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ABSTRACT

Ultrasound imaging is widely used in clinical imaging because it is non-invasive, real-time, and inexpensive. Due to the freehand nature of clinical ultrasound, analysis of an image sequence often requires registration between the images. Of the previously developed mono-modality ultrasound registration frameworks, only few were designed to register small anatomical structures. Monitoring of small finger vessels, in particular, is essential for the treatment of vascular diseases such as Raynaud's Disease. High frequency ultrasound (HFUS) can now image smaller anatomic details down to 30 microns within the vessels, but no work has been done to date on such small-scale ultrasound registration. Due to the complex internal finger structure and increased noise of HFUS, it is difficult to register 2D images of finger vascular tissue, especially under deformation. We studied a variety of similarity measurements with different pre-processing techniques to find which registration similarity metrics were best suited for HFUS vessel tracking. The overall best performance was obtained with a normalized correlation metric coupled with HFUS downsampling and a one-plus-one evolutionary optimizer, yielding a mean registration error of 0.05 mm. We also used HFUS to study how finger tissue deforms under an ultrasound transducer, comparing internal motion vs. transducer motion. Improving HFUS registration and tissue modeling may lead to new research and improved treatments for peripheral vascular disorders.

Keywords: image registration, high frequency ultrasound imaging, image processing

1. INTRODUCTION

Ultrasound imaging is one of the most popular medical imaging modalities which has been widely used in clinical field. In additional to its low-cost, non-invasiveness and non-ionizing, ultrasound imaging allows clinicians to monitor the condition of patient internally in real time. Image registration is a process of aligning two or more images, which is essential for image analysis because valuable information could be conveyed in more than one images depending on different acquisition time, different viewpoints and so on[1]. Because of the freehand nature of clinical ultrasound, analysis of an image sequence often requires registration between the images, which makes ultrasound image registration important.

Researchers have developed different ultrasound registration frameworks on human and small animals, but only few of them focused on registration of small anatomical structures. In 2002, a registration framework was proposed for real-time volume ultrasound registration of the heart[2]. It is based on mutual information and Nelder-Mead optimizer. In 2012, a registration frame for real-time tracking of 4D ultrasound date was proposed[3]. They used sum of squared differences (SSD) as similarity metric and Nelder-Mead algorithm as optimizer to validate their framework on liver scan. There are also novel registration algorithms developed in additional to popular registration frameworks. A near real-time registration algorithm (RESOUND) was developed for registering ultrasound volumes acquired before and after the resection of brain tumors[4]. The algorithm minimizes a cost function comprised of a similarity metric based on NCC and a smoothness term. The optimization was done by taking the analytic derivative of NCC, and using a stochastic gradient descent algorithm. Cubic B-spline was used to estimate the deformation field. The complex internal finger tissue is composed of various structures such as ligaments, tendons and phalanges (bones), making analysis of vascular structure even harder. However, there is an increasing need for registration of this small anatomical structures such as finger

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vessels, since problems in vessels may potentially cause a variety of vascular diseases related to hand and fingers. For example, Raynaud's Disease is defined as an episodic vasoconstriction of fingers or toes under certain conditions[5]. Considering this, we are interested in registration of small anatomical structures by applying High frequency ultrasound (HFUS), which allows us to view small anatomical details down to 30 microns within the vessels. Since the target area is so small that no work has previously been done to monitor the finger vessel using HFUS. Moreover, the deformation of finger tissue, due to the compression and movement of ultrasound transducer, makes it even more difficult to analyze and register ultrasound images. Therefore we conducted several experiments to develop an in-plane registration framework of high frequency ultrasound in deformable finger vessel.

2. METHODOLOGY

2.1 Experimental Setup & Protocol

As shown in Figure. 1, the ultrasound traducer is mounted on a linear stage which allows the operator to moves the probe along all three axis steadily. Right next to the operator is the ultrasound machine. Operators can see the images in real-time while performing the experiments. A foot petal is connected to capture the ultrasound images, which are saved to disk for further analysis. The ultrasound dataset is acquired using Vevo® 2100 System and Epiphan frame-grabber. The model of transducer we used is MS700, allowing the maximum frequency at 70 MHz. The code is implemented in C++ with the Insight Toolkit (ITK) and the OpenCV library. Two experiments were performed.

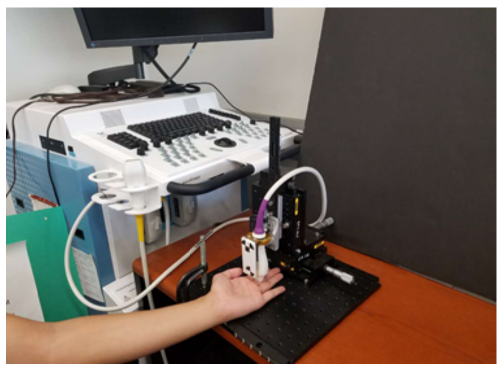

Figure 1 Experiment Setup

2.2 Similarity and pre-processing techniques experiment

A registration framework consists of several components. Choices of pre-processing algorithms and similarity metrics, in particular, should be informed in part based on the nature of the images being registered. In this initial study for 30-micron HFUS, we compared three popular image-registration similarity metrics: Mean Squared Error (MSE), Mutual Information (MI), and Normalized Correlation (NC). We also compared downsampling ratios: 1 by 2, 2 by 2, 2 by 4, and 4 by 4. In all cases, we initially applied Gaussian blurring to suppress noise. We studied image sequences from 5 different HFUS transducer motions: holding it still (noise still varies), pitching it forward and backward, translating it distally, translating it medially, and a composite motion that sweeps it around the finger so-as to remain perpendicular to the finger's surface. Each sequence contained 100 frames. For each similarity metric, downsampling ratio, and sequence triplet, we computed metric values between each two adjacent frames within the sequence and calculated the mean metric value, standard deviation, maximum/minimum values and 5%/95% percentiles.

2.2.1 Mean Squared Error (MSE)

Mean squared error is the simplest standard similarity metric in image registration. It computes sum of squared differences of pixel's intensity of both fixed and moving images. Since this metric requires both fixed and moving images to have the same intensity ranges, it is best-suited for mono-modality (ultrasound-to-ultrasound) registration.

2.2.2 Mutual Information (MI)

Mutual information is a well-established similarity metrics used in both rigid and non-rigid registration. It seeks a transform that aligns two images or volumes by maximizing their mutual information. As Viola et al.[6] proposed, both joint and individual entropies are used to obtain the MI value, which will be optimized when the individual entropies are maximized while joint entropy is minimized. Its robustness to outliers and efficiency to use in optimization make MI an excellent metric.

2.2.3 Normalized Correlation (NC)

Normalized correlation is another widely-used similarity metric. It calculates the correlation between two intensity values divided by the square rooted autocorrelation of both fixed and moving images. It works the best with mono-modality registration between two images acquired with the same characteristic curves, for example the same gamma curve.

2.3 Validation of registration framework

In this experiment, we used a linear stage to precisely translate the ultrasound transducer with a step size of 1 mm. Each motion consisted of 8 mm forward and then 8 mm backward across a proximal section of a finger, with an image acquired at each step, resulting in 17 images total including the initial frame. Manual registration using 3D Slicer was used for validation of each registration. The two purposes of this experiment were (1) to validate the registration algorithms on 70 MHz HFUS images and (2) to compare the HFUS transducer's global motion with its motion relative to internal anatomy.

The flowchart of this registration framework is shown in Figure. 2. As shown, pre-processing techniques Gaussian smooth and downsampling are applied on both fixed and moving images before registration process starts. In this registration framework, we used normalized correlation as similarity metric (validated in section 3.1) and One-Plus-One optimizer. A linear interpolator is selected to interpolate values when objects are resampled through the Transform.

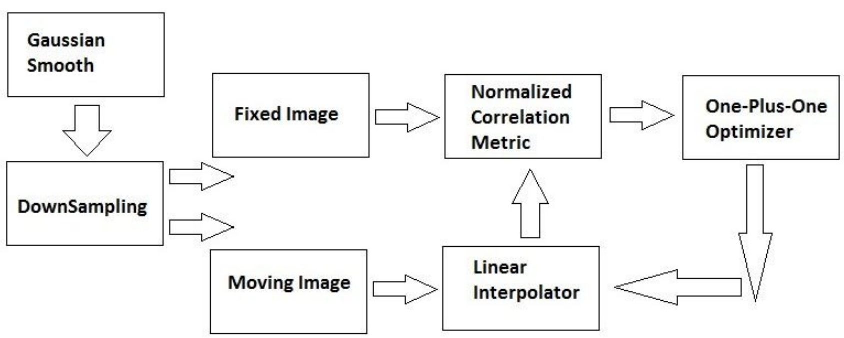

Figure 2 Flowchart of registration framework

2.3.1 One-plus-one evolutionary optimizer

In this registration framework, the optimizer used is one-plus-one evolutionary optimizer. The one-plus-one evolutionary optimizer follows a strategy that simulates the biological evolution of a set of samples in the search space. Random samples generator is needed to change the searching radius and position in the parametric space in order to find the global maximum[7].

3. RESULTS

3.1 Similarity and pre-processing techniques experiment

We presented the results by applying three different metrics and downsampling ratios pairs in all 5 motions. Varies of statistic methods such as mean, standard deviation, maximum/minimum value and 5%/95% percentiles have been applied and the comparison results are shown in Figure. 3,4 and 5. All values in the results are normalized based on standard deviation of motion "holding it still", which allows the same scale comparison among different pre-processing techniques. The vertical line in the graph is an indication of 95% percentile of metric values in "holding it still" motion. Three of these graphs were shown: MSE, MI and NC metrics with downsampling ratio of 4 by 4. The normalized correlation outperformed the MSE and MI since the majority of metrics values in all other motions, especially the medial motion for our registration framework since we are performing in-plane motion, are larger than the 95% percentiles of still motion, which indicates it can effectively differentiate images when the ultrasound transducer is translated medially. Thus, the normalized correlation with downsampling ratio of 4 by 4 is selected for our registration framework.

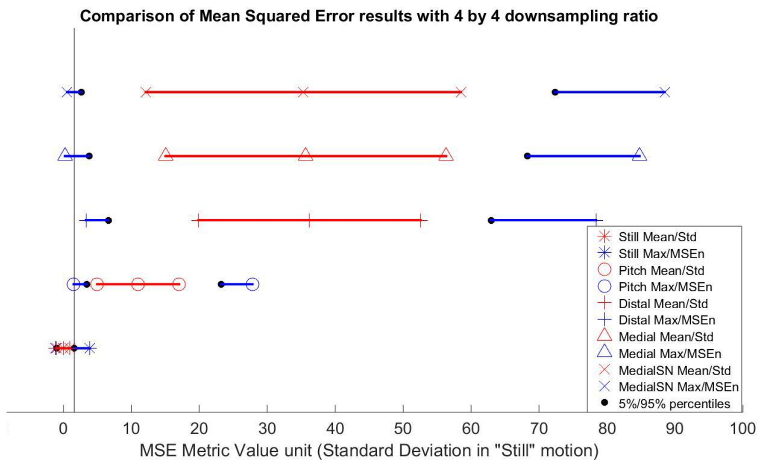

Figure 3 MSE result with 4 by 4 downsampling ratio

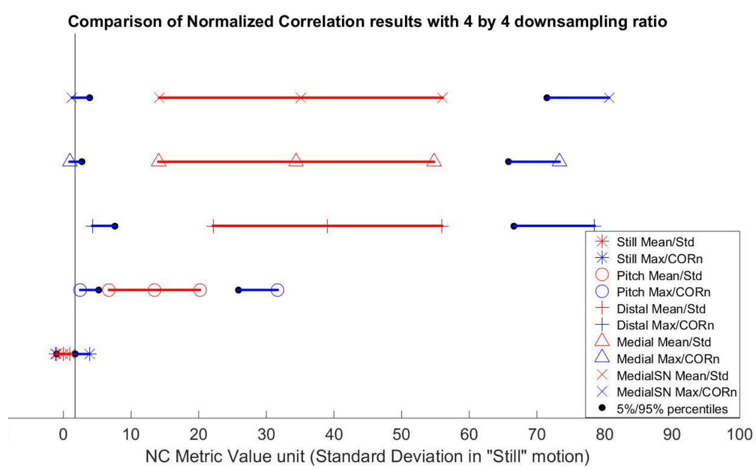

Figure 4 NC result with 4 by 4 downsampling ratio

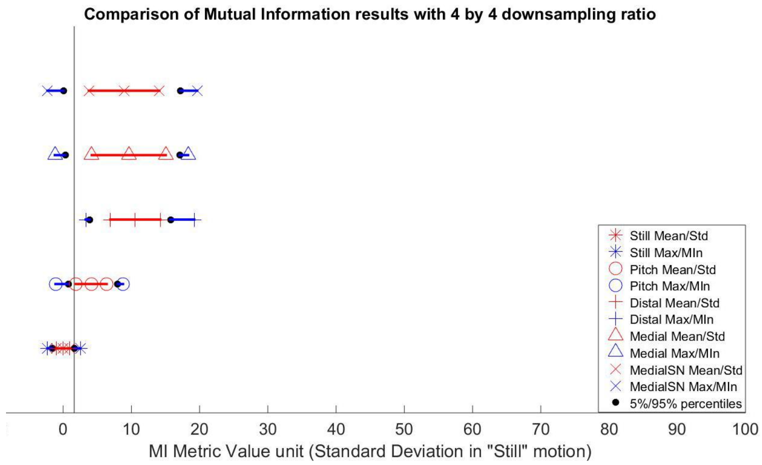

Figure 5 MI result with 4 by 4 downsampling ratio

3.2 Validation of registration framework

In Figure. 6 and 7, registration results are presented. Two of them were obtained by translating the probe first to right and then left (RL). The other two were obtained by translating the probe first to left and then right (LR). For each data sequence, we presented the total motion trajectory and the step movement of transducer, manual registration and auto registration with 4by 4 downsampling ratio. As shown in the results, internal tissue translates the same direction as the ultrasound probe. However, due to the effect of internal deformation, the step movement of internal tissue is usually less than the transducer, which causing the significant difference in total movement and trajectory between HFUS transducer's global motion and its motion relative to internal anatomy. Internal tissue would usually lead/lag behind transducer tip in a predictable way, but the exact amount of slipping and deformation varies considerably within bounds, making it difficult to create detailed a-priori model. However, there is a strong agreement between manual registration and automatic registration. Registration error of 8 sets of data were recorded a mean error of 0.051 mm is achieved. Moreover, in Figure. 8, finger vessel is shown before and after registration.

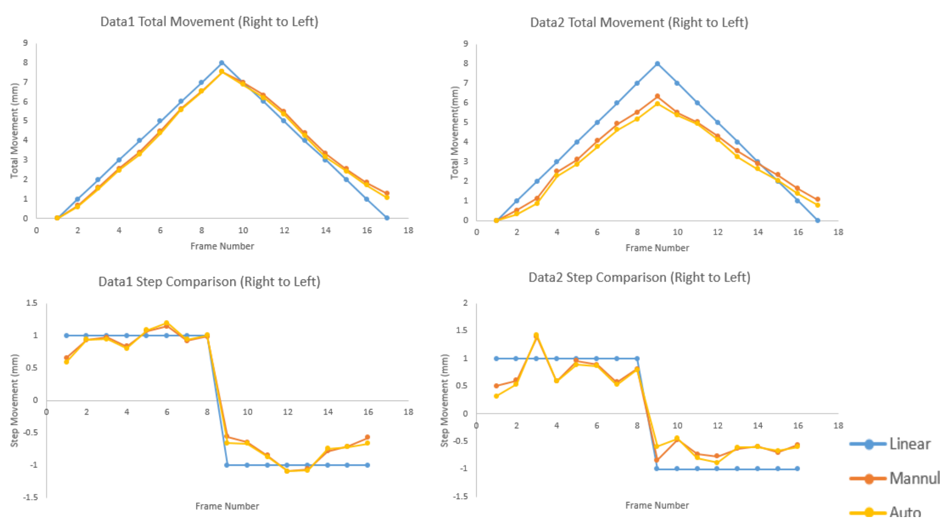

Figure 6 Left:(Top to bottom) Data1 total movement and step comparison with probe moving from right to left; Right:(Top to bottom) Data2 total movement and step comparison with probe moving from right to left

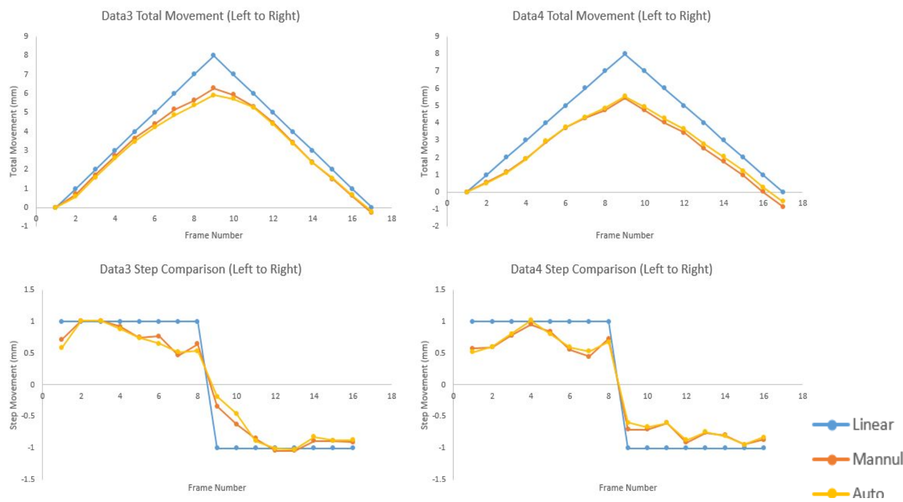

Figure 7 Left: (Top to bottom) Data3 total movement and step comparison with probe moving from left to right; Right:(Top to bottom) Data4 total movement and step comparison with probe moving from left to right

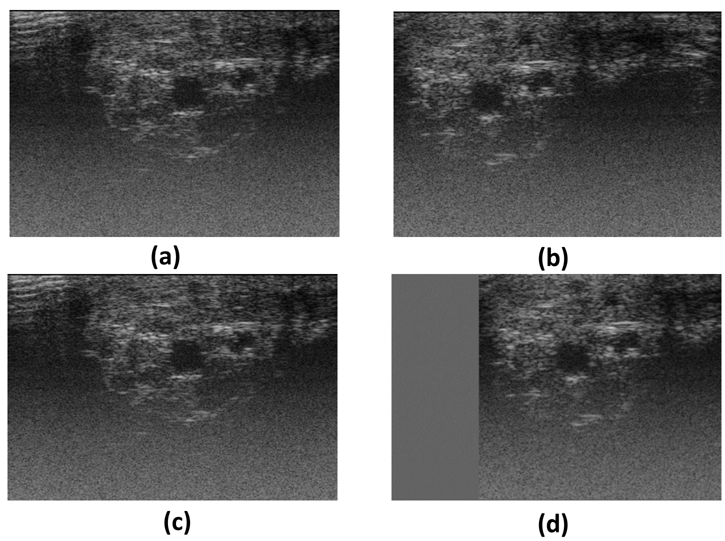

Figure 8(a)(b): fixed and moving image before registration; (c)(d): fixed and moving image after registration

4. CONCLUSION

In conclusion, we developed in-plane registration framework for deformable finger vessels using 50-70 Mhz HFUS system. We had the first results showing 50-70Mhz HFUS of finger anatomy, which shows more detail, more noise and less isotropic deformation. 50-70 MHz ultrasound can resolve small structures like nerve fascicles and layers of vessel walls, which could not previously be imaged using ultrasound, but noise is also increased and at this small scale individual microstructures exhibit more variation in their displacements under deformation. In addition, we performed the first automatic registration of this challenging HFUS dataset. We studied the efficacy of several established registration metrics on HFUS data, and surprisingly found that MSE and correlation usually outperform mutual information. We also found metric performance to be sensitive to preprocessing choices regarding blurring and down sampling. Lastly, we conducted the first detailed comparison of HFUS transducer's global motion vs. its motion relative to internal anatomy. We precisely translated the transducer within the ultrasound plane using micrometer-actuated linear stages, and we compared these results against both manual and automatic tracking of internal anatomy. There was strong agreement between manual vs. automatic tracking, but significant differences were observed against actual transducer motion, owing to significant internal deformation.

In the future, more research can be performed based on current results. For example, we can design and add external device to hold hands steadily and see how it affects the manual registration results of deformable finger tissues. Also, we can see how indentation of the probe to finger tissue would affect the movement of internal tissue so that a more realistic model can be obtained.

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