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Physiological Motion Reduction using Lagrangian Tracking for Electrode Displacement Elastography

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Abstract

Minimally invasive treatments such as microwave ablation (MWA), have been growing in popularity for extending liver cancer survival rates in patients, when surgery is not an option. As a nonionizing, real-time alternative to contrast-enhanced computed tomography (CECT), electrode displacement elastography (EDE) has shown promise as an imaging modality for MWA. Despite imaging efficacy, motion artifacts present due to physiological motion result in unintended speckle pattern variance thereby inhibiting consistent and accurate ablated region visualization. To combat these unavoidable motion artifacts, a Lagrangian deformation tracking (LDT) approach based on freehand EDE was developed to track tissue movement and better define tissue properties. For validating LDT efficacy, a spherical inclusion phantom as well as 7 *in vivo* data sets were processed, and strain tensor images compared to identical time sampled images estimated using a traditional Eulerian approach. *In vivo* results demonstrate greater consistency among visualized LDT strain tensor images, with segmented ablated regions showing standard deviation reductions of up to 98% when compared to Eulerian strain tensor images. Additionally, Lagrangian strain tensor images provided Dice coefficient improvements up to 25% and success rates improved from approximately 50% to nearly 100% for ablated region visualization.

Keywords

Elastography; Motion Artifact Reduction; Lagrangian Description of Motion; Electrode Displacement Elastography; Imaging Microwave Liver Ablations

Introduction

According to the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results Program (SEER), 1 in every 100 persons will be diagnosed with some type of primary liver cancer. Of those diagnosed, less than 18% will survive 5 or more years after diagnosis (Noone et al. 2018). Additionally, as of 2018, liver and intrahepatic bile duct

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cancers are the fifth leading cause of cancer related deaths in the United States with the number of cases more than tripling since 1980 (Society 2018). Unfortunately these statistics do not take into account the vast numbers of metastatic liver cancers originating from a variety of primary cancer locations, such as colorectal, lung, breast, and melanoma (de Ridder et al. 2016). As an example, over 50% of colorectal primary cancers (CRC) will result in liver metastasis leading to the high mortality of CRC patients due to hepatic failure (Group et al. 2010). To address these diseases, several liver cancer treatments have been adopted, namely liver transplantation (Palmer and Johnson 2009; Maluccio and Covey 2012), resection (Liu et al. 2009; Bruix et al. 2014), chemotherapies (Lencioni and Crocetti 2012; Bruix et al. 2014), and recently minimally invasive percutaneous treatments (Murakami et al. 1995; Goldberg et al. 2000; Dodd et al. 2001; Ganguli and Goldberg 2009; Tan and Ho 2009).

As a means of combating the growing trend of liver cancer diagnosis and low survival rates, minimally invasive approaches such as microwave ablation (MWA) have shown promise in extending patient's survival for up to 10 or more years (Palmer and Johnson 2009; Shiina et al. 2012; Bruix et al. 2014). Yet a main contingency, as for any minimally invasive method of treatment, is accurate and consistent imaging to ensure proper procedure execution (Dodd et al. 2001; Harari et al. 2016; Ryan et al. 2016). In the case of MWA, this is specifically aimed towards proper placement of ablation antennae as well as verification of 0.5 – 1.0 cm margin of normal tissue necrosis surrounding tumor cells to minimize any residual tumor progression (Lencioni and Crocetti 2007; Liu et al. 2009; Harari et al. 2016). Most often visualization takes the form of contrast enhanced computed tomography (CECT). Although this provides an accurate depiction of liver cancers and ablated regions, CECT is ionizing, time-consuming, and expensive for clinical use. Consequently, there is significant interest in developing other comparable imaging modalities.

As an alternative to CECT imaging, ultrasound is showing progress as a future comparable imaging modality for visualizing MWA. Ablated regions are depicted in B-mode ultrasound via a hyperechoic region surrounding ablated regions due to the high scatterer density of bubbles arising in tissue at high temperatures. Unfortunately, B-mode ultrasound visualization lacks the specificity necessary to delineate ablated regions accurately. The lack in accuracy is due to hyperechoic regions often overestimating areas of tissue necrosis and bubbles migrating during and after procedures leaving echogenicity as an unreliable predictor of MWA effectiveness (Kelekis & Filippiadis, 2016). Therefore B-mode ultrasound can only be considered as a rough estimate of induced tissue necrosis (Leyendecker et al., 2002). Contrast enhanced US (CEUS), has shown improved effectiveness in the assessment of ablation when compared to conventional B-mode US. In comparison to CECT, CEUS provides faster image acquisition, lower cost, and reduced nephrotoxicity (Mauri et al., 2014; Nolsøe et al., 2018). Additionally, CEUS and CECT have presented with similar sensitivity and specificity, however CEUS still fails to detect some liver masses detected with CECT (Chong et al, 2018).

Although CEUS may provide higher specificity than conventional B-mode US, elastography (Varghese and Ophir 1997; Ophir et al. 2002) has shown similar or improved diagnostic accuracy of hepatic masses as compared to CEUS. (Huang et al., 2019; Wege et al., 2012).

Fortunately, an elastography method, namely electrode displacement elastography (EDE), has overcome B-mode ultrasound's limitations for this application (Varghese et al. 2002). EDE uses the MWA electrode to induce localized, quasi-static deformations directly to the liver mass and ablated region (Varghese 2009). The tissue's response to these localized deformations is measured using ultrasound radiofrequency (RF) signals. RF echo signals are processed to estimate and present the tissue's elastic properties (Ophir et al. 1991; Ophir et al. 2002; Pareek et al. 2006). Additionally, gas bubble echogenicity that degrades thermal ablated region boundaries in B-mode ultrasound does not inhibit strain tensor estimation (Varghese et al. 2004). Many sequential publications have shown successes of EDE in simulation, phantom, *ex vivo*, and *in vivo* data (Bharat and Varghese 2006; Bharat et al. 2008; Jiang et al. 2009; Varghese 2009; Jiang et al. 2010; Rubert et al. 2010; DeWall et al. 2012; Peng et al. 2016; Yang et al. 2016) as well as high correlation between elastography strain tensor images and histopathology (Rubert et al. 2010). Further improvements to displacement estimation used for estimating tissue properties in EDE have greatly improved visualization of liver masses and ablated regions presented in (Pohlman et al. 2019b) and with the addition of machine learning in (Pohlman and Varghese 2018), yet low success rates and varying ablated region sizes hinder clinical utilization.

Despite improved visualization, a remaining constraint of EDE is low successful ablated region visualization rates and varying ablation sizes previously shown in (Yang et al. 2016; Pohlman et al. 2019b). A likely culprit of low success rates and ablation size variability are the various motion artifacts present within the 2D imaging plane. More specifically, as focused deformations are induced to the ablated region via electrode perturbations other physiological motion still occur, such as essential physiological motion, out-of-plane motion, freehand transducer movement, and electrode perturbation inconsistency. As a result, ideal cyclic electrode movements are corrupted with motion artifacts likely resulting in unintended speckle pattern changes. These speckle pattern changes may manifest as additional displacement estimation variance (Maurice and Bertrand 1999) and strain tensor visualization inconsistencies, thereby inhibiting accurate visualization of the ablated region and degrading delineation of ablated margins. This may have been perceived similarly in (Pohlman et al. 2019b) as low success rates and varying ablation sizes. Hence further improvements to EDE visualization require a reduction in these motion artifacts.

Several approaches have been pursued to alleviate the impact of motion artifacts. One common approach is to utilize increasingly robust displacement estimation approaches to reduce signal decorrelation. Displacement estimation algorithms have reduced decorrelation by regularization (Zahiri-Azar and Salcudean 2006; Brusseau et al. 2008; Jiang and Hall 2009; McCormick et al. 2011; Rivaz et al. 2011; Meshram and Varghese 2018), and recently machine learning (Hoerig et al. 2017; Ouzir et al. 2018; Wang et al. 2018; Wu et al. 2018). Although these methods improve displacement estimation, they do not necessarily account for large motion artifacts, likely seen *in vivo* during EDE. Alternatively, a possible solution may be to apply a known displacement or force to the electrode using a mechanical device such as linear actuators (Meyer 1998). With a known force acting on the liver mass, other motion artifacts can be accounted for, thereby reducing effects of motion artifacts. Although this may offer good results, this approach would add additional equipment, cost, and time;

undesirable for MWA. Therefore, other elastographic approaches, which encountered similar large motion artifacts, were examined.

Upon investigating elastographic approaches for other organs, a similar paradigm was observed with carotid and cardiac elastography (Maurice et al. 2004; Saber and Wen 2004; Geyer et al. 2010; Ma and Varghese 2012; Meshram and Varghese 2018). During cardiac elastography, translational motion and variability in the deformation present over the cardiac cycle impose large motion artifacts greatly impeding accurate description of tissue elastic properties over time. A traditional Eulerian description of motion was insufficient to describe tissue properties as it was limited to descriptions at specific time instances over a cardiac cycle. Cardiac elastography overcame this hurdle by utilizing a Lagrangian description of deformation for strain estimation. With a Lagrangian description, tissue deformation was tracked so that tissue properties may be accurately described locally. Following a similar logic to carotid and cardiac elastography, a Lagrangian description of tissue motion may be helpful in reducing the various motion artifacts seen during EDE. In this work, we show that Lagrangian deformation tracking (LDT) accounts for some of these motion artifacts. When properly tracked, accumulated displacements following a Lagrangian description present consistent, improved strain tensor image visualization and reduced ablation size variance.

Materials and Methods

Data Collection

Ultrasound radiofrequency (RF) data was collected from two different sources using a Siemens S2000 system with a 6C1 HD curvilinear transducer (Siemens, Mountain View, CA). First, RF data was collected from a CIRS ULTRASOUND QA 049 phantom with a 4.3 cm³ spherical 85 kPa inclusion embedded in 28 kPa background (Computerized Imaging Reference Systems, Inc., Norfolk, VA) during manual cyclic compressions. The second data set was collected from 7 patients shortly after a minimally invasive MWA procedure at the University of Wisconsin-Madison Hospital and clinics. *In vivo* data collections followed a protocol approved by the health sciences institutional review board at UW-Madison with all patients providing informed consent prior to the procedure. After verifying proper electrode placement, 80 frames of RF data were acquired during controlled ≈ 1 mm electrode perturbations by the operating clinician. Signal and image processing were performed offline using corresponding software packages in MATLAB.

Lagrangian Description of Motion

A Lagrangian deformation tracking (LDT) model for EDE was derived following an approach described by Maurice and Bertrand (Maurice and Bertrand 1999). A Lagrangian description of tissue motion describes a feature's position as its initial position and motion trajectory as a function of time. As a result, conservation of motion can be represented through inverse trajectory functions using a given trajectory of material features (speckle tracking). Following this logic, motion reduction may be achieved by transforming coordinates through a forward trajectory function, which may take the form of an affine transformation (Macovski 1983).

Flowchart

The LDT algorithm derived for EDE is shown in Fig. 1. First, features with higher echogenicity were automatically selected from B-mode images and then tracked over an EDE cycle. Following the trajectory of tracked features, affine transformations were estimated as a function of time and applied to a rectangular coordinate grid. With this transformed grid, displacements estimated for an Eulerian description of motion were interpolated onto the new coordinates of the transformed grid. The Lagrangian description of deformation, now spatially aligned, were accumulated over an EDE deformation cycle. The resulting LDT displacements were compared to the temporally aligned Eulerian displacements by segmenting thermally ablated regions from the strain tensor images.

Feature Selection

The first step for LDT involved selecting B-mode features to be tracked over an EDE cycle. The initial B-mode frame was chosen for selecting these features, as it offers visualization of the MWA antenna and ablated region. An obvious approach to obtain these features would be manual selection, yet this process may be time-consuming depending on the desired number of features. An alternative approach used in this work enabled features to be automatically selected from this image following a prior probability distribution derived as a function of brightness (hyperechoic intensity) in the B-mode image. This means that features were randomly sampled from weighted probability distribution function with weights defined using the relative pixel brightness of the B-mode image. Hyperechoic regions were chosen as they indicate tumors and ablated regions in B-mode images. This process resulted in selection of 20 or more pixels with a relative gray-scale intensity greater than 0.95 after normalizing gray values to a 0–1 scale. After a feature was selected from the probability distribution, all pixels within a 2 mm window around the feature in the B-mode image were removed from the distribution before sampling for the next feature. This process was then repeated for the required number of samples. To demonstrate similarities in the manual and automatic approaches, an example feature selection is shown in Fig. 2. Note the similar locations of the automatic and manually selected features.

Feature Tracking

After feature selection, a kernel size of 6 wavelengths by 3 A-lines was centered about each feature in RF frame n where n is the RF frame sampled at time τ_n for $n=1, \dots, N-1$ and N is the total number of RF frames sampled during EDE perturbations. Fixing this kernel in frame n , the same kernel location in frame $n+1$ was shifted in a range of 1 wavelength by 3 A-lines. The normalized cross correlation (NCC) values were estimated and the peak value defined the movement vector of that feature kernel. Since high resolution tracking was desired, RF data was then up-sampled after initial movement vector estimation using sinc interpolation. Data was up-sampled by a factor $2\times$ and $10\times$ for axial and lateral directions while the search range reduced by $2\times$ and $10\times$ respectively. The peak NCC and up-sampling process was repeated $6\times$ similarly to (Meshram and Varghese 2018). After tracking, any features where the peak NCC value dropped below 0.9 were removed. The x and y coordinates of remaining features were arranged into row vectors, $\vec{u}_n$ and $\vec{v}_n$.

Affine Transformation Estimation

After tracking these selected features, the next step was to estimate the trajectory functions to be applied to the displacement vector. For the purpose of EDE tracking, an affine transformation was used to allow linear transformations without introducing nonlinear distortions to negatively affect estimations. The affine transformation from τ_n to τ_{n+1} was calculated using (1).

$$\begin{bmatrix} \vec{u}_{n+1} \\ \vec{v}_{n+1} \end{bmatrix} = \begin{bmatrix} s_x(\tau)\cos\theta(\tau) - h_x(\tau)\sin\theta(\tau) \\ h_y(\tau)\sin\theta(\tau) \quad s_y(\tau)\cos\theta(\tau) \end{bmatrix} \begin{bmatrix} \vec{u}_n \\ \vec{v}_n \end{bmatrix} + \begin{bmatrix} T_x(\tau) \\ T_y(\tau) \end{bmatrix} \quad (1)$$

Where s is shear, h is scale, θ is rotation, and T is translation for x and y vectors as function of time τ solved using homologous coordinates. Affine transformation calculation required a minimum of 3 pairs of feature coordinates. Using more features may enable more robust transformation estimation (an additional benefit of automatic feature selection). For this work, approximately 20 features were automatically selected for each patient and the least squares solution of (1) was calculated resulting in a single universal affine transformation from τ_n to τ_{n+1} .

An example of this affine transformation coordinate tracking is shown in Fig. 3. Figure 3 (a) shows an example ablated region as an ellipse with inserted electrode with 5 selected features used for LDT. Additionally (a) shows the initialized rectangular coordinate grid encompassing the ablated region. Figure 3 (b) – (d) show how the ablated region was deformed via electrode perturbations as time elapsed. Features located in the B-mode image track this movement locally, with the corresponding features' relative position and displacement shown in (e) and (f), respectively, at sample times (a) - (d). (Note the cyclic motion of coordinates, as this is similar to what is seen for *in vivo* perturbations.) As a result of tracking features over time, affine transformations were estimated and applied to the rectangular coordinate grid. As shown in (b) – (d), the grid deforms and follows the ablated region using the feature coordinates as guides.

Coordinate Transformation

After calculating affine transformation variables of shear s , scale h , rotation θ , and translation T , the affine transformation matrix A can be formed shown in Eq. (2).

$$A(\tau) = \begin{bmatrix} s_x(\tau)\cos\theta(\tau) - h_x(\tau)\sin\theta(\tau) & T_x(\tau) \\ h_y(\tau)\sin\theta(\tau) & s_y(\tau)\cos\theta(\tau) & T_y(\tau) \\ 0 & 0 & 1 \end{bmatrix} \quad (2)$$

Next, we need to define the coordinate grid that will be tracked over τ . This was initiated after manual selection of the initial region of interest (ROI) including the ablated region. The x and y coordinates of the entire ROI were then sampled at 0.1 mm increments and placed into vectors X and Y , respectively.

These coordinates were transformed to remove tracked motion using Eq. (3).

$$\begin{bmatrix} X_n \\ Y_n \\ 1 \end{bmatrix} = A(\tau_n) \left(A(\tau_{n-1}) \cdots A(\tau_2) \left(A(\tau_1) \begin{bmatrix} X \\ Y \\ 1 \end{bmatrix} \right) \right) \quad (3)$$

where X_n and Y_n are new sample coordinates for the displacement estimate n . To obtain spatially aligned displacement ROI, the Eulerian displacement, I_{Eul} estimated from τ_n to τ_{n+1} and sampled at coordinates X_n and Y_n using bilinear interpolation were used to create the transformed displacement estimate, I_{Eul}^* . For future calculations, these transformed displacement estimates of the ROI were stacked into a 3D matrix I_{Eul}^* , where the first two dimensions are the size of the ROI and the third dimension is $N - 1$.

Frame Selection and Interpolation

However, using an affine transformation as the trajectory function does not consider the possibility of out-of-plane motion. Assuming tissue continuity, features neighboring each other should generally move together, thus low variation in feature movement was expected especially due to high NCC constraints on feature tracking ($NCC > 0.9$). Despite these considerations, some features presented with high variation in local movement, and thus a possible indicator of out-of-plane motion. Using this logic, a strategy was determined for reducing the effects of out-of-plane motion.

Movement of feature coordinates can be defined in terms of vectors $\vec{u}_n$ and $\vec{v}_n$ as

$\vec{\mu}_n = \frac{\partial \vec{u}_n}{\partial \tau} = \frac{\vec{u}_{n+1} - \vec{u}_n}{\partial \tau}$ and similarly $\vec{\nu}_n = \frac{\partial \vec{v}_n}{\partial \tau}$. The variance in feature trajectories at each sample frame n was then calculated using Eq. (4).

$$\begin{aligned} \vec{\mu}_n &= E \left[(\vec{\mu}_n - E[\vec{\mu}_n])^2 \right] \\ \vec{\nu}_n &= E \left[(\vec{\nu}_n - E[\vec{\nu}_n])^2 \right] \end{aligned} \quad (4)$$

With trajectory variation estimated at each sampled time, mean, λ , and variance, Λ , were calculated for each sample frame over the entire EDE data collection as shown in Eq. (5) and (6), respectively. The feature trajectory variation was then standardized so that values could be compared using z-scores (Milligan and Cooper 1988) as shown by Eq. (7).

$$\lambda = \frac{1}{N-1} \sum_{n=1}^{N-1} \sqrt{(\vec{\mu}_n)^2 + (\vec{\nu}_n)^2} \quad (5)$$

$$\Lambda = \frac{1}{(N-1)^2} \sum_{n=1}^{N-1} \left[\left(\sqrt{(\vec{\mu}_n)^2 + (\vec{\nu}_n)^2} - \lambda \right)^2 \right] \quad (6)$$

$$z_n = \frac{\sqrt{(\vec{\mu}_n)^2 + (\vec{\nu}_n)^2} - \lambda}{\sqrt{\Lambda}} \quad (7)$$

The vector $\vec{z}$ now contains the standardized feature trajectory variance at each sample n , and out-of-plane motion was defined as outliers of this standardized set determined using a z-score threshold, ζ . Using this terminology, good frames ℓ were chosen as frames where $|z_\ell| \leq \zeta$. The z-score threshold, ζ , was chosen heuristically as the minimum $\zeta \geq 1$ such that

$$0.8 \times (N - 1) \leq \sum_{i=1}^{N-1} \mathbb{I}_{\{|z_i| \leq \zeta\}}, \text{ where } \mathbb{I} \text{ is the indicator function that is 1 where } |z_i| \leq \zeta.$$

Plainly stated, ζ was chosen as the minimum value greater than 1 so that at most 20% of frames are deemed outliers. The choice for a maximum number of outlier frames was heuristically chosen as some *in vivo* cases may present with large deformations or out of plane motion resulting in many frames to be deemed as outliers, thereby reducing the accuracy of the later interpolation stage. As a compromise between removing outlier frames and retaining valid information for interpolation, outlier frames were limited to a maximum of 20% of the frames in a tracked cycle. The displacement matrix was then resampled at outlier frames using a spline interpolation estimated from good frames.

Finally the accumulated displacement matrix under a Lagrangian description of the deformation, I_{Lag} , was obtained by accumulating displacements over continuous sample frames of an EDE cycle, namely $\{\eta, \dots, \eta + \kappa - 1\}$ in the set n , where η is the starting sampled frame and κ is the number of sampled frames in the tracked EDE cycle shown by Eq. (8). The first two dimensions of the resulting LDT deformation matrix are the size of the ROI and the third dimension as the number of frames in the tracked EDE cycle.

$$I_{Lag, k} = \sum_{\alpha=0}^{k-1} I_{Eul, \eta + \alpha}^* \quad \forall k \in \{1, \dots, \kappa\} \quad (8)$$

Displacement and Strain Tensor Estimation

Initial Eulerian displacements were estimated using a Multilevel 2-D Normalized Cross-Correlation (MNCC) method developed by Shi and Varghese (Shi and Varghese 2007). This method operates in a pyramidal hierarchy first estimating local displacements using large 2D kernels to provide high SNR and following with smaller kernels to improve spatial resolution while maintaining high SNR by utilizing higher level estimations as initial displacements for the lower levels. To further improve displacement estimation, 2D sinc-interpolation in the DCT domain (Yaroslavsky et al. 2002) was utilized to estimate subsample displacements after each displacement estimation level. Displacement estimates with correlation coefficients less than 0.75 were interpolated using its nearest neighbors. For this work, four levels were used with kernel sizes of (8, 4, 2, 1) wavelengths by (8, 5, 3, 3) A-lines with the first, largest level using envelope data and the remaining levels utilizing RF data. Since a curvilinear transducer was used for RF data collection, estimated displacements were converted from a polar to Cartesian coordinate system using trigonometric functions. Following coordinate conversion, displacement maps were then

median filtered with a 1.9 mm × 1.9 mm kernel and then smoothed using dictionary representation with a patch size of 4.0 mm × 4.0 mm and 80% patch overlap. These estimated displacements were defined as the Eulerian displacements, I_{Eul} , and Lagrangian model for deformations, I_{Lag} , were estimated using Eq. (8). Finally, Eulerian and Lagrangian strain tensors were calculated using a 2D Savitzky-Golay digital differentiator of size 0.2 mm × 5.0 mm using 0th × 2nd order polynomials for x and y directions respectively (Savitzky and Golay 1964; Luo et al. 2005). The operation time for LDT algorithm, namely automatic feature selection, tracking of 20 points, affine transformation estimation, coordinate transformation, and frame selection/interpolation, is approximately 3–5 min for each patient largely dependent on number of points tracked and size of ROI.

Segmentation and Comparison of Strain Tensor Images

Eulerian and Lagrangian strain tensors images were used to segment ablated regions using active contours in the form of snakes. Snakes can conform to unique shapes and edges making them well suited for segmenting ablation regions due to the high-contrast boundary delineation obtained with strain tensor images (Kass et al. 1988; Ivins and Porritt 1995; Xu and Prince 1997). Snakes were initialized by a single manually segmented image for each patient. That single segmentation was used as an initial contour for axial and lateral strain tensor images of both Eulerian and Lagrangian descriptions of motion. By using the same initialization for all tracked frames axially and laterally, snake segmentation reduces the effects of observer bias. Following segmentation, areas were calculated by summing segmented pixels and normalizing based on pixel size. The mean and standard deviation of segmented regions over an EDE cycle were then compared.

In addition to segmented region areas, further comparisons were performed using center of mass differences and Sørensen-Dice coefficients, also known as the Dice similarity coefficient (DSC) (Sørensen 1948). Changes in center of mass (CoM) provided insight if subsequent segmented regions obtained over the strain tensor loop were centered similarly to each other, while DSC provides a measure of segmented area overlap throughout an EDE cycle. The center of mass for each image was determined by summing pixels within segmented region and normalized based on pixel size and CoM values were calculated using the 2-norm between centers of mass measured using Eq. (10). DSC was calculated using Eqn. (11) and values were averaged over the EDE cycle to obtain a single value for each patient.

$$C = (c_i, c_j) = \left(\frac{\sum_{i=1}^N \sum_{j=1}^M i \times \mathbb{I}\{B_{i,j}=1\}}{\sum_{i=1}^N \sum_{j=1}^M \mathbb{I}\{B_{i,j}=1\}}, \frac{\sum_{i=1}^N \sum_{j=1}^M j \times \mathbb{I}\{B_{i,j}=1\}}{\sum_{i=1}^N \sum_{j=1}^M \mathbb{I}\{B_{i,j}=1\}} \right) \quad (9)$$

$$CoM = \langle C_n, C_{n'} \rangle \quad (10)$$

$$DSC = \frac{2|B_n \cap B_{n'}|}{|B_n| + |B_{n'}|} \quad (11)$$

Where i, j are the x, y coordinates of the segmented image B , $\mathbb{I}\{B_{i,j} = 1\}$ is the indicator function that is 1 if the i, j lies within the segmented region and 0 otherwise, n is sample frame number, and $\langle \bullet \rangle$ is defined as the ℓ_2 -norm. DSC is defined as twice the number of elements common to both segmented images divided by the sum of elements in each image (Sørensen 1948). To compare the difference in segmented values, percent difference was calculated from traditional Eulerian to Lagrangian description shown by Eq. (12).

$$\frac{Lagr - Eul}{Eul} \times 100\% \quad (12)$$

Success Rates

Since qualitative visualization is also vital to EDE, a qualitative assessment of ablated region visualization was done using strain tensor success rates (Pohlman et al. 2019b). Success rates were calculated by a single blinded observer visualizing Eulerian and Lagrangian axial and lateral strain tensor images for a strain dynamic range of 0–1%.

Results

Phantom Tracking Results

Figures 4 and 5 show a visual comparison between axial strain tensor images of a tissue-mimicking phantom spherical inclusion with a stiffness of 85 kPa embedded within a 28 kPa background over a cycle of manual external compression. Lateral strain tensors were not considered for phantom data as manual compressions were performed axially. The B-mode image of the stiffest inclusion is shown in Fig. 4 (a). Additionally, the set of chosen tracking features are shown in Fig. 4 (a) along with the rectangular tracking grid in green. The axial position and displacement of the tracked features are shown in Fig. 4 (b) and (c), respectively over the manual compression cycle for 0.58 seconds. The feature position and corresponding displacement are tracked very accurately as illustrated by the alignment of the curve alignment in Fig. 4 (b) and (c). Figure 5 (a) and (b) show the strain tensor images for Eulerian and Lagrangian axial at 4 different time instants. Since Lagrangian tracked displacements are accumulated, note the difference in strain tensor magnitudes between the methods. All strain tensor images provide a very consistent inclusion size and location, but the Eulerian approach fails to visualize at time 0.332 seconds. This is a reasonable outcome due to the small displacement vectors at that time verified in Fig. 4 (b) and (c). On the contrary, since LDT accumulates displacements, the strain tensor image at 0.332 provides the maximum strain on the inclusion in Fig. 5 (b).

The inclusion strain tensor image segmentation results of area mean, and standard deviation, dice coefficient, and center of mass are shown in Table 1. The segmented area means were found to be nearly identical between the tracking methods, while there was a standard deviation reduction of 74%. The average Dice coefficient of LDT increased by 10% to almost 1 and all center of mass differences fell to below 1 mm. These results demonstrate the improved consistency of LDT, hence tracking results of *in vivo* data were investigated.

In vivo Ablated Region Tracking Results

Ablated regions were successfully tracked for 7 *in vivo* data sets for approximately one cycle of electrode perturbation. Examples of strain tensor images from both descriptions of motion can be seen in Fig. 6 – 9. Quantitative results of comparing segmented regions are shown in Table 2 and CoM and DSC in Table 3. Figures 6 and 7 shows visualization of an ablated region over an EDE cycle for Patient ID 2. A small subset of chosen tracking features can be seen in Fig. 6 (a) along with the rectangular grid used for tracking shown in green. Figures 6 (b) and (c) represent the axial position and displacement, respectively, of this subset of tracked features over the EDE cycle with color corresponding to feature colors in Fig. 6 (a). Figure 7 (a) – (d) show the strain tensor images for Eulerian axial, Eulerian lateral, Lagrangian axial, and Lagrangian lateral, respectively, at 4 different sample times over the EDE cycle. It is important to note that the Eulerian descriptions shown in Fig. 7 (a) and (b) failed to provide ablated region depiction at tracked sample times 0.649 seconds. On the other hand, the Eulerian description at sample times 0.081, 0.244, and 0.487 seconds successfully provided ablated region depiction, but the size, shape, and contrast of the ablated region delineation varied. In contrast the Lagrangian descriptions shown in Fig. 7 (c) and (d) show very consistent ablated region depiction, size, and shape at all sample times. A similar visual example is shown in Fig. 8 and 9 where lesion is shown tracked over two consecutive EDE cycles.

Table 2 provides a comparison of the mean and standard deviation of segmented ablated region sizes using Eulerian and Lagrangian descriptions of motion. Note that the perturbation frequency of the applied deformation varied with clinicians and depth of the liver mass varied with the patient. Therefore a single cycle of electrode perturbation varied in the number of frames (n) and total tracked time in seconds ranging from 0.43 to 0.87 seconds as shown in Table 2. For all the patients within each description of the deformation, the mean segmented area for axial and lateral directions showed similar sizes meaning little discrepancy between directions. On the contrary, Eulerian and Lagrangian descriptions differed with a segmented area mean and standard deviation reduction of 61.5% and 75%, obtained with the Lagrangian description respectively.

The Dice similarity coefficient and center of mass differences also provided insight into the consistency of ablated region location and size. Table 3 shows results of the DSC and CoM for all 7 patients in this study. All patients provided the same or higher DSC values using a Lagrangian description of motion when compared to that of a traditional Eulerian description of up to 25%. Minimum, mean, and maximum CoM differences over the EDE cycle are shown in Table 3. In all datasets, lower values of minimum, mean, and maximum are seen with LDT as opposed to Eulerian description, except for axial strain tensor image for patient 4.

Success Rates

Success rates offer valuable insight to visualization performance of the two descriptions of motion. Success rates are defined as an ablated region visualization by a single observer over the tracked EDE cycle. It is calculated as a percentage of sample frames that an ablated region can be seen over the number of sample frames in an EDE cycle. Examples of positive

visualization can be seen in Fig. 9 (a) and (b) at sample times 0.08 and 0.57 seconds and all sample times for Fig. 9 (c) and (d), while Fig. 9 (a) and (b) at sample times 0.33 and 0.49 seconds provide examples of failed ablated region visualization.

The success rates for each of the patients is shown in Table 4. It is shown that none of the patients using a Eulerian description show ablated region visualization for the entire EDE cycle, and the average of all patients only resulted 55% and 49% of frames in the EDE cycle be seen for axial and lateral strain tensors using Eulerian description. In contrast, LDT shows 100% success for axial and 91% success for lateral.

Discussion

In this paper, we propose the use of Lagrangian deformation tracking for ablation elastography in the liver. In our approach, clinician introduced ablation antenna perturbations are the primary deformation of interest, which may be corrupted by various physiological deformations due to respiratory, cardiac and patient movements, sonographer movement of the transducer. These extraneous deformation factors can differ greatly from patient to patient, and even within the same patient dependent on the liver lobe that is imaged.

Since the true ablated region size is not known, we are unable to draw any conclusions regarding the size or dimensions of the ablated region. For the phantom tracked cycle, the mean segmented area from the Lagrangian description did not differ from the traditional Eulerian description but showed improved consistency over time. For this reason, phantom results validated the consistency and accuracy of Lagrangian description of deformation as compared to the traditional Eulerian description. Although the true ablated region size is not known, we obtain a reduction in the segmented area standard deviations for the ablated regions, of at least 25% with the LDT approach when compared to the Eulerian approach for *in vivo* assessments. More importantly, we attain a large average reduction in the standard deviation by 75% demonstrating that LDT successfully provides more consistent segmented areas as opposed to the Eulerian approach. Additionally, LDT ablated regions resulted in much higher Dice coefficients and lower center of mass differences. This showed that segmented areas were similarly positioned and segmented overtime verifying the consistency of LDT and reduction in motion artifacts that plague the Eulerian description of motion. As a result of accurate tracking of ablated regions, success rates were greatly benefited with a nearly 100% successful visualization for axial and lateral directions using LDT.

Limitations

A major limitation of this work is that we do not know the true size or location of ablated regions for patients, therefore we are unable to make any claims directly on the accuracy of the Eulerian or Lagrangian description of the deformation. Future work will look to validate to the true sizes and locations of ablation zones using virtual slicing of the “gold-standard” CECT imaging for comparison to Eulerian and Lagrangian strain tensor images (Pohlman et al. 2019a). Although claims cannot be made on the accuracy of Eulerian or Lagrangian

descriptions of deformation for *in vivo* cases, we were able to gain insight from phantom data.

Segmented Area and Ablated Margin

The main goal of MWA is to induce thermal necrosis of cancerous tissue of the liver and a margin of normal tissue necrosis of 0.5–1.0 cm. It is beneficial to relate segmented areas to size and error of desired ablated margins. If we assume that microwave energy radiated from the electrode created an ellipsoidal shape of necrosis (Rubert et al. 2010), we can relate segmented area to ablated size and margin error by looking at Eq. (13).

$$Area \pm \Delta = \pi(\rho_1 \pm \delta)(\rho_2 \pm \delta) \quad (13)$$

Equation (13) is a modified equation for the area of an ellipse including the relationship of standard deviation on the area and radii of an ellipse, where ρ_1 and ρ_2 are the major and minor radii of the ablated ellipse, δ is the uniform radii standard deviation (ablated margin of error), and Δ is the segmented area standard deviation. Figure 10 visualizes this relationship between segmented area standard deviation and ablated margin error. Table 5 provides examples of expected area and deviation from an area given an ablative margin of error, δ .

As an example, if a clinician deems that the ideal ablation size for a patient is 2 cm – 3 cm, referring to Table 5, this results in an ideal segmented area of 18.9 cm². If a segmented area showed a standard deviation of $\Delta < 1.60$ cm², then we may assume that given an ellipsoidal ablation region the ablated margin should be within 0.1 cm of the ideal ablated margin. This of course only gives us a rough idea of the type of consistency required for a method to be deemed reliable in detecting the true ablative margin. We cannot make any claims as to the accuracy of location or true shape of ablated regions.

We can estimate that the segmented area of the phantom inclusion provides a circular radius of 1.25 cm, while the radius of a 4.3 cm³ inclusion is 1.01 cm. Although segmented inclusions from Eulerian and Lagrangian descriptions are slightly larger, area standard deviation of the Lagrangian description are well below a $\delta = 0.1$ cm using Table 5 as a guide. The Eulerian description on the other hand is greater than $\delta = 0.1$ cm. Additionally for *in vivo* cases, we can see that only one example, namely ID #6, of Eulerian segmented areas provided a standard deviation in the range of $\delta = 0.1$ cm for axial and $\delta = 0.25$ cm for lateral. This means that a high uncertainty of ablated margins was present using an Eulerian description of motion. On the contrary, standard deviations of Lagrangian segmented areas for ID #s 1, 2, 5, 6, and 7 demonstrated values representing close to $\delta = 0.1$ cm, or 10% of the ideal 1 cm margin and ID #3 of $\delta < 0.25$ cm. This result validates the importance of LDT's consistent segmented regions and resulting certainty that visualized ablated regions were relatively close ($\delta < 0.1$ cm) to the mean imaged ablated margin.

Conclusion

Success rates and consistency of ablated region visualization using EDE have been previously limited by physiological and non-ideal motions present during *in vivo* data

collection. To combat this issue, we proposed a Lagrangian deformation tracking approach (LDT) that tracks an ablated region temporally using affine transformations, significantly reducing the impact of these motions for ablated region visualization. Results of LDT showed a large decrease in segmented area standard deviation of nearly 100% on average and, using an ellipsoidal model, with low expected uncertainty of visualized ablative margins. Additionally, LDT showed higher consistency in ablated regions through an increase of Sørensen-Dice coefficients of up to 25% from the traditional Eulerian approach as well as lower differences in center of mass between segmented regions. The results of this work show that LDT will be a vital addition to EDE for providing increased consistency and success in visualizing ablated regions. Utilizing LDT reduces the negative effects present during EDE visualization. Physiological motion artifacts are an inevitable consequence during *in vivo* MWA procedures, yet LDT shows reduction of these motion artifacts resulting in more consistent visualization of ablation regions. Incorporation of LDT further closes the gap between ultrasound and contrast enhanced computed tomography for imaging MWA procedures in a clinical setting.

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Appendix

Segmentation using Snakes

The traditional snake is a curve, $\mathbf{x}(s)$, and is shown as Eq. (14). Active contour snakes aim to minimize the energy E , in Eq. (15) with additional energy terms derived from image intensities Eq. (16) and balloon force Eq. (17).

$$\mathbf{x}(s) = [x(s), y(s)], \quad s \in [0, 1] \quad (14)$$

$$E = \int_0^1 \frac{1}{2} (\alpha |\mathbf{x}'(s)|^2 + \beta |\mathbf{x}''(s)|^2) + E_{ext}(\mathbf{x}(s)) + F_b(\mathbf{x}(s)) ds \quad (15)$$

$$E_{ext}(\mathbf{x}(s)) = -|\nabla I(\mathbf{x}(s))|^2 - |\nabla(G_\sigma(\mathbf{x}(s))) * (I(\mathbf{x}(s)))|^2 \quad (16)$$

$$F_b(\mathbf{x}(s)) = k_1 \mathbf{n}(s) - k \frac{\nabla P}{\|\nabla P\|} \quad (17)$$

The image intensity energy allows the snake to be attracted or opposed to landmarks of an image (i.e., edges, lines, intersects, etc.), while the balloon force helps in avoiding issues when an active contour is initialized too far from an edge or does not have sufficient forces to keep the snake from shrinking on itself. Here α and β are weight parameters that control

the 1st and 2nd derivatives, namely the snake's tension and rigidity, respectively, ∇ denotes the gradient operator, $G_{\sigma}(\mathbf{x}(s))$ is the 2-D Gaussian filter with standard deviation σ , P is the pressure force, $\mathbf{n}(s)$ is a normal unit vector to the curve at $\mathbf{x}(s)$, k is the amplitude of the balloon force, and the sign of k_1 dictates whether the force is inflation or deflation. The external energy E_{ext} is found from the image itself such that smaller values occur at edges of interest. σ dictates the blur in image boundaries allowing the snake to detect the boundary from farther distances. The pressure force P dictates how strong edges will inhibit the balloon force.

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Figure 1.
Flowchart of the Lagrangian Deformation Tracking algorithm.

Figure 2.
Example of automatic feature selection (blue squares) vs. manual feature selection (red circles) in ultrasound B-mode image.

Figure 3.

An example of affine transformed coordinate tracking used in LDT. First frame (a), of image with ablated region as an ellipse, initialized coordinate grid as rectangle, and 5 sample tracking features. Panels (b-d) show transformation of coordinate grid over time as features follow antenna and ablated region. Relative position (e), and displacement (f), of the features at time steps a-d.

Figure 4.

Visual comparison between Eulerian and Lagrangian descriptions of motion in a phantom undergoing manual compression. Ultrasound B-mode image (a), showing the rectangular coordinate grid in green and sample of tracking features. Position (b), and displacement (c), of the tracked features over an EDE cycle.

Figure 5.

Visual comparison between Eulerian and Lagrangian descriptions of motion in a phantom undergoing manual compression. Axial strain tensor images at 4 sample times during a single compression cycle utilizing Eulerian (a), and Lagrangian (b), descriptions of motion, respectively.

Figure 6.

Visual comparison between Eulerian and Lagrangian descriptions of motion in EDE for patient ID 2. (a) Ultrasound B-mode image showing the rectangular coordinate grid in green and subsample of tracking features. (b) and (c) show the position and displacement, respectively, of the tracked features over an EDE cycle.

Figure 7.

Visual comparison between Eulerian and Lagrangian descriptions of motion in EDE for patient ID 2. Axial (a) and lateral (b) strain tensor images at 4 sample times during an EDE cycle utilizing an Eulerian description of motion. Axial (c), and lateral (d), strain tensor images at the same 4 sample times during the EDE cycle utilizing a Lagrangian description of motion.

Figure 8. Visual comparison between Eulerian and Lagrangian descriptions of motion in EDE for patient ID 6. (a) Ultrasound B-mode image showing the rectangular coordinate grid in green and subsample of tracking features. Position (b), and displacement (c) of the tracked features over two EDE cycles.

Figure 9.

Visual comparison between Eulerian and Lagrangian descriptions of motion in EDE for patient ID 6. Axial (a), and lateral (b), strain tensor images at 4 sample times during the tracked EDE cycles utilizing an Eulerian description of motion. Axial (c), and lateral (d), strain tensor images at the same 4 sample times during the tracked EDE cycles utilizing a Lagrangian description of motion.

Figure 10.
Example of the relationship between the standard deviation in the segmented area versus the standard deviation of ablative margins.

Table 1 -

Comparison between the segmented areas from Eulerian and Lagrangian descriptions of strain tensors over manual compression cycle of phantom.

SAMPLE SIZE (N)	Track Time (s)	Method	SEGMENTED AREA (CM ²)		DICE COEFFICIENT		CENTER OF MASS DIFFERENCE (MM)		
			Mean	Standard Deviation	Mean	Standard Deviation	Min	Mean	Max
21	0.58	Eulerian	4.9	1.1	0.88	0.09	0.004	0.13	0.37
		Lagrangian	4.9	0.29	0.96	0.02	0.002	0.024	0.049
		Percent Difference	-0.2%	-74%	10.0%	-73%	-64%	-81%	-87%

Table 2 –

Comparison between the segmented areas from Eulerian and Lagrangian descriptions of strain tensors over a single EDE cycle.

ID #	Sample Size (n)	Track Time (s)	Direction	EULERIAN SEGMENTED AREA (CM ²)		LAGRANGIAN SEGMENTED AREA (CM ²)		PERCENT DIFFERENCE	
				Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
1	9	0.61	Axial	23	11	10	0.89	-55%	-92%
			Lateral	24	7.0	9.8	0.40	-59%	-94%
2	8	0.65	Axial	22	11	11	0.37	-51%	-97%
			Lateral	20	6.5	9.6	1.7	-53%	-73%
3	13	0.83	Axial	32	4.1	24	2.9	-26%	-28%
			Lateral	28	5.3	16	2.7	-42%	-50%
4	15	0.87	Axial	30	6.6	14	5.0	-53%	-24%
			Lateral	28	6.0	21	2.8	-26%	-53%
5	8	0.43	Axial	25	7.6	5.7	0.18	-78%	-98%
			Lateral	25	7.9	6.3	0.19	-75%	-98%
6	9	0.73	Axial	40	1.2	6.0	0.35	-85%	-72%
			Lateral	38	3.0	3.4	0.39	-91%	-87%
7	7	0.47	Axial	18	9.7	3.5	0.74	-81%	-92%
			Lateral	26	8.0	3.4	0.30	-87%	-96%

Table 3 -

Segmented area comparisons for ablated regions with Eulerian and Lagrangian descriptions of motion.

ID #	Direction	DICE COEFFICIENT			CENTER OF MASS DIFFERENCE (CM)					
		Eulerian	Lagrangian	Percent Increase	Eulerian			Lagrangian		
					Min	Mean	Max	Min	Mean	Max
1	Axial	0.74	0.94	20%	0.048	0.39	1.0	0.004	0.15	0.27
	Lateral	0.83	0.96	13%	0.015	0.33	0.73	0.004	0.088	0.18
2	Axial	0.73	0.98	26%	0.11	0.43	1.1	0.001	0.016	0.050
	Lateral	0.81	0.94	13%	0.016	0.31	0.52	0.004	0.054	0.17
3	Axial	0.89	0.94	4.9%	0.056	0.43	1.0	0.004	0.22	0.74
	Lateral	0.86	0.91	5.2%	0.060	0.40	0.98	0.005	0.25	0.60
4	Axial	0.83	0.84	0.8%	0.026	0.57	1.2	0.008	0.51	1.3
	Lateral	0.84	0.89	5.1%	0.052	0.58	1.2	0.009	0.37	0.83
5	Axial	0.82	0.98	16%	0.025	0.42	0.77	0.004	0.021	0.046
	Lateral	0.78	0.97	19%	0.080	0.64	1.2	0.004	0.088	0.22
6	Axial	0.98	0.97	-1.3%	0.021	0.10	0.19	0.013	0.049	0.089
	Lateral	0.95	0.94	-0.5%	0.047	0.24	0.61	0.007	0.047	0.084
7	Axial	0.71	0.88	17%	0.11	0.67	1.5	0.011	0.21	0.42
	Lateral	0.81	0.95	15%	0.14	0.53	1.1	0.009	0.075	0.20

Table 4 –

Success rates over an EDE cycle of Eulerian and Lagrangian descriptions of motion for 7 patients

ID #	Eulerian		Lagrangian	
	Axial	Lateral	Axial	Lateral
1	89%	78%	100%	100%
2	63%	63%	100%	100%
3	31%	54%	100%	92%
4	67%	20%	100%	67%
5	38%	50%	100%	100%
6	44%	44%	100%	100%
7	57%	57%	100%	100%
ALL	55%	49%	100%	91%

Table 5 –

Reference to ellipse area and standard deviation given ellipse radii and uncertainty in radius.

<i>Ellipse Radii (cm)</i>		Area (cm ²)	(cm ²) given $\delta = 0.1$ cm	(cm ²) given $\delta = 0.25$ cm
ρ_1	ρ_2			
1	1	3.1	0.66	1.8
1.5	1	4.7	0.82	2.2
2	1	6.3	1.0	2.6
2	1.5	9.4	1.1	3.0
2	2	13	1.3	3.3
2.5	2	16	1.5	3.7
3	2	19	1.6	4.1
3	2.5	24	1.8	4.5
3	3	28	1.9	4.9