# The breast under pressure

*By Prof A. den Heeten & Prof K. Grimbergen*

## THE PHYSIOLOGY OF THE BREAST

The female breast develops during the menarche and consists mainly of protein, water, and fat.  The main categories of breast tissue are adipose tissue with a low X-ray attenuation coefficient, and fibrous and glandular tissue with an attenuation coefficient close to that of water. In mammography, the principal components contributing to image contrast are water, fat, and calcium. The surface skin consists of a substantial amount of protein reinforced with strong connective tissue fibers. From a mechanical point of view, three types of tissues can be distinguished, each displaying different mechanical properties under increasing pressure exercised by the mammographic paddle.

In this paper, the term "pressure" is taken to represent the mean contact area pressure, also known as interface pressure [1]. However, the actual physical parameter of pressure varies locally because of the shape of the breast and local pathology, so pressure gradients or areas of higher pressures can exist [2]. These features are of importance in mechanical imaging, but this aspect will not be dealt with in this paper.

For several reasons a certain level of compression of the breast is required in conventional full-field digital mammography and tomosynthesis.  Immobilization of the breast is needed to avoid movement and the consequent blurring of images. Flattening of the breast gives a more homogeneous exposure and a better dynamic range of luminance superimposing structures at different depths can be better depicted. Finally breast compression enables a quality image to be acquired, at a lower radiation dose [3, 4]. In routine practice ,the process is widely known as compression, even if, strictly speaking, the breast is actually incompressible; the more rigorous, appropriate term is that the breast is deformable.

## MECHANICAL PROPERTIES OF THE BREAST

The compression force applied during mammography is readily available as output from the mammography device, and is used to indicate the level of compression. The compression pressure is not directly available. In colloquial usage both terms force and pressure are frequently used randomly and interchangeably, which is a source of confusion in the understanding of what actually happens during the compression process [5].

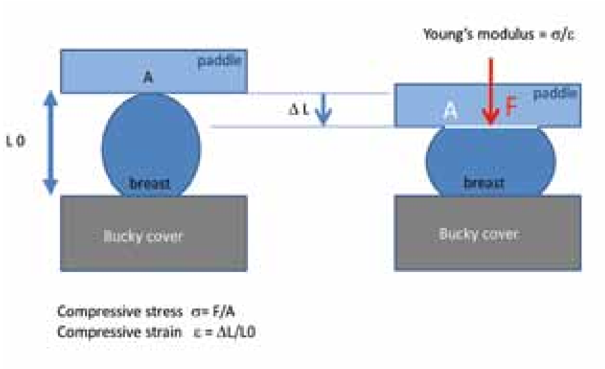


**Fig 1:** Schematic representation of mammographic compression; Young's modulus.

Using the mean Young's modulus — the ratio of the pressure (stress) and the deformation (strain) — it is possible to analyze the mechanical properties of the breast under compression [Figure 1]. The strain is itself the (dimensionless) ratio of the thickness reduction and the initial thickness. Thus, stress is equal to pressure and strain to flattening. These terms will be used in this paper interchangeably but are essentially the same.

Young's modulus thus has the dimensions of pressure and is expressed in (kilo)pascal. (It is confusing that Young's modulus is also sometimes described as an "elastic modulus" since it is not a measure of elasticity but rather of stiffness, the inverse of elasticity). During compression, the stress-strain relation of the breast can be recorded, with a strikingly large variation in the results [Figure 2]. We can distinguish linear relationships in cases of a constant (pressure-independent) Young's modulus to a progressively increasing Young's modulus and a saturating thickness with higher pressure.

From the experimental results of a large number of experimental measurements that we have amassed over the years, it can be concluded that the mechanical properties of breast tissue are very variable and differ significantly between women. In a premenopausal woman breast stiffness can even change significantly durinbg the menstrual cycle due to hormonal changes. Because of these  huge variations in the elastic properties of the breast, the usual aim of having a maximal reduction in breast thickness

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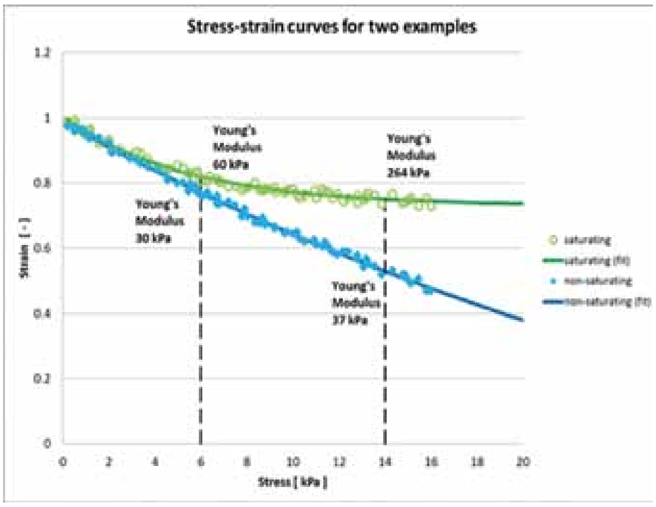


**Fig 2:** Non-saturating and saturating Young's modulus
A : The behavior of a breast (thickness 10 cm) with a linear relation, i.e., with increasing pressure a proportional decrease of thickness (constant Young's modulus (30kPa )); A proportional thickness decrease. Blue
B: The behavior of a breast (thickness 9 cm) with a non-linear relation, i.e., with increasing pressure a reduced decrease of thickness (Young's modulus (60kPa) at 6 kPa pressure): A saturating thickness decrease. Green

during mammography is actually a misconception, since this approach is based on the assumption that maximum reduction can be achieved in every breast without any *a priori* knowledge of its biomechanical properties. In addition to this, the measured Young's modulus can change per investigation, and in many women may continue without saturation as can be seen in Figure 2.

## MEAN COMPRESSION PRESSURE

When analyzing the mechanical properties of the breast, it becomes clear that pressure should be the preferred parameter to define compression [6, 7]. A complication is that breast tissue is not homogeneous and that Young's modulus is varies in the different tissues of the breast [8]. Consequently, we use the mean pressure of the contact area, also called interface pressure, which is calculated by dividing the force by the contact area between the breast and the paddle. To determine this contact area, we have developed a system based on capacitance measurement using a thin transparent conducting foil in the paddle [3]. In this way, we obtain a real-time value of the contact area, which, together with the force, enables a real-time mean pressure to be calculated during the actual breast compression. This can be directly displayed to the mammography technician or the patient. In addition, other mechanical properties can be determined and recorded, such as the evolution of the breast thickness, force, contact area and pressure, during compression [Figure 3]

## DETERMINATION OF THE OPTIMAL VALUE OF THE MEAN COMPRESSION PRESSURE

In the past, we advocated the use of a maximum of 10 kPa (75 mmHg) [6, 7] as the target for the mean compression pressure, which, it can be admitted, was initially an educated guess on our part. At the time, we reasoned that any pressure above diastolic blood pressure would be unnecessary. We considered that, because of its physiology and the effective incompressibility of the breast, the term compression gave the false impression that the breast could somehow be made smaller in volume. In fact only a very small amount of blood can be evacuated via the venous collaterals into the thoracic cavity. In addition the volume of the arterial compartment is low. Based on these considerations, a value of "somewhere in between the arterial diastolic pressure and the venous pressure" could have been advocated as the optimal compression pressure. However we knew that the skin — which has a much higher Young's modulus [8] than breast tissue — could have an influence. This is particularly relevant in lower volume breasts. In smaller breasts, the amount of skin relative to the total breast volume can even become dominant. For this reason, we decided to aim for a somewhat higher pressure, namely just below the diastolic arterial pressure.

## OTHER AREAS OF RESEARCH ON PRESSURE EFFECTS

In rehabilitation medicine, much research has been carried out on pressure sores. The focus in this field is on subcutaneous stiff bony structures, that are prone to result in pressure ulcers under certain pathologic conditions. One particularly interesting report described a comparison of the interface pressures between volunteers in different subject groups on specific seat cushions. In a group composed of relatively elderly but healthy subjects, the cushion made little difference; the measured interface pressure was consequently around 10 kPa (75 mmHg) [9]. This finding seems to indicate a physiologically determined regularity where the ratio of significantly different body weights (force) and seat contact areas became similar within in a certain range. However, this kind of research model involves much longer compression times and sometimes higher interface pressures in pathologic circumstances It was even shown that a pressure of 26,7 kPa applied for only a few minutes was sufficient to inhibit nerve conduction [9]. Similar and even higher pressures are routinely applied in current mammography practice, especially in women with small breasts [10].

## LARGE MAMMOGRAPHIC DATASETS

Large datasets of digital mammograms have been accumulated, particularly in hospitals and institutes involved in breast screening programs. Data mining of such datasets has become feasible thanks to newly developed software (Volpara enterprise) [11]. By this means, a large and growing amount of data has become available regarding pressure during mammography. Despite enormous variations between mammography practices, countries, and continents, the "center of gravity" of the pressure scatterplots is almost exactly 10 kPa. This was described in an earlier communication which reported the combined pressure values derived from the datasets using the Volpara software package [4]. Of course, there are areas in the world such as Asia where generally higher pressures are applied due to the women's smaller breasts [12]. Another reason for high pressure is the misinterpretation of the European guideline which in fact says that "*no optimal compression has been*

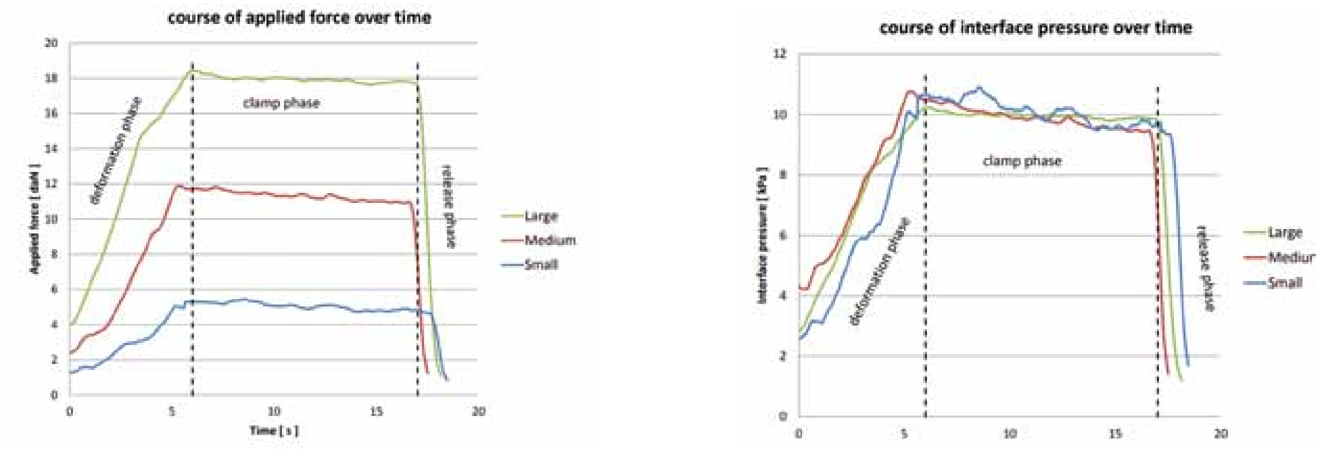


**Figure 3:** Real time recording during a typical mammographic compression with a dedicated paddle with a contact area measurement tool. The ratio with the force contact-area is calculated to the mean target pressure (10 kPa) [6]. Women with small breasts receive a lower force according the output of the mammographic machine but undergo the same pressure.

*determined*". On its own, this is perhaps not a very convincing argument. On the other hand, our collected data are based on over 150 000 mammograms [4] and show that a target pressure of 10 kPa has a clear correspondence with the mean daily practice throughout the world. As can be seen in figure 4 A, the "center of gravity" of 44,000 compressions (both data sets combined) also approaches 10 kPa (10,8 kPa). These data also show large variations. This enormous disparity in compression would diminish if a rational target pressure were to be used, together with real-time mean pressure measurement and monitoring during mammographic compression. A large decrease in variability when a pressure based compression procedure is carried out is shown in Figure 4. In a study comparing US and Dutch cohorts with a clinic where a pressure paddle was being used, it was found that with the pressure paddle, compression levels greater than 20 kPa occurred 30 times less frequently; likewise mean pressures under 5 kPa occurred 31 times less often.

## PRESSURE, YOUNG'S MODULUS, AND LESION DETECTION

In general, stiffening of breast tissue correlates with pathology. In inflammation, for example, the whole breast becomes harder,

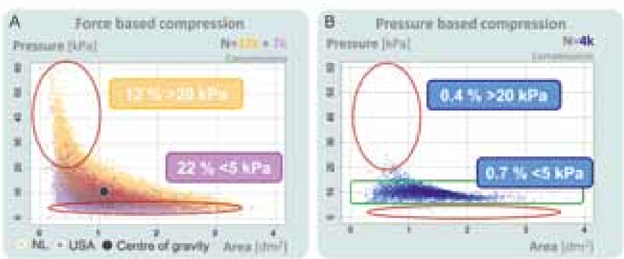


**Figure 4** : A: under the current way of working as calculated from a database (US and Dutch data), a large variation in pressure can be noted, in which the 20 daN limitation of the motor-drive of the paddle explains the banana shape of the plot. In fact women with small breasts are in no way protected by this limitation. B: Same plot as A in a hospital population with application of a pressure based compression. Figure adapted from [10]

with the result that Young's modulus differs sharply from that of the healthy breast. The primary goal of palpation in a physical examination is to find local differences in stiffness. But local and subtle areas with a higher Young's modulus can be hard to detect when the breast is large and/or stiff. It is known that the Young's modulus of different tissues can vary significantly, sometimes by as much as a factor of up to 15 times [13]. Such differences can be identified for example by using ultrasound imaging and can be quantified by shear wave elastography. In mammography of the compressed breast, differences in elasticity are sometimes the only indication of malignancy, for example in the more diffusely growing invasive lobular carcinomas. There are not many data in humans, but in tissue-mimicking phantoms, at different compression levels, it has been shown that most tumors will undergo smaller deformation than surrounding tissues. As a result of this, X-ray attenuation differences will be enhanced [14]. With further increases in pressure, the Young's modulus of fibroglandular, fat and tumor tissue converge [Figure 5]. Differences in stiffness thus become smaller at higher pressures [15] making it plausible that the X-ray attenuation differences will decrease again.

It is already known that the Young's modulus of invasive breast cancers can also vary substantially [16].

These effects may be the reason for the recent observations that at pressures higher than 10 kPa, there is a reduction in the detection of breast cancerous lesions and, perhaps more importantly, also in the one-year screening program sensitivity [17, 18]. The consequence of this is that there are relatively more interval cancers in the high pressure group.

## DISCUSSION

By far the most frequently carried out stress-strain test throughout the world is in the field of mammography. A conservative estimate shows that a number of nearly 500 million compressions in mammographies were carried out per year ( based on 125 million mammographies per annum times four exposures and compressions). This corresponds to a frequency of 16 compressions in mammography per second, 24 hours per day! Until recently, there was no apparent

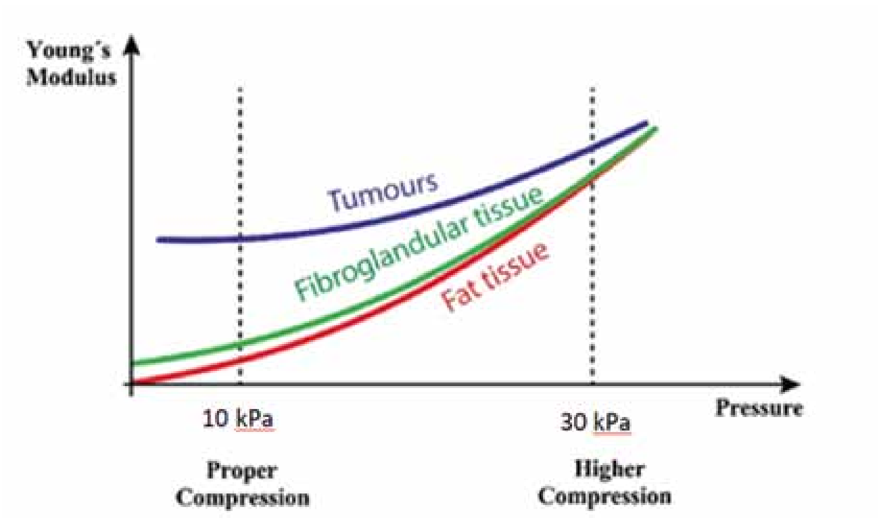


**Fig 5**. Converging stiffness curves at increasing compression pressure (Adapted from 13, 15).

awareness or concern that essential information (e.g. pressure) is lacking in the mammography examination.

Consequently it could be considered a medical procedure which is not adequately defined and therefore unreliable and sometimes perhaps not even safe or not safe enough. Pain and discomfort have been analyzed and reported in the literature because of the impact these factors have on compliance to screening. But serious incidents and reports about bruises and hematomas are more anecdotal. If mammographic compression without any method of measuring or objective monitoring of the pressure were to be introduced today as a brand new technique, it would probably never be accepted under current regulations because of patient safety concerns.

The justifiably strict and rigorous quality rules generally applied over the world (such as CE accreditation and FDA clearance), paradoxically seem to deter the medical equipment industry from taking simple remedial measures and considering mammographic compression as an *in vivo* stress-strain test that potentially can cause discomfort or even harm people.

## WHAT SHOULD BE DONE TO ACHIEVE A MORE CONTROLLED SITUATION?

**1.** A first step would be equipping mammographic machines with a pressure sensor. At the moment only the force parameter is displayed. Pressure — the ratio of the force to the contact area — is an essential parameter and can nowadays be measured without affecting the image quality or radiation dose [19], Such pressure data can allow the determination of a mean contact area pressure. It is this pressure that will cause strain and should be carried out within reasonable and conceivable physiologic boundaries. We have good reasons to advocate a pressure of 10 kPa to achieve enough strain in normal breast tissue and avoid extra radiation dose. This pressure is also enough to keep an invasive breast tumor relatively 10 to 15 times more stiff than normal breast tissue. The benefit of this is that such local differences in Young's modulus could enhance lesion conspicuity.

**2.** The guidelines in breast cancers screening should be revised because terms like "*stay within 10 -18 daN*" can in practice result in 18 daN on a contact area equal to or under 0,5 $dm^2$. Pressures over 36 kPa (270 mmHg) do happen and place all structures in a breast (pathologic and non –pathologic), roughly in the same stiffness range. Extreme (high and low) pressures can be found everywhere. In all mammographic databases that we were able to analyze from countries with moderate compression habits such as the US, UK, and Sweden, we noticed that a number of women fell within these extremes.

Without objective measurement, there is simply no way to estimate the pressure adequately.

## REFERENCES


1. Swain I. (2005) The Measurement of Interface Pressure. In: Bader D.L., Bouten C.V., Colin D., Oomens C.W. (eds) Pressure Ulcer Research. Springer, Berlin, Heidelberg.
2. Dustler M, Förnvik D, Timberg P, Andersson I, Petersson H, Brorson H, Tingberg A, Zackrisson S. Can mechanical imaging increase the specificity of mammography screening? Eur Radiol. 2017 Aug;27(8):3217-3225.
3. Grimbergen K, den Heeten A. Pressure controlled compression of the breast in mammography.DI Europe October 2016; 32:40-43
4. Grimbergen K, den Heeten A. Mammographic compression and diagnostic performance. DI Europe. October 2017; 33: 42-45
5. Grimbergen CA, den Heeten GJ. Pressure and breast thickness in mammography–what about physics? Br J Radiol. 2013 Jul;86(1027).
6. de Groot JE, Broeders MJ, Branderhorst W, den Heeten GJ, Grimbergen CA. A novel approach to mammographic breast compression: Improved standardization and reduced discomfort by controlling pressure instead of force. Med Phys. 2013 Aug;40(8)
7. de Groot JE, Branderhorst W, Grimbergen CA, den Heeten GJ, Broeders MJM. Towards personalized compression in mammography: a comparison study between pressure- and force-standardization. Eur J Radiol. 2015 Mar;84(3):384-391.
8. Liang X, Boppart SA. Biomechanical properties of in vivo human skin from dynamic optical coherence elastography. IEEE Trans Biomed Eng. 2010. Apr;57(4):953-9.
9. Swain ID, Bader DL. The measurement of interface pressure and its role in soft tissue breakdown. J Tissue Viability. 2002 Oct;12(4):132-4, 136-7, 140-6. Review.
10. Branderhorst W, de Groot JE, Highnam R, Chan A, Böhm-Vélez M, Broeders MJ, den Heeten GJ, Grimbergen CA. Mammographic compression–a need for mechanical standardization. Eur J Radiol. 2015 Apr;84(4):596-602.
11. https://volparasolutions.com/our-products/volparaenterprise/ approached 09-02-2018
12. Lau S, Abdul Aziz YF, Ng KH. Mammographic compression in Asian women. PLoS One. 2017 Apr 18;12(4):e0175781.
13. Barr RG, Zhang Z. Effects of precompression on elasticity imaging of the breast: development of a clinically useful semiquantitative method of precompression assessment. J Ultrasound Med. 2012 Jun;31(6):895-902.
14. Kim JG, Aowlad Hossain AB, Shin JH, Lee SY. Calculation of strain images of a breast-mimicking phantom from 3D CT image data. Med Phys. 2012 Sep;39(9):5469-78
15. Ramião NG, Martins PS, Rynkevic R, Fernandes AA, Barroso M, Santos DC. Biomechanical properties of breast tissue, a state-of-the-art review. Biomech Model Mechanobiol. 2016 Oct;15(5):1307-23.
16. Samani A, Zubovits J, Plewes D. Elastic moduli of normal and pathological human breast tissues: an inversion-technique-based investigation of 169 samples. Phys Med Biol. 2007 Mar 21;52(6):1565-7614
17. Holland K, Sechopoulos I, Mann RM, den Heeten GJ, van Gils CH, Karssemeijer N. Influence of breast compression pressure on the performance of population-based mammography screening. Breast Cancer Res. 2017 Nov 28;19(1):126.
18. Moshina N, Sebuødegård S, Hofvind S. Is breast compression associated with breast cancer detection and other early performance measures in a population-based breast cancer screening program? Breast Cancer Res Treat. 2017 Jun;163(3):605-613.
19. Pressure-standardised mammography does not affect visibility, contrast and sharpness of stable lesions de Groot, J.E. et al. European Journal of Radiology , Volume 86 , 289 – 295.