33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Palpation Nonlinear Reaction Force Analysis for Characterization of Breast Tissues

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Abstract— **This paper addresses a diagnostic palpation system based on the measurement of nonlinear elasticity. An indentation probe is used to press against breast tissue. Then, the measured reaction force is used to estimate the parameters of nonlinear elasticity, which enables the identification of tissue type, such as fat, muscle, mammary gland or tumor. Here, we present the basic concept of our study and preliminary experimental and simulation results from pilot studies. More specifically, we measured the nonlinear response of reaction force using the breast of a goat. In addition, we also simulated the reaction force using nonlinear biomechanical simulation with several tissue types. Large differences in reaction force occur only in the nonlinear range in both experimental and simulation situations. Our results confirmed the feasibility of our concept.**

I. Introduction

BREST cancer accounts for more than 1 million of the estimated 10 million malignancies diagnosed worldwide each year. In recent years, early detection of breast cancer has been possible because of advances in imaging technology. However, it is difficult to locate the exact position of a tumor and to make a definite diagnosis by palpation or imaging. In addition, invasive examinations such as biopsy are needed to diagnose whether a breast tumor is benign or malignant. Non-invasive and accurate diagnostic techniques are, therefore, desired to achieve accurate diagnosis and to alleviate the patient's mental burden.

The stiffness of malignant tumors has traditionally been qualitatively measured based on palpation by doctors. Many studies have reported systems for tissue characterization and for locating exact tumor position based on palpation. In particular, elastography imaging technologies have been explored. Elastography requires the induction of motion within the target tissue by an external force and conventional medical imaging modalities are used to measure tissue deformation, from which mechanical properties can be reconstructed.

There are limitations in the present elastography protocols. Elastography imaging typically provides contrast in linear stiffness under the assumption of very small deformations. It is actually very difficult to measure nonlinear properties using large deformations. On the other hand, tissues generally exhibit homogeneous, nonlinear, anisotropic elastic and viscous behaviors [1]. Krouskop et al. [2], Wellman et al. [3] and Samani et al. [4] measured the stiffness properties of breast tissues. These papers reported that breast tissue exhibits strong nonlinear properties. More specifically, tissues under low stress exhibit linear properties, but stiffness increased in tissues under high stress. The authors have also reported the measurement of nonlinear elastic properties of breast soft tissues, such as fatty tissue, muscles and mammary glands [5]. They reported that there are large differences in the magnitude of nonlinear elasticity among breast tissues, while differences in elastic properties in the linear range are small.

The goal of this study is to develop a diagnostic palpation system to identify the location of each tissue based on the measurement of nonlinear elasticity. Figure 1 shows our system concept. The indentation probe presses against breast tissue to the extent that the strains of breast tissue become large and such that nonlinear properties are exhibited. Then, the measured reaction force is used to estimate the parameters of nonlinear elasticity. The type of tissue, such as fat, muscle, mammary grand or tumor is identified by the estimated parameters of nonlinear elasticity. In addition, we consider that nonlinear elasticity measurement can be an effective method for the identification of tumor type because Krouskop et al. [2] have shown that nonlinear elasticity of malignant tumor is larger than that of benign tumor.

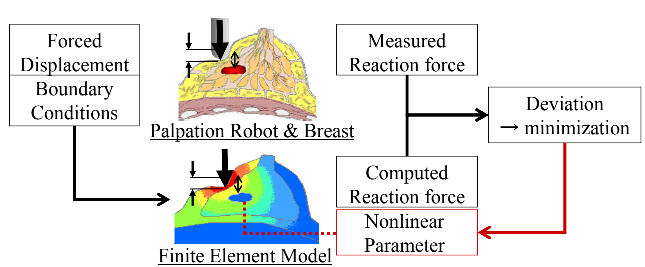

Fig.1. The conceptual scheme of our palpation method.

Manuscript received April 15th, 2011. This work was supported, in part, by the Global COE Program "Global Robot Academia" from MEXT (Ministry of Education, Culture, Sports, Science and Technology of Japan), a High-Tech Research Center Project from MEXT, a Grant-in-Aid for Scientific Research from MEXT (no. 22360108 and 22103512), a Waseda University Grant for Special Research Projects (no. 2010B-177) and Cooperative Research Project of the Institute of Development, Aging and Cancer, Tohoku University.

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It should be noted that there are some studies in the field of elastography addressing nonlinear elasticity. For example, Hall et al. present a system for nonlinearity imaging by 1% incremental strain [6]. Nitta et al. have described nonlinear elasticity parameter estimations for kidney phantom [7]. Wang et al. present an elastography method for reconstruction of nonlinear breast tissue properties and for simulation investigation [8]. These papers propose methods to identify nonlinear parameters but experimental evaluation with actual animal tissues were not conducted [7] [8]. Hall et al. [6] reported experiments and evaluation with actual tissue, although the experiment was conducted with only small displacements. In short, tissue characterization using analysis of nonlinear reaction force with large deformation has not been conducted.

The objective of the present paper is to investigate the basic concept of our study using preliminary experimental and simulation studies. More specifically, we used goat breast to measure the reaction force in response to large deformation. In addition, we also simulated the reaction force using nonlinear biomechanical simulation in several tissue types. The feasibility of our concept, tissue identification based on nonlinear properties of tissues, is discussed.

II. Method

A. Experiment

In this section, we describe the conditions under which the in vivo experiment was conducted. The method was performed using a test apparatus implanted in the breast of a goat. We intended to measure the reaction force from two indentation points in which the ratio of tissues (fats and mammary gland) are different under each point. The experimental details are described below (Fig. 2).

1) Ethical issues: All animals received humane care in accordance with "The Guidelines for the Care and Use of Laboratory Animals" published by the National Institute of Health (NIH publication 85-23, revised 1985), "The Guidelines for Proper Conduct of Animal Experiments" formulated by the Science Council of Japan (2006), and the guidelines determined by the Institutional Animal Care and Use Committee of Tohoku University.

2) Experimental setup: A goat breast was used for in vivo experiments. The goat was placed supine as shown in Fig. 2. In humans, the sternum is located under the breast, which acts as a stiff boundary (refer to Fig. 3). Unlike humans, goats have no sternum under their breast. As a boundary condition, considering the effect of the sternum in humans, we set the dorsal area of the goat breast as the fixed boundary by inserting a metal plate as shown in Fig. 3.

3) Experimental apparatus: The experimental manipulator has one degree of freedom of linear movement by an actuator. A force sensor (NANO 1.2/1, BL AUTOTEC) and a 7 mm diameter indentation probe were attached to the manipulator as shown in Fig. 2. We calculated the moving distance of the probe from the value of the encoder attached to the motor. The reactive forces exerted on the probe were sampled by the force sensor.

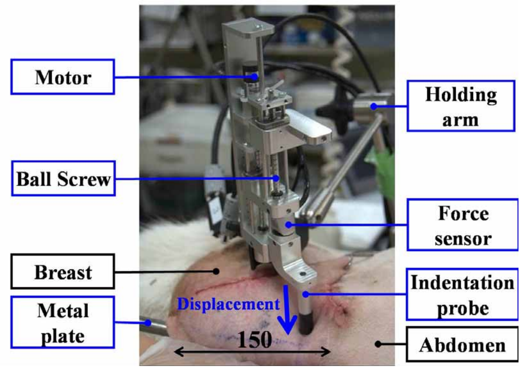


Fig.2. The arrangement of the goat breast and apparatus.

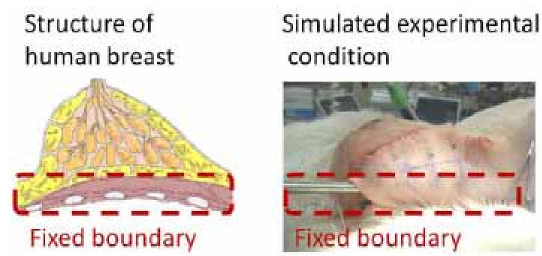
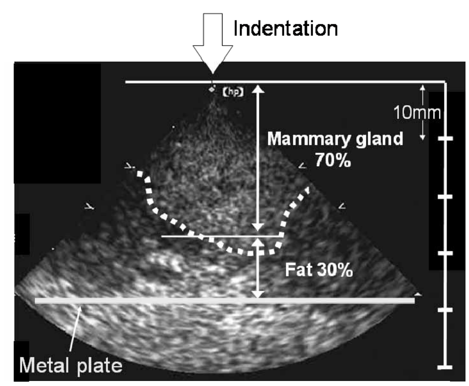
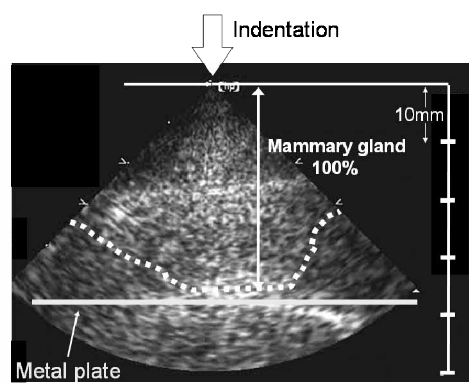


Fig.3. The boundary conditions of the breast in vivo.



(a) Point A



(b) Point B

Fig.4. Ultrasound images of hog breast at each point

4) Imaging modality: Ultrasound equipment (SONOS 5500, Hewlett Packard) was used for imaging because of its compatibility with the robot and for its ability to show real-time visualization.

5) Experimental conditions and procedures: First, we searched for an indentation point using an ultrasound probe. We judged the ratio of fats to mammary gland under the search point from the contrast of ultrasound images. We determined two points in which the ratio of fat and mammary grand are different: under point A, the tissue ratio was 70% mammary gland to 30% fat and at point B the tissue ratio was 100% mammary gland to 0% fat. The ultrasound images at each point are shown in Fig.4. For each point we positioned the experimental apparatus and fixed it in place using a laparoscope positioning device that can be changed between a free state and a locked state. The indentation was then carried out at constant velocity 3.0 mm/s and the force and displacement of the probe were recorded. Three indentations were performed at each point. We performed the experiment at point A and B.

B. Simulation

We have developed and reported mechanical liver and breast models in previous papers, in which we also gave specific descriptions of the material properties of the liver and of finite element based modeling (FEM) and of FEM validation [9]-[10]. The nonlinear force analysis was carried out using this modeling method. An overview of this modeling is presented as follows:

1) Material nonlinearity: We have previously reported the nonlinear elastic model of a pig liver [9] and breast [5]. This model was constructed by the torsional creep test using a rheometer (AR-G2, TA-Instrument). A creep test was carried out for various stresses to investigate material nonlinear properties. In our previous work, the steady state of the step response following sufficient elapsed time exhibits the low-frequency characteristics described in (1). Nonlinear properties can be modeled using the quadric function of strain described in equation (2). The parameters of these equations, measured by the experiment, are shown in Table I.

$$G\frac{d^k\gamma}{dt^k} = \tau \qquad (1)$$

$$G = \begin{cases} G_o & (\gamma < \gamma_0) \\ G_0(1 + a(\gamma - \gamma_0)^2) & (\gamma > \gamma_0) \end{cases} \qquad (2)$$

where G is the magnitude of stiffness, G_o is the viscoelastic modulus of the linear range, a_γ is the coefficient when the change of γ is the shear strain and γ_0 is the strain in which the characteristics of soft tissue change show nonlinearity.

2) Finite element modeling: We have previously reported our solution for the finite element model and have also provided specific descriptions of the development of this model [9]-[10]. As shown in Fig. 5, a model was constructed with a breast shape similar to that of the breast used in the experiment, which is explained in section A. The shape of the breast model was assumed to be 40 mm square. As a boundary condition, we set the dorsal side of the model as the fixed end simulating the effect of the sternum (we used a metal plate in the experiment). The mesh was developed using the Delaunay method, which involves dividing the object automatically into triangular elements, based on the outline of the target object. This is one of the most accepted methods because of the uniquely high reliability resulting from its geometric division. We created the two models with the same shape and mesh but having different material properties: one consisted of 70% mammary gland and 30% fat; the other consisted of 100% mammary gland and 0% fat. The configuration of mesh and each tissue is presented in Fig. 5.

3) Material properties: The stiffness parameter of the model was decided based on our previous work to measure the nonlinear elasticity of breast tissues [5]. Our previous work [9] revealed that there are large differences between the stiffness parameters of in vitro tissue and in vivo tissue. Considering the above, linear elasticity G_o was manually set to correspond with the experimental results shown in Fig.6. Meanwhile, the nonlinear elastic parameters a_γ and $\gamma_0$were not changed for the evaluation by difference in nonlinear elasticity. Table I shows the parameters of each tissue.

4) Simulation conditions: Nodes at probe contact at the center of the upper surface were displaced along the Y-axis at a rate of 3.0 mm/s. Time-series data for probe displacement and the external force were collected during the simulation. The simulations were carried out for both models.

III. Results

Figure 6 presents the experimental results of the reaction force during the indentations. Both reaction forces at point A and B increased linearly in response to small displacements of the indentation probe. The slopes of force increase were at similar magnitudes. The reaction force at point B exhibits a nonlinear increase after 4 mm of probe displacement. Meanwhile the force at point A remained linear after approximately 8 mm of displacement.

Figure 6 also presents the simulation results of the reaction force. The tendency was the same as in the experimental results; a small difference in reaction force in the linear range in response to small displacement and a large difference in the reaction force in the nonlinear range in response to large

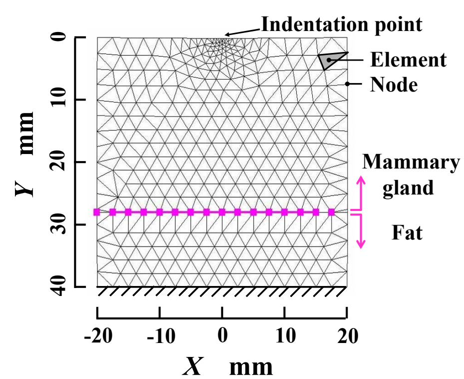


Fig.5. Boundary conditions of breast model mesh. The rear side of the model was set to be the fixed end.

TABLE I
Parameter of each tissue of the breast model

Tissue type	G_0 Pa	γ_0	a_γ
Fat	3.0×10^3	0.87	2.1
Mammary gland	4.8×10^3	0.44	2.1×10^1

displacement. The reaction force in the simulation was small in both nonlinear and linear ranges compared with the experimental result. The magnitude of nonlinearity in the simulation was also small compared with the experimental results.

IV. Discussion

1) Feasibility of our concept: There were small differences in the linear range in the reaction force during small displacements between the experimental and simulation results. On the other hand, this difference became large when the probe displacement became large and the reaction force became nonlinear. A small difference of reaction force may result in mischaracterization of tissue. Therefore, we suggest that it is preferable to identify tissue type by evaluating nonlinear elasticity rather than linear elasticity. These results support the feasibility of our concept to evaluate the nonlinear reaction force following large deformation of the breast.

2) Two dimensional analysis and model shape: we developed a 2D liver model and provided a 2D deformation simulation. It is acknowledged that a 3D model would provide more accurate results. However, an assumption, supported by related studies [11], was made that 2D simulation and manipulator movement would be sufficiently effective to enable accurate needle insertion. A comparative evaluation of 2D and 3D simulation will be undertaken in future work. The other limitation in our investigation is the shape of the model. We simulated the reaction force with a simplified structure.

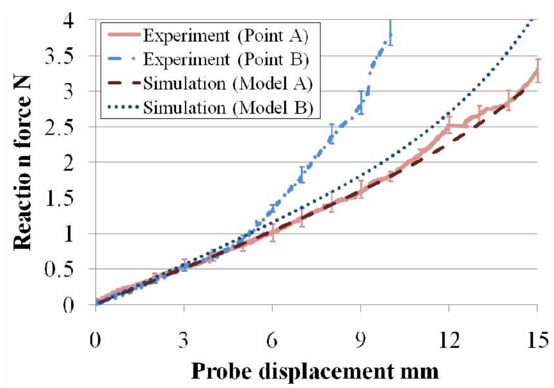


Fig.6. Experimental and simulation results of the reaction force (Average value of three experiments).

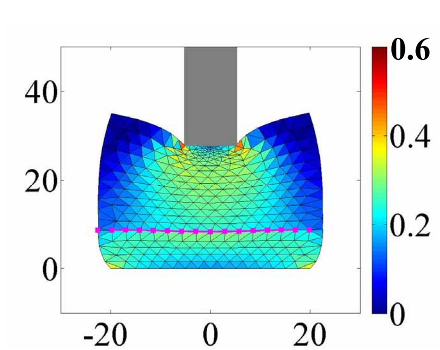


Fig.7. An example of model deformation. The color of each element represents the strain of the element.

The actual shape of the breast used in square breast model as the experiment was not square but a more complex structure. It is likely that the limitations of dimension and shape of the model result in the difference between the simulation and experimental results.

3) Tissue limitation: This article only covered mammary gland and fat as target tissues. The goal of our research is to characterize all the constituent breast tissues. Tissues such as muscle and tumor will be addressed in future work.

V. Summary And Future Work

We propose the palpation diagnosis system based on the measurement of nonlinear elasticity to identify the location of each breast tissue. Here, we have presented the basic concept of our study with preliminary experiment and simulation. More specifically, we performed an experiment to measure the nonlinear response of reaction force using the breast of a goat. In addition, we also simulated the reaction force using a nonlinear biomechanical simulation with several tissue types. Large differences in reaction force occur only in the nonlinear range in both experimental and simulation situations. Our results confirmed the feasibility of our concept.

In future work, we will examine the reaction force with a 3D breast model. We will perform an investigation that will include breast muscle and tumor. From these results, we will develop a palpation system for tissue characterization.

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