Optomechanical Imaging: Biomechanical and Hemodynamic Responses of the Breast to Controlled Articulation

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Abstract:
The biomechanical response of the breast was explored during fine articulation, as a function of the applied force protocol. Comparisons between calculated internal pressure or stress maps and reconstructed hemodynamic images show strong correlations.

Introduction:
There are many instances where the details of blood delivery to tissue and bulk fluid redistribution among the various vascular compartments can be impacted by disease or trauma. For instance, a common phenotype of breast cancer is derangements in hemodynamic states accompanied by increased tissue stiffness and local edema [1].

Motivated by the hypothesis that externally applied mechanical forces can produce distinct dynamic responses among these compartments, we have recently developed working technology as a new approach for assessment of pathology of the breast and other tissues. Principal elements of this technology, referred to as optomechanical imaging [2], include concurrent bilateral measures of the viscoelastic and hemodynamic properties of the breast in response to a wide range of controlled articulation maneuvers. Encouraging evidence was reported of high-contrast tumor detection in response to these maneuvers [2].

To better appreciate the influence that externally applied forces can be expected to have on internal fluid shifts, here we have compared the measured hemodynamic response of the breast to modeled estimates of internal mechanical forces, across a variety of applied articulation maneuvers.

Methods:
Simultaneous bilateral breast imaging was performed using a newly developed optomechanical imaging system described by Al abdi et al. [2]. The described system provides for high optical-density DODT imaging, accommodates a wide range of breast sizes, and simultaneously measures the viscoelastic response of the breast to finely controlled articulations. Fig. 1 shows a photograph of the sensing heads used for data collection and articulation. Fig. 2 shows the 16 articulating elements (AEs) and their classification based on their positions in relation to the breast.

Articulations include:
- Quasistatic full-compression protocols, which involved applying 7.1 N of force to every articulating element (AE); partial compression involved applying similar forces either to the medial-lateral AEs only, or to the cranio-caudal AEs only.
- Creep-compression was implemented by applying force to all AEs and holding this force constant by moving AEs to compensate for any decrease that might result from tissue relaxation.
- Uniaxial compression was implemented by applying force by all AEs and then returning to the initial force level in a short time (20 cycles, 15 cycle).
- Stepwise compression was implemented by increasing the force applied to all AEs by 0.5 N per step, then waiting only 20 s for tissue relaxation prior to the next step.
- Wave-like compression involves applying force to the different AEs in succession, starting with the lateral AEs and progressing to the medial ones, with an interval of 5 s per AE.

Thermodynamic pressure (p) and effective stress (\(\sigma\)) were calculated via a finite element analysis, performed on a homogenous model of breast tissue that has biomechanical properties appropriate for adipose tissue (i.e., Young's modulus = 19 kPa). Poisson’s ratio = 0.495 [3]. The geometric model considered, shown in Fig. 3b, contains 3,008 nodes and 16,761 elements, and represents an approximation to the geometry of a typical breast when placed inside the breast’s imaging sensor.

Mechanical pressure, principal stresses, and principal strains were computed using a nonlinear finite element software called Felix 4 [4]; \(\sigma\) and p were calculated using Eq. (1) and (2).

3D optical image reconstruction was performed using the Normalized Difference Method of Pel et al. [5].

Results:
Axial views of the calculated \(\sigma\) and p, following normalization of each image to its maximum value, are shown in Fig. 4a and 4b, respectively. Corresponding changes in the apparent total hemoglobin responses (\(\Delta Hb\)) derived from measurements taken on a healthy subject, shown in Fig. 5, suggest that the three compression protocols reveal that p is largest at the breast surfaces and decreases rapidly toward the center, while \(\sigma\) tends to increase in moving from the surface toward the breast center. The mechanical and thermal compression creates local maxima in p and \(\sigma\) maps in the medial and lateral regions, while the cranio-caudal compression creates local maxima in p and \(\sigma\) in the cranio-caudal regions. In the full-compression, high p and \(\sigma\) will produce pressure gradients within the breast tissue, which can produce directed blood flow and tissue displacement from high-pressure to low-pressure regions. Similar pressure and hemodynamic response patterns were noticed in the wave-like compression, which is shown in Fig. 5. Hence the direction of blood flow can be controlled by engaging different subset of AEs with different compression force values.

In the creep compression, tissue relaxation produces a decrease in the applied force, which triggers AEs to compensate for this decrease. Fig. 6a shows the average time-dependent movement of all AEs for a 43 year-old, otherwise healthy subject. As shown, the time-dependent deformation is essentially an exponential function.

The force-dependent hemodynamic response to step-wise compression, for the same subject as in Fig. 6a is shown in Fig. 6b. Inspection reveals that the rate of change of \(\Delta Hb\) is higher at low pressure, and this high rate indicates existence of a threshold from vascular compartments having high apparent vascular compliance (e.g., veins and capillaries). On the other hand, this rate decreases at high compression force, which indicates exclusion of blood from vascular compartments of low apparent vascular compliance (e.g., arteries). This force-dependent hemodynamic response was also reported by Capo et al. [8].

An example of the viscoelastic response observed during a quasi-static full-compression is shown in Fig. 8. Four phases are identified: loading, stress relaxation, unloading, and stress recovery.

To produce biomarkers sensitive to breast cancer, the spatial variability across the hemodynamic responses of transmission sensor array was calculated (standard deviation) for the left and right breast (SSD/SSDj). Fig. 8 shows a histogram of the calculated SSD/SSDj for two cancer subjects and a healthy control. As shown, the spatial variability in the affected breast is higher than in the contralateral unaffected breast.

Fig. 9 shows the mean and standard error for SSD/SSDj ratio for breast cancer and benign pathology subjects, and SSD/SSDj for healthy subjects. (See Table 1 for descriptive statistics on subject age and BMI). These ratios were calculated for deoxyhemoglobin (HbDeoxy) during the stress relaxation following mediolateral quasi-steady compression. The cancer group mean is significantly higher than that of the other subgroups.

Summary:
Applying pressure to the breast surface creates a complex heterogeneous pressure distribution within the tissue, and the spatial distribution of these forces is a function of the applied articulation maneuver and the tissue’s mechanical properties. The observation that there is a strong correlation between the measured hemodynamic response and computed spatial distributions of mechanical compression suggests that the simple poroelastic model considered [Eqs. (1,2)] can serve as a useful guide to predicting expected hemodynamic responses. A wide range of differential responses that serve to discriminate healthy from diseased breasts can be derived from hemodynamic responses during mechanical provocations.

References:

Acknowledgements:
This research was supported by the National Institutes of Health (grant 1R01CA130597) and the U.S. Army Grant DOD-MDAD-04-3-0013 through the Biomedical Engineering Training Program. The New York State Foundation for Science, Technology, and Innovation Technology Transfer Initiative Program (NYSTAR) and Multimodal Technologies International (MTI) also aided the technology transfer process.

Table 1: patient clinical information

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<thead>
<tr>
<th>Group</th>
<th>Age (y)</th>
<th>BMI</th>
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<tbody>
<tr>
<td>Cancer</td>
<td>56 ± 10.8</td>
<td>34 ± 0.8</td>
</tr>
<tr>
<td>Healthy</td>
<td>25 ± 4.8</td>
<td>34 ± 0.8</td>
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