the field of view at all angular positions. SPECT and micro-CT data were acquired as described above.

C. Registration Experiments

Before we performed image registration experiments, we preprocessed both micro-CT and SPECT image volumes. The original CT image volume has 512x512x497 voxels with 497 transverse slices. The voxel size is 0.10x0.10x0.10-mm. The SPECT image volume is 128x128x128-voxel with voxel size of 0.48x0.48x0.48-mm. We resample CT images and interpolated SPECT images generating two volumes with the same voxel size of 0.2x0.2x0.2-mm. We cropped both SPECT and CT images that have no signal of interest. The final volume images are 256x256x156 for phantom data and 256x256x232 for rats, respectively. We transform CT volumes and registered with corresponding SPECT volumes using our 3D registration algorithm.

D. Registration Evaluation

We used visual inspections to evaluate the registration. We used *RegViz*, a program written in IDL and created in our laboratory for visualizing and analyzing registered image volumes. First, color overlay displays were used to evaluate overlap of structures. One image was rendered in gray and the other in the "hot-iron" color scheme available in IDL. To visualize potential differences, it was quite useful to interactively change the contribution of each image using the transparency scale. Second, we manually segmented regions of interest (ROI) in image slices and copied them to corresponding slices. This enabled visual determination of the overlap of ROI over the entire volume. To evaluate registration of the phantom, we manually segmented the three tubes within the phantom from both CT and SPECT images. We calculated the central positions and computed the distance between corresponding central positions and the perimeters of the segmented tubes.

III. RESULTS

The fusion visualization of registered micro-CT and SPECT images shows that the tubes within the phantom are well matched (Fig. 1c). The distances between corresponding central points are less than 0.25-mm and the perimeter

differences are less than 0.33-mm. Hence, the phantom registration is quite accurate.

We determined the registration quality of the rat images by visually examining all image slices of registered volume pairs using one or more of the methods found in *RegViz*. A typical example is shown in Fig. 1 where the color overlays show that the rat lung aligned very well. Other transverse images were also well aligned indicating that the registration was successful in three dimensions. Contour overlap and sector display also demonstrate excellent registration.

IV. DISCUSSION & CONCLUSION

Using our three dimensional automatic registration method, we successfully registered high resolution micro-CT images with lung perfusion SPECT images of the rat. Phantom results show that the registration is quite accurate. As we are performing more rat imaging experiments, we believe that the registration and fusion visualization method could be a useful tool for many applications in small animal imaging.

ACKNOWLEDGMENT

The algorithm developed in this research was supported by DOD grant DAMD17-02-1-0230 to Baowei Fei and NIH grant R01-CA84433 to David L. Wilson.

The imaging work done for this research was supported by HL 19298, NSF BES 9818197, NIH BRP HL 64368, W.M. Keck Foundation, Bagozzi Graduate Fellowship and Department of Veterans Affairs.

REFERENCES

- [1] J.S.Lewis, S.Achilefu, J.R.Garbow, R.Laforest, and M.J.Welch, "Small animal imaging: current technology and perspectives for oncological imaging," *European Journal of Cancer*, vol. 38, pp. 2173-2188, 2002.
- [2] M.J.Paulus, S.S.Gleason, S.J.Kennel, P.R.Hunsicker, and D.K.Johnson, "High resolution X-ray computed tomography: An emerging tool for small animal cancer research," *Neoplasia*, vol. 2, pp. 62-70, 2000.
- [3] R.H.Johnson, H.Hu, S.T.Haworth, P.S.Chio, C.A.Dawson, and J.H.Linehan, "Feldkamp and circle-and-line cone-beam reconstruction for 3D micro-CT of vascular networks," *Physics in Medicine and Biology*, vol. 43, pp. 929-940, 1998.
- [4] C.Wietholt, R.C.Molthen, Johnson R.H., C.A.Dawson, and A.V.Clough, "SPECT imaging of pulmonary blood flow in a rat," *Proceedings of SPIE Medical Imaging on Physiology and Function: Methods, Systems, and Applications*, vol. 5031, 2003.
- [5] G.J.Forster, C.Laumann, O.Nickel, P.Kann, O.Rieker, and P.Bartenstein, "SPECT/CT image co-registration in the abdomen with a simple and cost-effective tool," *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 30, pp. 32-39, 2003.
- [6] B.W.Fei, A.Wheaton, Z.Lee, J.L.Duerk, and D.L.Wilson, "Automatic MR volume registration and its evaluation for the pelvis and prostate," *Physics in Medicine and Biology*, vol. 47, pp. 823-838, 2002.

- [7] B.W.Fei, J.L.Duerk, and D.L.Wilson, "Automatic 3D Registration for Interventional MRI-Guided Treatment of Prostate Cancer," *Computer Aided Surgery*, vol. 7, pp. 257-267, 2002.
- [8] F.Maes, A.Collignon, D.Vandermeulen, G.Marchal, and P.Suetens, "Multimodality image registration by maximization of mutual

information," *IEEE Transactions on Medical Imaging*, vol. 16, pp. 187-198, 1997.

- [9] J.Nelder and R.A.Mead, "A simplex method for function minimization," *Computer Journal*, vol. 7, pp. 308-313, 1965.

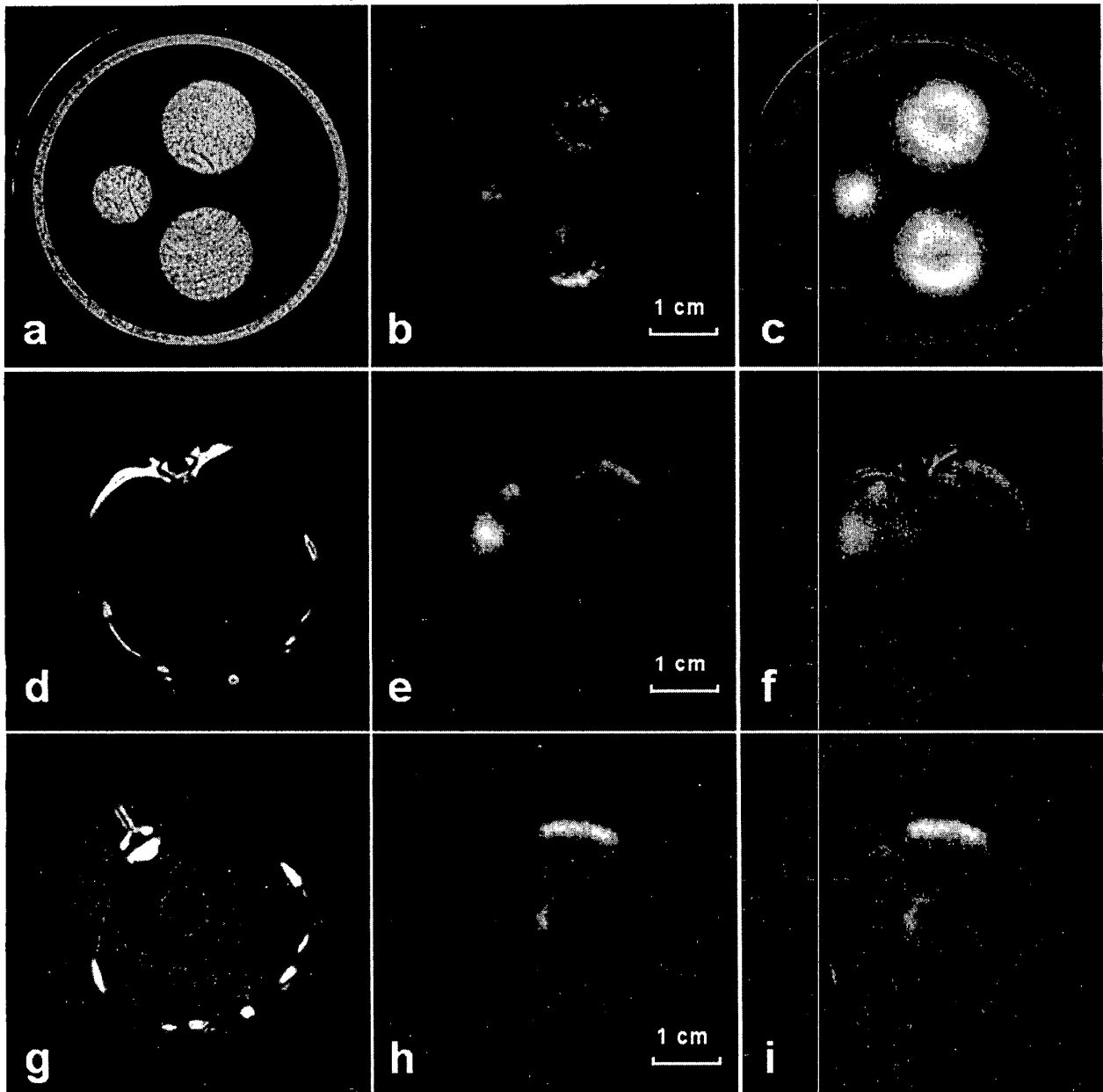


Fig.1. Images of Micro-CT (a,d,g), SPECT (b,e,h), and fusion visualization (c,f,i). a,b,c: Images of the phantom. In the fused image (c), the three tubes within the phantom are well aligned. d,e,f: Normal lung images showing the lung field (d) and perfusion (e) of both the left and right lungs of the rat. g,h,i : Images obtained from a rat with occluded left pulmonary artery. Perfusion (h) is observable only in the right lung in this case. The registered fusion visualization (i) excellently represents both structural and functional information.