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Silicone phantom validation of breast cancer tumor detection using nominal stiffness identification in digital imaging elasto-tomography (DIET)

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ABSTRACT

Background and objective: Cancerous tumors exhibit considerably higher stiffness than healthy breast tissues. This research develops a hysteresis loop analysis detection method for breast cancer diagnosis, which is validated using silicone phantom tests to provide an initial proof of concept of the overall DIET diagnostic approach.
Methods: Steady state sinusoidal displacements induced by mechanical actuation are captured using the DIET system for 4 silicone breast phantoms (1 homogeneous "healthy"; 3 with 10–20 mm stiffer inclusion "tumors" at different locations). Hysteresis loops for each measured reference point on the breast surface (N≈14,500/phantom) are constructed from the measured displacements and a calculated mass normalized restoring force. The distribution of nominal elastic stiffness over breast surface is estimated using a hypothesis test and regression analysis. A small motion threshold, Δd, is used to reduce errors in identified elastance and its values determined from sensitivity analysis.
Results: Sensitivity analysis shows displacement reconstruction errors from very small motions can be eliminated using a threshold $\Delta d = 6\,\mu$m to clearly reduce errors in identified nominal elastance. Results for all 4 phantoms indicate stiffer inclusions induce a greater number of reference points with stiffness $\geq 2\times$ higher in the segment with the inclusion than the nominal stiffness in the "healthy" segments in the x, y and total net 2D displacement directions. Therefore, the presence of a stiffer "tumor" inclusion is automatically detected and located by comparing the nominal stiffness to a calculated threshold, k_t. Inclusion segments are finally localized algorithmically using an inclusion indicator, K_{index}.
Conclusions: The overall results validate the capability of the proposed method to accurately detect and locate a stiff inclusion in typical, representative silicone breast phantoms without misidentifying other regions or a healthy no-inclusion phantom in the non-invasive DIET system. The methods are entirely generalizable to human clinical data from a DIET system, and the results justify such clinical trials.

1. Introduction

Breast cancer is a severe international health problem. Over one million women are diagnosed annually and it causes over 400,000 mortalities [1]. Successful early detection provides a means to reduce mortality [2], where a tumor size of 10–14 mm at first detection has been shown to lead to 15-year survival rates of over 85% [3].

The current standard screening technique is X-ray mammography. Mammography causes patient discomfort due to breast compression reducing screening compliance [4], requires radiation exposure limiting the applicable age group [5,6], and is less available in remote areas [7]. In addition, mammography can have low sensitivity as the radio-density of cancerous tissue varies only 5%–10% from healthy tissue, which can lead to false-positive rates up to 24% [8,9]. However, the evident 400%–1000% contrast in elastic stiffness between healthy and cancerous breast tissue [10,11]

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has been recognized for its diagnostic potential in high resolution elastographic breast imaging.

Elastography for breast cancer diagnosis is an imaging modality to identify the differences of elastic properties between the normal and abnormal human tissues. Elastography can be described by three steps: applying mechanical excitation to the tissue, imaging or measuring the tissue response, and calculating mechanical parameters from the measured response for diagnosis. The current successful elastography methods include magnetic resonance elastograpy (MRE), ultrasound elastography and digital imaging elasto-tomography (DIET)[12].

In particular, MRE offers unique information regarding the extent of disease, staging, and recurrence regardless of breast density compared to mammography [13]. However, such methods require a mathematical inversion algorithm incorporating complex boundary conditions, tissue anisotropy, and nonlinearity, to reconstruct the elastic properties in 3D volume [12,14–16], which is thus computationally expensive [17,18] and can suffer identifiability issues [19]. In addition, the specificity of the MRE technique can also be a problem leading to a numerous false positives and unnecessary biopsies [20]. Finally, MR imaging equipment is still too expensive and time consuming as a practical screening tool for general population. Ultrasound elastography (UE) identifies stiffer regions by measuring the relative speed and attenuation of ultrasound through tumors and healthy tissue, and is less expensive and widely used [20,21]. However, it is a highly operator-dependent measurement in terms of controlling probe pressure and acoustic window [20,22,23], which thus increases the potential cost of diagnostic operation.

Digital Image Elasto-tomography (DIET) is a non-invasive and low-cost breast cancer screening approach [21,24–27]. In the DIET system, steady-state, low amplitude sinusoidal motion of the breast volume is mechanically actuated with an amplitude of 0.5 mm. Cameras arranged in a ring capture 2D images of the breast surface at 10 points in the sinewave (every 36°) over a full vibration cycle. The cameras and actuator are synchronized by strobing a set of LEDs at specific phases in the cycle. Consecutive sets of 2D images are converted into a 3D description to measure the surface displacement of each reference point between frames [21,28]. The DIET system is intended to be compact and can be easily deployed, event in remote areas, where people have little access to the breast cancer screen facilities [27]. The DIET system is focusing on measuring the surface displacement of the breast subject rather than the response of the full volume as the MRE and UE require, which thus highly reduce the potential computational complexity and cost. In addition, the measured displacement can be directly used as input signal to an automatic identification algorithm for calculating elastic properties for cancer diagnosis, which could thus enable an automatic implementation of the overall approach. Finally, the diagnosis would not require specialist operator and radiologist skills by developing an automatic identification method.

Early detection methods employed with the DIET system include finite element model (FEM) based reconstruction algorithms and modal analysis methods. FEM method applies the three-dimensional amplitude of each reference point's motion in an inverse reconstruction algorithm to generate an elastic modulus distribution with the three-dimensional breast volume for tumor detection [25,26]. However, the inverse reconstruction problem has even greater computational intensity than full volume problems due to lack of data and also requires an expert operator to process the results [26]. Modal analysis identifies stiffer inclusions by how they increase the effective local elastance based on how the inclusion modifies transmission of the sinusoidal shear wave through the breast tissue volume [27,29,30]. The modal analysis approach is computationally inexpensive, and has shown its ability to detect the presence of 10 ~ 20 mm stiffer inclusion in the experimental phantom tests. However, the order of the fitted natural frequency for detection can be shifted due to the change of inclusion size, which thus also require a skilled operator. In addition, the inclusion locations cannot be accurately identified for even 20 mm size of inclusions for some phantoms [27].

In the search for rapid, effective and computationally light solutions, this study develops a practical hysteresis loop analysis based method to identify the nominal elastic stiffness across the surface of the breast. The identification method is applied to 4 silicone breast phantoms with comparable properties to human tissues [27,31] to experimentally demonstrate and validate the feasibility and robustness of this approach. The detection and localization of stiffer inclusions in the breast phantom is achieved by identifying clearly changes of nominal stiffness in the region of inclusion, along with consistent, lower stiffness values in the remainder of the phantom mimicking healthy tissues.

2. Method

2.1. 3D displacement reconstruction of the breast surface

The breast hangs freely in the DIET system while being mechanically actuated with an amplitude of approximately 0.5 mm. The 3D motion of the ~14500 reference points on the breast surface are reconstructed using a set of 5 × 10 images captured by 5 cameras. In particular, the reconstruction process consists of four stages[21]:

(1) Using colour-based segmentation to extract the approximated actuator and breast positions by applying Kadane's 2D maximal Subarray Algorithm [32] to the segmented images. The actuator and breast profiles are then refined using the Levenberg-Marquardt's optimization;
(2) Estimating a 3D parametric model of the breast surface from the segmented images so that the profile of breast model projected back into the images matches the contours detected in the images;
(3) Implementing a modern dense optical flow algorithm [33] for each pair of consecutive frames for every camera to recover the skin surface motion.
(4) Projecting optical flow onto 3D surface model to minimize the projection function to recover the 3D surface motion of each reference points. These reference points provide input for the following DIET diagnostic method.

2.2. Hysteretic response of the breast surface

The dynamic hysteretic behaviour in the horizontal direction for each reference point at the breast surface can be represented using a single-degree-of-freedom (SDOF) model:

$$f_s(v(t), \dot{v}(t)) = -m \cdot \ddot{v}(t) \tag{1}$$

where m is the mass attributed to the selected point, $f_s(v(t), \dot{v}(t))$is the restoring force, and$\ddot{v}(t)$ is the relative acceleration of the reference point to the fixed base in the DIET system. Gravity and input actuation forces are ignored, as they are vertical forces and the equation only assesses stiffness in the horizontal direction. Thus, Eq. (1) can be rewritten:

$$f_s(v(t), \dot{v}(t))/m = k_e \cdot v(t) = -\ddot{v}(t) \tag{2}$$

where $f_s(v(t), \dot{v}(t))/m$ is a mass normalized, generalized restoring force approximated by a nominal or effective stiffness, k_e, and the relative actuated tissue displacement $v(t)$.