Correlating 2D Histological Slice with 3D MRI Image Volume Using Smart Phone as an Interactive Tool for Muscle Study

Aydin Eresen, Peng Li and Jim Xiuquan Ji*

Abstract— in muscle dystrophy studies, registration of histological image with MRI image volume enables cross validation of MRI biomarkers using pathological result. However, correlation of 2D histology slice with 3D MRI volume is technically challenging due to the potentially non-orthogonal slice plane and incomplete or distorted histological slice. This paper presents an efficient method to directly perform the 2D-3D registration. The method is unique in that it uses smart phone as a navigation tool for initial alignment followed by an overlap invariant mutual information-based refinement. Experimental results using animal muscle samples images from a 3T MRI and HE stained histological images show that the proposed method is capable of aligning the histological slice with an oblique slice in MR volume.

I. Introduction

Muscle dystrophy is a disorder that affects both human and animals [2]. MRI has been an effect noninvasive tool for imaging in muscle dystrophy studies for longitudinally tracking the natural progression of the disease or the responses to therapies. Although many biomarkers are volume-averaged quantities such as muscle volume, length or average relaxation parameters, previous studies show heterogeneity in muscle may be import quantitative maker [2]. In order to understand the structural as well as the pathological heterogeneities, it is important to be able to register MRI images or measurements with pathological test results shown on histological slices.

Three general methods have been tested to align histology slices with MRI volume. First one is to use 3D histology and 3D MRI volume registration [3]. In this approach, reconstruction of histology volume using a large number of slices is required. It is proposed that deformations during histology sample slicing can be overcome by such volume registration. However, to create 3D volume of histology, large numbers of histological slices with known inter-space are needed and the required preparation by pathologists is time consuming in practical applications. The second kind of methods is based on 2D histological and 2D MRI slice registration. Due to deformations caused during sectioning of tissue and preparation of histology image, similarity between histology and MR slice may not be always existed [4].

The last kind is based on 2D slice and 3D volume registration [5-7]. In [5], Satish et. al. implement registration between T2-weighted and dynamic contrast enhanced MR images to assist detection of prostate cancer. In [8], Xiao et. al. propose a 3-step registration method for slice to volume registration in prostate cancer studies. The method first finds MRI slices that are closest to the histology slice. Then it performs 2D slice-slice registration before a final 3D-3D refinement. There methods require multiple steps, which could be time consuming and errors from early steps can propagate to the final result.

In this paper, we propose a new direct 2D-3D registration method. In the first step, an interactive alignment is applied to determine initial orientation for MR slice using smartphone as the navigation tool. At the second step involves an automatic 2D slice and 3D volume registration using mutual information. Preliminary results using a dog muscle show that proposed algorithm can present good spatial correlation between histology slice with oblique slice in the MRI volume.

The paper is organized as follows: Section 2 explains the method. Section 3 discusses the experimental results. Section 4 summarizes the discussion.

A. E. is with the Electrical and Computer Engineering Department, Texas A&M University, College Station, TX 77840 USA (e-mail: aeresen@tamu.edu).

P. L. is with the Electrical and Computer Engineering Department, Texas A&M University, College Station, TX 77840 USA (e-mail: billlipeng@tamu.edu).

*J. X. J. is with the Electrical and Computer Engineering Department, Texas A&M University, College Station, TX 77840 USA (Phone: 979-458-1468; fax: 979-845-6259; e-mail: jimji@tamu.edu).
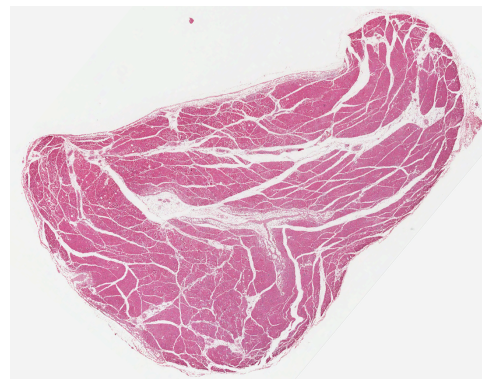
Figure 1. Histology slice cut from the middle of the muscle

II. Method

A. Acquisition of Histological Images and MR Images

Histological images are created from dog muscle. Sharp knives are used to prevent movement of the tissue during slicing but cutting surface has distortions caused by changing pressure over knifes. After muscle is sliced, slice is stained with Hematoxylin & Eosin dye. Histological slice after staining is given in Figure 1. The Histological image has 40X magnification and its resolution is 90084 × 67706 for 22.67mm × 17.64mm area. Pixel size is around 0.25µm.

MR slices are acquired on a 3T Siemens Magnetom Verio MR Machine. During T1-weighted acquisition, echo time=12.7ms, repetition time=555ms, slice thickness=1mm and echo sequence is spin echo. Field of view is calculated as 49 mm for both *x* and *y* directions. A representative set of MR slices are shown in Figure 2.
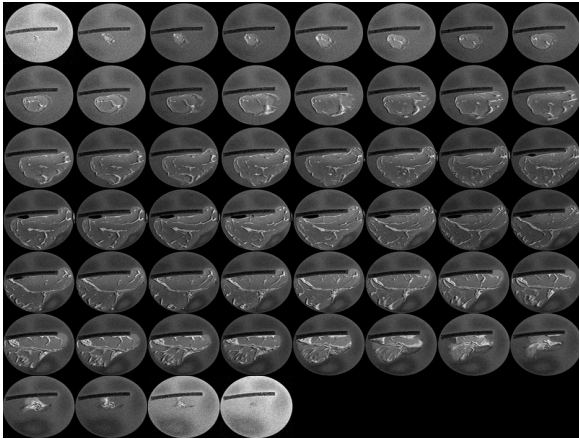

Figure 2.   The set of MRI slices of muscle acquired on the axial plane

B. Registration Procedure

One of the challenges for registration of MRI and histology image is enormous difference between MR and histology. The length of each MRI pixel is 0.1276mm, which has lower resolution compared to the same length of histology image that is 0.0180mm. Hence, there are 49 pixels in histology corresponding to every pixel in MRI image. Voxel size of MR and histology should be adjusted to obtain acceptable results on registration. For this purpose, histology image is down sampled to reach voxel size of MRI. After that, following steps are executed as in Figure 3.

During registration process, a 201px × 201px sized grid is created using physical space value for each direction(*x, y, z*) and orientation of the grid is changed at each step of the refinement. After that the grid is used to generate oblique MRI slice from 3D MRI volume with the aid of linear interpolation. In here, the generated oblique slice is accepted as registered MRI and MI is used to refine the registration

accuracy. Pixel size are defined as x = 0.1276mm, y = 0.1276mm and z = 1.050cm.
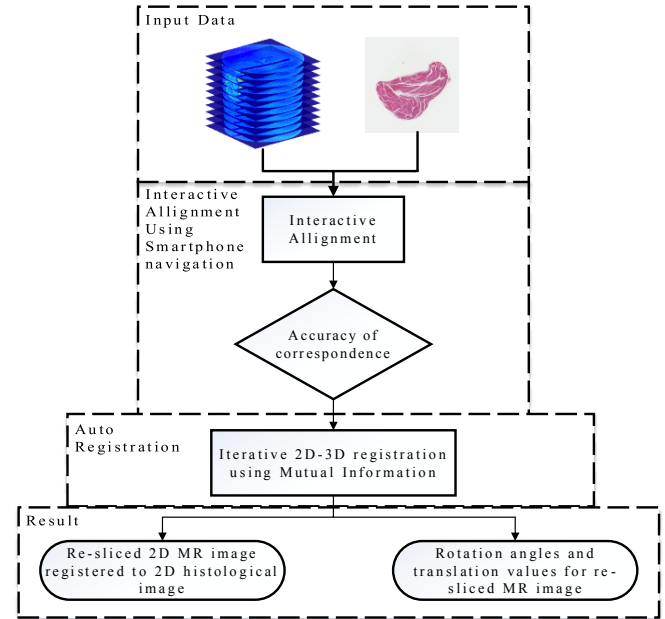

Figure 3.   Flow diagram of the proposed system

The spatial transformation of the MR slice that matches with the histological slice can be defined as,

$$I_m = V_m \left\{ \mathrm{T}_{\{\rho,\theta,\varphi,x,y,z\}} \left(Grid(\hat{x},\hat{y}) \right) \right\} \tag{1}$$

where V_m is MR volume, I_m is MRI slice that aligns with the histology slice, T is the spatial transformation with ρ, θ, φ, rotation angles and *x*, *y*, z translation values, Grid($\hat{x},\hat{y}$) is a 2D spatial grid defined the same pixel size as histology slice at the mass center of the V_m and in the axial plane.

B1. Interactive Alignment Using Smartphone as a Navigation Tool

A smartphone application is implemented to ease defining orientation parameters rotation angles and translation values by user. Inertial Measurement Unit (IMU) existing inside smartphone is used to define orientation of MR slice. An application is created to be able to read orientation and position data of any android smartphone with IMU sensors. Afterwards, they are sent to the server run on Matlab® through user defined protocol in real time. App interface is shown in Figure 4.

After the data is received, the position and rotation values are interpreted to use during interactive alignment. MR slice with new orientation, result of histology and MR slices alignment are presented in GUI (Figure 5). Orientation values are showed as live for defining initial position of the MR slice during iterative slice to volume registration to increase user's intuition.

orientationA	GyroscopeX
orientationP	GyroscopeY
orientationR	GyroscopeZ
linAccX	MagnetometerX
linAccY	MagnetometerY
linAccZ	MagnetometerZ
AccelerometerX	scale
AccelerometerY	
AccelerometerZ	

ip

port

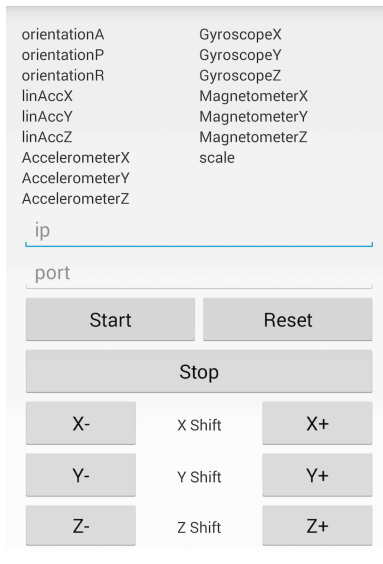| Start | Reset |
Stop	
X-	X Shift	X+
Y-	Y Shift	Y+
Z-	Z Shift	Z+

Figure 4.   User interface of controller app running on android smartphone

Rotation and translation values defined at the end of this process are used as initial for iterative registration.

B2. *Interpolate MR slice on the grid*

As mentioned in [9], we're losing valuable 3D integrity of the tissue during slicing process and orientation of slicing plane is not known. Hence, we do not receive reasonable similarity between MRI and histology slice. We create an MR slice with new orientation obtained from user's intuition to be able to overcome this problem.

Utilizing from interpolation techniques is used for various purposes in medical imaging. Obtaining new slice with interpolation is accepted as accurate. In our implementation, 3D linear interpolation is used for that purpose because texture is not changing very fast in tissue. During interpolation method, the user defines required orientation parameters. An interface is created to show results of the manual registration as seen in Figure 3.

B3. *Iterative 2D-3D Registration Using MI as Similarity Metric*

After determining of reference orientation by user interaction, we refine parameters for rotations and translations. While maximizing the correspondence between MR and histology slice, mutual information (MI) is used as similarity metric [11].

Throughout the iterative registration, slice orientation is changed and oblique slice is created using linear interpolation. After that, MI between oblique MRI and histology slice is calculated using histology information and recorded for all possible orientation of MR slice. The orientation of oblique slice is accepted as candidate parameter set for rigid transformation. During calculation of MI, we created 64 bins to group intensity of slices and exhaustive search algorithms are applied as similarity maximizing procedure.
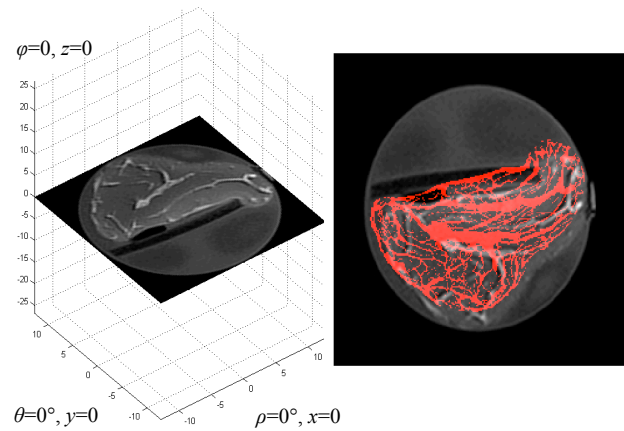

Figure 5.   User interface utilized during interactive allignment

III.   EXPERIMENTAL RESULTS

During implementation of our procedure, we used 52 T1-weighted MR slices to reconstruct 3D volume, and inter-slice is defined as used during MR imaging which is 1mm. Our slice thickness is 1 mm and resolution in axial direction is 0.1276mm for each pixel. Resolution is calculated by utilizing from MRI dicom header file. At first step, field of view is measured and after that voxel size is calculated. During reconstruction linear interpolation is used since the change in muscle tissue is not changing very fast. During real-time manual registration, linear interpolation takes less time than more complex techniques and increase the frame rate per second. In our implementation, each iteration takes nearly 0.5 seconds due to required computational burden during obtaining new MR slice with desired orientation parameters. Throughout the experimentation, a Windows[®] 7 pc which has Intel[®] i7-920 processor, 1.8GB graphic card and 9GB DDR3 memory is used and Matlab[®] software is utilized for implementation.

Histological slice has higher resolution than MR; hence, it needs to be down-sampled to reach resolution of MR slices. Our histological slice has 40x magnification and its sizes are nearly 90k pixels for each directions in space for nearly 4 cm area. Image software is used for viewing our large file. Obtaining a lower resolution histology image is the first step of down sampling, and resampling in both directions follows it. After first step, resolution of histological slice is 0.0180mm and it is scaled nearly 1/90 of original scale image. After down-sampling process manual segmentation is started.

An interface, that shows new slice whose orientation is controlled by the user in 3D MR volume, and combination of MRI and histology slice is prepared to ease manual registration by supporting user intuition. Orientation parameters for each axis are given in figure for informing user. In the left part of the interface, combined slices are shown for result of registration. Due to narrow intensity histogram of histological slice, which is related to type of dye and textural structure, fusion of these slices are not defined as very clearly.

After concluding interactive alignment, determined orientation values (ρ=-10˚, θ=-10˚, φ=3˚ and x=-6.38mm, y=-6.38mm, z=21mm) are stored and boundaries for each parameter are measured with predefined constraints. Later, optimization process is processed with exhaustive search algorithm to maximize similarity parameter in which mutual information is used in our implementation. Due to looseness of exhaustive search algorithm and complexity of 6D space, optimization process is continued nearly 4 hours. The obtained results show highest MI value is measured with following rotation angles and translation values, ρ=7˚, θ=7˚, φ=-2˚ and x=6.38mm, y=6.38mm, z=31mm respectively.

In Figure 6, we present three MR slices and three alignment results for them. In Figure 6.a, slice is selected from MR data and rigid transformation is applied and results is shown in 6.d. Figure 6.b shows oblique slice created after interactive alignment and results after transformation is applied is shown in 6.e. Figure 6.c shows oblique slice created after iterative alignment and 6.f shows that the result of registration.
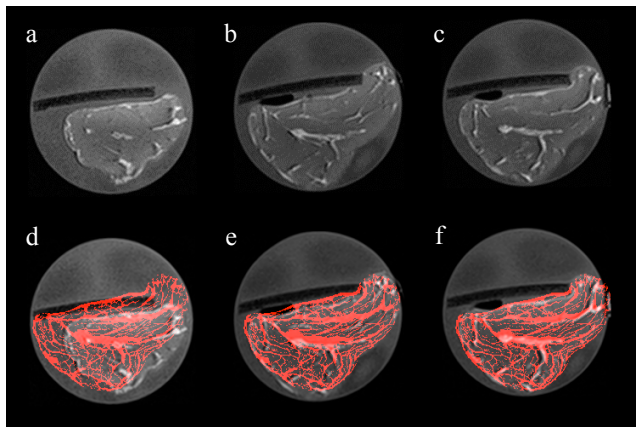

Figure 6. The registered MRI slices showing on top row and with the histological image slice (in red) overlapped. (a-d) initial slice, (b-e) oblique MRI slice after interactive alignment, (c-f) oblique MRI slice after-mutual information based refinement

IV. DISCUSSION

This paper presented a novel method that directly registers the 2D histology slice with the 3D MRI volume within two steps. First step of the method includes user-based interactive alignment using smartphone as navigation device for initial alignment. At the second step, an iterative 2D-3D registration process is implemented using MI as similarity metric. Throughout execution of the method, orientation of the MRI grid is changed and oblique slice is created. Moreover, similarity between an oblique MRI slice and histology image is tried to maximize inside the defined parameters boundary. The presented method is efficient by using a smartphone as navigate device initial alignment and the registration accuracy is improved by using mutual information-based iterative refinement. The preliminary results shown that the method can be correlated oblique MR slice with the histology slice. This will be useful for muscle

dystrophy study or other studies that involve registering 2D histological image with 3D volumetric images.

REFERENCES

[1] D.W. Townsend, "Multimodality imaging of structure and function", *Physics in Medicine and Biology,* vol. 4, pp. 1-39, 2008.

[2] Z. Fan, J. Wang, M. Ahn, Y.S. Malawsky, N. Chahin, S. Elmore, C.R. Bagnel Jr, K. Wilber, H. An, W. Lin, H. Zhu, M. Styner, J.N. Kornegay, Characteristics of magnetic resonance imaging biomarkers in a natural history study of golden retriever muscular dystrophy, *Neuromuscular Disorders*, vol. 24, pp. 178-191, 2013.

[3] L. Alic, J.C. Haeck, K. Bol, S. Klein, S.T. van Tiel, P.A.Wielepolski, M. de Jong, W.J. Niessen, M. Bernsen, J,F, Veenland, "Facilitating Tumor Functional Assessment by Spatially Relating 3D Tumor Histology and In Vivo MRI: Image Registration Approach", *PLoS One*, vol. 6, pp. 1-10. 2011.

[4] H. Park, M.R. Piert, A. Khan, R. Shah, H. Hussain, J. Siddiqui, T.L. Chenevert, C.R. Meyer, "Registration methodology for histological sections and in vivo imaging of human prostate", *Academic Radiology*, vol.15, pp. 1027-1039, 2008.

[5] S. Viswanath, B.N. Bloch, M. Rosen, J. Chappelow, N. Rofsky, R. Lenkinski, E. Genega, A. Kalyanpur, A. Madabhushi, "Integrating structural and functional imaging for computer assisted detection of prostate cancer on multi-protocol in vivo 3 Tesla MRI", *Proceedings of SPIE Medical Imaging*, vol. 25, pp. 607-619, 2009.

[6] S.G. Jhavar, C. Fisher, A. Jackson, S.A. Reinsberg, N. Dennis, A. Falconer, D. Dearnaley, S.E. Edwards, S.M. Edwards, M.O. Leach, C. Cummings, T. Christmas, A. Thompson, C. Woodhouse, S. Sandhu, C.S. Cooper, R.A. Eeles, "Processing of radical prostatectomy specimens for correlation of data from histopathological, molecular biological, and radiological studies:a new whole organ technique", *Journal of Clinical Pathology*, vol.58, pp. 504-508, 2005.

[7] V. Shah, T. Pohida, B. Turkbey, H. Mani, M. Merino, P.A. Pinto, P. Choyke, M. Bernardo, "A method for correlating in vivo prostate magnetic resonance imaging and histopathology using individualized magnetic resonance-based molds", *Review of Scientific Instruments*, vol. 80, 2010.

[8] X. Gaoyu, B.N. Blochb, J. Chappelowa, E. M. Genegae, N.M. Rofskyc, R.E. Lenkinskid, J. Tomaszewskif, M. D. Feldmanf, M. Rosenf, A. Madabhushia, "Determining histology-MRI slice correspondences for defining MRI-based disease signatures of prostate cancer", *Computerized Medical Imaging and Graphics*, vol. 35, pp. 568-578, 2011.

[9] O. Yangming, S. Dinggang, M. Feldman, J. Tomaszewski, C. Davatzikos, "Non-Rigid Registration between Histological and MR Images of the Prostate: A Joint Segmentation and Registration Framework", *Computer Vision and Pattern Recognition Workshops*, 2009, pp. 125-132.

[10] A. Klein, S.G. Satrajit, B. Avants, B.t.t. Yeo, B. Fischl, B. Ardekani, J.C. Gee, J.J. Mann, and R.V. Parsey, "Evaluation of Volume-based and Surface-based Brain Image Registration Methods", *NeuroImage*, vol. 51, pp.214-220, 2010.

[11] R. Cilibrasi, P. Vitanyi, "Clustering by compression", *IEEE Transactions on Information Theory*, vol. 51, pp. 1523-1545, 2008.