Non-contrast Doppler Microvessel Image Reconstruction by semi nonrigid Motion Compensation and Localized Clutter filtering; a Qualitative and Quantitative Evaluation

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Abstract—Vascular networks can provide invaluable information about tumor angiogenesis. Ultrafast Doppler imaging enables ultrasound to image micro-vessels by applying tissue clutter filtering methods on the Spatio-temporal data obtained from plane-wave imaging. However, motion is an intrinsic part of microvasculature imaging due to various reasons e.g breathing and vessel pulsation. Part of such a motion is taken care of by using Spatio-temporal cluttering filtering. Nonetheless, the remaining part of the motion who manifests itself as blurring or generating ghost vessels should be corrected using another level of motion compensation. We proposed a robust and computationally efficient motion compensation algorithm for Ultrasound micro-vessel imaging. We successfully evaluated the performance of the algorithm by a simulation study. Finally, we tested the proposed motion compensation method on the in vivo data of microvasculature in different organs including breast and thyroid. Results show blurring and ghost vessel problems are significantly reduced using the proposed algorithm. Moreover, our quantitative assessment demonstrated that image correlation among different frames in Ultrafast Doppler imaging is significantly improved utilizing the proposed motion correction method.

Index Terms—Doppler imaging, small vessel imaging, motion compensation, contrast free imaging.

I. INTRODUCTION

EARLY detection of cancer with minor invasiveness and method availability plays a key role in survival rate. The alteration of cancerous tissue can be studied through the associated vascular network and angiogenesis to assist the accuracy of cancer diagnosis [1]. For instance, the thyroid is a vital organ that affects the metabolic rate and protein synthesis. To evaluate the thyroid for the presence of nodules, High-frequency sonography has been used [2]. However, it cannot be used to differentiate cancerous from benign thyroid nodules. Invasive Fine-needle aspiration biopsy (FNAB) remains the golden standard for the diagnosis of thyroid malignancy even if it has a 1.5–11.5% false-negative rate and an approximately 10% rate of being non-diagnostic [3]. Therefore, there is a persuasive need for a better noninvasive diagnostic method that can help to distinguish between malignant from nonmalignant thyroid tissues. The study of thyroid nodules angiogenesis may provide valuable information on being benign or malignant. Moreover, potential biomarkers for diagnosis of breast cancers the major cause of mortality among women [4] can be extracted via quantification of morphological features of small vessel image [5]. Among the existing methods for visualizing the vascularity of the tumor for breast cancer, non-contrast Ultrafast Doppler imaging equipped with high frame rate plane-wave compounding imaging offers the map of microvascular network with promising sensitivity [6]. Thanks to advances in rank revealing decomposition methods based on the orthogonal transformations such as singular value decomposition (SVD) on the rich spatiotemporal data of power Doppler, two sub-spaces of blood flow and tissue can be distinguished efficiently via a thresholding operation [7-11]. Even though SVD can significantly extend the domain for separation of blood and tissue components, the recovered blood data still inherit the same transformational motion imposed by tissue which will undermine the quality of power Doppler images. Furthermore, motion is an intrinsic part of microvasculature imaging due to various reasons e.g breathing and vessel pulsation. In particular, even in a controlled in vivo set-up, for thyroid nodule microvessel imaging, there are some key factors such as pulsating carotid artery results in generating motion artifact/ blurring and the manifestation of artificial shadow and make the small vessel map reconstruction even more challenging. If the lateral motion is smaller than half of the lateral resolution, Doppler-based motion estimation works well as reported by Poree et al. [12].

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While it is demonstrated that the axial motion compensation alone is not sufficient when the total motion in a lateral direction is large in comparison to the wavelength [13]. In line with the same hypothesis, a motion correction by tracking the positions of the pixels in each low-resolution image was introduced using the synthetic transmits the aperture method similar to the super-resolution imaging paradigm [15]. The standard technique to address the motion correction problem is to compute an upscaled cross-correlation (CC) between two images. Several groups reported the cross correlation based motion correction for preclinical in vivo studies of animal models for contrast-enhanced ultrasound [14]. Those studies included mapping the microvessel of mouse ear to mitigate the breathing artifact [15], imaging an in vivo rat brain [16], and in vivo study on a tumor xenograft-bearing mouse [17] and a two-stage motion algorithm applied to super-resolution US imaging [18]. However, the main drawback of those studies is using an exogenous contrast medium. In vivo, human imaging introduces an additional level of complexity to the thyroid motion during image acquisition as additional complexity that obstructs the precise quantification of the microvascular network for thyroid nodules. To the best of our knowledge, there is only one or few research studies on motion correction of contrast-free ultrasound power Doppler imaging which is on small vessel imaging of human thyroid A cross-correlation based motion correction of the clutter-filtered Doppler ensemble for human thyroid nodules using a spline-based interpolation was reported recently [19]. However, the study is not efficient in terms of time and needs a GPU workflow. Besides, there is no study on motion correction of the in vivo breast data using contrast-free Ultrafast Doppler imaging.

In this paper, we introduced a computationally efficient robust motion compensation algorithm for Ultrasound microvessel imaging. The robustness of the algorithm is a result of being a template-based method at a subpixel resolution. We first present a brief overview of signal separation via a local low-rank approximation and its utility in clutter removal for imaging small vessels. For this purpose, we provide simulation models that closely model tissue and blood motions under different translational and shearing motions. We then introduce a motion compensation algorithm that provides a coherent integration of post-SVD ensembles for the formation of power Doppler-like images. We then present several in vivo examples where the proposed coherent integration method provides significant gain over conventional SVD in recovering small vessels. We successfully evaluated the performance of the algorithm by a simulation study. Finally, we tested the proposed motion compensation method on the in vivo data of microvasculature in different organs including thyroid and breast.

II. MATERIALS AND METHODS

Our proposed motion-compensated method for ultrasound Doppler micro-vessel image is summarized in Figure 1. The method is mainly based on a computationally efficient and robust registration method on the power Doppler image sequence which is obtained using a local SVD clutter tissue removal filter. The evaluation was performed using a simulation study and in vivo ultrasound images of malignant and benign breast lesions, thyroid nodules. The study was approved by the Institutional Review Board (IRB) of Mayo Clinic and was the Health Insurance Portability and Accountability Act (HIPPA) compliant. A signed written informed consent was obtained from all participants before the study. The methods were carried out following the approved guidelines. Details of the methods are given in the following sections.

![Fig.1 schematic diagram of flow for the proposed method](image-url)
A. Data acquisition

We evaluated the performance of the proposed method on in vivo patient data. The data set was reconstructed using breast, thyroid conditions. The focus of study was mainly on the vessel structure within the tumor boundaries. We acquired all in vivo data using an Alpinion Ecube12-R ultrasound machine (ALPINION Medical Systems, Seoul, Korea). The L3-12H linear array (ALPINION Medical Systems, Seoul, Korea) with a centered imaging frequency of 8.5 MHz was used for studying subjects with thyroid nodules and breast lesions. The system provided a sequence of frames at a high frame rate with five-angle compounded ultrasound raw data (at ~600 frames per second) in the form of raw IQ beam-formed data, for a total duration of 3.2 s on the lesion site.

B. Local SVD filtering on the spatiotemporal data

Signal \( s(x, z, t) \) corresponds to tensor \( S \in \mathbb{R}^{N_x \times N_z \times N_t} \), where \( N_x \) and \( N_z \) are the number of spatial samples along the x-direction and z-direction, respectively, and \( N_t \) is the number of samples over time. The data tensor \( S \) is reshaped to form a Casorati matrix by transforming tensor \( S \) into a 2-D spatiotemporal matrix \( S_C \in \mathbb{R}^{(N_x \times N_z) \times N_t} \) to provide information of each frame in one column of matrix. The full plane wave data can be decomposed into local small blocks with arbitrary shapes. In each block tissue signals are assumed to be locally coherent and noise locally stationary. This, in turn, enables the effective separation of tissue, blood, and noise via SVD. These arbitrary shapes can be selected based on the displacement of different regions of the tumor and the sounding area. It is possible to cluster different regions of one microvasculature image based on the clustering displacement of each pixel. Since, displacement tracking of each pixel in an image over time even using fast-displacement tracking algorithms like time delay estimation based on dynamic programming [20] for a large number of frames takes time, limit the real-time application of this method. A simplified version of local SVD is used here, which only considers SVD inside the breast lesion and thyroid nodule areas. This simplification is done based on the hypothesis that the displacement of the tumor is mainly different from displacement of other parts of tissue when ultrasound pulse is applied to that tumor. The block has arbitrary shape the number of elements in each frame is considered \( n_f \), and number of time samples is considered as \( n_t \), in this paper we consider \( n_t = N_t \). The data inside the polygon \( P_L \) is represented by a prism of \( \varrho_L \) over time, which is reshaped to form a local Casorati matrix by transforming prism of \( \varrho_L \) into a 2-D spatiotemporal matrix \( C_L \in \mathbb{R}^{n_f \times n_t} \) to provide information of each frame in one column of matrix. Using singular value decomposition (SVD) of \( C_L \) we have

\[
C_L = U \Delta V^*
\]  

where \( \Delta \in \mathbb{R}^{n_f \times n_t} \) is a non-square diagonal matrix, \( U \in \mathbb{R}^{n_f \times n_f} \) and \( V \in \mathbb{R}^{n_t \times n_t} \) are orthonormal matrices, and \( ^* \) indicates conjugate transpose. Columns of \( U \) and \( V \) matrices correspond to the spatial and temporal singular vectors of \( C_L \). Based on the definition of SVD, matrix \( C_L \) can be decomposed into sum of rank one matrix \( A_i = u_i \otimes v_i \) as follows:

\[
C_L = \sum_{i=1}^{n} \lambda_i A_i = \sum_{i=1}^{n} \lambda_i u_i \otimes v_i
\]  

where \( u_i \) and \( v_i \) are \( i^{th} \) columns of \( U \) and \( V \), respectively. \( \lambda_i \) is \( i^{th} \) ordered singular values of \( C_L \) and \( \otimes \) denotes outer product operation. Each column \( v_i \) is a temporal signal with length \( n_t \). Each column \( u_i \) is spatial signal with dimensionality of \( n_f \). In fact, each vector of \( u_i \) maps to the polygon, which is selected for local SVD, \( I_i \) which is modulated by a temporal signal \( V_i \). Hence, for any pixel inside of polygon, \( P_L \) we have

\[
s_{\text{blood}}(x, z, t) = s(x, z, t) - \sum_{i=1}^{n} \lambda_i I_i(x, z)v_i(t)
\]  

In this paper threshold \( n \) is selected based on setting a threshold on the slope of the second order derivative of eigenvalues decay, as described by Bayat, et al. in [21]. Let us consider \( R_{\text{Blood}} \) be the SVD filtered ultrasound power Doppler sequence. The filtered signal \( s_{\text{blood}}(x, z, t) \) is used to produce the power Doppler image as

\[
I(x, z) = \sum_{n=1}^{N_t} |s_{\text{blood}}(x, z, nT)|^2
\]  

where \( T \) is the sampling time between two successive ultrafast ultrasound frames.

C. Semi-nonrigid motion correction

To compensate for the motion, we divide images after local SVD to \( K \) overlapping patches with size \( P_1 \times P_1 \) pixels
and the number of overlapping pixels are \( q_I \). We register these overlapping patches using the registration of B-mode images. Then after registration first layer, we divide each patch into second layer overlapping patches [22].

### C.I. Initial Displacement Estimation for Patches

In the proposed a method the spatio-temporal data are registered based on calculating the information of shifts from the in phase-quadrature (IQ) data. We applied a Fourier based registration method [23] and aligned every frame alongside a calculated template [24], to improve the precision of image registration. The miss-registration information i.e row and column shifts are calculated for the B-mode plane wave frames and have been employed to compensate for the motion error in US cluttered removed data. For fractional shifts, a frequency domain interpolation is used. Let the plane wave ultrasound sequence be \( S \equiv \{ S_i; t = 1, ..., k \} \), where \( S_i \) is the matrix of each frame and it is given by \( S_i = \mathcal{F}(x_{ij}, t_k) \), sampling locations are represented by the variable \( x_{ij} = [x_i, z_i] \) for lateral; \((x_i)_{i=1...n_x} \) and \((z_i)_{i=1...n_z} \) for axial; and \((t_k)_{k=1...n_t} \) for time. The template \( T_i \) corresponding to a split of the tensor \( S \) over time \( t \) is defined as the median of \( n \) frames locally averaged over selected part of sequence where \( S_i \) belongs but not over the whole sequence and it is given by:

\[
T_i = \left\{ \begin{array}{l}
\text{median}(S_i); \quad n \leq t \leq k \\
S_i; \quad 1 \leq t \leq n
\end{array} \right.
\]

(5)

We minimize the normalized error between frames \( S_i \) and corresponding templates i.e. \( T_i \). The measure of difference between \( S_i \) and \( T_i \) is defined based on a normalized mean square error (NMSE) which is insensitive to multiplicative constant [25] and it is given by

\[
e_{\text{NMSE}}(t) = \min_{\alpha(t), x_0(t), z_0(t)} \left( \frac{\sum_x \sum_z |\alpha T_w(x - x_0(t), z - z_0(t), t) - S_{tw}(x, z, t)|^2}{\sum_x \sum_z |S_{tw}(x, z, t)|^2} \right)^{1/2},
\]

(6)

where

\[
T_w(x, z, t) = T(x, z, t) \ast w(x, z),
\]

(7)

and

\[
S_{tw}(x, z, t) = S_i(x, z, t) \ast w(x, z),
\]

(8)

and

\[
w(x, z) = F^{-1}[W(u, v)].
\]

(9)

The weighting function is selected based on SNR of image over depth. Due to convexity of (6) in terms of \( \alpha \), the optimum phase constant of \( \alpha \) is derived by setting partial derivative of (6) with respect to \( \alpha \) as follows

\[
\alpha(t) = \frac{\sum_x \sum_z S_{tw}(x, z, t)T_{w}^{*}(x - x_0(t), z - z_0(t), t)}{\sum_x \sum_z T_{w}^{*}(x, z, t)}.
\]

(10)

By replacing (10) in (6) and using Parseval’s theorem, we have

\[
e_{\text{NMSE}}(t) = 1 - \frac{\max_{x_0(t), z_0(t)} |\mathcal{F}(x_0(t), z_0(t), t)|^2}{\sum_x \sum_z |S_{tw}(x, z, t)|^2 \sum_x \sum_z |T_{w}(x, z, t)|^2}
\]

(11)

where

\[
\mathcal{F}(x_0(t), z_0(t), t) = \sum_{u} \sum_{v} \mathcal{F}(u, v, t)T_{w}^{*}(u, v, t)\exp\left[i2\pi\left(\frac{ux_0(t)}{M} + \frac{vz_0(t)}{N}\right)\right]
\]

(12)

\( u \) and \( v \) are spatial frequency, \( S_{tw}(u, v, t) \) and \( T_{w}(u, v, t) \) are discrete Fourier transforms (DFTs) of \( S_{tw}(x, z, t) \) and \( T_{w}(x, z, t) \) which are defined as follows.
\[
S_{tw}(u,v,t) = \sum_{x} \sum_{z} S_{tw}(x,z,t) \exp\left(-i2\pi \left(\frac{ux(t)}{M} + \frac{vz(t)}{N}\right)\right) \\
T_{tw}(u,v,t) = \sum_{x} \sum_{z} T_{tw}(x,z,t) \exp\left(-i2\pi \left(\frac{ux(t)}{M} + \frac{vz(t)}{N}\right)\right)
\]  

(13)

(14)

where \(M\) and \(N\) are image dimension in \(x\) and \(z\) direction, sparse matrices multiplication method based on fractional Fourier transform paradigm in a 1.2-pixel neighborhood is used for performing DFT [26] and the data were initially up sampled by factor of \(\alpha = 1.5\). The subpixel registration is then performed by fining the peak in an array with size of \((1.2\times, 1.2\times)\) pixels. The translation estimate then is refined. In a semi-nonrigid motion correction manner, each frame split into set of overlapping blocks with determined dimension and register against the template (which is updating every \(n\) frames). The final motion corrected image is then generated by interpolating all registered sub-blocks. Estimated [18, 27, 29].

C_II. Tuning Displacement Estimation for Patches

The estimated displacement of \(x_0(t)\) and \(z_0(t)\) are used for registration of first layered patches in tensor of blood images with size of \(P_1 \times P_1\). The tensor of blood image sequence be \(S_b = \{S_{0i}; t = 1, ..., k\}\), where \(S_{0i}\) is the matrix of each frame of blood and it is given by \(S_{0i} = S_b(x_{1i}, t_k)\). Then the output tensor is used for second layer registration of blood image tensor. In the second layer registration initial size of patches is \(P_1 \times P_1\) and registration will be performed for all patches with this size. Table 1 shows steps of registration algorithm.

C_II. Quality Assessment metrics

The spatio-temporal data are registered based on calculating the information of shifts from the in phase quadrature (IQ) data i.e., users observe the data (or a temporally down sampled version of it) before and after registration to assess the outcome of the registration. This makes the comparison of different algorithms difficult and subjective especially when applied to real datasets. Here, we use a series of simple metrics to quantify the performance of different algorithms.

-To evaluate the results of the motion correction algorithm across the different frames, we use a metric that is based on the similarity (pixel-wise, Pearson's correlation coefficient) between the mean image across time and each individual frame. Intuitively, an increase in the correlation coefficient for a given frame indicates a better alignment with the mean. Similar metrics have been used before for assessing the quality of registration algorithms in the context of other imaging modalities [28]. To account for border effects during registration, a number of pixels around each boundary (e.g., equal to the maximum shift in each direction over time) is removed prior to computing the correlation coefficients.

| TABLE I. Units for Pseudo code of iterative algorithm for registration. |
|-------------------------------------------------------------|
| **Initialization**                                         |
| Set \(K, P, q_0\)                                          |
| Estimate \(s_0(t), x_0(t), z_0(t)\) using (1) from prism of \(g\) |
| For \(k = 1\) to \(K\)                                    |
| \(i = 0\)                                                  |
| while \(|TF_{kt}| < \text{THR}\) do                         |
| \(1. k^{th}\) cube of \(S_{0i}\) \(\leftarrow\) Register \(k^{th}\) cube from tensor of \(S_{0i}\) with size \(P_1 \times P_1\) |
| and overlapping \(q_i\) pixels window using \(s_0(t), x_0(t), z_0(t)\) from tensor |
| \(2. TF_{ki} \leftarrow\) Estimate tensor flow in \(k^{th}\) patch at \(i^{th}\) iteration |
| \(3. i = i + 1\)                                          |
| \(4. \) Estimate \(s_{0i}(t), x_{0i}(t), z_{0i}(t)\) using (1) for \(k^{th}\) tensor at \(i^{th}\) iteration |
| \(5. P_i \leftarrow f(K, P_{i-1}, g_{i-1})\)             |
| \(6. q_i \leftarrow g(K, P_{i-1}, g_{i-1})\)              |
| end                                                        |

The mean correlation metric can be used to identify frames where the registration is successful or not, or to compare different motion correction algorithms at the level of individual frames. The correlation coefficient (CC) between \(S_{0i}(x, z, t)\) and \(I(x, z)\) is defined as
\[ CC(S_t, I(x, z)) = \frac{\sum_x \sum_z \left( S^2_t(x, z, t) - \overline{S^2_t}(t) \right) \cdot (I(x, z) - \overline{I})}{\sqrt{\sum_x \sum_z \left( S^2_t(x, z, t) - \overline{S^2_t}(t) \right)^2} \cdot \sqrt{\sum_x \sum_z (I(x, z) - \overline{I})^2}} \]  

(15)

where \( \overline{S^2_t}(x, z, t) \) and \( \overline{I}(x, z) \) are the average values of \( S^2_t(x, z, t) \) and \( I(x, z) \) respectively and are defined as follows:

\[ \overline{S^2_t}(t) = \frac{1}{MN} \sum_x \sum_z S^2_t(x, z, t) \]  

(16)

\[ \overline{I} = \frac{1}{MN} \sum_x \sum_z I(x, z) \]  

(17)

An alternative measure is to quantify how crisp is a summary image before and after registration. This can be done by computing the norm of the gradient field of the image at all pixels. If \( I \) is the summary image then its Conciseness [28] can be defined as

\[ cm(I) = \| \nabla I(x, z) \|_F \]  

(18)

where \( \nabla I(x, z) \) denotes the gradient vector field of \( I(x, z) \) in all directions, \( | \cdot | \) denotes the entry-wise magnitude, and \( \| \cdot \|_F \) denotes the Frobenius norm. Examples of summary images include the mean image and the correlation image (CI).

III. RESULTS

1) Simulation Study

The method presented in [19] was adopted to simulate combined tissue-blood motions. Briefly, tissue motion was modeled as a stochastic flow which was implemented as an affine transformation with both translational and shears components. The mean velocity and maximum shear strain were 0.01. The maximum blood velocity was with a laminar pattern such that the mean blood velocity was half of the maximum velocity Vessel diameter. A multi-angle compounding plane wave imaging with a maximum steering angle of was simulated. The simulation was performed to acquire 3 seconds of complex raw data. Additive white Gaussian noise was added to the blood+tissue echo to create a signal to noise ratio (SNR) of 20dB. Fig. 2(a) shows a power doppler image of the vessel after SVD clutter filtering without inducing motion, which is called ground truth image. In Fig. 2(b) motion is induced to power the Doppler image of Fig.2(a). Fig. 2(c) shows the power doppler image of Fig.2(b) after the semi non-rigid motion-corrected image. Qualitatively, it can be seen Figs 2(a) and 2(c) are similar which indicates the motion correction algorithm is working well. Fig. 2(d) compares the CC in (11) for ground truth, power doppler image with motion, and semi non-rigid motion-corrected image for a different number of frames. It is obvious the correlation coefficient of semi non-rigid motion-corrected image is enhanced in comparison with the motion-induced image and converges to that of the ground truth image. Fig. 2(e)-(f) show the corresponding binary images of Fig. 2(a)-(c), it is evident that the vessel diameter of Power doppler image with induced motion, i.e. Fig. 2(c) has more fluctuations in comparison with the vessel diameter of Power doppler images of ground truth and semi non-rigid motion-corrected images in Fig. 2(d) and (h). Finally, Fig. 2(h) compares estimated vessel diameter from images in Fig.2(e) – (g), it can be observed that the mean and standard deviation of estimated vessel diameter of images in Fig. 2(e) and (f) are similar, while it is significantly different for Power doppler image with induced motion.
2) Evaluation performances on in-vivo clinical data

We also evaluated the performance of the proposed method on the in vivo data from patients with breast lesions and thyroid nodules. The data sets were reconstructed using breast lesion and thyroid nodules conditions including benign and malignant. The focus of the study was mainly on vessel structure within the benign nodule/tumor boundaries applying local SVD. Experiments were approved by the Mayo Clinic Institutional Review Board (IRB). Before our study, all subjects signed the IRB-approved consent forms. We acquired all in vivo data using an Opinion Ecube12-R ultrasound machine (OPINION Medical Systems, Seoul, Korea) equipped with an L3-12H linear array (ALPINION Medical Systems, Seoul, Korea) with a centered imaging frequency of 8.5 MHz. The system provided a sequence of frames at high frame rate with 5-angle compounded ultrasound raw data (at ~600 frames per second) in the form of raw IQ beamformed data for a total duration of 3.0 seconds on the lesion site. Fig. 3(a) and (b) show the SVD clutter filtered image of malignant breast lesion before and after semi non-rigid motion correction. Fig. 3(c) compares the Correlation coefficient in (15) for SVD clutter filtered images in Fig. 3(a) and (b) for different frames, it is evident that the CC is increased after using semi non-rigid motion correction. Fig. 3(d) compare norms of gradient i.e. $cm$ defined in (18) for images in Fig. 3(a) and (b), it is obvious that after motion correction, $cm$ significantly increased which means the edges of vessels are preserved better after motion correction. Fig. 3(e) and (f) show a larger view in region A of Fig. 3(a) and (b), it is obvious that after motion correction double vision in the vessel is disappeared after motion correction (see Fig. 3(f)). Fig. 3(g) and (h) show a larger view in region B of Fig. 3(a) and (b), it is obvious that the flattening of vessels and double vision of the vessel is disappeared in Fig. 2(h).
Fig. 3. SVD clutter filtered image of malignant breast lesion (a) before correction (b) after semi non-rigid motion correction (c) Correlation coefficient in (15) for semi non-rigid motion corrected image and original image (d) norm of gradient in original image and semi non-rigid motion corrected image. (e) SVD clutter filtered image in region A (f) semi non-rigid motion corrected image in region A (g) SVD clutter filtered image in region B (h) semi non-rigid motion corrected image in region B.

Fig. 4(a) and (b) show the SVD clutter filtered image of benign breast lesion before and after semi non-rigid motion correction. Fig. 4(c) compares the CC in (15) for SVD clutter filtered images in Fig. 4(a) and (b) for different frames, it is evident that the CC is increased after using semi non-rigid motion correction. Fig. 4(d) compare norms of gradient i.e. $cm$ defined in (18) for images in Fig. 3(a) and (b), it is obvious that after motion correction, $cm$ significantly increased which means the edges of vessels are preserved better after motion correction. Fig. 4(e) and (f) show a larger view in region A of Fig. 3(a) and (b), it is obvious that after motion correction flattening of the vessel is disappeared after motion correction (see Fig. 4(f)).

The first and second columns in Fig. 5 show the SVD clutter filtered images of thyroid nodules before and after semi non-rigid motion correction, respectively. The third column in Fig. 5 compare the CC in (15) for SVD clutter filtered images in the first and second column of Fig. 4 and (b) for different frames, it is evident that the CC is increased after using semi non-rigid motion correction. The fourth column of Fig. 4 compares norms of gradient i.e. $cm$ defined in (18) for images in first and second columns of Fig. 5, it is obvious that after motion correction, $cm$ significantly increased which means the edges of vessels are preserved better after motion correction.
Fig. 5. SVD clutter filtered image of thyroid nodule (a, c, i, m, q, u) before registration (b, f, j, n, r, v) after semi non-rigid motion correction (c, g, k, o, s, w) Correlation coefficient in (15) for semi non-rigid motion corrected image and original image (d, h, l, p, t, x) norm of gradient in original image and semi non-rigid motion corrected image.

Fig. 6. (a) Average gradient of vasculature image before and after registration for different thyroid nodules. (b) Normalized increment of gradient in percent for different patients.
VI. DISCUSSIONS AND CONCLUSIONS

Non-contrast vascular imaging using high frame rate plane-wave imaging and tissue clutter removal techniques can play a major role in the visualization of neovascularization in tumors. However, a part of physiological motion caused by reasons such as breathing, and vessel pulsation or sonographer movement remains after clutter filtering and it can obstruct the small vessels and degrade image quality. The overall objective of our study was to develop a robust fast computationally efficient motion compensated framework for Doppler micro-vessel imaging. The robustness of the algorithm is a result of being a template-based method at a subpixel resolution. We successfully evaluated the performance of the algorithm by a simulation study. Moreover, we tested the proposed motion compensation method on the in vivo data of microvasculature in different organs including breast and thyroid. Results show blurring and ghost vessel problems are significantly reduced using the proposed algorithm. Our quantitative assessment demonstrated that image correlation among different frames in Ultrasound Doppler imaging is significantly improved utilizing the proposed motion correction method. This multi-stage motion correction pipeline was developed based on the assumption that the motion is heterogeneous. While this semi-nonnrigid and a patch-based algorithm can be considered almost a nonrigid motion compensation, some other factor such as deformable shape which is variable during data acquisition and between should be considered. We performed a simulation study to prove the concept of the proposed algorithm and obtained desirable outcomes. We also showed pathological cases in which the motion-compensated algorithm took care of the major visual signature of the given pathologic angiogenesis. Despite compelling results for the in vivo experimental dataset where the ground truth was unknown, the outcome of the method cannot be optimal. To improve upon these results, a further investigation should be conducted based on using another imaging modality like microCT, which can more precisely estimate and can fine-tune the algorithm parameter. The preliminary qualitative and quantitative results presented here suggest that the proposed motion correction algorithm is effective and can also be used for further analysis such as vessel quantification.

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