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Noninvasive Two-Dimensional Strain Imaging of Atherosclerosis: A Preliminary Study in Carotid Arteries *In Vivo*

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Abstract

Atherosclerosis remains a major cause of mortality all over the world and the sudden rupture of atherosclerotic plaque is the most important assassin. Vascular ultrasound elastography has shown promise in estimating the elastic properties to evaluate the plaque vulnerability. Contrary to intravascular elastography, noninvasive applications use a transcutaneous ultrasound transducer that is inexpensive, re-useable and convenient. To estimate the strain map, we employ a cross-correlation method in complex field to extract both the magnitude and phase messages of the ultrasound RF-echo signal. Two-dimension noninvasive carotid elastography was studied in atherosclerotic rats and New Zealand Rabbits and also in healthy volunteer, and the results indicate huge potential for diagnosis of the vulnerability of atheromatous plaques.

Keywords: atherosclerosis; vascular ultrasound elastography; noninvasive; carotid; strain

1. Introduction

With the approach of aged society and the acceleration of aging, atherosclerosis remains a major cause of mortality all over the world, and the sudden rupture of atherosclerotic plaque, which generally occurs in certain atherosclerotic lesions known as rupture-prone or vulnerable plaques, is perhaps the most important factor that should be in charge of the Acute Coronary Syndrome (ACS) [1, 2]. Pathological studies shown

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that the vulnerable plaque has been associated with several pathologic features including a thin fibrous cap (<65um or ≤3 layers of cells) covering a large lipid core (more than 30%~40% proportion of plaque), and increased inflammatory cell infiltration within the cap [3, 4]. Detecting the composition and morphology of a rupture-prone plaque is thereby very important and, however, a big challenge. Over the last several years, ultrasonic elastography has shown promise as a technique to determine plaque composition and morphology based on the difference in tissue stiffness [5-7].

Studies shown that atherosclerosis in the carotid artery are related to the diseases of coronary arteries, the aorta and the arteries of the lower extremities, and carotid atherosclerosis also predicts coronary heart disease and cerebrovascular disease in a strong and graded manner [8, 9]. Because the carotid artery is a superficial artery, it's well suitable for noninvasive ultrasound elastography and it has been studied in phantoms and rats [9, 10] and in patients in the longitudinal direction [11]. For noninvasive vascular elastography of an atherosclerotic plaque, the deformation of lesions induced by the periodic variation of blood pressure is surveyed by transcutaneous ultrasonic imaging system. Contrary to the intravascular ultrasound elastography, where the special one-off intravascular transducer is needed to be inserted into the artery [12-14], the transcutaneous ultrasound transducer is inexpensive and re-useable, and is simple and quick operation.

In this investigation, 2D noninvasive carotid elastography is surveyed in atherosclerotic rats and New Zealand Rabbits and also in healthy volunteer. We employ a cross-correlation method for accurately tracking the displacement (deformation) filed using both the magnitude and phase of the ultrasound radio-frequency signal.

2. Materials and methods

2.1. Atherosclerotic Animal model

Four rats and eight New Zealand white rabbits were included in this study. The animals were fed a high cholesterol diet (21% fat and 0.15% cholesterol, radiation sterilization, provided by Guangdong medical laboratory animal center) for at least eight weeks prior to study. Before the experiment, the animal hairs in the carotid region were removed for benefit at the ultrasonic detection. The experimental procedure involved scanning the carotid artery with B-mode ultrasound imaging to trace the atherosclerotic regions (i.e. the region of interest, ROI) and then collecting the ultrasonic radio-frequency (RF) signals in the longitudinal section of the ROI for elasticity reconstruct with RF mode of the ultrasound system. After the noninvasive ultrasound detection, the animals were sent to pathology laboratory for pathology analysis.

2.2. Experimental Setup and Data acquisition

Ultrasound B-mode images and raw RF data were acquired with a VisualSonics Vevo 770® High-Resolution Imaging System equipped with an RF interface, and the sample frequency of the system was 250MHz. Rat experiments were done using an array transducer with a central frequency of 17.5MHz for B-mode imaging and 21MHz for RF data acquisition. The electrocardiogram (ECG) was record simultaneously during the RF signals investigation, and three neighbouring cardiac cycles were selected to match the RF data to compute the diastole and systole strains. The New Zealand white rabbits were studied using a single element transducer with frequency of 30MHz, and the Pulse Repetition Frequency (PRF) was 100Hz and each frame of picture included 100 lines, altogether 100 frames were acquired.

2.3. Estimation of strain with autocorrelation method in complex domain

The deformations of vessel wall induced by periodic heart beat introduce time-shifts in the received RF-echo, and they are varying from the sub-sample range to a few samples of the RF-echo. It is necessary to obtain the micro shifts that are smaller than the RF-echo sampling interval so that we can get accurate displacement estimates. Several approaches of autocorrelation techniques for time-shifts estimation have

been described in the literature [15, 16]. In this study the micro shifts are estimated using the phase information of two subsequent frames of the RF-echo based on 2-D autocorrelation in complex field. The two dimensions studied in this work are axial and longitude.

The ultrasound RF signal can be represented by $S(h,l,t_n)$, where h is the index along the axial direction, l is the index along the lateral direction (longitude), and t_n is the frame index. The complex analytic signal along the axial direction can be obtained as follows:

$$\tilde{S}(h,l,t_n) = S(h,l,t_n) - j\breve{S}(h,l,t_n) \tag{1}$$

$$\breve{S}(h,l,t_n) = S(h,l,t_n) * H(h) \tag{2}$$

where the symbol $*$ represents convolution and $H(h)$ is FIR Hilbert transformation operator. The 2D complex auto-correlation function at time (frame number) t_n is then defined as follow:

$$\tilde{R}(h_c,l_c,t_n) = \sum_{m=-\frac{M}{2}}^{\frac{M}{2}-1}\sum_{n=-\frac{N}{2}}^{\frac{N}{2}-1} \tilde{S}(h+m,l+n,t_n) \bullet \tilde{S}^*(h+m+q,l+n,t_n+1) \tag{3}$$

where M and N represent the observation window that includes M samples along the axial direction and N samples along the lateral direction, and $q = -Q:1:Q$ where Q represents search length; the superscript * denotes complex conjugation.

If the time-shifts of the ultrasound RF-echo caused by deformation of the vascular wall are bigger than the sampling period t_s, the time-shifts could be acquired by the index of the peak of the magnitude of the auto-correlation and the search length:

$$\breve{\delta t}(h,l,t_n) = [h_{c\max} - (Q+1)] \cdot \frac{1}{f_s} \tag{4}$$

where $h_{c\max}$ represents the max value index of the cross-correlation coefficients $\tilde{R}(h_c,l_c,t_n)$ along the axial direction, and $f_s = 1/t_s$ is the sampling frequency.

With regard to the micro time-shifts which are smaller than t_s, they could be computed by the phase information involved in the cross-correlation coefficients:

$$\hat{\delta t}(h,l,t_n) = \frac{2\angle\tilde{R}(h_{c\max},l_c,t_n)}{\angle\tilde{R}(h_{c\max}+1,l_c,t_n) - \angle\tilde{R}(h_{c\max}-1,l_c,t_n)} t_s \tag{5}$$

where the symbol $\angle$ denotes the angle operator, i.e., $\angle(a+jb) = \arctan(b/a),\ a,b \in R$. The total time-shifts then can be acquired as

$$\delta t(h,l,t_n) = \breve{\delta t}(h,l,t_n) + \hat{\delta t}(h,l,t_n) \tag{6}$$

Then the displacement field can be estimated by the time-shifts and velocity of ultrasound in tissue:

$$\delta d = \delta t \cdot \frac{c}{2} \tag{7}$$

Finally, strain in the axial direction is estimated from the displacements as:

$$st(h,l,t_n) = \frac{\delta d(h+\Delta h,l,t_n) - \delta d(h,l,t_n)}{\Delta h \cdot t_s \cdot \frac{c}{2}} \tag{8}$$

where Δh is defined as the strain sample points and is one of the main factors determining the strain image resolution [17].

3. Results and discussion

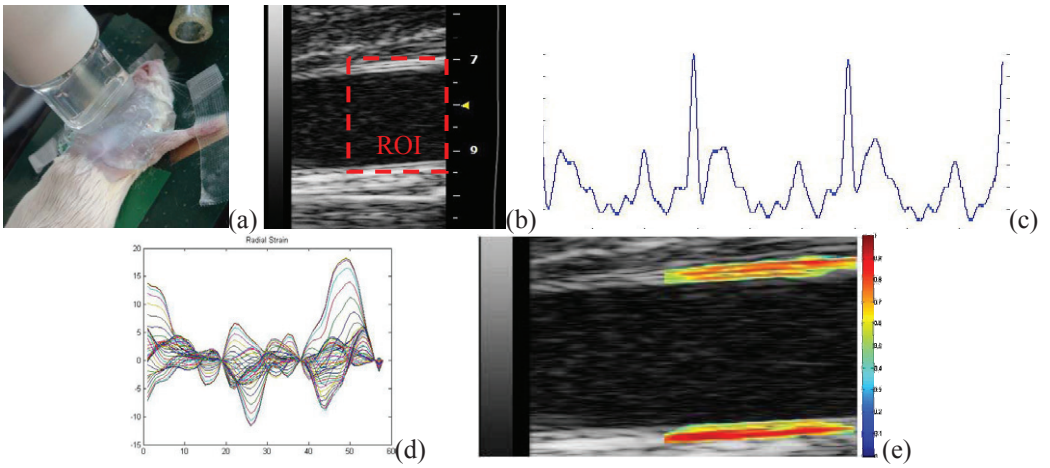

Fig. 1. The carotid experiment of rat model (a) to obtain (b) B-mode image and (c) three neighbouring cardiac cycles were selected to match the RF data to compute the diastole and systole strains of the ROI marked in (b), and the axial strain lines of some points in ROI were shown in (d), and (e) represents the strain map fused with the B-mode image.

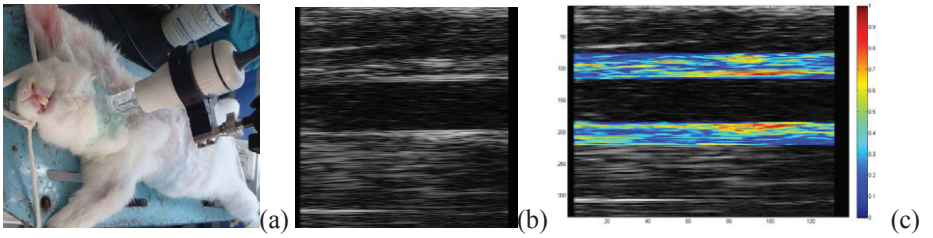

Fig. 2. The carotid study of New Zealand white rabbits (a) to obtain (b) B-mode image and (c) fused with strain map.

Figure 1(b) and figure 2(b) represent the B-mode ultrasound images of a longitudinal section of an atherosclerotic rat's and New Zealand white rabbit's carotid respectively. The region of interest (ROI) marked in the picture figure 1(b) was selected to estimate the diastole and systole strains as shown in figure 1(d), and the ECG was record simultaneously during the RF signals obtaining and three neighbouring cardiac cycles as shown in figure 1(c) were employed to match the RF data. From the B-mode images we can find that the vessel wall is smooth and of course there is no stenosis, which would be diagnosed as health status in clinical. Actually, based on B-mode ultrasound imaging system the calcific and fibrous plaques can be classified with high sensitivity and specificity [18], but it is helplessness in diagnosing lipid plaque which is formed at an early stage of atherosclerosis and always has smooth vessel wall and no lumen narrow, and it is noteworthy that the lipid plaque is generally considered as unstable, i.e. the vulnerable plaque [19, 20]. Scholar H. Kanai and H. Hasegawa and et al. [11] has been pointed out that the elastic modulus of lipid (about 81 ± 40KPa) is more less than that of smooth muscle and collage fiber (about 1.0 ± 0.63MPa). As the deformation or strain is inversely proportion to the elastic modulus, the big value (corresponding to color map) in strain map as shown in figure 1(e) indicates that there indwells a large amount of lipid in the vascular wall, which implies the ROI is not health anymore.

The similar case can be seen in figure 2(b) and figure 2(c). The strain map indicates that the strain of healthy vessel is well-distributed and relatively small, whereas the lipid tissue has a heterogeneous and

larger strain which can be considered as a defining characteristic of lipid plaque or the early stage of atherosclerosis.

Figure 3 shows the study of human carotid in a healthy volunteer. The results are consistent with the above analysis and give a moderate uniform strain map.

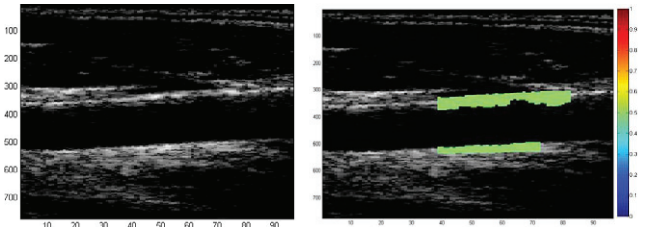

Fig. 3. Ultrasound B-mode image of a longitudinal section of human carotid and embedded strain map in healthy volunteer.

4. Conclusion

Two-dimension noninvasive carotid elastography was studied by transcutaneous ultrasonic imaging system in atherosclerotic rats and New Zealand Rabbits and also in healthy volunteer. The approach of estimation of strain based on autocorrelation method in complex domain was employed for accurately tracking the deformation using both the magnitude and phase information of the ultrasound radio-frequency signal and this technique was chosen because it provides good performance when estimation time-delays smaller than the sampling period. This preliminary study offers potential for diagnosis of the vulnerability of plaque in a clinical setting. Further investigation will be carried out to improve the sensitivity and specificity of the noninvasive vascular ultrasound elastography.

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