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Mechanical Imaging – a Technology for 3-D Visualization and Characterization of Soft Tissue Abnormalities. A Review

A. Sarvazyan* and V. Egorov

Artann Laboratories, Trenton, NJ, USA

Abstract

Mechanical Imaging (MI) is a branch of Elastography. MI differs from conventional ultrasonic and MR elastography in that it evaluates soft tissue mechanical structure using stress data rather than dynamic or static strain data. MI closely mimics manual palpation because the MI probe with a force sensor array attached to its tip acts as a palpating finger. MI is intrinsically a three-dimensional imaging modality because the surface stress patterns obtained at different levels of tissue compression are defined by three-dimensional mechanical structure of the tissue. This review presents the biomechanical basis of MI and its applications for breast cancer screening, and the differentiation of benign and malignant lesions, the visualization and evaluation of prostate conditions, and for the characterization of vaginal wall elasticity.

Keywords

Elastography; elasticity imaging; soft tissue; mechanical imaging; tactile imaging; breast; prostate; cancer

INTRODUCTION

Mechanical Imaging (MI), a.k.a. “tactile imaging” or “stress imaging”, is a method of medical diagnostics capable of 3-D visualization of internal structures in terms of their elasticity [1]. MI is a branch of Elasticity Imaging (EI). MI closely mimics manual palpation. The MI probe has a force sensor array mounted on its contact surface that acts like human fingertips during clinical examination. By slightly compressing soft tissue with the MI probe, the force sensor array detects the resulting changes in the surface stress pattern, similar to the sense of touch. The sequence of stress patterns, corresponding to different levels of applied pressure, is used for 3-D image reconstruction of the examined tissue in terms of its elasticity.

Actually the first EI devices described in the literature were MI devices [2–4]. There are two major differences between MI and all other types of EI based on either ultrasound [5–10] or magnetic resonance (MR) [11–14]. The first difference is that MI reconstructs the internal mechanical structure of tissue using the data of stress pattern over the compressed tissue, while ultrasound or MR elasticity imaging are based on detection of strain induced in the tissue by various static or dynamic means. Therefore, MI may be called “stress imaging”, in contrast to other elasticity imaging techniques, which are estimating tissue displacement and referred to as “strain imaging”.

The second difference is that MI uses much simpler means for obtaining 3-D tissue elasticity images than MR or ultrasonic EI, and therefore is low cost and easy-to-use. Current MI devices described in more detail below, employ a simple pressure sensor array composed of two layers of conductive strips forming a grid of capacitors. Applied pressure changes the distance between the electrodes and respectively, the capacitance value. We reviewed the diagnostic accuracy, procedure cost and cost-effectiveness of currently available technique for breast screening and diagnosis including mammography, ultrasound, MRI and MI [15] and demonstrated that the MI has the potential to provide the best cost-effective solution. For many of the applications, where tissue abnormalities are located within a few centimeters under the accessible tissue surface, the sensitivity and specificity of MI may be comparable to those of sophisticated MR and ultrasonic elasticity imaging devices. However, MI cannot be used for imaging tissue structures located well below the limit of manual palpability.

During the last decade, numerous methods and devices have been developed implementing MI technology in various medical applications, such as the visualization and evaluation of prostate conditions, breast cancer screening, the differentiation of benign and malignant lesions, and the characterization of vaginal wall elasticity [1, 15–29].

BIOPHYSICAL BASIS OF MECHANICAL IMAGING

Tactile Sensor Sensitivity and the Role of Brain in the Analysis of Touch in Manual Palpation

Understanding mechanisms of tactile sensing is important for optimal MI system design. Over the last 30 years, attempts to develop elasticity imaging devices using principles of manual palpation had very limited success [2–4]. In the late 1970s Frei *et al.* [2, 3] proposed an instrument for breast examination that used a plurality of spaced piezoelectric force sensors. The sensors were pressed against the breast by a pressure member which applied a given periodic or steady stress to the tissue. A different principle for evaluating the pattern of pressure distribution over a compressed breast was proposed by Gentle [4] eight years later. The pressure distribution was monitored optically by using the principle of frustrated total internal reflection to generate a brightness distribution. Using this technique, simulated lumps in breast prostheses were detected down to a diameter of 6 mm. But the author was unable to obtain any quantitative data on lumps in a real breast. The failure has been explained by the insufficient sensitivity of the registration system, and that “the load, that the volunteers could comfortably tolerate, was less than that used in the simulation.”

The limited success of these prior attempts to mimic palpation by devices detecting stress patterns over compressed tissue can be explained by a number of reasons, the most important of which is the underestimation of the role of the examiner's brain interpreting the sense of touch in the manual examination process. Palpation skills involve complex analysis of temporal and spatial variations of force exerted on the tip of a finger. Palpation efficiency depends equally on the sensitivity of the tactile receptors in the fingertips, and the data processing capabilities in the brain of the experienced examiner. This analogy introduces several reasons why “the brain” of an MI device is as equally important as the design of the tactile array. One obvious reason is related to the necessity to relate the signals from the tactile sensors to the motion of the fingers for accurate spatial and temporal image reconstruction. Another reason is related to the necessity to filter the “noise” resulting from heterogeneity and variability in the mechanical properties of soft tissues in a manner similar to experienced clinicians discerning tissue abnormalities. For example, the heterogeneity and variability of even a healthy breast, together with a significant dependence of viscoelastic properties of breast tissue on age, on physiological status, on the character of breast pathology, etc., make the problem of examination of the breast by direct mechanical

measurements highly dependent on the experience of the examiner. Because of the heterogeneity and variability of tissue mechanical properties, not much additional information can be obtained via higher sensitivity of the tactile sensors. The solution to the problem is designing adequate algorithms to process the temporal and spatial dependences of tactile data and filter the “noise” arising from tissue heterogeneity. Addressing this problem was one of the challenging tasks that Artann Laboratories successfully accomplished in the development of MI devices.

Tactile Sensing as a Means for Evaluating Tissue Shear Elasticity

Elasticity represents a property which is easy to grasp and interpret. An image, color coded in terms of elasticity, provides an answer to a very natural question: “is the region of interest hard or soft?” The force experienced by a finger pressing a uniform tissue is at the first approximation a linear function of tissue shear elasticity modulus G . This can be shown by a simple mathematical model describing a circular piston with a radius R , mimicking the tip of the finger, acting on the semi-infinite elastic media having the shear and bulk moduli G and K [30]. The relationship between the force P applied to the piston and its displacement W in the case when $G \ll K$ is described by equation: $P = 8GRW$ [30]. Therefore the force experienced by the fingertip pressing on tissue is at the first approximation a linear function of displacement and of tissue shear elasticity modulus.

Extensive studies with the aim to visualize tissue internal structure using a pressure sensor array (“tactile imaging”) were conducted by researchers at Harvard University in the applications related to documentation of breast masses [19, 20, 31]. The relationship between soft tissue elasticity moduli and its structure and composition is discussed in detail in [32, 33].

Delectability of an Inclusion in soft Tissue by MI

The problem of delectability of an inclusion as a function of relative hardness, size and depth was analyzed in several publications [34–36]. The changes in the pressure profiles over a simple two-dimensional tissue model with inclusions of different parameters were calculated using the classical solution of Goodier, i.e. the problem of compressing a medium with a spherical inclusion [37]. Some representative results of this analysis are presented in Fig. (1) adapted from [28].

Fig. (1A) shows results of a theoretical evaluation of relative changes of pressure profiles over a compressed tissue phantom with an inclusion (a nodule). Pressure profiles are shown as a function of nodule/tissue relative hardness. Here E and E_0 are the Young's moduli of nodule and tissue respectively, H and L are the height and the length of the tissue phantom layer, h and d are the depth and the diameter of a nodule, a is the distance from the edge of the phantom to the nodule and $P = P - P_0$ is the difference between pressure profiles for the tissues with and without a nodule. Panel B illustrates the dependence of the P/P_0 maximum on the diameter d of the nodule located at the depth 10 mm and elasticity moduli ratios 5 and 2. The dotted line at the level of 5% of the relative pressure changes denotes the assumed sensitivity of the force sensors in the array used for measuring pressure profile. As it follows from the shown data, this level of sensitivity of the sensors may provide detection of a nodule with 2–3 mm diameter at the depth of 10 mm.

Experiments have been conducted on nodule detectability by MI in comparison with manual palpation [26]. A soft tissue phantom with a set of inclusions having diameters from 6 mm to 14.5 mm pre-positioned at depths from 7.5 mm to 35 mm was designed and tested. The experiments demonstrated superior sensitivity of electronic palpation which allowed detection of hard nodules up to 30% greater depth than manual palpation.

As it is seen in Fig. (1A), dependence of pressure profile maximum on the hardness of a nodule is significant only in the limited range of nodule/tissue relative hardness E/E_0 . We made a series of experiments with breast phantoms having inclusions with different relative hardness [26, 38]. The experimental data are shown in Fig. (2) together with a theoretical curve [39]. It is clearly seen that quantitative assessment of nodule elasticity is feasible only in a limited range of relative hardness ranging from 1 to about 5–10, depending on the sensitivity of the sensor array.

Evaluation of Elasticity Moduli of Bulk Tissue

An image produced by MI reflects the relative hardness of an inclusion versus the surrounding tissues. Therefore it is necessary to have the absolute value of the elastic modulus of the bulk tissue to be able to evaluate the absolute values of the nodule elasticity modulus. The possibility to get absolute values of Young's modulus of a lesion holds a promise for quantitative differential diagnostics of pathology.

The pressure pattern produced by a force sensor array depends upon numerous factors partly related to the elasticity modulus and structural parameters of the examined tissue and partly to geometrical characteristics of the array, the curvatures of the contacting surfaces of both the tissue and the sensor array.

Fig. (3) shows finite element simulation (left panels) for the pressure profile for homogeneous phantoms with different Young's moduli, and right panels illustrate an experiment on measuring the pressure profile over phantoms with the same values of elasticity modulus. Theoretical results are in excellent agreement with experimental data. It is seen that there is a significant dependence of pressure profiles on integral elasticity, which can be utilized in algorithms for assessment of absolute values of tissue elasticity modulus.

Size and Depth of the Nodule

It was shown both theoretically and experimentally that the diameter and the depth of a hard inclusion differently affect the pressure profile [34–36, 39]. Fig. (4) presents results of experiments with tissue phantoms comprising hard inclusions of different diameter located at different depth in a soft tissue phantom. It is seen that although the peak amplitude of the pressure profile could be the same for a smaller nodule closer to the surface as for the bigger nodule located deep inside the tissue, the shape of the pressure peak is distinctly different for these two cases. Specifically, visually might be seen difference in a ratio of peak value to its width and curvature the peak. Right graph of the Fig. (4) including overlaid plots helps to compare these cases.

Spatial Resolution

Spatial resolution for the MI, which could be important for certain applications such as biopsy guidance, highly depends on the mode of examination. In case of a pressure profile measured as a static stress pattern on the surface of a compressed object, the theoretical spatial Nyquist limit for the typical sensor with 2.5 mm sensor element spacing is twice that period and is equal to 5 mm. In the dynamic mode of examination, when the sensor array is moved laterally over the examined tissue, the spatial resolution could be an order of magnitude higher than the characteristic dimension of a single sensor [1]. In the dynamic mode of examination, the spatial resolution is closely related to the temporal resolution since more frames of pressure pattern per unit of displacement is recorded, the better the effective spatial resolution. Fig. (5) presents experimental data obtained by a pressure sensor array placed under a soft tissue phantom containing a hard inclusion while moving a roller over a region of the inclusion, as shown in the diagram on the top of the figure [1]. Pressure patterns were recorded at 100 frames per second. At such frame rate, the roller motion

trajectory is represented in submillimeter increments, which appeared to be the main factor defining the spatial resolution in detecting the position of the inclusion, while the dimensions of single sensor in the array are of secondary importance. A topographic map shown at the bottom of the figure presents the levels of amplitude of the signal displayed as a function of time (vertical axis) and coordinate (horizontal axis). One can see that even without any mathematical processing, the centroid of the rings in the topographic image of Fig. (5) can be estimated with the accuracy of better than 1 mm in the horizontal plane, while the spacing between the sensors in the array used in that experiment was 4 mm. This experiment was performed with sensors of different size [1]. It was shown that in this dynamic mode of examination the spatial resolution of 1 mm does not get worse even when the spacing is increased to 10 mm because the spatial resolution is closely related to the temporal resolution: the more frames of pressure pattern per unit of displacement are made, the higher is the spatial resolution.

Pressure Pattern Analysis and Image Formation

Translating raw pressure pattern data into a 2-D or 3-D image of the internal mechanical structure of the examined object is one of the most challenging tasks in the development of MI technology. The data processing and analysis algorithms highly depend on the mode of examination, on hardware of the MI system, such as the dimensions and number of elements in the pressure sensor array and sensitivity and noise level of the sensors. In most of the applications of MI technology, the dimensions of the sensor array are much smaller than the imaged object. Consequently, formation of an image of the examined part of an object often requires compounding multiple spatially separated pressure patterns. Description of the steps in the pressure pattern analysis, tissue 3-D mechanical structure reconstruction and visualization, with explanation of physical and mathematical bases of algorithms implemented in the MI software, can be found in [24]. Here we will just present two examples illustrating composite images of a soft tissue model with embedded inclusions (Fig. 6 and 7). The images were obtained by pressing the MI probe against the model while gradually moving along the site of the model containing inclusions. Fig. (6) shows a perspective view of a model with dimensions 120 mm × 120 mm × 62 mm comprising three inclusions: a narrow rectangular strip, a triangle and a circle (middle panel). The inclusions located 12 mm beneath the model surface were made of a 3 mm thick rubber sheet with Young's modulus of $E=350$ kPa. The tissue phantom was 62 mm thick and had Young's modulus of $E = 15$ kPa. Right panel of Fig. (6) shows the composite image assembled from successive images obtained by scanning the MI probe over the model.

Fig. (7) shows results of an experiment on a soft tissue model with an embedded inclusion having thin elongated spikes. The inclusion simulated stellate lesions in breast which often appear as a central mass surrounded by spicules radiating outwards. The thickness of the central mass of the inclusion was about 5 mm and the diameter was 10 mm. The inclusion was located at the depth of 12 mm. The spikes were thin and it was impossible to feel them by manual palpation. The model, made of a transparent silicon rubber, was 45 mm thick and its Young's modulus was $E=7$ kPa. The Young's modulus of the inclusions was $E=75$ kPa. The assembled image is shown in Fig. (7) which demonstrates good correspondence with the examined object. Structural details which are impossible to feel by manual palpation are well pronounced in the compound image.

Three-Dimensional Image Reconstruction

There is a theoretical possibility for rigorous 3-D reconstruction of a complex soft tissue structure by solving the inverse problem for 2-D input patterns. Such an approach would require numerous assumptions and huge computational power which is far from being

practical. We have developed an alternative semi-empirical way of 3-D image formation [13], which is briefly described below.

The input data for 3-D reconstruction comprises a continuous sequence of 2-D filtered stress patterns. The initial hypotheses enabling 3-D reconstruction are: (a) the higher the compression force, the greater the representation of deeper structures in the imprint image; and (b) the total pressure is proportional to the tissue deformation in the Z-direction (normal to the probe surface). The 3-D reconstruction starts with the formation of an initial (seed) 3-D structure by stacking the series of 2-D structure images along Z-coordinate during first tissue compression. Every 2-D imprint is further integrated by a parallel translation inside the 3-D structure image by matching algorithm [13]. After the examination is complete, a smoothing and 3-D interpolation is applied to the constructed structures. The final 3-D structure visualization is deployed by the computation of iso-surfaces related to the hardness distribution of the underlying structure. Fig. (8) presents an example of 3-D image reconstruction of a composite inclusion in a test phantom. The ability of this approach to reproduce the underlying tissue structures was demonstrated on a variety of phantom models and clinical data. [24–26].

CLINICAL APPLICATIONS OF MECHANICAL IMAGING

During the last two decades, several devices for soft tissue imaging and elasticity assessment based on the MI technology were developed and tested in clinical studies. These devices include the Breast Mechanical Imager (BMI) for breast cancer detection [1, 15, 26–28], the Prostate Mechanical Imager (PMI) for 3-D prostate visualization in elasticity terms highlighting prostate nodularity [16–18, 21, 24, 25] and the Vaginal Tactile Imager (VTI) for pelvic floor prolapse assessment [29, 40]. The data obtained by MI allow for calculation of numerous parameters of tissue and tissue abnormalities, such as Young's modulus, elasticity contrast, nonlinearity (strain hardening), heterogeneity index, nodule size and shape, which are shown to be useful in differentiating benign and malignant lesions [27].

Prostate MI

PMI provides a real-time 3-D image of the prostate and detects the presence and location of abnormalities within the gland. PMI enables a physician to visually examine and store a 3-D reconstructed image of the prostate and evaluate prostate volume, elasticity and elasticity contrast. The utility of PMI is similar to the utility provided by digital rectal examination (DRE), which is currently considered a standard of care for men over the age of 50. The *American Urological Association* in 2009 in their Best Practices Statement recommended that: “Men who wish to be screened for prostate cancer should have both a PSA (prostate specific antigen) test and a DRE” [41].

Many doctors performing DRE are general practitioners, not urologists, and are often not as skilled in diagnosing abnormalities or as comfortable in conducting a DRE procedure. DRE performed on the same prostate on the same day by two different examiners could result in different findings. Palpatory findings are consistent among experienced urologists in about 80% of the exams while agreement between inexperienced practitioners is much lower, reaching only 50% [42].

PMI can minimize subjectivity in the DRE by providing an easy-to-use and accurate tool for visualizing abnormalities of the prostate. This claim is fully supported by the data obtained in the bench and clinical studies [21, 25]. PMI facilitates the sharing of information between clinicians by providing an objective digital image of the prostate at the time of the exam that can be stored in the patient's file or saved/transmitted electronically as part of the information provided when referring the patient to a clinical specialist.

Fig. (9) illustrates the PMI examination as an electronic palpation and shows a characteristic example of clinical data. The general view of PMI is shown in Fig. (10). PMI includes a transrectal probe with two separate pressure sensor arrays and an orientation sensor, a data acquisition and processing unit, and a laptop computer. The first pressure sensor array with 128 sensors installed on the head of the probe collects a sequence of pressure patterns while pressing the probe against the prostate. The obtained data are translated into 2-D and 3-D prostate images through a temporal and spatial filtering and subsequent signal processing. The second sensor array with 48 sensors located on the shaft of the probe measures the forces applied from the sphincter and tracks the location of the probe head relative to the sphincter. The orientation sensor located in the handle of the probe provides data on relationship between acquired stress patterns and position of the probe relative to the prostate.

Prior to clinical studies the performance of PMI was extensively tested on phantoms to determine imaging accuracy, reproducibility, inter-system and inter-operator reproducibility for generating a real time digital image [24, 44]. An anatomical model of the male pelvis with an anal canal, rectal wall, and interchangeable silicone models of the prostate gland was designed to accurately represent elasticity of real tissue. Several sets of prostate models of varied dimensions, shapes and elasticity, with structural inclusions mimicking nodules of various diameters and elasticity, were manufactured for the bench tests. Hard nodules were positioned in specific locations within the prostate models to simulate various prostate elasticity distributions. It was demonstrated through extensive bench testing that the PMI can reproducibly visualize abnormalities and produce images of nodules in prostate models in the pelvic simulator.

The assessment of the PMI's ability to image the human prostate and detect areas of hardness was first addressed by a comparison of the MI data with manual palpation and pathology results on removed prostate glands [7]. Histological findings from posterior segments of nine excised prostates were compared to the PMI generated images of the gland. Study findings confirmed that all PMI depicted abnormalities correlated closely with the palpated nodules and pathology findings. In a 168 patient study, the factors affecting PMI image reconstruction capabilities were evaluated [25]. Following a standard DRE performed by an urologist, the PMI examination was conducted. The examiner was able to observe and inspect, in real-time, two orthogonal cross-sections of the prostate. The PMI scan took approximately 40 to 60 seconds and the collected data were saved in a digital format. As an outcome of the study, the PMI provided data sufficient for image reconstruction of the prostate in 84% of study cases. Based on a patient survey, the level of comfort of the PMI was judged to be similar to that of a DRE examination [25].

Breast MI

Fig. (11) shows a general view of Breast Mechanical Imager (BMI). The device includes a probe with a pressure sensor array, an electronic unit, and a laptop computer. This device is currently produced by Medical Tactile, Inc., Los Angeles, CA, (MTI) under the trade name SureTouch™. The device is approved by the FDA as a visual mapping system for documentation of the findings at clinical breast examination. BMI can quantitatively evaluate multiple mechanical and structural properties of breast and breast lesions, such as Young's modulus, elasticity contrast, tissue nonlinearity (strain hardening), heterogeneity index, nodule size, shape and mobility, which could be altered by cancer development [26]. Clinical data collected at four different sites for 179 cases have demonstrated BMI's capability for characterizing and differentiating benign and malignant breast lesions [27]. Histologically confirmed malignant breast lesions demonstrated increased hardness and strain hardening as well as decreased mobility in comparison with benign lesions. Statistical analysis of data on 147 benign and 32 malignant lesions revealed BMI's average sensitivity

of 91.4% and specificity of 86.8% with a standard deviation of $\pm 6.1\%$ [27]. Examples of cysts and ductal carcinoma images recorded by BMI are shown in Fig. (12).

A detailed description of the lesion features used in benign versus malignant discrimination is given in the original publication [27]. The ROC analysis for output of Bayesian classifier employed six input parameters for differentiation of benign and malignant lesions yielded sensitivity 87.5%, specificity 84.4%, and area under ROC curve 86.1%. Based on these findings, it may be concluded that BMI has the potential to be used as a cost effective device for cancer detection as a diagnostic modality. We further believe the BMI can be used not only for binary classification but for calculating the probability distribution for multiple possible outcomes subdividing various benign and malignant classes. In other words, the BMI has the potential to be used for breast pathology diagnostics in a wider sense to distinguish between fibroadenoma, cyst, fibrosis, ductal, lobular carcinoma and other conditions. We estimated that the use of the BMI after standard screening procedures (mammography alone or combination of mammography and conventional ultrasound) could reduce the benign biopsy rate. Specifically, a 23% reduction of the benign biopsy is possible without missing cancer cases, and a 50% reduction of the benign biopsy with 4.6% missed cancer cases [27].

MI for Vaginal Wall Assessment

We designed and built the Vaginal Tactile Imager (VTI) for assessing conditions of vaginal walls. VTI includes a transvaginal probe, an electronic unit, and a laptop computer. The vaginal probe comprises a pressure sensor array (120 sensors) and a simple orientation sensor (two-axis tilt sensor). In a pilot clinical study with 13 patients [40], the VTI capability to assess vaginal wall elasticity conditions was assessed. It was shown that VTI can clearly visualize the increased rigidity at the mesh graft site after reconstructive surgery with the use of adjuvant materials for vaginal support (Fig. 13). The elasticity images such as that shown in Fig. (13) may be considered as a documentation of the vaginal wall state after such surgery. Any significant changes in the elasticity pattern of vaginal walls in time (months or years) might be observed by repetitive VTI scanning after establishing confidence intervals for quantitative values. The collected VTI data for sites with increased hardness allowed elasticity assessment of these sites by calculating the slope of the peak value in the pressure pattern versus total applied force to the scanhead.

It was also demonstrated that VTI might be used for pelvic organ prolapse characterization [29] (Fig. 14). VTI data demonstrated statistically significant quantitative decrease in the vaginal walls elasticity for prolapsed conditions which were defined by physical examination.

A critical review of published data on the urogynecologic aspects of female sexual dysfunction demonstrates a lack of standardized instruments for assessing biomechanical conditions of the pelvic floor. Clinicians highlight the need for studies to assess the anatomical, physiological, and sensory mechanisms related to female sexual dysfunction [43]. Our clinical results demonstrate applicability of the MI technology for 3-D imaging of the vagina and surrounding structures and characterization of normal and pelvic organ prolapse conditions.

Our findings suggest that MI may offer a non-invasive, quantitative evaluation of vaginal elasticity with the potential for a more comprehensive evaluation of overall vaginal support structures. The prospective gynecologic application of the MI could impact our further understanding of the etiology of prolapse, individual variations in biomechanical properties and provide insight into optimal approaches for surgical repair.

CONCLUSIONS

Mechanical imaging is a promising field in biomedical engineering. MI has already established a distinct niche among other methods of elasticity imaging. Major accomplishments of MI are currently limited to breast and prostate cancer detection and assessment of conditions of the vaginal wall. Results of clinical testing of MI accumulated to date suggest that MI meets the basic requirements for a practical method of day-to-day detection monitoring of breast and prostate cancer: it is simple, fast, inexpensive and safe. However, the full extent of its clinical application has yet to be explored. Larger studies will be needed with controls including biopsy and other elasticity imaging modalities to reveal full diagnostic potential of the MI in assessment of diseases accompanied by changes in mechanical properties of tissues and specifically to provide more accurate data on the ability of MI to differentiate benign and malignant lesions. MI technology is potentially applicable to any field of medical diagnostics and treatment monitoring where manual palpation is used. We believe that there are numerous unexplored applications of MI in surgery. Information obtained by manual palpation is one of the factors defining success of certain surgical operations on removing malignant masses. A compact hand held MI probe may help surgeon to more accurately and objectively map the boundaries of affected tissue. The challenges in expanding the field of applications of MI are mainly in adapting the geometry of the probe with the force sensor array to new anatomical sites and tissue types, creating data processing algorithms and MI probe manipulation techniques for new users and applications.

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REFERENCES

- [1]. Sarvazyan AP. Mechanical Imaging: A new technology for medical diagnostics. *Int J Med Inform.* 1998; 49:195–216. [PubMed: 9741894]
- [2]. Frei, EH.; Sollish, BD.; Yerushalmi, S. Instrument for viscoelastic measurement. United States patent US4144877. Mar. 1979 inventors; Yeda Research and Development Co. Ltd., assignee
- [3]. Frei, EH.; Sollish, BD.; Yerushalmi, S. Instrument for viscoelastic measurement. United States patent US4250894. Feb. 1981 inventors; Yeda Research and Development Co. Ltd., assignee
- [4]. Gentle CR. Mammobarography: a possible method of mass breast screening. *J Biomed Eng.* 1988; 10(2):124–126. [PubMed: 3361866]
- [5]. Lerner, RM.; Parker, KJ. Sono-elasticity in imaging. In: Kessler, LW., editor. *Acoustic imaging.* Plenum Co.; New York: 1988. p. 317-27.
- [6]. Yamakoshi Y, Sato J, Sato T. Ultrasonic imaging of internal vibration of soft tissue under forced vibration. *IEEE Trans Ultrason Ferroelectr Freq Control.* 1990; 37(2):45–53. [PubMed: 18285015]
- [7]. Parker KJ, Huang SR, Musulin RA, Lerner RM. Tissue response to mechanical vibrations for “sonoelasticity imaging”. *Ultrasound Med Biol.* 1990; 16(3):241–46. [PubMed: 2194336]
- [8]. Ophir J, Cespedes I, Ponnekanti H, Yazdi Y, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. *Ultrason Imaging.* 1991; 13:111–34. [PubMed: 1858217]
- [9]. De Korte CL, Cespedes EI, van der Steen AF, Lancee CT. Intravascular elasticity imaging using ultrasound: feasibility studies in phantoms. *Ultrasound Med Biol.* 1991; 23:735–46. [PubMed: 9253821]
- [10]. Sarvazyan AP, Rudenko OV, Swanson SD, Fowlkes JB, Emelianov SY. Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics. *Ultrasound Med Biol.* 1998; 24:1419–35. [PubMed: 10385964]

- [11]. Fowlkes JB, Emelianov SY, Pipe JG, et al. MRI techniques for detection of elasticity variation. *Med Phys.* 1995; 22:1771–78. [PubMed: 8587532]
- [12]. Multhupillai R, Lomas DJ, Rossman PJ, Greenleaf JF, Manduca A, Ehman RL. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science.* 1995; 269:1854–57. [PubMed: 7569924]
- [13]. Plewes DB, Betty I, Urchuk SN, Soutar I. Visualizing tissue compliance with MR imaging. *J Mag Res Imaging.* 1995; 5:733–38.
- [14]. Sinkus R, Lorenzen J, Schrader D, Lorenzen M, Dargatz M, Holz D. High-resolution tensor MR elastography for breast tumour detection. *Phys Med Biol.* 2000; 45(6):1649–64. [PubMed: 10870716]
- [15]. Sarvazyan A, Egorov V, Son JS, Kaufman CS. Cost-effective screening for breast cancer worldwide: current state and future directions. *Breast Cancer: Basic and Clinical Research.* 2008; 1:91–99. [PubMed: 19578481]
- [16]. Niemczyk P, Sarvazyan AP, Fila A, et al. Mechanical Imaging, a new technology for prostate cancer detection. *Surg Forum.* 1996; 47:823–25.
- [17]. Sarvazyan, AP. Proc. MEDTEC'97. Tysons Corner; VA, USA: Aug. 1997 Knowledge-based mechanical imaging of the prostate; p. 87-94.
- [18]. Niemczyk P, Cummings KB, Sarvazyan AP, Bancila E, Ward WS, Weiss RE. Correlation of mechanical imaging and histopathology of radical prostatectomy specimens: a pilot study for detecting prostate cancer. *J Urol.* 1998; 160(3):797–801. [PubMed: 9720551]
- [19]. Wellman, PS.; Howe, RD.; Dewagan, N.; Cundari, MA.; Dalton, E.; Kern, KA. Tactile Imaging: A Method for documentation breast masses. *Proceeding of the First Joint BMES/EMBS Conference; IEEE Computer Society Press; 1999.* p. 1131-32.
- [20]. Wellman PS, Dalton EP, Krag D, Kern KA, Howe RD. Tactile imaging of breast masses: first clinical report. *Arch Surg.* 2001; 136(2):204–08. [PubMed: 11177142]
- [21]. Weiss R, Hartanto V, Perrotti M, et al. In vitro trial of the pilot prototype of the prostate mechanical imaging system. *Urology.* 2001; 58(6):1059–63. [PubMed: 11744495]
- [22]. Sarvazyan A. Model-based imaging. *Ultrasound Med Biol.* 2006; 32(11):1713–20. [PubMed: 17112957]
- [23]. Kaufman CS, Jacobson L, Bachman B, Kaufman L. Digital documentation of the physical examination: moving the clinical breast exam to the electronic medical record. *Amer J Surg.* 2006; 192:444–49. [PubMed: 16978946]
- [24]. Egorov V, Ayrapetyan S, Sarvazyan AP. Prostate Mechanical Imaging: 3-D image composition and feature calculations. *IEEE Trans Med Imaging.* 2006; 25(10):1329–40. [PubMed: 17024836]
- [25]. Weiss RE, Egorov V, Ayrapetyan S, Sarvazyan N, Sarvazyan AP. Prostate mechanical imaging: a new method for prostate assessment. *Urology.* 2008; 71(3):425–429. [PubMed: 18342178]
- [26]. Egorov V, Sarvazyan AP. Mechanical imaging of the breast. *IEEE Trans Med Imaging.* 2008; 27(9):1275–87. [PubMed: 18753043]
- [27]. Egorov V, Kearney T, Pollak SB, et al. Differentiation of benign and malignant breast lesions by mechanical imaging. *Breast Cancer Res Treat.* 2009; 118(1):67–80. [PubMed: 19306059]
- [28]. Sarvazyan, AP.; Egorov, V. Mechanical imaging in medical applications. In: *IEEE Eng Med Biol Society, 2009. Proceedings of Annual International Conference; Minneapolis, MN, USA. 2009 Sep 3–6; p. 1975-78.* 2009
- [29]. Egorov V, van Raalte H, Sarvazyan A. Vaginal Tactile Imaging. *IEEE Trans Biomed Eng.* 2010; 57(7):1736–44. [PubMed: 20483695]
- [30]. Sarvazyan, AP.; Skovoroda, AR.; Emelianov, SY., et al. Biophysical bases of elasticity imaging. In: Jones, JP., editor. *Acoustical imaging 21.* Plenum Press; New York and London: 1995. p. 223-240.
- [31]. Howe RD. Tactile sensing and control of robotic manipulation. *J Advanced Robotics.* 1994; 8(3): 245–61.
- [32]. Sarvazyan, AP. Elastic properties of soft tissues. In: Levy, M.; Bass, HE.; Stern, RR., editors. *Handbook of Elastic Properties of Solids, Liquids and Gases. Vol. Volume III.* Academic Press; New York: 2001. p. 107-27.

- [33]. Sarvazyan, AP.; Hill, CR. Physical chemistry of the ultrasound-tissue interaction. In: Hill, CR.; Bamber, JC.; Ter Haar, GR., editors. *Physical Principles of Medical Ultrasonics*. John Wiley & Sons; 2004. p. 223-235.
- [34]. Sarvazyan, AP.; Skovoroda, AR. Method and apparatus for elasticity imaging. United States patent US 5524636. Jun. 1996 inventors; Artann Laboratories, assignee
- [35]. Pashko DA, Pyt'ev YP, Sarvazyan AP. Minimax evaluation of parameters of a nodule in diagnosing breast cancer with the use of a force sensor array. *Bulletin of Moscow State University, Ser. 3, Physics, Astronomy*. 1996; 5:18–25.
- [36]. Pashko DA, Pyt'ev YP, Sarvazyan AP, Skovoroda AR. On the ultimate potentialities of classification of pathologies in the problem of diagnostics of breast cancer. *Pattern Recognition and Image Analysis*. 1996; 6:510–22.
- [37]. Goodier JN. Concentration of stress around spherical and cylindrical inclusions and flaws. *Trans. ASME*. 1933; 55(39):39–44.
- [38]. Sarvazyan AP. Computerized palpation is more sensitive than human finger. *Proceedings of the 12th International Symposium on Biomedical Measurements and Instrumentation 1998*. Dubrovnik-Croatia. 1998:523–24.
- [39]. Sarvazyan, A. Intrinsic limitations in differential diagnostics based on quantitative elastography. *Abstracts of the third International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity*; 2004 Oct 17-20; Cumbria, UK: Lake Windermere; p. 622004
- [40]. Egorov, V.; van Raalte, H.; Lipetskaia, L. Assessment of the vaginal wall elasticity by mechanical imaging. *Proceedings of the 7th International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity*; Austin, Texas USA. 2008 Oct 27-30; p. 472008
- [41]. AUA [homepage on the Internet] Clinical Guidelines. www.auanet.org/guidelines
- [42]. Smith DS, Catalona WJ. Interexaminer variability of digital rectal examination in detecting prostate cancer. *Urology*. 1995; 45:70–4. [PubMed: 7529449]
- [43]. Dalpiaz O, Kerschbaumer A, Mitterberger M, et al. Female sexual dysfunction: a new urogynaecological research field. *BJU Int*. 2008; 101(6):717–21. [PubMed: 18190620]
- [44]. Egorov, V.; Sarvazyan, A. Operator training and performance descriptor for prostate mechanical imaging. *Proceedings of the 7th International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity*; Austin, Texas. 2008 Oct 27–30; p. 272008

Fig. (1).
 Dependence of pressure profile data on parameters of a nodule. Adapted from [28]. See text.

Fig. (2). Dependence of the pressure profile maximum (normalized to P/P_0 for $E/E_0=100$) on the relative elasticity of the nodule.

Fig. (3). Experiments have demonstrated the use of the pressure profile for estimating integral elasticity. Experimental results (right panel) agree well with finite element simulations (left panel).

Fig. (4).
Pressure profiles for different inclusion diameter, d and depth h . See text.

Fig. (5). Spatial-temporal pressure profiles obtained by moving a linear array of sensors over a phantom with an inclusion. Reproduced with permission from [1].

Fig. (6).
Image matching procedure yields a compound image which closely corresponds to the examined structure. See text.

Fig. (7).
Compound image shows good correspondence with the examined object. See text.

Fig. (8).

Illustration of an algorithm for 3-D image reconstruction.

A - a schematic top view of a test phantom ($E = 8$ kPa) with 3 inclusions ($E = 125$ kPa, $D1 = 15$ mm, $D2 = 8$ mm and $D3 = 5$ mm) at about 8 mm depth; B – a sequence of 2-D stress patterns obtained at different levels of compression; C - reconstructed 3-D image. See text for details.

Fig. (9). PMI closely mimics DRE while offering superior sensitivity and capability of 3-D imaging and storing examination data.

Fig. (10).
General view of the Prostate Mechanical Imager.

Fig. (11). General view of Breast Mechanical Imager. The device comprises a probe with 2-D pressure sensor array (1), an electronic unit (2), and a laptop computer with touch screen capability. Reproduced with permission from [26].

Fig. (12).
Processed data for two clinical cases demonstrate the ability of MI technology to produce 3-D images of lesions. A - two cysts; B - invasive ductal carcinoma.

Fig. (13). Mechanical imaging of anterior and posterior vaginal walls allows visualization and quantitative elasticity evaluation of increased rigidity at mesh grafts. Adapted with permission from [29].

Fig. (14). Box plots demonstrating discrimination of normal from prolapse vaginal wall conditions assessed by VTI. Adapted with permission from [29].