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### Image Data-Driven Thermal Dose Prediction for Microwave Ablation Therapy

#### Alice K. Ding<sup>1,2,3</sup>, Jon S. Heiselman<sup>1,3</sup>, Michael I. Miga<sup>1,3,4,5,6</sup>

<sup>1</sup> Vanderbilt Institute for Surgery and Engineering, Nashville, TN USA; <sup>2</sup> SyBBURE Searle Undergraduate Research Program; <sup>3</sup> Vanderbilt University, Department of Biomedical Engineering, Nashville, TN USA; <sup>4</sup> Vanderbilt University Medical Center, Department of Radiology and Radiological Sciences, Nashville, TN USA; <sup>5</sup> Vanderbilt University Medical Center, Department of Neurological Surgery, Nashville, TN USA; <sup>6</sup> Vanderbilt University Medical Center, Department of Otolaryngology, Nashville, TN USA

#### ABSTRACT

Because many patients diagnosed with hepatocellular carcinoma are not eligible for liver transplantation or resection, there has been a great deal of interest in developing locoregional therapies such as thermal ablation. One such thermal ablation therapy is microwave ablation. While benefits have been gained in the management of disease, local recurrence in locoregional therapies is still very common and represents a significant problem. One suggested factor is the presence of soft tissue deformation which is thought to compromise image-to-physical targeting of diseased tissue. This work focuses on presenting a hepatic phantom with an embedded mock tumor target and studying the effects of deformation on ablation when using image-to-physical rigid and non-rigid alignment approaches. While being deformable, the hepatic phantom was designed to enable optical visibility of the ablation zone with target lesion visibility in CT images post-treatment using albumin, agar, formaldehyde, and water constituents. Additionally, a physical mock tumor target phantom was embedded in the hepatic liver phantom and contained CT contrast agent for the designation of lesion prior to mock intervention. Using this phantom, CT scans and sparse-surface data were collected to perform rigid and nonrigid registrations. The registrations allowed for the navigation of the ablation probe to the center of the mock lesions using a custom-built guidance system; this was then followed by microwave ablation treatments. Approximately 96.8% of the mock lesion was ablated using nonrigid registration to guide delivery while none of the mock lesion was ablated using the rigid alignment for guidance, i.e. a completely missed target. This preliminary data demonstrates an improvement in the accuracy of target ablation using a guidance system that factors in soft tissue deformation.

Keywords: Microwave ablation, phantom development, deformation, image-guided surgery, liver, registration

#### 1. INTRODUCTION

Liver transplant and resection are currently the preferred methods of treating hepatocellular carcinoma; however, many patients are not candidates for such treatment methods. As a result, there has been considerable focus on loco-regional therapies for treatment such as thermal therapies. In particular, microwave ablation (MWA) has many advantages such as having the ability to deposit power to a large spatial extent resulting in a more uniform ablation of tumor lesions as well as the ability to ablate up to and around large vessels [1]. While radiofrequency ablation (RFA) is another more common thermal ablation technique, there has been some suggestions that RFA has increased recurrence rate compared to MWA [2].

Currently, image-guided ablation procedures have assisted in probe placement using interventional imaging techniques (ultrasound, biplanar fluoroscopy, CT), optical tracking, and image-to-physical registration methods. However, the alignment of pre-procedural imaging to the intraprocedural environment can be confounded by soft tissue deformations [3]. This could result in incomplete treatment and local recurrences from inaccurate ablations [4]. Soft tissue deformation correction approaches using image-to-physical nonrigid registration methods have been presented previously but have largely been evaluated retrospectively. For example, in a retrospective study [5], nonrigid registration methods were shown to improve ablation targeting for more accurate realization of thermal dose planning.

The purpose of this work will be to use a hepatic phantom with clinically relevant features to determine the effects of factoring soft tissue deformation in prospectively guiding the MWA treatment and to quantitatively evaluate the potential

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treatment efficacy of the predicted MWA zone at a specific target location through identifying the overlap between the navigated ablation zone and mock therapeutic targets.

#### 2. METHODS

#### 2.1 Development of Hepatic Phantom

The necessary requirements for the hepatic phantom were deformability similar to its *in vivo* counterpart, optical visibility of an ablation zone within gross pathology, and the ability to depict a target lesion in CT images. The hepatic phantom was developed using water, agar powder (Thermo Fischer Scientific, Waltham, MA), albumin powder (Sigma-Aldrich, St. Louis, MO), 37 % formaldehyde solution (Thermo Fischer Scientific, Waltham, MA), and barium sulfate powder (Thermo Fischer Scientific, Waltham, MA), and barium sulfate powder (Thermo Fischer Scientific, Waltham, MA), and barium sulfate powder (Thermo Fischer Scientific, Waltham, MA), and barium sulfate powder (Thermo Fischer Scientific, Waltham, MA). An egg white solution was created through a combination of 10 wt. % albumin powder and water. An agar-formaldehyde solution was also created from 1 wt. % agar powder and water by heating to a boil in the microwave, and then adding 0.002 wt. % formaldehyde solution. Equal amounts of both solutions were combined once the agar-formaldehyde solution was cooled to less than 56°C in order to prevent the albumin protein from denaturing. This denaturing property later will be used for optical visibility of the ablation zone. This dilution yielded an agar-albumin solution of approximately 0.5 wt. % agar, 5 wt. % albumin, and 0.001 wt. % formaldehyde. The agar-albumin solution was then poured into an acrylic box mold, as well as a plaster hepatic mold containing five multimodal fiducial markers (IZI Medical, Owlings Mills, MD) around its base and two targets suspended within the liver using a thread. Both gels were allowed to set for at least two hours.

In the hepatic phantom mold, the two suspended phantom mock tumor targets were created using the same protocol above with additions of 0.1 wt. % of barium sulfate powder as CT contrast and a small volume of food dye for optical visibility. The phantom targets were poured into a spherical mold to create a standard shape. Each were then suspended distant from each other but in the same lobe of the liver. **Figure 1a** depicts the developed hepatic phantom, **Figure 1b** demonstrates an example of a mock lesion and an ablation zone annotated with dimensions for a comparison in size, and **Figure 1c** shows a CT slice featuring a target lesion contrasted by barium sulfate (circled) and a multimodal fiducial (boxed).



**Figure 1. (a)** The hepatic phantom made up of 0.5 wt. % agar powder, water, and albumin in its plaster mold. (b) The dimensions of the ablation zone after the phantom was treated with MWA. The pink (a result of using food dye for better visibility) area in the image is the target tumor location. (c) A CT slice of the phantom with the target (circled) and a multimodal fiducial (boxed) visible.

#### 2.2 Registration Process

Initial CT imaging data of the hepatic phantom was taken for planning and registration purposes (Figure 2a). Once acquired, a planning utility was employed to segment the liver and mock tumors. Upon completion, the liver phantom was removed from its plaster mold and a systematic deformation similar to that experienced in surgical cases was imparted on the phantom to simulate the presence of intraprocedural shape change (Figure 2b). To simulate image guided ablation in the open surgical environment, an optically tracked stylus was used to collect sparse anterior surface data. Often for open procedures, only the anterior surface can be digitized and the liver typically experiences significant shape change from mobilization and perihepatic packing. Image-to-physical registration began with a salient feature weighted iterative closest

point rigid registration [6] followed by a linearized iterative boundary reconstruction nonrigid registration method that accounts for soft tissue deformation [7]. Point data was also collected for each centroid of the multimodal fiducials using the optically tracked stylus.

With registration complete, the guidance system was used to direct a tracked MW ablation probe to the center of a lesion as designated on the guidance display using (1) rigid and (2) nonrigid registration methods for the two mock tumor targets embedded inside the phantom. Point data were also collected for the final probe placement where the window of the probe was positioned (**Figure 2c**). The locations were then treated with a 915 MHz MWA probe (ST antenna, Perseon, Salt Lake City, Utah) for 15 minutes; a CT scan of the ablated, deformed liver phantom was then collected for validation.



Figure 2. (a) CT slice of the phantom in its plaster mold prior to deformation. (b) The deformation applied to the hepatic phantom in a plaster base which was held in place by a piece of silicone (pink). (c) The tracked ablation probe inserted into the target in the phantom based on nonrigid guidance.

#### 2.3 Registration Analysis

For consistency, all components (points, phantom, mock tumors, and the ablation zones) were all registered to the same computational space. A rigid-body point based registration between fiducial positions in the post-deformation CT scan and the physical positions collected with optical tracking allowed alignment of the tracked position of the ablation antenna with the measured positions of the tumors from CT imaging. This experimental setup allows a quantitative comparison of the predicted location of the ablation zone navigated to the mock tumor target with the true position of the tumor after deformation has been applied.

Although the ablation zone cannot be visualized in CT imaging, the boundary of the ablation zone was created through the following process for the purpose of comparing the overlap between the ablation zone and the target to which it was navigated. The phantom material that was allowed to set in the box mold was treated with 915 MHz MWA for 15 minutes and its dimensions (**Figure 3a** and **3b**) were used to generate an ellipsoid model. An assumption is made here that both ablation zones resulting from rigid and nonrigid guidance had the same dimension as observed in the box mold and were

perfectly shaped ellipsoids. These ellipsoids were registered so that their centers aligned with tracked positions of the ablation probe window and their orientations were in the same direction of vectors created by segmentation of points in the CT scan where a void was created along the track of the ablation probe (Figure 3c). The resulting model of co-registered ablation and tumor positions is shown in Figure 3d.



Figure 3. (a) The height of the ablation zone inside the box mold; it is approximately 33.4 mm. (b) The diameter of the ablation zone in the box phantom; it is approximately 24.1 mm. (c) Because the ablation zone is not visible on CT imaging, it's location was determined by segmenting the point where the probe entered the phantom and its tip. (d) The components of the experiment registered in the same space. The grey is the liver; the yellow is the ablation zone created from nonrigid registration guidance in targeting the turquoise tumor. The red is the ablation zone as a result from rigid registration guidance in targeting the dark blue tumor. The result of fiducial points used for point-based registration are the five green points below the liver.

To assess the effectiveness of the ablation zone in removing target lesion for both rigid and nonrigid registration cases, the positive predictive value (PPV) as defined by:

$$PPV = \frac{V_{T \cap A}}{V_T} \cdot 100\%$$

where  $V_{T \cap A}$  is the volume of the tumor successfully ablated and  $V_T$  is the total volume of the tumor. The PPV for the nonrigid registration case was 96.8% and for rigid registration, 0.0%.

#### 3. RESULTS

**Figure 4** shows a qualitative comparison between the displays used to position the ablation probe into the center of the tumor. **Figure 4a** depicts the guidance display used when positioning the probe using rigid-body registration and ablating the first tumor, while **Figure 4c** shows the same display for the same tumor at the same probe position except if the nonrigid guidance display. More specifically, **Figure 4c** suggests that the point navigated to in **Figure 4a** will be in fact a missed ablation as the registration used in **Figure 4c** suggests the tumor is in a different location. We should note that the tumor ablated in **Figure 4a**, and **4c** was guided by the rigid guidance display. **Figure 4d** depicts the nonrigid guidance used when positioning the ablation probe inside the second tumor, while **Figure 4b** shows the same display for the same tumor at the

same probe position but if the rigid-body registration display were to be used instead (in contrast to **Figure 4a/4c**, the nonrigid registration was used to guide and deliver the ablation to this mock tumor target). In this case, the probe position in **Figure 4b** is a reconstructed location assuming rigid registration.



**Figure 4.** The guidance display when predicting the location of tumor with respect to the ablation probe position. The actual displays used for ablation are boxed in red. (a) The guidance display when positioning the probe (in green) into the tumor (in brown). This display used rigid registration. (b) The guidance display when positioning the probe (green) into a different tumor (brown) using rigid registration. (c) The location of the ablation probe for the same tumor in 4a except the guidance display is depicting the probe location with respect to the tumor using nonrigid registration. (d) The ablation probe is in the same position for the same tumor as in 4b except the guidance display depicts the prediction using rigid registration. The alignment displays shown in 4a and 4d were used to prospectively guide the ablation probe for the respective tumor targets, and the displays in 4b and 4c were generated retrospectively after the microwave ablation had commenced.

For verification, **Figure 5** shows a qualitative comparison of the spatial relationships between the tumor and the ablation zone in the hepatic agar-albumin phantom and the generated computational model. **Figure 5a** and **5b** depict the ablation-tumor overlap in the computational environment under rigid, and nonrigid guidance, respectively. Gross pathology dissections in **Figure 5c** and **Figure 5d** depict the ablation-tumor overlap in the physical phantom under rigid, and nonrigid guidance, respectively.



**Figure 5. (a)** The computational liver model (white) with the ablation zone (red) and tumor (blue) for rigid registration oriented in the same configuration as gross pathology in 5c. (b) The computational liver model (white) with the ablation zone (red) and tumor (blue) for nonrigid registration oriented in the same configuration as gross pathology in 5d. The overlap between the ablation zone and tumor is in purple. (c) The agar-albumin phantom sliced after treatment to depict the ablation zone guided with rigid registration (white) and the target lesion (dyed green and circled in red). (d) The same agar-albumin phantom sliced open to depict the ablation zone guided with nonrigid registration (white) and the target lesion (dyed green and circled in red).

#### DISCUSSION

#### 4.1 Post-Treatment Analysis

The qualitative results found in **Figure 4** are consistent with the quantitative findings. The nonrigid registration display of the probe (**Figure 4c-reconstructed**, **4d**) targets the tumor better as compared to its rigidly registered counterparts (**Figure 4a**, **4b-reconstructed**). Similarly, the evidence for this better targeting can be seen in **Figure 5b**, deformation corrected, when compared to that of **Figure 5a**. This suggests that the nonrigid registration gave a more accurate prediction of the probe location with respect to the tumor than rigid.

Quantitatively, the nonrigid registration showed profound improvement in ablating the target lesion both in prediction shown in **Figure 4** and in outcome **Figure 5b**. Although, according to the PPV, it is implied that some of the tumor during the nonrigid registration case was not fully ablated as can be seen in the protruding side of the tumor in **Figure 3c**. It is difficult to verify whether tumor was actually missed in gross pathology of the post-ablation phantom due to the configuration slice shown in **Figure 5b**. This is a potential limitation of this experiment as the dimensions of the ablation zone used to computationally model and calculate PPV were taken from an ellipsoidal model of the ablation zone taken from the box phantom. It is important to note, however, that current manufacturer standards for characterizing ablation zone volumes are similar in design to the box experiment presented here except that the ellipsoidal models are measured from ablations performed in *ex vivo* tissue.

#### 4.2 Registration Error Analysis

In order to analyze the registration error during this work, a virtual simulation was used to compare the rigid and nonrigid registration techniques (Figure 6). To quantify registration error, the distances between each registered tumor centroid from the initial planning image and the centroid of the ground truth tumor derived from post-operative imaging of the phantom after treatment were compared (Table 1). For the tumor that was targeted using nonrigid guidance, the position of the tumor predicted by nonrigid registration was compared with the ground truth tumor position. In this case, the centroid distance was approximately 5.1 mm. A simulated experiment was performed to see how the position of the same tumor would have compared if rigid registration was used for guidance instead, and found that the centroid distance between the virtual position of the rigidly registered tumor and the ground truth would have been 9.2 mm. Likewise, the same was done to the tumor targeted using rigid guidance. Between the ground truth tumor and the rigidly registered prediction of the tumor tumor was instead predicted distance was 7.0 mm. When the tumor location was instead predicted

using nonrigid registration, the centroid distance was only 3.0 mm. This reaffirms the results of this work that the registration error involved with guidance was lower for the nonrigid than the rigid registration method.



**Figure 6.** A comparison between the locations of the tumor positions with the ground truth tumor (brown). On the left, the ground truth (brown) and predicted (yellow) positions of tumors using nonrigid registration as guidance are depicted, while the pink tumor shows the predicted position of the tumor if rigid registration were to be used. On the right, the predicted position of the tumor using rigid registration as guidance is depicted with yellow, while the predicted position of the same tumor if nonrigid registration were applied is shown in pink.

 Table 1. The centroid distance between each tumor compared with the ground truth.

REGISTRATION	CENTROID
	DISTANCE
Nonrigid Actual	5.1 mm
Rigid Virtual	9.2 mm
Rigid Actual	7.0 mm
Nonrigid Virtual	3.0 mm
	REGISTRATION Nonrigid Actual Rigid Virtual Rigid Actual Nonrigid Virtual

#### 4.3 Imaging Error Analysis

As mentioned previously, the ablation zones are not visible on CT scans and as a result, geometric models were generated from gross pathology performed on a box phantom. This assumes that the ablation zone was a perfect ellipsoid, had the same dimensions between the hepatic phantom and the box phantom, and did not change between each tumor ablation in the hepatic phantom. Additionally, the volumes of the segmented tumors between the initial imaging and the post-treatment imaging were found to change by approximately 25%. This change is hypothesized to be caused by the diffusion of contrast agent between preoperative and postoperative imaging which results in blurring of the tumor boundaries that can segmentation of the region of interest less consistent.

#### 4.4 Localization Error Analysis

To determine the error between where the ablation probe was believed to have been placed versus where it was actually placed, the actual position of the probe was found by segmenting the tip point of the ablation probe from CT images (Figure 7a). Using an optically tracked probe, the position of the probe was also measured as point data during ablation; this is where the probe was believed to have been placed with respect to intraoperative tool tracking (Figure 7b). After co-registering both points into the same space using the transformation derived from the multimodal fiducial set, the distances between the tracked and observed probe tip locations were calculated (Figure 7c). It was found that the probe using nonrigid registration as guidance had a localization error distance of 11.2 mm while the probed placed using rigid registration had a localization error of 17.7 mm. This suggested significant localization error in the probe

placement. However, the confirmation work using gross pathology to analyze the tumor and ablation zone spatial positions did not seem to indicate this level of error. Based on the post-experiment analysis, it is hypothesized that this error may have been caused by changes to the measured probe tip localization at the time of acquisition due to flexure of the needle. In future work, a more controlled process of probe delivery and stabilization during guidance and ablation is necessary in order to confirm these preliminary findings.



**Figure 7. (a)** The true position of the ablation probe was determined by segmenting the probe tip from the needle track seen in the CT images. **(b)** The probe position was also collected using an optical tracker placed on the probe. **(c)** The distance between the two points were calculated to find the localization error of the ablation probe.

#### 4. CONCLUSION

Soft tissue deformation is a continual challenging factor for the development of image-guided therapeutic delivery in the liver. The experiment reported provides preliminary results toward prospective guidance of microwave ablation using nonrigid, sparse-data-driven, image-to-physical registration as compared to guidance using conventional rigid registration. The results indicate that there is considerable potential for improving the accuracy of targeted ablation delivery with methods to compensate for soft tissue deformation. This improvement is represented by vastly superior PPV which implies more effective treatment of the target lesion. Additionally, nonrigid registration gives a more accurate prospective prediction of the ablation probe location with respect to the tumor when using the guidance displays. The next steps of this study would be to replicate the experiment for multiple cases and tumor locations. Additionally, the cause for the high localization error needs to be investigated and corrected. Accuracy of the analysis can also be improved by exploring ways to computationally model the ablation zone more correctly in terms of its dimensions.

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