

Modeling breast biomechanics for multi-modal image analysis—successes and challenges

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Biomechanical modeling of the breast is a burgeoning research field that has potential uses across a wide range of healthcare applications. This review describes recent developments regarding multi-modal breast image analysis, and outlines some of the key challenges that researchers face in introducing the models into the clinical arena. Deformable breast models have demonstrated capabilities across a wide range of breast cancer diagnoses and treatments. Specific applications include magnetic resonance (MR) image guided surgery, registration of x-ray and MR images, and breast reduction/augmentation surgery planning. Challenges lie in improving the fidelity of these models, which are presently simplistic and use many unverified parameters. Specific challenges include characterization of individual-specific mechanical properties of breast tissues, precise representation of loading and boundary constraints during different clinical procedures, and validation of modeling techniques used to represent key mechanical aspects such as the suspensory Cooper's ligaments. Scientists must also work towards translating their research tools into the clinical setting by developing efficient tools with user-friendly interactivity. Widespread adoption of such techniques has the potential to significantly reduce the numbers of misdiagnosed breast cancers and enhance surgical planning for patient treatment. © 2009 John Wiley & Sons, Inc. *WIREs Syst Biol Med* 2010 2 293–304

Breast cancer is a leading cause of cancer death among women worldwide. X-ray mammography is considered to be the gold-standard modality for early detection of breast cancer. With its high throughput (scans taking typically 10 s) and relatively low cost (a typical MRI costs four times that of a mammogram), it is presently the only feasible imaging modality for screening. Nevertheless, x-ray mammograms alone cannot be used to identify and characterize all cancers, partly because of their two-dimensional representation of a 3D compressed breast and also because of their limited applicability to women with dense breasts. Therefore, when a suspicious lesion is identified on a mammogram, clinicians typically acquire additional views of the

breast using different imaging modalities such as magnetic resonance imaging (MRI), ultrasound or positron emission tomography (PET). However, these other modalities also have drawbacks. For example, MRI scans, while providing three-dimensional views of the breast in a relatively benign manner (as opposed to harmful x-rays), have a low specificity and hence often require the use of contrast agents to detect cancers. PET scans can highlight the spread of disease and help monitor treatment response, but provide poor resolution (3–5 mm as opposed to 50 μ m on an x-ray mammogram). Thus, PET images have good specificity, but poor sensitivity, especially to small tumors that are typically found in screening population.¹

These modality-specific drawbacks may be overcome by using the information from different imaging modalities in a complementary manner. Indeed, research has shown that breast cancer detection is more effective when clinicians analyze

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image patterns across multiple imaging modalities.² However, accurately fusing the information from different imaging modalities is non-trivial. This is not only because of differences in the physics of each imaging modality, but also because the internal tissues deform differently as a result of the differing loading conditions applied during breast imaging. For example, the breast is compressed between two plates during x-ray mammography, whereas the breast is typically pendant (loaded under gravity) in a receiver coil during MR imaging.

Extensive research has been conducted to develop non-rigid registration algorithms that can determine transformation maps between different medical images. Traditionally, algorithms were developed to find a transformation that minimizes the difference in image texture or other intensity-based similarity measurements.^{3–8} However, such algorithms permit physically implausible transformations, which limit their reliability. Thus, constraints such as volume preservation have been applied to ensure transformations are more physically realistic.^{8,9}

Algorithms have been developed to apply transformations that are constrained by the laws of physics, subject to the loading conditions on the breast during an imaging procedure. One of the first attempts to directly incorporate breast movement into breast image registration was conducted by Kita et al.^{10,11} Their model of breast deformation was purely geometrical and used a deformable cylinder to account for the kinematic transformations, but not for stress equilibrium. The breast tissue was assumed to deform uniformly under compression. While such kinematic modeling is not strictly biomechanics based, this work was an important step towards illustrating the utility of registration techniques based upon breast deformation models.

Since the work of Kita et al., the ability to represent realistic breast deformations has gained significant interest. More recent studies have taken the kinematics and elasticity of the different tissues into account to predict the deformation by applying the laws of continuum mechanics. The potential of such biomechanical models is being investigated across a range of breast-cancer-related medical applications, including multi-modal image registration,^{12,13} surgical planning for mastectomies,¹⁴ and image-guided breast biopsies.¹⁵

In this paper, we provide an overview of the state of the art in breast biomechanics modeling for breast cancer identification and treatment. Biomechanical modeling of the breast is an active area of research, and important challenges must be addressed before such models can be widely accepted as practical tools

in the clinical arena. We present an overview of current technologies followed by an outline of some of the important challenges in developing clinically applicable biomechanical models. We then provide a brief outlook of future developments in this research field, and potential applications of biomechanics modeling for breast cancer diagnosis and patient care.

STATE OF THE ART IN BREAST BIOMECHANICS MODELING

Biomechanical models of the breast have predominantly been developed using the finite element (FE) method. The first continuum mechanics models simulated breast deformation under gravity loading,¹⁶ mammographic compression,¹⁷ and MR guided breast biopsy.¹⁸ In the decade following these studies, a number of groups have initiated research programs to develop more reliable biomechanical models of the breast. Table 1 provides a summary of some of the groups that are currently active in this field, and highlights the performance of the different models, taking account of the application and the modeling approach adopted by each group.

Zygantidis et al.²⁰ avoided the use of finite elements and continuum theory entirely, and developed an algorithm they deemed to be faster and easier to implement. The algorithm represents the breast as a system of springs, assuming each voxel in a three-dimensional image to be a linear elastic spring (with stiffness depending on the type of tissue the voxel represents), which must maintain equilibrium with surrounding voxel springs when a load is applied. A unique approach was also taken in solving for the deformed configuration. The typical assembly of a stiffness matrix was avoided by solving for the equilibrium of each mass-spring iteratively, using a simplified equilibrium equation, until all nodes are in equilibrium. Because of the lack of experimental validation, the trade-off between speed and accuracy of simulations using this technique is unclear.

Roose et al.²⁶ showed that mass-spring models can lead to non-physical local phenomena when modeling large deformations. They were also motivated by ease of implementation and speed of computations, using mass-tensor models of small strain deformations to predict breast deformation for MRI registration and breast augmentation planning.^{14,19} Mass-tensor methods involve a FE solution of the general, dynamic Newtonian laws of motion,²⁷ thus enabling real-time deformations to be simulated. Unlike Zygantidis et al., Roose et al. validated their method using patient data. In the case of MRI registration, breast images taken 6 months apart were registered with the

TABLE 1 | A Survey of Biomechanical Models of the Breast

Lead Author	Application/Mode of Deformation	Computational Technique	Material Characteristics	Performance
Roose et al. ¹⁹	Temporal registration of breast MRI and breast augmentation	Small strain, via mass-tensor models using finite element methods (FEM)	Homogeneous, linear elastic material	Breast augmentation planning errors in range of 2.5 mm to 3.5 mm
Ruiter et al. ¹²	Register MRI to x-ray mammogram	Finite strain, continuum mechanics, FEM	Tested different heterogeneous model combinations—linear elastic to exponential	Predicted center of lesion lay within actual lesion volume from image
Zygantidis and Bliznakova ²⁰	Register CC and MLO x-ray mammograms	Small strain, spring system modeling	Heterogeneous, linear elastic materials	Validation not reported
Zhang et al. ¹³	Register CC and MLO x-ray mammograms	Small strain, continuum mechanics, FEM	Homogeneous, linear elastic material	Avg distance between actual and predicted lesion location was 2.2 mm
Del Palomar et al. ²¹	Simulation of gravity loading for surgical planning	Finite strain, continuum mechanics, FEM	Heterogeneous, fat, fibrous (neo-Hookean) and skin (polynomial function)	Avg distance between model surface and real surface was 2.4 mm
Tanner et al. ²²	MR-mammography	Finite strain, continuum mechanics, FEM with statistical techniques	Heterogeneous model consisting of linear elastic and exponential material models	Statistical deformation models captured deformations to within 2.5 mm
Carter et al. ¹⁵	MR-guided surgery	Finite strain, continuum mechanics, FEM	Homogeneous, neo-Hookean function	5 mm error in predicting tissue movement during surgery
Pathmanathan et al. ²³	Gravity, and compression	Finite strain, continuum mechanics, FEM	Heterogeneous model for fat, fibro (polynomial equation) and skin (exponential)	Validation not reported
Rajagopal et al. ^{24,25}	Gravity and compression	Finite strain, continuum mechanics, FEM	Individual-specific, homogeneous, neo-Hookean model	Predicted feature location to within 4–6 mm

biomechanical model, reducing the sum of squared differences in intensity between the images by 44, 29 and 24% of the sum of squared differences of the non-registered images for each of three patient image sets. In the case of breast augmentation planning, accuracy of simulating a post-operative breast configuration was assessed by measuring the difference in skin configuration between simulated and real post-operative breast image data for four patients. The model predictions were within a clinically acceptable range of 2.5 mm and 3.5 mm.

While small strain deformations are straightforward to implement and fast to compute, these models do not adequately represent the rotations and large deformations that the breast experiences.²⁸ Hence, such approaches could lead to unacceptable errors when attempting to map tumors between medical

images. Because of this, groups that are interested in such applications typically use the FE implementation of large deformation elasticity for modeling the large nonlinear deformations in the breast.

There are significant differences in the performance of continuum models (Table 1). Most models are simplistic with many unverified parameters. For example, mechanical properties of the breast are known to vary significantly between individuals,²⁹ yet many studies,^{12,13,22–24} have used mechanical properties published in the literature. In contrast, Rajagopal et al.^{24,25} have estimated individual-specific mechanical properties, but assumed tissue homogeneity without accounting for the different tissue types. Such differences also exist in the application of loading and boundary conditions, as it is difficult to accurately measure and simulate the imaging conditions.

Sensitivity studies by Ruiter et al.,¹² Pathmanathan et al.,²³ and Tanner et al.³⁰ have compared models of mechanical behavior and approaches to loading and boundary conditions. However, because of the complex nonlinear effects of these different parameters, and the lack of substantial experimental data, the conclusions from such studies are questionable and sometimes contrary. For example, Ruiter et al.¹² demonstrated the importance of skin in deformation predictions, whereas Pathmanathan et al.²³ reported contrary findings.

A question that arises when comparing the different modeling approaches and performance measures in Table 1 is “how accurate does a breast biomechanical model need to be?” The required level of accuracy is dictated by the application. For instance, a software tool for tracking suspicious lesions across different images needs to be highly accurate to ensure that a reliable diagnosis is made. However, a surgical training tool may only need to be visually realistic, and a reasonable speed of interaction may be achieved by sacrificing model accuracy.

The accuracy itself is dependent on the level of detail to which models represent reality. From the reported successes of the different groups in Table 1 one could conclude that the required accuracy for the applications can be achieved with naive models. Indeed, even the simple kinematic model proposed by Kita et al.¹⁰ has been reported to provide clinical success to reconstruct the three-dimensional position of microcalcification clusters from x-ray mammograms.³¹

However, the utility of these models is often limited to the application for which they were originally developed due to the different requirements of accuracy in the applications. For example, a surgery training tool has a different set of requirements to a microcalcification tracking tool.

From a biomechanical modeling perspective, a thorough understanding and quantification of the sources of error in breast deformation predictions would be of immense value. Models could be tuned or simplified to specific applications with the confidence that the critical parameters and details of the model that are needed for each specific application have been represented adequately. Such confidence can only be gained by working towards a physically realistic, detailed model of the breast.

While state of the art biomechanical models of the breast have achieved some successes, further research, development, and validation will provide us with a better understanding of breast biomechanics and enable the transfer of knowledge into the clinical arena with greater confidence. In the following

section, we describe some of the key challenges facing the development of such anatomically and biomechanically realistic models.

CHALLENGES IN BREAST BIOMECHANICS MODELING

There are three major requirements for developing a realistic biomechanical model of the breast:

1. accurate geometric representation of the anatomy of the breast;
2. constitutive models that faithfully represent the mechanical behavior of the different tissues;
3. realistic and precise representation of boundary and loading conditions.

The fidelity of these aspects determines the accuracy of breast mechanics predictions. However, acquiring the necessary information to satisfy these requirements is not trivial. Mechanical properties must be acquired in a non-invasive manner, but commonly used imaging technologies do not adequately highlight key structural details such as the Cooper's ligaments and the muscle–breast tissue interface. These challenges are compounded by the fact that a biomechanical model can only be applied in the clinical setting if it is simple and efficient to use, and does not impose undue discomfort to patients. These are not insurmountable difficulties, as will be discussed in the following sections.

Modeling Breast Geometry

The breast is a heterogeneous body, extending from the level of the second rib on the platysma myoides muscle, to the seventh rib on the external oblique muscle (see Figure 1). On the sternal margin, the breast sits over the pectoralis major and rib cartilage while at the axillary margin, it sits on the serratus major, external oblique muscles and fascia of the thorax. Internally, the breast consists of two layers of superficial and deeper connective tissue (fascia mammae) that are attached to the ligamentous tissue of the sternum, between which fatty, fibrous and other functional components (such as lactiferous ducts) are situated. The superficial layer forms a fibrous cover, passing between the gland and the skin and also enters the interior of the gland. Fibrous extensions from this layer, called suspensory (Cooper's) ligaments, proceed to the posterior surface of the skin to support the breast.

MR imaging can provide a detailed 3D view of the internal structural organization of an

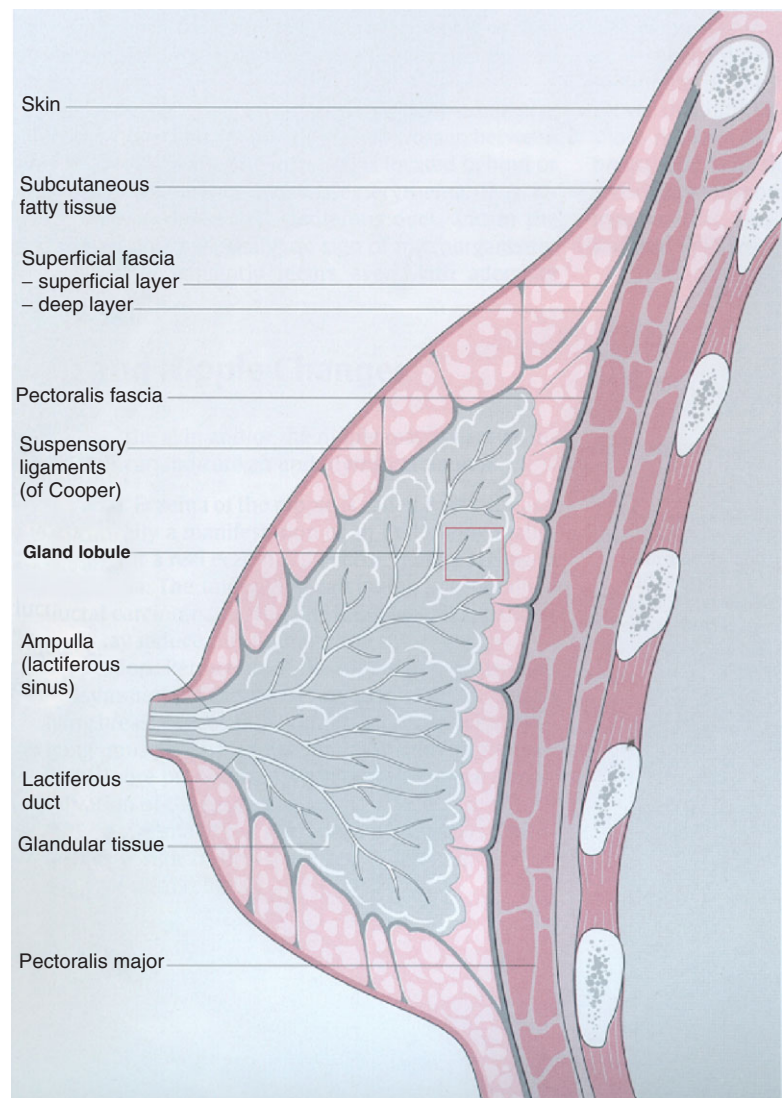


FIGURE 1 | Anatomy of the breast (Adapted and reprinted with permission from Dronkers et al. *Practice of Mammography*. Copyright 2002 Thieme Medical Publishers Inc.).

individual's breasts (see Figure 2) with reasonable contrast between skin, fat, and fibrous tissues. Modeling the breast geometry with MR data using FE methods is straightforward, with most groups using either tetrahedral or hexahedral elements to accurately represent the individual-specific geometry with high accuracy (see Figure 2). Algorithms have also been developed to rapidly create anatomically realistic FE models of the breast, customized to each individual.²⁴

While the skin, fat, and fibrous tissues are readily identifiable, the suspensory Cooper's ligaments and the breast tissue to muscle borders are typically difficult to identify and segment from MR images. Although techniques exist for modeling the mechanical anisotropy introduced by the suspensory ligaments, their reported structural reinforcement has often been neglected in models due to the identification

issue.^{32,33} Identifying a clinical imaging protocol that highlights these structures is challenging. Histological samples, such as those from Guinebretiere et al.³⁴ although not providing a view of the entire breast, may help in developing models of anisotropy in the breast. Lack of clarity of the muscle to breast tissue boundary has also meant that groups typically assume the breast to be rigidly fixed to the chest muscles. However, sensitivity studies^{12,30} suggest that this assumption must be investigated further to accurately reproduce breast deformation near the chest wall.

There are further modeling challenges in attempting to faithfully represent tissue heterogeneity in the breast. While the distribution of fat and fibrous tissues can be represented using classical FE techniques, modeling of the mechanical interaction of the skin with the internal breast tissue requires further investigation. The simplest options involve

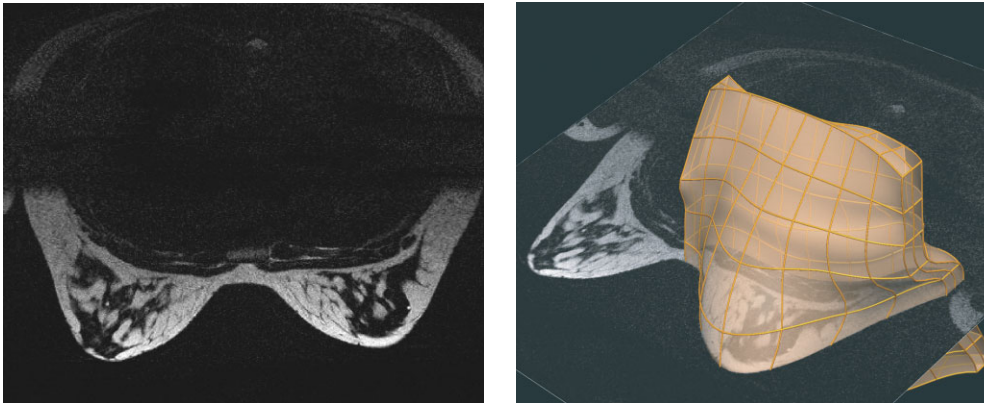


FIGURE 2 | Left: MR image slice of the breast in the prone orientation. Right: A geometric model fitted to the prone MR image set using hexahedral finite elements with cubic-Hermite interpolation functions.

modeling the skin layer as additional 3D elements that surround the internal tissue elements, or coupling 2D membrane (skin) elements to 3D fat/fibrous elements.^{23,35} However, it is clear from sensitivity analyses^{12,23,30} that little is known about the accuracy of these representations. More robust clinical validation experiments, along with more controlled phantom studies³⁵ should provide further confidence.

Another aspect that is typically overlooked by researchers is the fact that all images of the breast are taken under some type of loading condition (gravity, compression, etc). Hence, all images of the breast represent a loaded configuration. However, correct use of finite deformation elasticity theory requires reliable knowledge of the stress-free configuration, which is used as a reference state from which deformation predictions can be determined. Therefore, errors in model predictions may arise if, for example, the prone gravity-loaded deformed configuration was used as the reference state for the prediction of the supine gravity-loaded configuration. Rajagopal et al.²⁴ provided one of the first estimates of the unloaded state of the breast, by assuming that its density was similar to that of water^{36,37} and imaging the breasts while immersed in water (see Figure 3). While neutral buoyancy imaging may be clinically impractical, it does provide excellent data for validating novel computational techniques for determining the unloaded configuration of the breast from a set of deformed geometries.^{38,39} These techniques have been validated analytically and experimentally using controlled silicon gel phantom experiments.^{38,40} They have also been applied to modeling breast deformations under gravity loading conditions with reasonable success,⁴¹ but it remains to validate these methods clinically (see Figure 3).

Characterizing the Mechanical Behavior of Breast Tissues

There is a paucity of data available regarding the *in-vivo* mechanical properties of breast tissues.

Several studies^{29,42–45} have quantified the mechanical properties of the breast constituents using linear elastic Young's moduli to relate the stiffness to the type of tissue. These studies have shown that tumors are much stiffer than normal breast tissues. For example, ductal carcinomas have been reported to be 13 times stiffer than normal fatty or fibroglandular tissue.⁴³ However, two observations can be made from these experiments, which must be accounted for when modeling breast deformations: (1) the wide range of stiffness values reported; and (2) the nonlinear mechanical behavior of the different tissues.

Research groups have accounted for the nonlinear mechanical response of breast tissues by using polynomial and exponential constitutive models (Table 1). For example, Samani et al. developed experimental and material parameter estimation techniques to measure and fit hyperelastic constitutive parameters.^{46,47} Importantly, the mechanical properties of breast tissues differ between individuals and over time due to the variability in breast morphology, age, and physiological condition.⁴⁸ Table 2 shows the range of the mechanical properties reported by different research groups. Such variability makes it difficult to use statistical data to model individual breast properties.

Specialized instrumentation and software tools must be developed to characterize the mechanical behavior of an individual's breast tissues to accurately predict deformations using biomechanical models. Han et al.⁴⁹ illustrates the possibility of *in vivo* material parameter estimation by performing ultrasonic indentation tests on breast tissues. Their experiments combined a force sensor with an optical tracking system that was integrated into an ultrasound machine. This technique falls into the broader category of elastography^{29,45,48,50} where stiffness is measured by cyclic loading and unloading of the tissue at different rates. As such, these experiments measure dynamic stiffness as opposed to quasi-static stiffness that is

FIGURE 3 | Estimating the unloaded state of the breast. (a) MR image slice of the breast of a volunteer in the prone gravity-loaded state. (b) Prone MR image slice embedded in a finite element model that was fitted to the 3D prone MR dataset. (c) Predicted unloaded shape of the breast with prone image warped to unloaded shape. (d) Synthetic MR image slice of the predicted unloaded configuration of the breast acquired using the biomechanical model. (e) MR image slice of the neutrally buoyant breast immersed in water (represented by the white block in the image). An indication of tissue displacement between this neutral buoyancy image and prone gravity-loaded image in (a) is given by the distance between nipple and pectoral muscle surface.

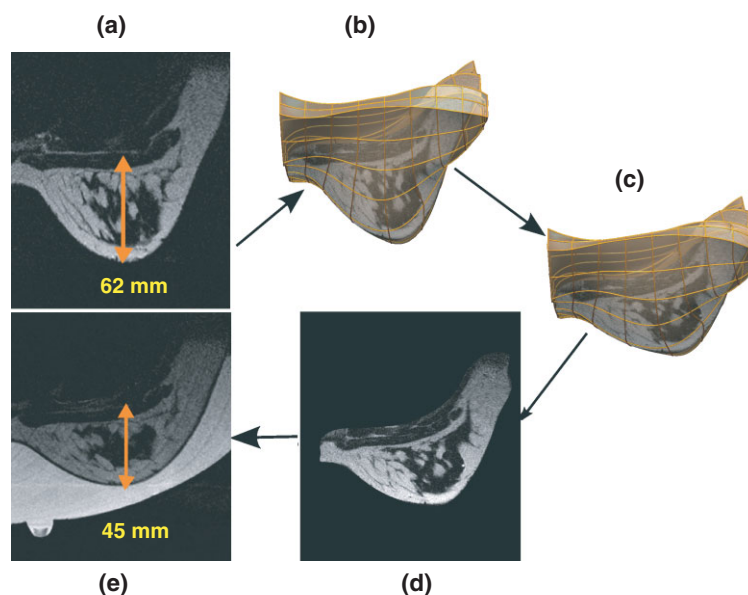


TABLE 2 | A Wide Range of Mechanical Properties of the Breast have been Reported

Lead Author	Experimental Condition	Constitutive Model	Fat Stiffness	Fibroglandular Tissue Stiffness	Tumor Stiffness
Wellman et al. ⁴⁴	<i>Ex vivo</i> punch indentation	Linear elastic and exponential relations	$E = 17.4 \pm 8.4$ kPa at 15 % strain	$E = 271.8 \pm 167.7$ kPa at 15% strain	$E = 2162$ kPa for ductal carcinoma <i>in situ</i> (DCIS)
Krouskop et al. ⁴³	<i>Ex vivo</i> compression loading	Linear elastic relation	$E = 20 \pm 8$ kPa at 20% compression	$E = 48 \pm 15$ kPa at 20% compression	$E = 290 \pm 67$ kPa for DCIS
Del Palomar et al. ²¹	<i>In vivo</i> gravity loading	Neo-Hookean relation	$C_1 = 3$ kPa	$C_1 = 12$ kPa	N/A
Samani et al. ^{42,46,47}	<i>Ex vivo</i> compression loading	Linear elastic model and polynomial functions	$E = 3.25 \pm 0.9$ kPa at 5% compression.	$E = 3.24 \pm 0.61$ kPa at 5% compression	$E = 16.38 \pm 1.55$ kPa for DCIS
Rajagopal et al. ²⁴	<i>In vivo</i> gravity loading	Neo-Hookean relation	$C_1 = 0.08$, and 0.13 kPa for two volunteers	$C_1 = 0.08$ kPa, and 0.13 kPa for two volunteers	N/A

required for modeling deformations such as breast compression. Nevertheless, these techniques do provide estimates of relative stiffnesses of the different tissue types.

Rajagopal et al.²⁴ acquired individual-specific neo-Hookean material parameter values by using an optimization technique to identify the parameter value that allows the biomechanical model to reliably predict a number of gravity-loaded configurations of the breast (acquired using MRI). Such model-based techniques are applicable in the clinical setting, but require further development to individually characterize the different breast tissue types.

In vivo measurement of skin properties is also a challenging task.^{51,52} The skin must be stretched in a variety of ways (multi-axially) to acquire sufficient

force and deformation data for reliable identification of the nonlinear anisotropic mechanical properties. While there is a body of work on estimating mechanical properties of skin *ex vivo*, *in vivo* measurement of the anisotropy has been challenging, requiring the development of specialized devices.⁵³ These devices and the associated modeling techniques must be further miniaturized and optimized before the tools will be applicable for the estimation of individual-specific mechanical properties in a clinically routine manner.

Loading Conditions During Breast Imaging

The breast is subject to a variety of complex loading conditions during the various imaging

procedures, from gravity-loading during MRI or biopsies, indentation for ultrasound, to compression for x-ray mammography or tomosynthesis. Simulating each of these loading conditions is a significant challenge to the application of biomechanical models.

During MR imaging, the breast is subject to gravity-loading, but the mechanical design of breast MR coils makes it likely that the breast is subject to a more complex set of loading conditions as it comes into contact with the sides of the coil. While such conditions could be simulated using contact mechanics theory, the changing conditions due to breathing increases the complexity of the problem, and may require modeling of, or accounting for respiration dynamics.

X-ray mammography imaging conditions also pose specific challenges. For instance, the breast is extended and placed on the x-ray mammography apparatus before compression. Research must be conducted to quantify the extent of the friction between the plates and the breast. The implications of such loads on the breast must be determined to ensure reliable tracking of tumors from the x-ray image to the 3D MR image and *vice versa*.

Several research groups have focused their efforts on simulating breast MR and x-ray mammography using quasi-static loading conditions (Table 1). Ultrasound, biopsies, and reconstruction surgeries involve dynamic loading conditions, because ultrasound probes and needles are typically in motion involving complex interactions with the breast tissues throughout the procedure. While quasi-static simulations involving linear strain approximations have been used,¹⁵ dynamic simulations are rare.

Translation into the Clinical Arena

The challenges outlined above are important problems that must be addressed to create reliable biomechanical models of the breast. However, if it was difficult to use, even a highly reliable biomechanical model may be irrelevant to a clinician. Hence, another challenge that researchers face is to translate their technical achievements into practical tools and workflows in the clinical setting—from model creation to simulation and data visualization.

Model creation must be fast and user-friendly, allowing a clinician to use an intuitive and possibly automated approach to generating geometric models of the breast from medical images. While automated techniques have been previously developed,²⁴ they still involve some manual intervention to ensure that the fitting algorithm produces regularly shaped discretization elements. Biomechanics modelers favor

such elements due to their numerical stability in simulations. Often the critical step is to create an initial geometry with relatively undistorted elements that grossly represents the specific breast shape. This manual step could be performed intuitively by superimposing an image set with a model and providing the clinician with tools to drag vertices of the model to grossly follow the boundaries of the images. Such segmentation tools are already commonly used in heart models for studying heart disease.^{54,55} These interfaces make use of efficient image-segmentation and geometric fitting algorithms to provide a semi-automatic model-fitting workflow. There are a number of image segmentation techniques available to segment MR and mammographic images of the breast⁵⁶ that could become part of a repository of tools that a clinician can use to quickly segment boundaries and fit models to breast images.

A significant bottleneck for the transformation of breast biomechanics research into the clinical arena relates to the availability of suitable images. At present, MR images provide the best starting point from which 3D models of the uncompressed breast can be created. However, MR images are expensive to acquire. In addition, x-ray mammograms are the starting point from which breast cancer diagnosis is performed in the clinic. Hence, an open challenge is how a 3D model of the breast can be created when one only has access to 2D mammograms. To this end, Yam et al.³¹ approximated the 3D uncompressed breast shape using 2D mammograms and a prior generic geometric model. Another possibility is to develop statistics based models (similar to Tanner et al.²²) where a model from a database could be chosen based on a few measurements of the patient's breast (bra size etc.). Those who require accurate representations of a specific individual's breast may have to resort to acquiring surface scans and estimating breast tissue distribution from the clinical images at hand.

Development of streamlined clinical methods for identifying mechanical properties of the breast *in vivo* is also critical to clinical translation. This may require research to identify the best combination of mechanical tests on the breast (indentation, gravity, vibration, etc.) that produce sufficient data for robustly estimating the mechanical properties of the breast. Breast elastography^{50,57} may also play a role in this aspect. A critical factor will be patient comfort, as patients should not be subjected to added stress from having unfamiliar mechanical tests being conducted on them.

Once a geometric model incorporating individual-specific mechanical properties of the breast is created, simulations must produce results

quickly and reliably for real-time applications such as image-guided surgery. With current computers having multiple-core processors, we anticipate that parallel processing techniques will be more commonly used to provide timely simulation results. Graphical processing units are also showing promise in speeding up computations for real-time simulations.⁵⁸

Note that it may not be necessary to address all of the challenges outlined above for successful transformation into the clinical setting. Indeed, an application that does not require a highly accurate model, such as a surgical training tool that only needs a qualitatively realistic simulation of breast deformation, may not require highly accurate information about breast geometry and/or mechanical properties. Thus, the transformational challenges are application specific.

With model accuracy being application specific, researchers must also ensure that users are informed of the limitations of the models they analyze. Model developers must validate their tools using data from clinical trials, and provide information on the confidence of model predictions, based on the required accuracy of the inputs (such as the mechanical properties) for each application. Researchers should keep in mind that clinicians typically do not wish to master the techniques used to develop biomechanical models. Hence, the clinical applicability of biomechanical models is critically dependant on the efforts the researchers put into translating their skills into user-friendly and reliable software applications.

OUTLOOK

A biomechanical model that simulates breast deformations during the various imaging procedures and faithfully captures the variety of breast shapes and mechanical properties has the potential to be a useful and versatile tool in a variety of applications in medical care and cosmetics.

Individual-specific biomechanical models of the breast will provide clinicians with visualization tools to fuse diagnostic information from different imaging technologies, such as x-ray mammography, MRI, ultrasound, and breast tomosynthesis, within a unified three dimensional environment. Biomechanical models may help to reduce the number of images that need to be obtained, if they can be used to reconstruct additional views that a clinician may require. For example, after fusing information from x-ray images of the compressed breast and ultrasound images of the breast in the supine position using a biomechanical model, a clinician may propose a biopsy that requires

the patient to lie on their side. The biomechanical model could be used to simulate this additional view so that the clinician can follow the suspicious lesion without having to reimage the breast.

The applicability of biomechanical models is also being investigated in the wider scope of patient care, such as MR-guided surgery and breast reconstruction surgery (Table 1). A lack of extensive data on the dynamics of the normal breast³³ begs for the development of realistic, physics-based biomechanical models. Such models could also provide valuable insight into the mechanical characteristics of the breast appropriate for the design of implants.

CONCLUSION

Biomechanical modeling of the breast is an active research field that shows potential in a number of clinical applications. Present models of breast mechanics have achieved reasonable success, demonstrating their capabilities in applications such as image-guided surgery, x-ray to MR image registration, and surgical planning. However, there are significant differences in the accuracy of these models due to differing assumptions and the use of unverified parameters in the models.

Future developments might include: (1) representation of the structural organization and interaction of different tissues such as skin and the suspensory Cooper's ligaments; (2) constitutive models of the mechanical properties of the different tissue types; and (3) the accurate representation of the loading and boundary conditions on the breast during different imaging procedures. Modeling techniques for representing the structural organization of tissues and the interactions between skin, breast tissue, and muscle require systematic validation. Substantial research is needed to develop tools that can estimate individual-specific and regionally varying mechanical properties of breast tissues. Further effort must be put into modeling the loading conditions that the breast experiences during an examination, to account for clinically useful loads (such as positioning the breast in an x-ray imaging apparatus) that may be complex to simulate.

While these are significant research challenges, they are compounded by the fact that the technologies developed in the research laboratory must be efficient and straightforward for translation into the clinical environment. As such, researchers face the challenge of translating their technologies into user-friendly and efficient software tools that have the clinician's needs and patient's welfare in mind.

Biomechanical models of the breast have demonstrated their utility in a number of areas. The challenges above are not insurmountable. Successful development and validation of solutions will ensure

that biomechanical models are useful over a wide range of applications, from medical image analysis to virtual surgery applications and cosmetics.

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