Comparison of three dimensional strain volume reconstructions using SOUPR and wobbler based acquisitions: A phantom study

Wenjun Yang^{a)}

Department of Medical Physics, University of Wisconsin School of Medicine and Public Health,
University of Wisconsin-Madison, Madison, Wisconsin 53705

Atul Ingle

Department of Electrical and Computer Engineering, University of Wisconsin-Madison,
Madison, Wisconsin 53706

Tomy Varghese^{a)}

Department of Medical Physics, University of Wisconsin School of Medicine and Public Health,
University of Wisconsin-Madison, Madison, Wisconsin 53705 and Department of Electrical
and Computer Engineering, University of Wisconsin-Madison, Madison, Wisconsin 53706

(Received 26 October 2015; revised 10 January 2016; accepted for publication 15 February 2016;
published 7 March 2016)

Purpose: Ultrasound strain imaging is a relatively low cost and portable modality for monitoring percutaneous thermal ablation of liver neoplasms. However, a 3D strain volume reconstruction from existing 2D strain images is necessary to fully delineate the thermal dose distribution. Tissue mimicking (TM) phantom experiments were performed to validate a novel volume reconstruction algorithm referred to as sheaf of ultrasound planes reconstruction (SOUPR), based on a series of 2D rotational imaging planes.

Methods: Reconstruction using SOUPR was formulated as an optimization problem with constraints on data consistency with 2D strain images and data smoothness of the volume data. Reconstructed ablation inclusion dimensions, volume, and elastographic signal to noise ratio (SNRe) and contrast to noise ratio (CNRe) were compared with conventional 3D ultrasound strain imaging based on interpolating a series of quasiparallel 2D strain images with a wobbler transducer.

Results: Volume estimates of the phantom inclusion were in a similar range for both acquisition approaches. SNRe and CNRe obtained with SOUPR were significantly higher on the order of 250% and 166%, respectively. The mean error of the inclusion dimension reconstructed with a wobbler transducer was on the order of 10.4%, 3.5%, and 19.0% along the X, Y, and Z axes, respectively, while the error with SOUPR was on the order of 2.6%, 2.8%, and 9.6%. A qualitative comparison of SOUPR and wobbler reconstruction was also performed using a thermally ablated region created in *ex vivo* bovine liver tissue.

Conclusions: The authors have demonstrated using experimental evaluations with a TM phantom that the reconstruction results obtained with SOUPR were superior when compared with a conventional wobbler transducer in terms of inclusion shape preservation and detectability. © 2016 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4942814>]

Key words: 3D ultrasound elastography, strain imaging, SOUPR, wobbler transducer

1. INTRODUCTION

Both diffuse and focal hepatic diseases such as fibrosis or liver neoplasms, respectively, exhibit increased local tissue stiffness.^{1–7} For diagnosis of liver fibrosis, liver stiffness below 6 kPa is considered to be normal, while values between 8 and 12.5 kPa are considered as the threshold for advanced fibrosis and cirrhosis, respectively.⁵ Liver stiffness was reported to be even higher among patients diagnosed with hepatocellular carcinoma (HCC), due to liver cirrhosis.⁶ In Jung's study,⁶ the average liver stiffness for 57 patients with HCC was 16.1 kPa which was significantly higher than the fibrosis threshold.

Traditionally, manual palpation has been considered to be a fast and effective diagnostic method for detecting local tissue stiffness changes for differentiating liver diseases. Ultrasound

elastography,⁸ which provides quantitative and sensitive examination of liver stiffness, represents a medical imaging analog to palpation. It has been applied for the clinical diagnosis of liver fibrosis and cirrhosis, using approaches such as transient elastography (FibroScan; Echosens, Paris, France).^{1–6} In addition to the diagnosis of pathological tissue stiffness, monitoring of thermal ablation-induced local tissue stiffness contrast is another important application of ultrasound elastography.^{9–16} Radiofrequency or microwave ablations are minimally invasive alternatives to surgical resection for HCC or metastatic liver cancers. The thermal dose delivered to the tumor causes coagulative necrosis of tumor cells and is associated with increased local tissue stiffness.^{9–14} Conventional ultrasound B-mode imaging is commonly used for ablation needle guidance. However, it is not an effective modality for ablation monitoring

due to the similar echogenicity between the ablated region and surrounding normal tissue.^{9–14} On the other hand, ultrasound elastography utilizes the underlying tissue stiffness contrast as an effective alternative for ablation monitoring.^{9–14,17,18}

Ultrasound elastography is based on analyzing sequential ultrasound radiofrequency (RF) echo-signal frames in response to an internal^{19–21} or external^{8,22,23} mechanical stimulus. Local tissue strain,⁸ shear wave velocity,²⁴ or wavelength²⁵ are commonly used as parameters to reconstruct the Young's modulus of the local tissue. In this study, we focus on evaluating 3D strain imaging for ablation monitoring to overcome limitations of current 2D ultrasound elastography. Due to the 1D nature of most ultrasound transducers, almost all of current ultrasound elastographic imaging in use is confined to 2D imaging planes. The lack of out of plane tissue stiffness limits information on tumor volumes and reduces ablation region monitoring to a single slice intersecting the 3D treated volume. It could result in an inaccurate estimate of the tumor size or thermal dose delivered because the tumor or ablated region may have a different shape on other intersecting imaging planes.

To obtain the entire 3D distribution of tissue stiffness, 3D elastography has been utilized including its application with free-hand 1D transducer scans^{26,27} or wobbler transducer^{28,29} based acquisitions. 3D reconstruction using free-hand transducer scanning is based on transducer position tracking and 3D coordinate interpolation.^{26,27} With a 1D transducer placed on the surface of a patient, laser/optical/acoustic tracking systems are used to record the relative position of the transducer. After a series of scans, 2D strain, modulus, or shear wave elastograms and their position information are input into the 3D coordinate system and an interpolated 3D elastogram is generated. The advantage of this type of 3D elastography is the flexible positioning of the transducer. Nevertheless, position tracking always introduces errors and it is relatively difficult to record the tilt angle of each imaging plane, and the final interpolation results may be biased by imprecise 2D imaging plane coordinates.

An alternative 3D ultrasound elastography approach is based on using a mechanically driven “wobbler” transducer.^{28,30} The wobbler transducer is an encapsulated 1D transducer whose translational movement can be controlled by a mechanical driver. It provides more accurate imaging position information than free-hand 1D transducer acquisitions. 3D elastographic imaging with wobbler transducers can be categorized into two types: in one, the target 3D volume image is interpolated from the discrete 2D imaging planes, and a volume before and after the tissue deformation is recorded with local displacement and strain values calculated based on the volumetric data acquired. However, the computational complexity of volume-based algorithms is relatively steep, and thus the local tissue displacement search range is usually confined in a small range.³⁰ The other type is based on the interpolation of 2D strain images obtained at each mechanical position of the transducer in a step and shoot mode.^{28,29} A series of quasiparallel 2D strain images are generated at each position of the wobbler transducer and are then interpolated to generate a 3D volume based on their position. The

reconstruction algorithm is similar to that used for free-hand 1D transducer based acquisitions, except that the imaging planes are better controlled.

In spite of the relatively accurate position information obtained with a wobbler transducer, there may be mismatches between the quasiparallel imaging planes and a spherical or ellipsoidal region mimicking a tumor or ablated region. These quasiparallel 2D imaging planes may intersect with the ellipsoidal regions enclosing only a small area near the target boundaries. Thus, the effective information in each 2D plane decreases as the imaging planes move from the center to target edges. The lack of effective strain information on these imaging planes toward the edges and the resulting interpolation may lead to distortion of the target shape and inaccurate estimation of the target volume. In order to overcome the mismatch of the imaging planes and the ellipsoid target shape, we introduced a rotational acquisition method for 3D US elastography in a previous study, referred to as sheaf of ultrasound planes reconstruction (SOUPR).³¹ Instead of linearly translating the US transducer along the target surface, the acquisition planes are positioned rotationally with a specified angular increment. The sheaf of imaging planes is rotated along the central axis of the spherical or ellipsoidal target. As a result, the strain information is maximized in each of the 2D imaging planes.

In this study, we experimentally evaluate and compare SOUPR-based acquisitions and 3D volume reconstruction to that obtained using a wobbler transducer on a tissue mimicking (TM) phantom with an ellipsoidal inclusion mimicking a tumor or ablated region. 2D strain images generated with eight different cross correlation kernel sizes at each SOUPR and wobbler imaging plane were utilized for 3D volume reconstruction. The reconstructed inclusion dimensions, volume, signal to noise ratio (SNRe) and contrast to noise ratio (CNRe) of the SOUPR, and wobbler acquisitions were compared. 3D reconstruction was further tested on a thermal ablation created in *ex vivo* bovine liver tissue.

2. MATERIALS AND METHODS

2.A. Experimental setup

3D strain image reconstructions using SOUPR and wobbler were applied on ultrasound RF data acquired on a cubical TM phantom with an ellipsoidal inclusion placed at a depth of 3.5 cm. The dimension of the TM phantom was 80 × 80 × 80 mm. The major axis of the embedded ellipsoid was 19 mm and the other two minor axes were both 14 mm. The shear modulus ratio of the inclusion to background was 2.9, measured using an Aixplorer system (Supersonic Imagine Corporation, France), with a similar sized region at the same depth.

An Ultrasonix SonixTOUCH system (Analogic Corporation, MA, USA) was used to acquire US RF echo signals. The transducer utilized for SOUPR was a L14-5/38 linear array transducer, as shown in Fig. 1(a), and a 4D L14-5/38 transducer was used for the wobbler based acquisition as shown in Fig. 1(b). The linear array transducer encapsulated in the

FIG. 1. Ultrasound transducers used for SOUPR and wobbler 3D reconstruction. (a) The L14-5/38 linear transducer used for SOUPR. (b) The 4DL14-5/38 transducer used for wobbler transducer reconstruction. The linear array transducer inside the wobbler transducer is identical to the linear transducer used for SOUPR.

wobbler was identical to the L14-5/38 transducer used for SOUPR. The imaging planes for SOUPR were perpendicular to the phantom surface and rotated around the central axis of the inclusion at a 30° angle as illustrated in Fig. 2(a). Mechanical translation of the linear transducer inside the wobbler was approximated by a series of quasiparallel planes with 2.02 mm intervals, which were calculated from the stepping angle and the source to target distance as shown in Fig. 2(b). There was a 1° divergence between these imaging planes because of

the small angular rotation of the linear array wobbler transducer, which was approximated by the translation. This divergence correction is discussed in Sec. 2.C. Ten independent data acquisition experiments were performed on the TM phantom for the two 3D reconstruction methods. A total of six imaging planes were used for each 3D SOUPR reconstruction, while the number of imaging planes of the wobbler transducer that intersect the inclusion was between seven and eight planes among the ten independent acquisitions. For both SOUPR and wobbler acquisitions, the transducers were operated at a 6.7 MHz center frequency, using an image depth of 6 cm with a single focal zone located at 4 cm. The imaging width of both SOUPR and the wobbler transducer was 38 mm. RF echo signals were acquired at a 40 MHz sampling frequency. The L14-5/38 and 4D L14-5/38 transducers were inserted into a 10×10 cm plexiglass plate to apply a uniform mechanical deformation as shown in Fig. 2(c). A 1.6 mm compression³² was applied along the vertical direction, which is 2% of the phantom height of 80 mm. The compression ratio is within the linear stress-strain range of the material due to the small compression.

2.B. 2D strain image generation and segmentation

A 2D cross correlation based tracking algorithm³³ was implemented to estimate the local displacement in the

FIG. 2. Experimental setup and 2D ultrasound imaging plane geometry. Top view of 2D US scan plane geometry for (a) SOUPR and (b) wobbler based reconstruction. (c) The compression apparatus and TM phantom. (d) 2D strain image generated with cross correlation kernel size of $4.8 \text{ wavelength} \times 7 \text{ A-lines}$. The red contour denotes segmentation results using an active contour algorithm.

TM phantom caused by the external compression for both SOUPR and wobbler acquisition methods. Eight different window dimensions based on a combination of four different axial lengths and two lateral widths were used to compare the reconstruction results in terms of the inclusion volume, SNRe, CNRe, and ellipsoidal axis lengths. Axial dimensions of the windows were 3.4, 4.8, 6.1, and 7.5 wavelengths and the lateral widths were three and seven A-lines, respectively. The two adjacent cross correlation kernels overlap 80% along the beam direction and an A-line in the lateral direction.

Strain values were calculated as the gradient of local displacement. A 15-point linear least square fit was applied to reduce noise artifacts caused by the gradient calculation. Stiffer regions experience less strain and thus appear as dark regions in the strain image as shown in Fig. 2(d). Only the axial component of the strain was estimated because the deformation was applied uniformly along the axial or beam direction.

In order to define the boundary of the inclusion, segmentation was applied to the 2D strain images. An “active contour” algorithm³⁴ was used for segmentation with the results shown in Fig. 2(d). An initial circular contour was placed at the center of the inclusion. It was found that 600 iterations were sufficient to converge to a reasonable solution. The final contours were expanded with a disk kernel of seven pixels in diameter to close the gaps of segmented contours caused by noise in strain images and then shrunk by the same kernel to delineate a sharp edge. The segmentation algorithm was applied to the strain images generated with the eight different windows for both SOUPR and wobbler based acquisitions. 2D binary masks were generated based on these segmentation results with a value of 1 inside the inclusion and a value of 0 in the background. Volume estimation of the 3D reconstructed inclusion was based on these binary masks as discussed in Sec. 2.C.

2.C. 3D strain volume and binary mask reconstruction

3D strain volume estimation of the inclusion was divided into two parts: the first stage was the reconstruction of a 3D strain image from the 2D imaging planes, while the second stage was the generation of a 3D binary mask. The purpose of the binary mask was to estimate the inclusion volume without any observer errors in delineating inclusion boundaries on the 3D strain image. On the other hand, SNRe and CNRe were measured on the 3D strain image to compare the detectability of the reconstructed inclusion using the SOUPR and wobbler acquisition methods.

For SOUPR, a 3D binary mask of the inclusion was reconstructed with the 2D segmented binary masks as discussed in Sec. 2.B using a reconstruction algorithm developed by our group,³¹ which is described below:

$$\min_x \|Ax - b\|^2 + \eta \|Bx\|^2, \quad (1)$$

where x denotes the 3D volume to be estimated, A is the grid sampling matrix, b is the observed value located in the sheaf of planes, $\eta > 0$ is a regularization parameter that controls the amount of smoothing, and B represents the Laplacian operator calculating the second derivative of the 3D volume as an indicator of the smoothness.

The reconstruction was formulated as an optimization problem on a user defined 3D coordinate system with known data sampled at specific planes as shown in Fig. 2(a). The interpolation was subject to an optimization process with an objective function shown in Eq. (1) consisting of preserving data consistency with the known data at those 2D imaging planes and a data smoothness constraint. Data consistency is aimed at keeping the reconstructed 3D strain or binary mask to be within a small variation from the known data measured at those 2D planes, and the data smoothness constraint was based on the assumption that the inclusion possessed a smooth ellipsoidal shape, which is common for thermal lesion.³¹ The solution

FIG. 3. Wobbler transducer imaging plane step angle correction. (a) Lateral view of the imaging plane of the wobbler transducer assuming that they are parallel. (b) Lateral view of imaging plane after angle correction with the 2D projective transform applied to the lateral slices.

to this optimization problem and tuning of the regularization parameter η was described in detail in the paper by Ingle and Varghese.³¹ A reconstructed 3D binary mask was used for inclusion volume estimation which is discussed in Sec. 2.D. The 3D strain images were reconstructed with the same algorithm except that they were reconstructed directly from the 2D strain images without segmentation. The SNRe and CNRe were calculated on these 3D strain images, as discussed in Sec. 2.D.

For the reconstruction with the wobbler transducer, 3D binary masks and strain images were reconstructed with a conventional bicubic interpolation to assemble the 2D binary masks and strain images to create a 3D volume. The 2D images were first interpolated with an assumption that the imaging planes were parallel, as shown in Figs. 2(b) and 3(a). Then a projective transformation³⁵ was applied to the 3D coordinate system to project the reconstructed 3D cube into a trapezoid to account for the 1° divergence of the imaging planes which was induced by the step angle of the wobbler transducer as shown in Fig. 3(b). The projective transformation was applied to each lateral plane of the 3D interpolated volume. Thus, the original square plane was transformed to a trapezoid with a shrunk top and an expanded bottom region. The projection transform is formulated as follows:

$$P_s = M_{ds} P_d, \quad (2)$$

where $P_s = \begin{pmatrix} u \\ v \\ q \end{pmatrix}$ is the coordinate of points before transformation and $P_d = \begin{pmatrix} x \\ y \\ w \end{pmatrix}$ is the coordinate of points after transformation. The effective coordinate of the points is the first two dimensions and the third dimension is added to account for scaling. $M_{ds} = \begin{pmatrix} a & b & c \\ d & e & f \\ g & h & i \end{pmatrix}$ is the projection matrix, and without loss of generality, $i = 1$ since a scalar product yields the same projection. Thus, there are eight parameters to be determined for this matrix. The coordinate of the four vertexes

of the projection plane before and after projection was used to calculate the matrix elements as shown in the following:

$$M_{ds} = \begin{pmatrix} u_0 & v_0 & 1 & 0 & 0 & 0 & -u_0x_0 & -v_0x_0 \\ u_1 & v_1 & 1 & 0 & 0 & 0 & -u_1x_1 & -v_1x_1 \\ u_2 & v_2 & 1 & 0 & 0 & 0 & -u_2x_2 & -v_2x_2 \\ u_3 & v_3 & 1 & 0 & 0 & 0 & -u_3x_3 & -v_3x_3 \\ 0 & 0 & 0 & u_0 & v_0 & 1 & -u_0y_0 & -v_0y_0 \\ 0 & 0 & 0 & u_1 & v_1 & 1 & -u_1y_1 & -v_1y_1 \\ 0 & 0 & 0 & u_2 & v_2 & 1 & -u_2y_2 & -v_2y_2 \\ 0 & 0 & 0 & u_3 & v_3 & 1 & -u_3y_3 & -v_3y_3 \end{pmatrix} \begin{pmatrix} a \\ b \\ c \\ d \\ e \\ f \\ g \\ h \end{pmatrix} = \begin{pmatrix} x_0 \\ x_1 \\ x_2 \\ x_3 \\ y_0 \\ y_1 \\ y_2 \\ y_3 \end{pmatrix}, \quad (3)$$

where u_k and v_k are the coordinate of the k th vertex on the source plane, and x_k and y_k are the coordinate of the k th vertex on the destination plane.

The final interpolated 3D grid resolution was similar to that used for SOUPR, which was around $0.25 \times 0.25 \times 0.25$ mm.

2.D. Volume, SNRe, and CNRe calculation

Inclusion volume comparisons were conducted using the 3D binary masks. Nevertheless, due to the interpolative nature of the 3D reconstruction algorithms, these 3D binary masks did not preserve a sharp boundary. There was a transition gradient from the inclusion to background with the value varying from 1 to 0. A threshold value between 0 and 1 was selected to define the boundary of these binary 3D masks. In this study, a threshold of 0.45 was applied to preserve a smooth and reasonably segmented boundary of the reconstructed volume, as shown in Fig. 4. For all the 3D binary masks generated from the eight displacement tracking kernels, all voxels greater than 0.45 were set to be 1 while the others were set to be 0.

FIG. 4. Threshold value for the 3D binary masks. A C-plane denoting a horizontal slice of the reconstructed 3D mask using SOUPR is shown. Pixel values decrease from 1 around the center to 0 toward the background. A threshold value of 0.45 was selected between the two values shown in the expanded figure. A threshold value outside this range would result in a distorted surface.

With the boundary defined by the threshold value, the volume of the inclusion was estimated as shown in the following:

$$V = N \times \Delta v, \quad (4)$$

where V is the volume of the inclusion, N is the number of voxels inside the inclusion, and Δv is the voxel volume defined by the resolution of the 3D coordinate grid. Spatial resolution of the 2D strain images generated with different displacement tracking kernels was registered with the same B-mode image to keep the voxel size estimation robust through those eight tracking kernels.

In this study, SNRe was defined as in Eq. (5).³⁶ An SNRe value of at least 5 is needed to distinguish image features at 100% certainty based on the Rose criterion,³⁷

$$\text{SNRe} = \frac{\mu}{\sigma}, \quad (5)$$

where μ is the mean value within the region of interest (ROI) which is a cubical region defined inside the reconstructed inclusion with a volume of around 0.25 cm^3 (approximately $0.8 \times 0.8 \times 0.4 \text{ cm}$); σ is the standard deviation within the ROI.

The CNRe was used to evaluate lesion detectability on strain images. The CNRe takes into consideration the contrast of the target and background and their contribution to the noise level as defined in the following:

$$\text{CNRe} = \frac{|\mu_i - \mu_b|}{\sqrt{\sigma_i^2 + \sigma_b^2}}, \quad (6)$$

where μ_i is the mean value of the ROI, which is a cubical region defined inside the inclusion, and also used for SNRe calculations; μ_b is the mean value within a similar sized cubical ROI defined in the background. σ_i and σ_b denote the standard deviation of the estimates within the inclusion and background ROI, respectively.

2.E. Sensitivity analysis when the SOUPR center does not coincide with inclusion center

A simulated spherical phantom was used to study the volume and shape preservation of the 3D reconstruction when the center of the SOUPR planes does not coincide with the center of the inclusion. The radius of the simulated spherical phantom was 0.6, and the maximum distance the center of SOUPR was shifted was 0.2, which corresponds to 33.3% of the radius. At each shifted SOUPR center, a series of 2D imaging planes was calculated theoretically based on the sphere geometry, using the same 30° rotation angle. The simulation was performed for two distinct conditions; the first where information on the inclusion center or axes was known and the second with an unknown inclusion center. For the first condition with a known target center, each 2D image slice was placed at

FIG. 5. 3D reconstruction of strain images and corresponding segmented regions obtained using the binary mask. 3D strain volume distribution (a) and segmented region (c) for SOUPR. Similarly, the 3D strain image (b) and inclusion segmented (d) using a wobbler transducer. These images were reconstructed based on 2D strain images generated with a cross correlation kernel size of $4.8 \text{ wavelength} \times 7 \text{ A-lines}$.

FIG. 6. Comparisons of reconstructed inclusion volume, SNRe, and CNRe metrics. (a), (c), and (e) are based on the 2D strain images generated with cross correlation kernels width of seven A-lines, while (b), (d), and (f) are based on a cross correlation kernel width of three A-lines. The kernel lengths on the horizontal axis were 3.4, 4.8, 6.1, and 7.5 wavelengths. (a) and (b) present a comparison of the inclusion volume estimates between SOUPR and wobbler. The dotted line on top denotes the actual inclusion volume. (c) and (d) are the SNRe comparisons for the same series of kernel sizes, while (e) and (f) present the CNRe comparisons. The error bar for each kernel size denotes the standard deviation of ten independent measurements. The star notation represents the p -value of a one sided t test for the hypothesis that SOUPR estimates are equal to those obtained using the wobbler transducer. A single star notation denotes that $0.01 < p < 0.05$, while two stars denote $p < 0.01$.

the corresponding position intersecting the spherical phantom shown in Fig. 7(a). Both the volume and Jaccard index of the reconstructed phantom were calculated based on the SOUPR algorithm described in Eq. (1). The Jaccard index denotes a parameter that is used to measure the similarity between two data sets, which is formulated in the following:

$$\text{Jaccard index} = \frac{A \cap B}{A \cup B}, \quad (7)$$

where A denotes the reconstructed 3D volume, while B represents the volume of the simulated phantom.

In a similar manner, for the second condition tested, we assumed that the position of target was not available, and

TABLE I. Inclusion axis estimates with SOUPR and wobbler reconstruction using seven A-line kernels.

Window length (wavelengths)	Axis length of the 3D inclusion reconstructed with SOUPR (mm)			Axis length of the 3D inclusion reconstructed with wobbler (mm)		
	X	Y	Z	X	Y	Z
3.4	14.73 $\pm$ 0.52	14.59 $\pm$ 0.52	16.16 $\pm$ 0.86	14.05 $\pm$ 0.76	13.53 $\pm$ 0.99	13.77 $\pm$ 0.83
4.8	14.28 $\pm$ 0.55	14.25 $\pm$ 0.57	16.85 $\pm$ 0.96	14.18 $\pm$ 0.27	13.53 $\pm$ 0.99	14.21 $\pm$ 0.37
6.1	13.43 $\pm$ 0.43	13.43 $\pm$ 0.43	17.48 $\pm$ 1.08	11.31 $\pm$ 0.16	13.53 $\pm$ 0.99	16.98 $\pm$ 0.21
7.5	13.96 $\pm$ 0.58	13.84 $\pm$ 0.59	18.24 $\pm$ 1.12	11.12 $\pm$ 0.26	13.45 $\pm$ 0.96	16.61 $\pm$ 0.98

SOUPR center was set as the default central axis. Each 2D image slice was aligned with this central axis and the 3D volume was reconstructed with this default coordinate system. The volume and Jaccard index obtained was compared between these two conditions. The simulation was performed using the MATLAB software (Mathworks, Inc., MA, USA).

2.F. Feasibility on *ex vivo* tissue

3D reconstructions using SOUPR and wobbler were also validated on *ex vivo* bovine liver tissue with an ablated region created using a Neuwave Medical Certus 140 (Madison, WI, USA) system. Fresh bovine liver tissue was obtained from a local slaughter house. The ablated region was created using a general clinical setting using a 55 W power level for 3 min ablation duration and a single antenna. The 2D imaging planes were positioned using the same geometry as that utilized for the TM phantom scans as shown in Figs. 2(a) and 2(b). 2D strain images were generated with a 2% compression corresponding to the tissue height. The volume of the ablated region was calculated using a 3D binary mask previously described and shown in Eq. (4).

3. RESULTS

Due to the data smoothness constraint associated with SOUPR based reconstructions, the noise level within the inclusion and background was lower when compared to the wobbler based reconstructions as shown in Figs. 5(a) and 5(b). The 3D reconstructed strain volume with SOUPR was visibly closer to the ellipsoidal shape of the phantom inclusion while the shape reconstructed with the wobbler transducer was more cylindrical as illustrated in Figs. 5(c) and 5(d).

The comparisons of the reconstructed inclusion volume, SNRe, and CNRe obtained using correlation kernels with the width of seven A-lines are shown in Figs. 6(a), 6(c), and 6(e). The average inclusion volume obtained using SOUPR over the 4 kernel lengths was 1.64 cm³, which was 7.7% larger than the volume of 1.53 cm³ obtained with the wobbler transducer shown in Fig. 6(a). The average SNRe obtained with SOUPR over the four kernel lengths was 30.6, which was 208.5% higher than the SNRe value of 9.9 estimated with the wobbler transducer, as shown in Fig. 6(c). An improved CNRe with SOUPR was also obtained with a mean value of 5.1, which was 101.6% higher than the mean of 2.5 obtained with the wobbler transducer, as shown in Fig. 6(e). The $p < 0.05$ held for all comparisons except $p = 0.06$ for the volume comparison with the kernel length of 4.8 wavelengths as shown in Fig. 6(a).

Comparison results using kernels with the width of three A-lines are shown in Figs. 6(b), 6(d), and 6(f). The average inclusion volume over the four kernel lengths was similar for both SOUPR and wobbler approaches, around 1.57 cm³. However, improved SNRe and CNRe were observed with SOUPR, which was similar to the results with seven A-lines kernels. The average SNRe with SOUPR was 25.5, which was 250.3% higher than the average value of 7.3 obtained with the wobbler transducer, while the CNRe of SOUPR was 5.0, which was 166.0% higher than the CNRe value of 1.9. The $p < 0.01$ held for all the SNRe and CNRe comparisons.

Comparisons of the reconstructed ellipsoidal inclusion axis lengths are shown in Tables I and II, which were computed from the 3D reconstructed binary masks as illustrated in Figs. 5(c) and 5(d). The axes length in Table I was measured from the 3D binary masks reconstructed from 2D strain images generated with seven A-line cross correlation kernels as in Figs. 5(a), 5(c), and 5(e). The axis length in Table II

TABLE II. Inclusion axis estimates with SOUPR and wobbler reconstruction using three A-line kernels.

Window length (wavelengths)	Axis length of the 3D inclusion reconstructed with SOUPR (mm)			Axis length of the 3D inclusion reconstructed with wobbler (mm)		
	X	Y	Z	X	Y	Z
3.4	14.45 $\pm$ 0.44	14.37 $\pm$ 0.57	16.24 $\pm$ 0.92	16.52 $\pm$ 0.60	13.53 $\pm$ 0.99	12.34 $\pm$ 0.28
4.8	14.14 $\pm$ 0.37	14.00 $\pm$ 0.46	16.68 $\pm$ 0.92	16.44 $\pm$ 0.36	13.53 $\pm$ 0.99	12.55 $\pm$ 0.23
6.1	13.40 $\pm$ 0.38	13.35 $\pm$ 0.33	17.13 $\pm$ 1.04	13.85 $\pm$ 0.88	13.53 $\pm$ 0.99	15.08 $\pm$.033
7.5	13.36 $\pm$ 0.42	13.27 $\pm$ 0.39	17.62 $\pm$ 1.06	13.14 $\pm$ 1.24	13.45 $\pm$ 0.96	13.85 $\pm$ 0.88

Fig. 7. Simulation of the sensitivity of volume estimations for a shift in the SOUPR center with respect to the inclusion center. (a) Schematic diagram of the geometry of the simulated phantom and the shifted SOUPR center. (b) C-plane image of the reconstructed phantom using a shifted SOUPR center, with the known target position. (c) Volume of the reconstructed phantom estimated at different shift. The red (solid) curve was obtained when the target center is known, while the blue curve (dashed) was obtained for the unknown target center case. The center of SOUPR planes was assumed to be the target center when the target position is unknown. (d) The Jaccard index measured at the same shifted distance as (c).

was measured from the 3D binary masks based on three A-line kernels as in Figs. 5(b), 5(d), and 5(f). The mold of the inclusion in the phantom used in this study was constructed with a size of $14 \times 14 \times 19$ mm (X , Y , and Z axes, respectively).

For the comparisons with kernels of seven A-lines' width shown in Table I, the mean error between the measured axes length and the dimensions of the inclusion mold with SOUPR was 2.6%, 2.8%, and 9.6% for the X , Y , and Z axes, respectively. The mean error of the 3 axes using the wobbler method was 10.4%, 3.5%, and 19.0%, respectively. The comparison with kernel width of three A-lines is shown in Table II. The mean error with SOUPR for the three axes was 3.3%, 3.1%, and 11.0%, respectively, while the mean error with the wobbler transducer was 10.7%, 3.5%, and 30.2%.

Sensitivity analysis on the misalignment between the SOUPR and inclusion center is shown in Fig. 7. Figure 7(a) presents a schematic diagram of the misalignment between the SOUPR and target center, with the corresponding C-plane of the inclusion illustrated in Fig. 7(b). When the location of the shift in SOUPR center with respect to the inclusion center is known, the volume measurement of the reconstructed phantom remains stable and corresponds to the zero-shift case

indicated by the solid curve shown in Fig. 7(c). On the other hand, when the location of the target center is not known and the SOUPR center is considered to be the target center, the volume of the reconstructed phantom decreases slightly with an increase in the shift. For a shift of 33.3% of the radius, the volume measured dropped to 93% of the value at zero-shift indicated as the dotted curve shown in Fig. 7(c). A similar trend is also observed for the Jaccard index as shown in Fig. 7(d). The similarity between the reconstructed phantom using SOUPR and the original simulated phantom remains around 0.9 even as the center of SOUPR is shifted to 33.3% of the radius with the known target position. In the absence of target center information, the Jaccard index drops to 92% of the value measured with zero-shift.

A qualitative comparison of the SOUPR and wobbler reconstruction approaches on a microwave ablation procedure performed in *ex vivo* bovine tissue is shown in Fig. 8. 2D strain images are illustrated in Figs. 8(a) and 8(b), while the corresponding 3D volume reconstructions are shown in Figs. 8(c) and 8(d), respectively. The shape of the ablated region reconstructed with SOUPR was visibly closer to an ellipsoid, which is the most commonly observed shape for thermally coagulated regions, as shown in Figs. 8(c) and 8(d).

FIG. 8. SOUPR and wobbler 3D strain reconstruction of an ablated region created in *ex vivo* bovine liver tissue. (a) Strain image of the thermal lesion using SOUPR, generated with 6.1 wavelengths $\times$ 7 A-lines tracking kernel. (b) Strain image of the thermal lesion for the wobbler, generated with the same parameters as that for SOUPR. (c) The reconstructed inclusion using SOUPR. (d) The reconstructed inclusion using the wobbler transducer.

4. DISCUSSION AND CONCLUSIONS

In this study, we compared our previously developed 3D strain reconstruction algorithm, SOUPR, to a conventional method based on RF data acquired using a wobbler transducer, in terms of TM phantom inclusion dimensions, volume, SNRe, and CNRe. Reconstruction results were also compared based on the accuracy of the reconstructed inclusion shape in terms of ellipsoidal axis lengths. The reliability of SOUPR based reconstructions was further validated using an *ex vivo* ablation procedure performed on bovine liver tissue.

The dependence of reconstructed inclusion volume on the displacement tracking kernel is illustrated in Figs. 6(a) and 6(b). For the tracking kernels with a width of seven A-lines shown in Fig. 6(a), SOUPR provides a closer volume estimation to the actual value when compared to wobbler based estimations for almost all kernel lengths (with $p < 0.05$ or $p < 0.01$). When the kernel width is reduced to three A-lines, volume estimation with SOUPR displays a similar trend to that obtained using seven A-lines. The only deviation occurs for volumes estimated with a kernel length of 7.5 wavelengths, which decreases significantly. However, the volume estimation with wobbler transducer provides a closer value to SOUPR with this smaller displacement tracking kernel, as illustrated in Fig. 6(b). This comparison indicates that the volume estimation with SOUPR is less sensitive to the size of the displace-

ment tracking kernels than the wobbler and provides overall more stable volume estimation. In addition to the relatively stable estimation at various tracking kernel sizes (for each specific kernel), the standard deviation of the volume estimation with SOUPR is smaller than that with a wobbler, which is indicated by the length of the error-bar in Figs. 6(a) and 6(b).

Estimation of inclusion volumes with SOUPR and wobbler was both below the actual value of 1.9 cm³ as shown in Figs. 6(a) and 6(b). Underestimation with wobbler transducer might be due to the fact that the number of 2D imaging planes was limited and thus only part of the inclusion may have been delineated on the strain images. The ellipsoidal volume outside the outermost imaging planes was not accounted as shown in Figs. 5(d) and 7(b). Visualization and improved volume estimation results can be obtained by using smaller step-and-shoot angles, and consequently a larger number of 2D imaging planes, to reconstruct the 3D volume using the wobbler transducer. In this study, we attempted to have similar number of imaging planes for both SOUPR and wobbler based reconstructions. On the other hand, the underestimation of inclusion volume with SOUPR may be caused by the fact that the intersecting imaging plane may not perfectly align with the central axis of the inclusion. The imaging plane passing through the central axis of the inclusion would provide the largest intersection area of the inclusion. The current reconstruction algorithm with SOUPR assumes that

every imaging plane would align with the central axis of the inclusion. However, if the imaging plane fails to intersect with the central axis, a smaller intersection area would be input to the SOUPR algorithm resulting in an underestimation of the inclusion volume. This situation can be mitigated by using 2D matrix array transducers, where the SOUPR intersecting planes would be better aligned.³⁸ Another probable reason for the underestimated volume with SOUPR might be caused by the threshold value selected for the binary masks. The boundary of the 3D binary masks decreases from value of 1 to 0 as shown in Fig. 4. A too large or too small threshold value would result in a distorted volume surface. To keep a smooth surface of the 3D volume, threshold values between 0.37 and 0.47 can be utilized. We used a threshold value of 0.45 in our study to reduce the volume increase caused by the interpolation, while keeping a smooth surface of the 3D volume. This threshold has been validated from the 3D masks shown in Fig. 4. A robust 3D segmentation method applied directly to the 3D strain volume might be helpful as a further study to replace the 2D thresholded binary masks.

The detectability of the reconstructed inclusion is evaluated in terms of the SNRe and CNRe metrics for SOUPR and wobbler based reconstructions as shown in Figs. 6(c)–6(f). The SNRe and CNRe of the reconstructed inclusion with SOUPR were higher than that of wobbler with statistical significance ($p < 0.01$). This improvement in the SNRe and CNRe for SOUPR when compared to the wobbler may result from two sources: the additional outer layer present with the wobbler transducer and the reconstruction algorithm. As shown in Fig. 1(b), there is a layer for the wobbler transducer that houses the linear array transducer. Although this layer is designed to avoid ultrasound energy loss, it could have an impact on ultrasound propagation. Another factor that would contribute to SNRe and CNRe enhancement is the different reconstruction algorithms applied for SOUPR and wobbler 3D reconstruction, respectively. The 3D reconstruction for SOUPR is modeled as an optimization problem with an objective function consisting of data consistency and smoothness constraints.³¹ The data smoothness constraints utilized may result in the 3D volume reconstructed with SOUPR having lower data variance when compared to wobbler based data acquisition where the reconstruction is accomplished with a 3D cubical interpolation. The standard deviation of the SNRe metric for each displacement tracking kernel size is larger for SOUPR when compared with wobbler based reconstructions as illustrated in Figs. 6(c) and 6(d). However, the standard deviation for CNRe estimates shows an inverse relationship as shown in Figs. 6(e) and 6(f), where it is larger for wobbler than SOUPR based reconstructions.

Besides the quantitative metrics including inclusion volume, SNRe, and CNRe, one important goal of 3D strain reconstruction is to visualize the reconstructed volume, in our case the thermally coagulated region in the liver. Thus a full characterization of the target shape is critical to judge the thermal dose distribution in the ablated region. From Figs. 8(c) and 8(d), it is shown that the reconstructed inclusion obtained with SOUPR is more consistent with the ellipsoid shape anticipated while the results with wobbler are more

cylindrical which is caused by the quasilinear interpolation among the 2D imaging planes. Although an angle correction has been applied to the reconstruction, it has to be noted that the overall translation angle was only 6° – 7° which does not differ significantly from a parallel approximation. In order to quantify the shape preservation, the three axes of the ellipsoidal inclusion were compared between SOUPR and wobbler reconstructions. From Tables I and II, it is shown that except for the Y axis, the error of X and Z axes is quite large with the wobbler. In other words, the wobbler reconstruction preserves the Y axis length reasonably well while a large distortion appears for the other two axes. The comparison was further validated on an *ex vivo* bovine model with a thermal lesion created by microwave ablation as shown in Fig. 8. The volume estimation was similar between SOUPR and wobbler with a small increase of 0.7 cm^3 which was with the same trend as observed on the TM phantom.

One limitation of SOUPR is that it assumes that the rotating imaging planes are along the central axis of the target. For liver ablation monitoring, the microwave antenna can serve as a marker for the central axis due to the homogeneous ablation volume anticipated around the antenna. Under other circumstances where the target position is impractical to measure, from the numerical simulation, a 7% underestimation of the target volume will occur with a 33.3% shift from the target center when the target location is unknown. For most imaging situations due to the local nature of ultrasound scanning, we do not anticipate a significant shift from the center of the SOUPR imaging planes to the inclusion center. Another limitation of SOUPR is that the target shape is assumed to be smooth. If the ablated region is surrounded by large vessels, this assumption might not hold since the large heat sink caused by vessels might cause a large distortion of the inclusion shape. Thus, the reconstruction of an irregular shaped target would require additional 2D SOUPR imaging planes passing through the irregular region and iterative reconstruction approaches,³⁸ which is a topic for study in the future.

The 3D reconstruction applied on TM phantoms with SOUPR provided superior results when compared to the method based on a wobbler transducer in terms of inclusion volume, SNRe, CNRe, and shape preservation. The *ex vivo* experiment demonstrates the ability to use this approach for thermal ablation monitoring. A statistical comparison of these 3D reconstruction algorithms on *ex vivo* tissue will be the next step to validate our reconstruction algorithm.

ACKNOWLEDGMENTS

The authors acknowledge funding support from NIH-NCI Grant No. R01 CA112192-08. The authors also thank Dr. Timothy J. Hall, Ph.D. for use of the compression apparatus.

^{a)}Electronic addresses: wyang37@wisc.edu and tvarghese@wisc.edu; Telephone: 608/265-8797; Fax: 608/262-2413.

¹M. Ziol, A. Handra-Luca, A. Kettaneh, C. Christidis, F. Mal, F. Kazemi, V. de Ledinghen, P. Marcellin, D. Dhumeaux, J. C. Trinchet, and M. Beaugrand, "Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C," *Hepatology* **41**(1), 48–54 (2005).

- ²H. L. Chan, G. L. Wong, P. C. Choi, A. W. Chan, A. M. Chim, K. K. Yiu, F. K. Chan, J. J. Sung, and V. W. Wong, "Alanine aminotransferase-based algorithms of liver stiffness measurement by transient elastography (FibroScan) for liver fibrosis in chronic hepatitis B," *J. Viral Hepatitis* **16**(1), 36–44 (2009).
- ³J. Foucher, L. Castera, P. H. Bernard, X. Adhoute, D. Laharie, J. Bertet, P. Couzigou, and V. de Ledinghen, "Prevalence and factors associated with failure of liver stiffness measurement using FibroScan in a prospective study of 2114 examinations," *Eur. J. Gastroenterol. Hepatol.* **18**(4), 411–412 (2006).
- ⁴J. Vergniol, J. Foucher, E. Terrebbonne, P. H. Bernard, B. le Bail, W. Merrouche, P. Couzigou, and V. de Ledinghen, "Noninvasive tests for fibrosis and liver stiffness predict 5-year outcomes of patients with chronic hepatitis C," *Gastroenterology* **140**(7), 1970–1979.e3 (2011).
- ⁵S. Mueller and L. Sandrin, "Liver stiffness: A novel parameter for the diagnosis of liver disease," *Hepatic Med.* **2**, 49–67 (2010).
- ⁶K. S. Jung, S. U. Kim, S. H. Ahn, Y. N. Park, Y. Kim do, J. Y. Park, C. Y. Chon, E. H. Choi, and K. H. Han, "Risk assessment of hepatitis B virus-related hepatocellular carcinoma development using liver stiffness measurement (FibroScan)," *Hepatology* **53**(3), 885–894 (2011).
- ⁷R. J. DeWall, S. Bharat, T. Varghese, M. E. Hanson, R. M. Agni, and M. A. Kliever, "Characterizing the compression-dependent viscoelastic properties of human hepatic pathologies using dynamic compression testing," *Phys. Med. Biol.* **57**(8), 2273–2286 (2012).
- ⁸J. Ophir, I. Cespedes, H. Ponnekanti, Y. Yazdi, and X. Li, "Elastography: A quantitative method for imaging the elasticity of biological tissues," *Ultrason. Imaging* **13**(2), 111–134 (1991).
- ⁹T. Varghese, U. Techavipoo, W. Liu, J. A. Zagzebski, Q. Chen, G. Frank, and F. T. Lee, Jr., "Elastographic measurement of the area and volume of thermal lesions resulting from radiofrequency ablation: Pathologic correlation," *AJR, Am. J. Roentgenol.* **181**(3), 701–707 (2003).
- ¹⁰T. Varghese, J. A. Zagzebski, and F. T. Lee, Jr., "Elastographic imaging of thermal lesions in the liver *in vivo* following radiofrequency ablation: Preliminary results," *Ultrasound Med. Biol.* **28**(11–12), 1467–1473 (2002).
- ¹¹S. Bharat, T. Varghese, E. L. Madsen, and J. A. Zagzebski, "Radio-frequency ablation electrode displacement elastography: A phantom study," *Med. Phys.* **35**(6), 2432–2442 (2008).
- ¹²B. J. Fahey, R. C. Nelson, S. J. Hsu, D. P. Bradway, D. M. Dumont, and G. E. Trahey, "In vivo guidance and assessment of liver radio-frequency ablation with acoustic radiation force elastography," *Ultrasound Med. Biol.* **34**(10), 1590–1603 (2008).
- ¹³R. Righetti, F. Kallel, R. J. Stafford, R. E. Price, T. A. Krouskop, J. D. Hazle, and J. Ophir, "Elastographic characterization of HIFU-induced lesions in canine livers," *Ultrasound Med. Biol.* **25**(7), 1099–1113 (1999).
- ¹⁴N. Rubert, S. Bharat, R. J. DeWall, A. Andreano, C. Brace, J. Jiang, L. Sampson, and T. Varghese, "Electrode displacement strain imaging of thermally-ablated liver tissue in an *in vivo* animal model," *Med. Phys.* **37**(3), 1075–1082 (2010).
- ¹⁵T. Varghese and H. Shi, "Elastographic imaging of thermal lesions in liver *in vivo* using diaphragmatic stimuli," *Ultrason. Imaging* **26**(1), 18–28 (2004).
- ¹⁶S. Bharat, U. Techavipoo, M. Z. Kiss, W. Liu, and T. Varghese, "Monitoring stiffness changes in lesions after radiofrequency ablation at different temperatures and durations of ablation," *Ultrasound Med. Biol.* **31**(3), 415–422 (2005).
- ¹⁷O. Kolokythas, T. Gauthier, A. T. Fernandez, H. Xie, B. A. Timm, C. Cuevas, M. K. Dighe, L. M. Mitsumori, M. F. Bruce, D. A. Herzka, G. K. Goswami, R. T. Andrews, K. M. Oas, T. J. Dubinsky, and B. H. Warren, "Ultrasound-based elastography: A novel approach to assess radio frequency ablation of liver masses performed with expandable ablation probes: A feasibility study," *J. Ultrasound Med.* **27**(6), 935–946 (2008).
- ¹⁸A. Mariani, W. Kwiecinski, M. Pernot, D. Balvay, M. Tanter, O. Clement, C. A. Cuenod, and F. Zinzindohoue, "Real time shear waves elastography monitoring of thermal ablation: *In vivo* evaluation in pig livers," *J. Surg. Res.* **188**(1), 37–43 (2014).
- ¹⁹T. Varghese, J. A. Zagzebski, P. Rahko, and C. S. Breburda, "Ultrasonic imaging of myocardial strain using cardiac elastography," *Ultrason. Imaging* **25**(1), 1–16 (2003).
- ²⁰E. E. Konofagou, J. D'Hooge, and J. Ophir, "Myocardial elastography—A feasibility study *in vivo*," *Ultrasound Med. Biol.* **28**(4), 475–482 (2002).
- ²¹U. Bae, M. Dighe, T. Dubinsky, S. Minoshima, V. Shamdasani, and Y. Kim, "Ultrasound thyroid elastography using carotid artery pulsation: Preliminary study," *J. Ultrasound Med.* **26**(6), 797–805 (2007).
- ²²A. P. Sarvazyan, O. V. Rudenko, S. D. Swanson, J. B. Fowlkes, and S. Y. Emelianov, "Shear wave elasticity imaging: A new ultrasonic technology of medical diagnostics," *Ultrasound Med. Biol.* **24**(9), 1419–1435 (1998).
- ²³K. R. Nightingale, M. L. Palmeri, R. W. Nightingale, and G. E. Trahey, "On the feasibility of remote palpation using acoustic radiation force," *J. Acoust. Soc. Am.* **110**(1), 625–634 (2001).
- ²⁴S. Catheline, F. Wu, and M. Fink, "A solution to diffraction biases in sonoelasticity: The acoustic impulse technique," *J. Acoust. Soc. Am.* **105**(5), 2941–2950 (1999).
- ²⁵A. Manduca, T. E. Oliphant, M. A. Dresner, J. L. Mahowald, S. A. Kruse, E. Amromin, J. P. Felmlee, J. F. Greenleaf, and R. L. Ehman, "Magnetic resonance elastography: Non-invasive mapping of tissue elasticity," *Med. Image Anal.* **5**(4), 237–254 (2001).
- ²⁶J. E. Lindop, G. M. Treece, A. H. Gee, and R. W. Prager, "3D elastography using freehand ultrasound," *Ultrasound Med. Biol.* **32**(4), 529–545 (2006).
- ²⁷A. Gee, R. Prager, G. Treece, C. Cash, and L. Berman, "Processing and visualizing three-dimensional ultrasound data," *Br. J. Radiol.* **77**(Suppl. 2), S186–S193 (2004).
- ²⁸G. M. Treece, J. E. Lindop, A. H. Gee, and R. W. Prager, "Freehand ultrasound elastography with a 3-D probe," *Ultrasound Med. Biol.* **34**(3), 463–474 (2008).
- ²⁹S. Bharat, T. G. Fisher, T. Varghese, T. J. Hall, J. Jiang, E. L. Madsen, J. A. Zagzebski, and F. T. Lee, Jr., "Three-dimensional electrode displacement elastography using the Siemens C7F2 fourSight four-dimensional ultrasound transducer," *Ultrasound Med. Biol.* **34**(8), 1307–1316 (2008).
- ³⁰H. Rivaz, E. Boctor, P. Foroughi, R. Zellars, G. Fichtinger, and G. Hager, "Ultrasound elastography: A dynamic programming approach," *IEEE Trans. Med. Imaging* **27**(10), 1373–1377 (2008).
- ³¹A. Ingle and T. Varghese, "Three-dimensional sheaf of ultrasound planes reconstruction (SOUPR) of ablated volumes," *IEEE Trans. Med. Imaging* **33**(8), 1677–1688 (2014).
- ³²H. Chen and T. Varghese, "Multilevel hybrid 2D strain imaging algorithm for ultrasound sector/phased arrays," *Med. Phys.* **36**(6), 2098–2106 (2009).
- ³³L. Chen, G. M. Treece, J. E. Lindop, A. H. Gee, and R. W. Prager, "A quality-guided displacement tracking algorithm for ultrasonic elasticity imaging," *Med. Image Anal.* **13**(2), 286–296 (2009).
- ³⁴T. F. Chan and L. A. Vese, "Active contours without edges," *IEEE Trans. Image Process.* **10**(2), 266–277 (2001).
- ³⁵O. Faugeras, *Three-Dimensional Computer Vision: A Geometric Approach* (MIT, Cambridge, MA, 1993), Vol. 10, pp. 817–844.
- ³⁶T. Varghese and J. Ophir, "A theoretical framework for performance characterization of elastography: The strain filter," *IEEE Trans. Ultrason., Ferroelectrics, Freq. Control* **44**(1), 164–172 (1997).
- ³⁷A. Rose, *Vision: Human and Electronic* (Plenum, New York, 1973).
- ³⁸T. Varghese and A. N. Ingle, "Method and apparatus for rapid acquisition of elasticity data in three dimensions," U.S. Patent No. 20,150,330,832, Application No. 14/276019 (19 November 2015).