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A Method for Measuring the Accuracy of Multi-modal Image Fusion system for Catheter-based Cardiac Interventions Using a Novel Motion Enabled Targeting Phantom

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***Abstract*—Targeted stem cell therapy offers great potential for the repair of infarcted cardiac tissue following heart attack. Safe delivery of stem-cells via catheter based interventions remains a challenge. A multi-modal image fusion approach has been considered for safe targeting of myocardial infarct border zones. In this paper we present an apparatus and method for measuring the accuracy of catheter-based injections using a multi-modal image fusion system. We also present results of the accuracy of our image fusion system under varying levels of cardio-respiratory motion.**

I. INTRODUCTION

Myocardial infarction (MI) affects 1.1 million Americans each year. Minimally invasive interventions, such as percutaneous transluminal coronary angioplasty, are a feasible option for over a million patients in the US alone. However, patients who present late, or fail early treatment can develop progressive ventricular enlargement, heart failure, and sudden death. Stem cell therapy has recently generated interest due to its potential for cardiac cell repair. Landmark small animal studies show that direct intramuscular injection of bone marrow derived stem cells precisely targeting the infarct border zone offers dramatic functional recovery post-MI [1]. Preliminary studies suggest that a catheter-based, transendocardial approach that delivers stem cells directly into the infarct borders from within the heart may improve cell retention and curb adverse remodeling post MI.

However, limitations exist with conventional interventions to safely deliver stem cell treatment to the infarct border. In recent MI patients, the infarct zone is delicate, thereby increasing the risks of perforation with catheter based injection (a life-threatening event). Thus, accurate targeting is critical for the safe delivery of stem cells. X-ray fluoroscopy is the de facto modality to guide catheter procedures - predominantly due to excellent device visualization. However, it offers little cardiac tissue visualization. For this reason, image fusion systems that can combine anatomical and functional road-maps based on MR or CT images with real-time information such as ultrasound images and spatially tracked devices are desirable for this application. We have developed a system that is capable of fusing i) magnetic resonance imaging (MRI) based cardiac road map to best define the cardiac surfaces and infarct borders, with ii) live 3D ultrasound (3DUS) to permit real-time motion compensation and iii) electromagnetic (EM) tracking sensors to enable a registration framework. We have shown that this multi-modality registration is feasible in pig experiments [2]. This imaging technology will enable future investigations of optimal injection site location, and the impact of multiple injections to the same location for multiple dose strategies. In order to translate this image fusion system to the clinic, it is necessary to quantify the registration accuracy.

We introduce a method and apparatus for quantifying the injection accuracy of a multi-modal image fusion system for catheter based interventions. We present a novel cardio-respiratory motion enabled phantom, as well as an EM tracked injection catheter for performing injections. We also present accuracy results for a set of catheter based injections at different levels of respiratory motion. We later discuss future steps to further improve the accuracy of this system, such as the implementation of motion compensation algorithms.

II. METHODS

A. Novel Motion-Enabled Cardiac Phantom

A polyvinyl alcohol (PVA) based cardiac phantom was molded from a real human heart and has similar mechanical properties to soft-tissue [3]. The apex from the cardiac phantom was then removed and replaced with a detachable "targeting slab" (Fig. 1). This "targeting slab" is easily removed and then re-attached to the apex of the heart phantom. Within this slab were four circular holes where removable targets can be placed (Fig. 2). The purpose of this configuration was so that injections and corresponding analysis could be conducted efficiently, allowing for a large number of iterations for each experiment. The phantom consists of replaceable parts including targets, to ensure consistent physical integrity of the model for numerous experiments.

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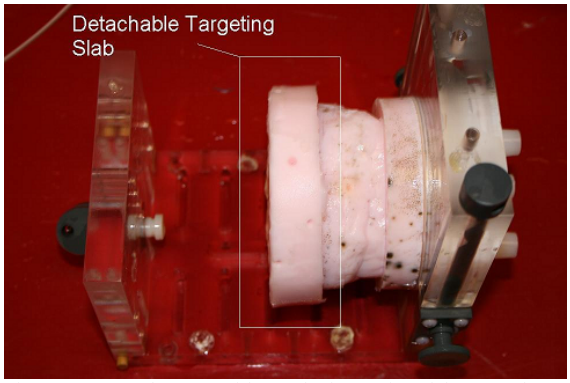

Figure 1. Heart phantom with attached targeting slab. A catheter enters from the ports on the right, and injects into the targeting slab.

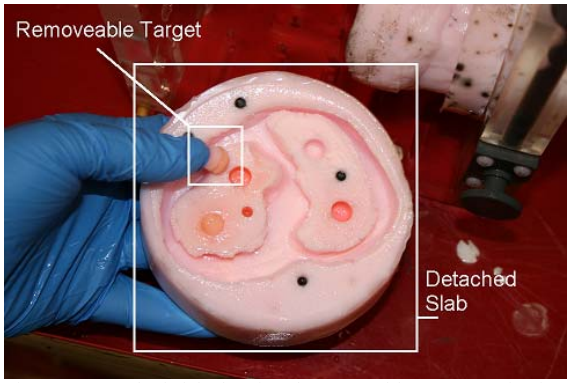

Figure 2. Detached slab showing the removable targets. Injections of dye are made into the targets, and afterwards accuracy measurements are made. Targets are easily replaced so that numerous injection experiments can be made rapidly.

The cardiac phantom was mounted onto a pneumatically controlled, closed-loop motion actuator. A RAPU micro-controller (Remote Advanced Playback Unit, Brookshire software) was used to control a linear pneumatic actuator cylinder. The position signal from the RAPU controller and the position error signal from the output of a string potentiometer attached to the pneumatic cylinder are fed into a differential amplifier. The signal from this amplifier controls a differential pneumatic valve, which in turn controls the position of the pneumatic cylinder. This closed-loop feedback ensures precise and repeatable movement of the phantom. A schematic of the control system is shown in Figure 4. The actuator cylinder is attached to the phantom and moves the phantom back and forth over a ramp, which allowed for the imitation of the coupled superior-inferior and posterior-anterior cardio-respiratory motion present in most humans. Respiratory motion-like signals were created to control the linear position of the phantom as a function of time. Beating-heart motion is not included in this version of the phantom, due to the fact that most interventionalists only inject at end-diastole. A future version of the phantom will include this capability.

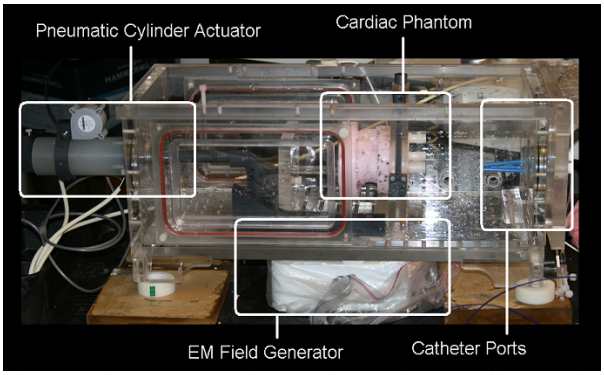

Figure 3. Phantom setup. The PVA phantom is mounted into a tank and is controlled by a pneumatically controlled motion system. Catheters are introduced from ports located on the sides.

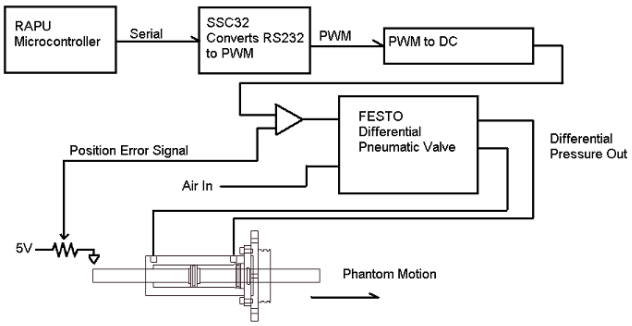

Figure 4. A schematic of the phantom motion control system. User-generated positions signals are downloaded into the RAPU microcontroller, and the closed-loop system moves the phantom

B. EM Tracked Catheter

A prototype steerable EM tracked injection catheter was fabricated from an off the shelf steerable catheter sheath ('Channel' Model, Bard Medical), nitinol hypotube (Johnson-Matthey Medical), and a 5DOF EM tracking sensor (NDI) (Fig. 5). The EM sensor was fixed in the lumen tip of the catheter, while the hypotube was able to advance freely through the lumen in order to penetrate the PVA. The EM sensor has a 1mm offset from the hypotube, introducing a source of error into the system.

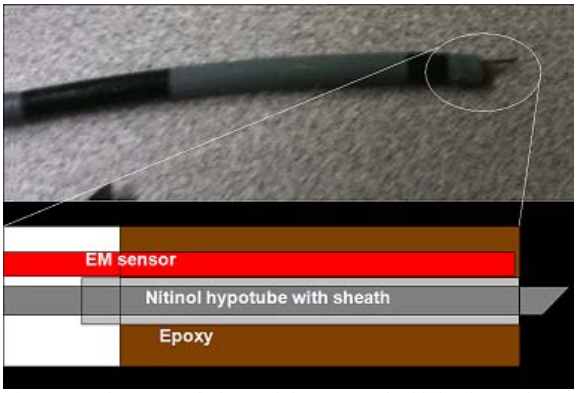

Figure 5. Diagram and photo of the EM tracked injection catheter. The EM sensor is fixed in place at the tip the catheter, while the sharpened hypotube is able to move freely within the lumen.

C. MR Acquisitions

Axial MR scans of the phantom were acquired on a 1.5T system (Signa HDxt, GE Healthcare, Milwaukee, WI) with the following parameters: 8-channel cardiac coil; 3D balanced SSFP (bSSFP/FIESTA) pulse sequence; TR/TE/Flip = 3.6ms / 1.5ms / 55 deg.; FOV/Matrix = 35cm/384x384; Num. Slices/Sl. Thickness = 256/1mm. After the images were acquired, we digitally altered the MR volumes so that a small point appeared in the center of each target (Fig. 6) using a circular Hough transform on each slice. This allowed the system operator to aim for the exact center of the circle rather than an interpretation of the center. The MR images are acquired once pre-operatively, and the same image is used for registration in all subsequent targeting experiments. This is acceptable due to the fact that the PVA structure is rigid over a long period of time (years) if properly maintained.

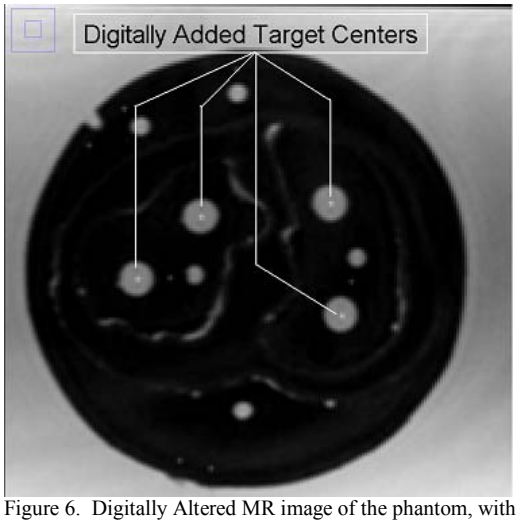

Figure 6. Digitally Altered MR image of the phantom, with enhanced signal at the center of each target.

D. Registration

Registration is performed in the cathlab at the time of the injection experiment. MR images are registered to the EM coordinate space by matching the location of fiducials in the MR series to location of fiducials in EM space. The fiducial locations are segmented in the MR images, and an EM tracked sensor is touched to the corresponding fiducials. The resulting set of points clouds are registered by finding the rigid transformation matrix that minimizes error between the point locations segmented from MR and the transformed point locations measured in the EM space. The associated error is known as the "fiducial registration error" (FRE).

Fiducials consisted of 5 indentations on the exterior of the targeting slab. This was done so that any incidental movement between the PVA phantom and its holding frame would not affect the resulting MR to EM registration. The geometric configuration of the fiducials was similar in configuration to what is typical of a clinical fiducial scenario, except the spatial distribution in the axial direction was smaller, and the distance between the fiducials, targets, and the centroid of the fiducial configuration was smaller, which affects the expected targeting error and is explained later in the paper.

E. Accuracy Measurements

The most clinically relevant measure of accuracy is the distance between the actual injection and the center of the target, what we refer to as the "combined error" (CE). The CE is a vector sum of two errors: the "system error", also known as the "target registration error", (TRE), and the "operator error" (OE). The TRE is the distance between the actual injection location and the catheter tip location reported by the fusion system at the time of the procedure. The OE is the distance between the catheter tip and the target center as displayed by the fusion system at the time of injection, and is a function of the operator's ability to guide the catheter to a specific location. In this study, it was difficult to measure the OE at the exact time of injection when respiratory motion was present, so we only report CE for respiratory motion experiments.

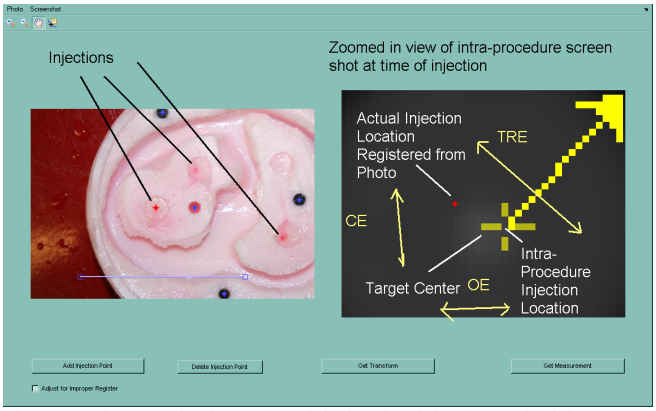

Figure 7. Photograph of targeting slab showing injections, which is registred to an intra-procedure image of the target at the time of injection. The target is zoomed in.

Accuracy measurements were carried out by taking a high resolution photograph of the PVA "slab" and a ruler following a set of injections. This was used to measure the distance between the target center and the actual injection location to obtain the CE. To measure TRE and OE, a screenshot of the injection was registered to the photograph by matching landmarks (5 small circles shown in figures 2 and 6). By doing this, the intra-procedural location of the catheter tip at time of injection could be compared to the actual injection location, as well as the center of the target (Fig. 7). The registration error for this technique was very low, 0.19 mm, compared to the typical system error in this study.

CE was characterized as a function of respiratory motion amplitude and registration error. Respiratory motion amplitude corresponds to the amount of translation the phantom makes during a single cycle. Targeting experiments were done at translations of 0, 5, and 20 mm, which cover most of the range found in humans. The respiratory rate was 15 cycles per minute for all

experiments. Injections were performed at "end expiration" which corresponds to the respiratory phase of fiducial based registration initialization. To determine end expiration, the US volume was registered to the MR volume at the beginning of the experiment at the end expiration position, and end expiration was determined qualitatively as the moment that the US volume seemed to be best registered with MR. This is clinically comparable to pre-procedural registration during a breath hold.

III. RESULTS

A total of 41 injections were performed. Table I shows the mean and standard deviation of the accuracy measures for all respiratory motion scenarios.

Without respiratory motion, the fusion system is very accurate. The 1.44 mm RMS TRE is only slightly larger than the 1mm offset between the needle and the EM sensor. These values of error are slightly larger than what was reported in [4] (RMS error 1.00mm), and are reasonable considering that the measurements make in this study were made using an injection catheter with a built in offset.

We found that the injection error general increased with respiratory motion, as well as the variance of the error, which is expected. The error did not increase linearly with amplitude, however. This is most likely due to the fact that, when making an injection during end expiration, the source of error is from the user not having much time (roughly 1 second at a breathing rate of 0.25 Hz) to aim the catheter at the target, whereas with no motion the user has an unlimited amount of time to precisely maneuver the catheter. This means that error is more likely a function of breathing rate rather than motion amplitude.

IV. DISCUSSION

The CE under these scenarios was well within the recommended 10 mm bounds, although there are many confounding issues found in a clinical setting that are not present in our set-up.

First, cardiac motion due to the beating of the heart is also present in the clinic, and creates additional challenge for an interventionalist attempting to guide a catheter toward a target. The most common strategy for dealing with cardiac motion is to simply attempt to make injections during end-diastole; the fact that our heart phantom is always in end-diastole eliminates lots of the challenge.

Furthermore, the fiducial configuration in a clinical scenario is different than in our set-up. We refer to theoretical results in [5] to compare the effect of fiducial configuration on TRE in our setup with that of a clinical fiducial configuration.

According to [5], the TRE is approximately a function of the "fiducial localization error" (FLE), the number of fiducials used, and the location of the target relative to the fiducial configuration:

$$< TRE^2(r) > \approx \frac{< FLE^2 >}{N}\left(1+\frac{1}{3}\sum_{k=1}^{3}\frac{d_k^2}{f_k^2}\right) \qquad (1)$$

Where N is the number of fiducials used d_k is the distance of the target from the principle axis and f_k is the RMS distance of the fiducials from the principle axis. We calculated the quantity $\left(1+\frac{1}{3}\sum_{k=1}^{3}\frac{d_k^2}{f_k^2}\right)$, the "fiducial configuration error factor" (CEF), for our phantom setup, as well as from a fiducial configuration from a pig experiment done by our group in the past, in order to compare how the fiducial configuration in a clinical scenario would affect TRE differently than in our experiment. Table II shows the results. For both scenarios, we see values ranging from 3 to roughly 8.5. Therefore, the values for target registration error achieved in these experiments should be roughly the same as those achieved in a clinical setting *given the same level of FLE and amount of cardiac motion*. This may not always be the case, as FLE is a function of distance from the EM field generator when making the EM measurements, and heart motion is more complicated in a clinical setting.

In future experiments, we would like to expand the range of motion covered, and to perform experiments with different operators to test the inter-operator variability. We are also currently developing a real-time 3DUS based motion compensation algorithm, and will test the ability of it to reduce injection errors.

V. CONCLUSION

In this study, we have presented a novel motion phantom and methodology to test injection accuracy of a multimodality image fusion system under varying levels of cardiac motion from respiration. We have also simulated how varying levels of error in the registration step impact the resulting target accuracy. Targeting accuracy varied from 1.56 in the no motion case, to 2.81 in the 2.0 cm motion case. In future scenarios, we will examine the role of image based respiratory motion compensation in decreasing errors associated with respiratory motion of the heart, as well as test the error due to beating heart motion in a modified phantom.

TABLE I
MEAN VALUES OF FRE AND ERROR FOR EACH SET OF INJECTIONS.

			RMS Error (mm)±Std. Deviation		
Samples	Respiratory Motion (mm)	Mean FRE (mm)	TRE	OE	CE
15	0.0	0.76	1.44 ±0.54	1.00 ±0.51	1.56 ±0.79
16	5.0	0.86	-	-	2.57 ±1.33
10	20.0	0.85	-	-	2.81 ±1.27

TABLE II
ROTATIONAL ERROR COMPONENT FOR THE FIDUCIAL AND TARGET CONFIGURATIONS IN A PIG AND A PHANTOM.

Target Number	Fiducial Configuration Error Factor (CEF)
Phantom	
1	3.07
2	8.47
3	6.03
4	3.14
Pig	
1	8.57
2	3.21
3	3.40
4	4.41
5	8.36

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