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Evaluation of tomosynthesis elastography in a breast-mimicking phantom

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ABSTRACT

Objective: To evaluate whether measurement of strain under static compression in tomosynthesis of a breast-mimicking phantom can be used to distinguish tumor-simulating lesions of different elasticities and to compare the results to values predicted by rheometric analysis as well as results of ultrasound elastography.

Materials and methods: We prepared three soft breast-mimicking phantoms containing simulated tumors of different elasticities. The phantoms were imaged using a wide angle tomosynthesis system with increasing compression settings ranging from 0 N to 105 N in steps of 15 N. Strain of the inclusions was measured in two planes using a commercially available mammography workstation. The elasticity of the phantom matrix and inclusion material was determined by rheometric analysis. Ultrasound elastography of the inclusions was performed using two different ultrasound elastography algorithms.

Results: Strain at maximal compression was 24.4%/24.5% in plane 1/plane 2, respectively, for the soft inclusion, 19.6%/16.9% for the intermediate inclusion, and 6.0%/10.2% for the firm inclusion. The strain ratios predicted by rheometrical testing were 0.41, 0.83 and 1.26 for the soft, intermediate, and firm inclusions, respectively. The strain ratios obtained for the soft, intermediate, and firm inclusions were 0.72 ± 0.13, 1.02 ± 0.21 and 2.67 ± 1.70, respectively for tomosynthesis elastography, 0.91, 1.64 and 2.07, respectively, for ultrasound tissue strain imaging, and 0.97, 2.06 and 2.37, respectively, for ultrasound real-time elastography.

Conclusions: Differentiation of tumor-simulating inclusions by elasticity in a breast mimicking phantom may be possible by measuring strain in tomosynthesis. This method may be useful for assessing elasticity of breast lesions tomosynthesis of the breast.

1. Introduction

Tomosynthesis of the breast is a new imaging technique that reduces superimposition of breast lesions by overlying structures such as glandular tissue and allows more precise visualization of lesion borders [1]. This may lead to better detection and characterization of breast masses compared to digital mammography [2,3].

Assessment of the elasticity of breast lesions using ultrasound elastography has been shown to be helpful in differentiating benign from malignant breast lesions [4–6]. Other methods of assessing elasticity, such as MR-elastography are under investigation [7]. In sonographic elastography, the deformation of a target lesion in relation to the surrounding tissue under different amounts of physical compression is used for judging elasticity. Compression is also applied in radiographic techniques such as mammography and tomosynthesis of the breast; to the best of our knowledge, however, this has so far not been used to obtain elastographic data.

A variety of methods can be used for ultrasound elastography [8]. In this technique, results are often shown as strain maps, which display relative tissue displacement under compression. Strain can also be expressed as change in diameter in one or more planes.

While in conventional mammography, lesion borders are often somewhat indistinct, improved depiction of lesion borders by tomosynthesis may increase the potential to accurately and reproducibly measure lesion diameter [9]. Mechanical strain imposed on the breast by variable deformation forces and captured by tomosynthesis can potentially provide information on the elasticity of lesions if lesion diameter is measured accurately (Fig. 1). A similar approach was used successfully in ultrasound elastography before more sophisticated techniques were available [10]. The aim

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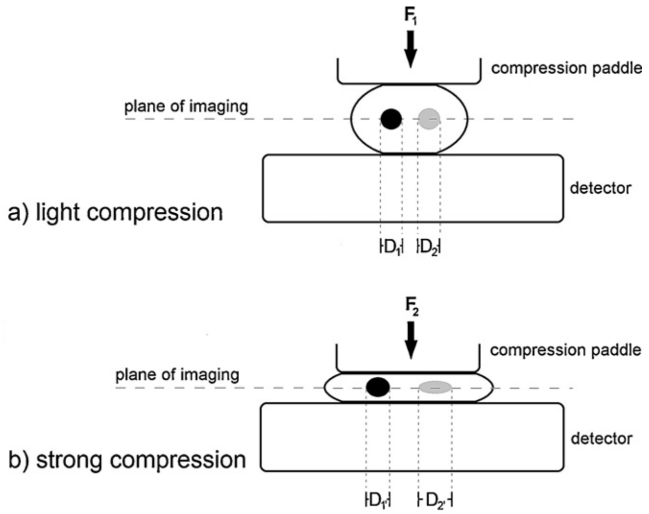

Fig. 1. The effects of compression on breast lesions of different elasticity (represented by different shades of gray) in tomosynthesis and mammography; F_1 – light compressive force; F_2 – strong compressive Force; D_1, D_2 – diameters of inclusions under light compression; $D_{1'}$, $D_{2'}$ – diameters of inclusions under strong compression.

of this study was to evaluate whether measurement of strain under static compression in X-ray tomosynthesis of a breast-mimicking phantom can be used to distinguish tumor-simulating inclusions of different elasticities and to compare the findings to rheometrical analysis of elasticity as well as established methods of ultrasound elastography.

2. Materials and methods

2.1. Tomosynthesis phantoms

We prepared three cylindrical phantoms that measured 63 mm in diameter and 100 mm in length and were made of soft, pliable silicone gel (Shore hardness A 4; PlatSILITA® 22-4T, PolyConForm GmbH, Düsseldorf, Germany) (Fig. 2). The phantoms contained gelatinous spheres of an agar–agar-based substance (WiroGel® M, BEGO GmbH, Bremen, Germany) made with 1, 2 or 3 parts of water-soluble contrast agent (Peritrast® 350 mg iodine/100 ml, Dr. Franz Köhler Chemie GmbH, Alsbach-Hähnlein, Germany) to achieve different degrees of stiffness. In the remainder of this work, these will be referred to as firm (1 part WiroGel® M/1 part contrast agent), intermediate (1 part WiroGel® M/2 parts contrast agent) and soft (1 part WiroGel® M/3 parts contrast agent) inclusions. The diameter of the inclusions ranged from 14 to 21 mm.

2.2. Image acquisition and analysis

The phantoms were imaged using a wide angle Tomosynthesis system (Tomosynthesis Inspiration, Siemens, Erlangen, Germany; CE-marked, non-FDA-approved) with increasing compression settings ranging from 0 N to 105 N in steps of 15 N. Images were acquired parallel to the long axis of the phantom as shown in Fig. 2b. To obtain a measure of the matrix elasticity, transverse deformation and indentation area of the phantoms were measured. The phantom was then rotated 90° along the long axis and imaged again at the same compression setting, as shown in Fig. 2c. The projections obtained this way were named "plane 1" and "plane 2". The phantom was repositioned after each set of images.

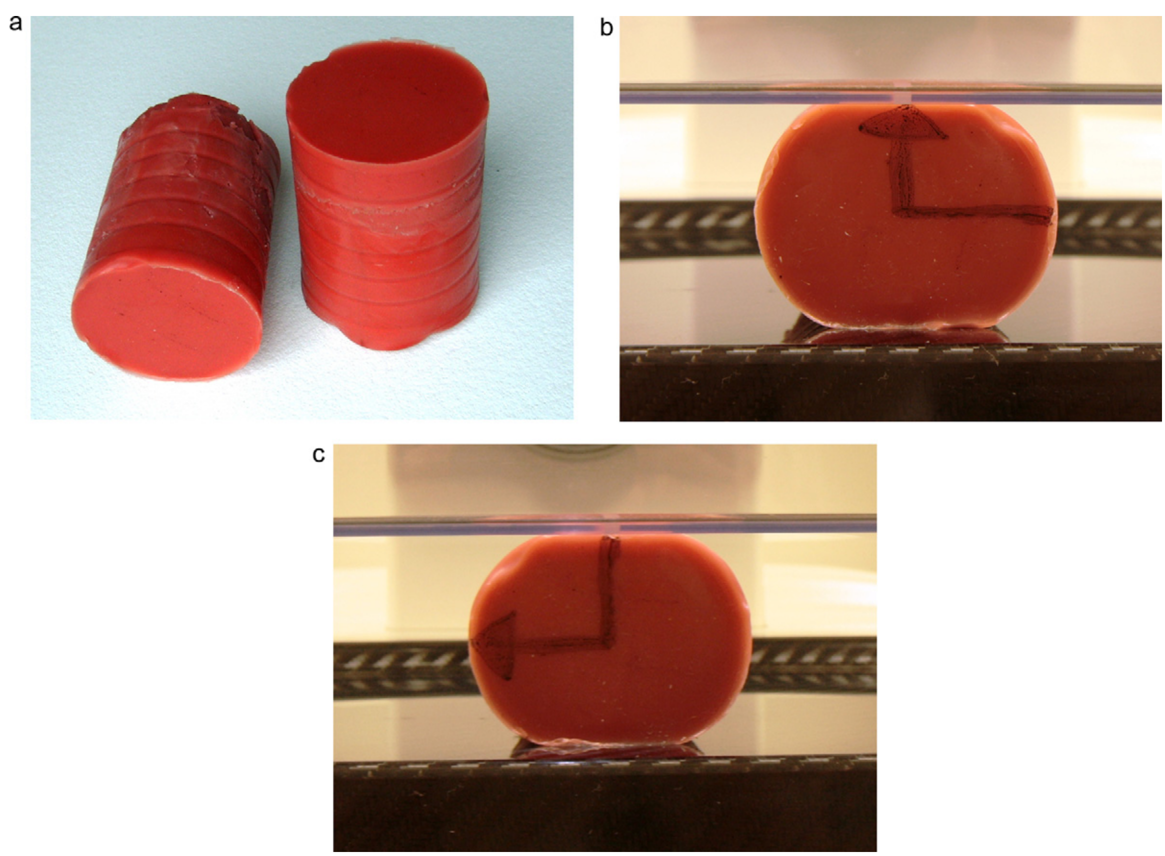

Fig. 2. (a) Two of the phantoms used for the experiments. The phantoms were of cylindrical shape, 63 mm diameter and 100 mm length. (b) A phantom during image acquisition, position 1 and (c) position 2 (rotated 90°).

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The greatest diameter of the inclusions was measured on the central slice (relative to the inclusion) in both planes using the 'distance measure'-function on a commercially available Mammography Workstation (General Electricity RA1000). A single measurement, orientated at 90° to the long axis of the phantom, was taken. Image acquisition and analysis was performed by a radiologist with 5 years of experience in clinical mammography.

2.3. Calculation of strain and Young's modulus

Strain e is defined as the change in diameter of an inclusion, expressed as a fraction of the uncompressed diameter as follows:

$$e = \frac{d - D}{D} \quad (1)$$

where d is the diameter of an inclusion in the compressed state and D is the diameter prior to compression. The strain ratio was calculated by dividing the strain of the phantom by the strain of the inclusion.

The Young modulus is defined as stress divided by strain, or

$$E = \frac{F/A}{d - D/D} \quad (2)$$

where F is the compressive force acting onto the area A of the phantom.

According to Eq. (2) the Young modulus of the inclusions was derived for each applied force in the range of 15–105 N by measuring d and A. The so obtained E-values were averaged over both projections for providing a mean Young modulus for each inclusion. Correspondingly the Young modulus of the phantom matrix material was calculated by measuring the deformation of the phantoms in the same axis as the inclusions.

2.4. Rheometric analysis

The elasticity of samples of the inclusion material and of the matrix was measured using an oscillatory rheometer (Physica MCR 301, Anton Paar GmbH, Ostfildern, Germany) at 20 °C at a frequency of 1 Hz and a strain of 0.3%. The rheometer measured shear elasticity, which was converted to a Young's modulus by multiplication by a factor of 3 [11].

2.5. Ultrasound elastography

The phantoms were scanned using two sonography systems that employed different elastography algorithms (Real-time elastography on Hitachi Preirus with Linear Broadband Transducer 13-5, 9 MHz, Software Version 1, Hitachi Medical Systems Europe Holding AG, Zug, Switzerland; Tissue strain imaging on Toshiba Aplio XG, PLT805AT Linear Ultrasound Transducer, 9 MHz, Software Version 5, Toshiba Medical Systems, Otawara, Japan). Details of these methods have been published elsewhere [12,13]. Measurements were performed by a radiologist with 15 and 5 years experience in ultrasound and ultrasound elastography, respectively.

3. Results

An example image is shown in Fig. 3.

The measured diameters of each inclusion under increasing compression are shown in Table 1. Strain at maximal compression in plane 1/plane 2 was as follows: 24.4%/24.5%, respectively, for the soft inclusion, 19.6%/16.9%, respectively, for the intermediate inclusion, and 6.0%/10.2%, respectively, for the firm inclusion. Differences in strain between the different inclusions increased with increasing compression. Strain of the inclusions under increasing compression are shown in Figs. 4 and 5.

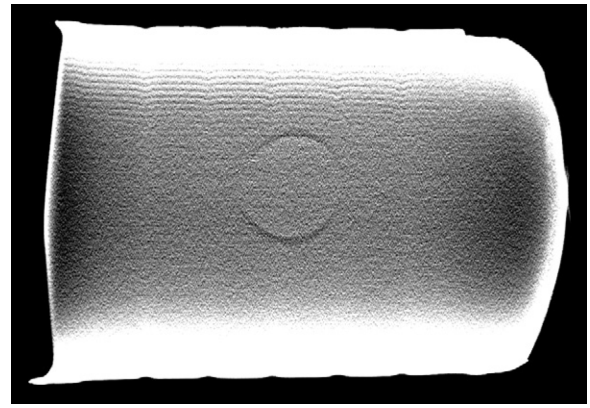

Fig. 3. 1 mm reconstructed tomosynthesis slice of one of the phantoms showing an inclusion.

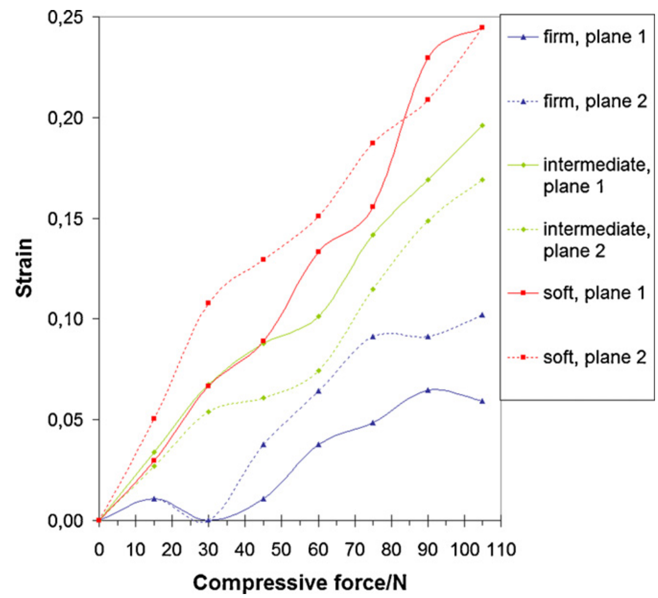

Fig. 4. Strain of the phantom inclusions, each measured transversally in two planes. The plots illustrate strain measurements for three different inclusions, i.e., soft, intermediate, and firm.

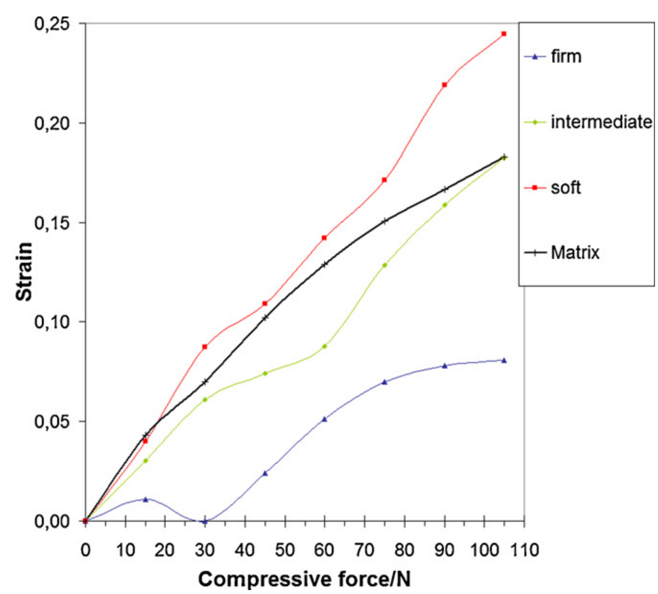

Fig. 5. Strain of the phantom inclusions averaged from transverse measurements in two planes and strain of the phantom matrix averaged from measurements of three phantoms.

Table 1
Absolute diameters of the inclusions at increasing compression.

Compression force/N	Diameter of inclusions in plane 1/plane 2/mm			Diameter of phantoms/mm
	Soft inclusion	Intermediate inclusion	Firm inclusion	
0	13.5/13.9	14.8/14.8	18.5/18.6	63/63/63
15	13.9/14.6	15.3/15.2	18.7/18.8	65/64/65
30	14.4/15.4	15.8/15.6	18.5/18.6	66/66/67
45	14.7/15.7	16.1/15.7	18.7/19.3	68/68/69
60	15.3/16.0	16.3/15.9	19.2/19.8	70/70/70
75	15.6/16.5	16.9/16.5	19.4/20.3	72/71/71
90	16.6/16.8	17.3/17.0	19.7/20.3	73/72/72
105	16.8/17.3	17.7/17.3	19.6/20.5	74/73/73

Rheometric analysis yielded a matrix elasticity of 37.2 kPa and elasticities of 15.3 kPa, 30.9 kPa and 46.8 kPa for the soft, intermediate and firm inclusions, respectively. The average matrix elasticity obtained by measurement of deformation of the phantoms according to Eq. (2) was 199.7 ± 90.3 kPa. The Young's modulus of the inclusions was 139.3 ± 53.0 kPa, 193.4 ± 59.7 kPa and 505.6 ± 357.1 kPa for the soft, intermediate and firm inclusions, respectively.

The strain ratios obtained from ultrasound elastography and tomosynthesis elastography are shown in Table 2.

4. Discussion

Determining the elasticity of breast masses can yield useful information for distinguishing benign from malignant lesions [5–7]. While elastography has been successfully established as an adjunct to ultrasound examination of the breast, other techniques may, in theory, yield similar information. Tomosynthesis has so far not been used to obtain elastographic data.

There are a number of obstacles that have to be overcome to perform an accurate assessment of tissue strain from tomosynthesis data sets. Problems arise from (a) measurement error and (b) non-uniform stress distribution. The former may be the result of multiple factors such as superimposition of overlying structures, three-dimensional irregularities of shape of the target lesions, projection error and calibration error. The latter results from difficulties in predicting force distribution in irregularly and variably shaped bodies like the human breast, inhomogeneities resulting from different tissue consistencies and, again, irregularities in shape of the target lesions.

By reducing superimpositions and improving depiction of breast masses, X-ray tomosynthesis reduces some of the sources of measurement error [9]. If accuracy of measurement is increased enough to reliably detect small changes in diameter of breast lesions at variable deformation forces, the elasticity of suspicious lesions may be measurable. Kim et al. recently demonstrated the feasibility of calculating strain-maps using computed tomography images of an X-ray phantom [14]. As breast CT produces images similar to tomosynthesis of the breast, their findings are potentially transferable to this technique. However, they used a solid phantom made of epoxy resin, which differs considerably from biological tissues in terms of elasticity. In this study, we investigated whether inclusions of different elasticities in a breast-mimicking phantom can be distinguished using one-dimensional measurement of strain under static compression and compared the results to rheometrical measurement of elasticity as well as established ultrasound elastography techniques.

The strain ratios of the inclusions obtained with tomosynthesis were comparable to the results of ultrasound elastography. All three techniques obtained strain ratios larger than those predicted by rheometrical testing. Nevertheless, relative differences could be detected by all techniques.

With regard to comparing this phantom model to actual breast lesions, little data on absolute elasiticities of human tissues are available in the literature. Venkatesh et al. performed a study using MR-elastography of benign and malignant liver lesions and obtained shear elasticities of 2.3 kPa, 2.7 kPa and 10.1 kPa for normal liver, benign liver tumors and malignant liver tumors, respectively [15]. Converting these values to Young's moduli according to [11] results in elasticities of 6.9 kPa, 8.1 kPa and 30.3 kPa, respectively, which represents a similar range to the tumor-simulating inclusions used in this study.

Measurement of lesion diameters was performed in two rectangular planes. Strain was similar in both planes, indicating reasonable reproducibility of the measurements. The data shows that some measurement error exists, which may affect the accuracy of the results particularly when strain is small. The measurement error may have partly been due to the relatively small contrast between the inclusions and the surrounding silicone matrix. A further bias may have been introduced by small irregularities in the shape of the inclusions, which impair reproducible measurements. The latter problem clearly applies to in vivo tissue with arbitrarily shaped lesion geometries. However, it is a fundamental result of this feasibility study that small amounts of deformation in near-spherical inclusions are detectable by clinical X-ray tomosynthesis.

It should be noted that this technique, in theory, allows direct measurement of elasticity of inclusions. However, elasticity becomes markedly non-linear when strain exceeds values of a few percent. This may explain the large discrepancy in the Young's moduli obtained using tomosynthesis elastography from values measured in rheometrical analysis, since the former was performed at a range of compression settings commonly used in tomosynsthesis of the breast and produced strain values ranging from 6 to 25%. Other reasons may include uni-dimensional, as opposed to multi-dimensional, measurement of strain. Therefore, a

Table 2
Strain ratios of the inclusions obtained by ultrasound and tomosynthesis elastography.

	Strain ratio			
	Strain ratio predicted from rheometry	Tissue strain imaging	Real-time elastography	Tomosynthesis elastography
Soft inclusion	0.41	0.91	0.97	0.72 ± 0.13
Intermediate inclusion	0.83	1.64	2.06	1.02 ± 0.21
Firm inclusion	1.26	2.07	2.37	2.67 ± 1.70

more reliable direct measurement of elasticity would require much smaller compression forces (much below the values used in clinical tomosynthesis) along with highly accurate, multidimensional measurement of strain. The use of image registration with calculation of strain maps may be offer an increase in accuracy of strain measurement.

A potential drawback of the technique is that it requires a minimum of two exposures with different amounts of compression. Since, with X-ray tomosynthesis, maximal compression may be less crucial to image quality than with mammography [16,17], the technique could be combined with other techniques requiring sequential exposures, such as contrast enhanced tomosynthesis [18]. Initial results of applying this technique on image data obtained from contrast enhanced tomosynthesis appear promising.

Limitations of this phantom experiment are related to the regular, cylindrical shape of the phantom and the regular, near-spherical shape of the inclusions. As the intention of the study was a proof of principle, the phantom shape was chosen intentionally in order to produce a homogenous distribution of the compressive force throughout the phantom. With a conical, less homogenous structure like the human breast, force distribution becomes much more complicated and this may be a source of error when the technique is applied to actual breast lesions. The size of the inclusions was variable for technical reasons, which leads to a relatively larger effect of measurement error with the smaller inclusions. Some lesions detected in tomosynthesis may be significantly smaller than the inclusions used, increasing the demands on accuracy in the measurements.

5. Conclusions

We conclude that tomosynthesis elastography allows assessment of strain of tumor-simulating inclusions in a breast-mimicking phantom, which can be used to differentiate inclusions of different elasticities. This novel method may be useful for assessing the elasticity of breast lesions in tomosynthesis of the breast, yielding results similar to ultrasound elastography. In a clinical setting, this technique may be combined with other tomosynthesis techniques, such as contrast-enhanced tomosynthesis.

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