Mammography and Digital Breast Tomosynthesis: Technique

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Abstract

The introduction of mammography as a radiographic imaging modality optimized for breast imaging revolutionized breast cancer care. Throughout the decades, conventional, screen-film-based mammography has given way to digital mammography, resulting in many benefits, including a streamlined workflow and improved performance in certain subgroups of patients. More importantly, the introduction of digital technology in mammographic imaging resulted in the development of even more advanced technologies, such as digital breast tomosynthesis. Tomosynthesis, with its ability to result in pseudo-tomographic imaging of the breast with a system that has the same footprint and workflow as mammography, has had an important impact in the breast imaging clinic.

In this chapter, the basic concepts of X-ray-based breast imaging, common for both mammography and tomosynthesis, are reviewed. The major components of these imaging systems are described, and the resulting and potential clinical and screening performance of these modalities is discussed. Finally, considering their widespread use in asymptomatic women during screening, the dosimetry aspects of X-ray-based breast imaging are explained.

1 Introduction

Even after years of research and development of more advanced imaging techniques, some of them involving acquisition of functional, multiparametric, and/or dynamic data, mammography is still the most common modality used for breast cancer imaging. Its relatively high performance, ease of use, affordability, few requirements for installation, and speed of acquisition and interpretation have made it, and its newly developed offspring, digital breast tomosynthesis, the main workhorse of breast imaging.

Mammography is based on the principles of standard radiography, but modified and optimized to image the breast. Due to specific clinical and physical requirements, breast imaging, especially for detection of features that suggest the presence of cancer, necessitated the development of a separate system. The end result is a device that can acquire an image of the breast in a couple of seconds, with the ability to depict both very fine calcifications and very subtle masses and spiculations at the same time. These different suspicious features, which can be the result of malignancy, require very different imaging capabilities, a problem that has been solved by the optimization of a radiography system for this specific clinical application.

Due to its benefits, mammography is not only used in clinics and hospitals for diagnosis of breast disease in (mostly) women presenting with symptoms, but more importantly, for screening for breast cancer in asymptomatic women. Mammographic screening for breast cancer has become common practice throughout the industrialized world, with some countries even implementing population-based screening programs. As part of these programs, all women of a certain age group are invited to undergo mammographic imaging for detection of suspicious findings that may indicate the presence of breast cancer. This widespread use of mammography can only be performed due to its aforementioned advantages, such as noninvasiveness, affordability, ease and speed of use, and high detection performance.

In this chapter, the basics of mammography and digital breast tomosynthesis, their capabilities and limitations, clinical use, and other characteristics, such as radiation dose, are discussed.

2 Basics of X-Ray-Based Breast Imaging

Mammography is an X-ray-based transmission imaging technique. This means that the mammographic image is formed by transmitting a field of X-rays through the breast and detecting the X-rays that exit it. The resulting mammogram shows the differences in how the different breast tissues attenuate the X-rays traveling through them (Fig. 1). At the macroscopic scale, in terms

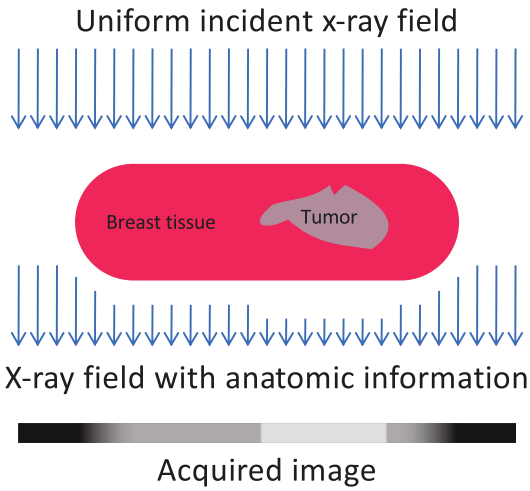

Fig. 1 Diagram of the acquisition of a mammogram. An incident X-ray field, as uniform as possible, is emitted towards the breast. The tissue attenuates the field, with each type of tissue attenuating the field differently. The differences in the intensity of the X-ray field that exit the other side of the breast reflect the differences in attenuation of the tissues contained inside the breast. The detector captures the X-rays and the resulting image is related to the amount of X-ray energy arriving at the detector. In this diagram, the length of the arrows representing the X-rays corresponds to the number of X-rays at each location

of absorption of X-rays, the breast can be assumed to be composed of largely three different tissues: skin, adipose, and fibroglandular tissue. Adipose tissue attenuates X-rays less than fibroglandular tissue (Hammerstein et al. 1979). Therefore, a dense area of the breast, composed mainly of fibroglandular tissue, appears brighter in a mammogram than a more fatty area.[1] Meanwhile, malignant tissue attenuates X-rays at a very similar rate to that of fibroglandular tissue (Hammerstein et al. 1979; Johns and Yaffe 1987). This means that a malignant lesion can appear with the same brightness in a mammogram as normal fibroglandular tissue. Therefore, detection of lesions depends on their irregular shape being visible against an adipose background. If a lesion is completely surrounded or superimposed by fibroglandular tissue, then it might not be visible. This is why the sensitivity of mammography is substantially reduced with increasing breast density (Wanders et al. 2017).

[1]Dense areas appear brighter in the already processed "for presentation" mammogram. In the original raw "for processing" mammogram, dense areas appear darker. The image is inverted during the image processing that every digital mammogram undergoes.

2.1 Breast Lesions

The main types of suspicious features that mammography aims to depict in the detection and diagnosis of breast cancer are the following:

- Masses: In general, dense areas, usually with low contrast, of round, oval, or irregular shape, well-defined or ill-defined margins which could include spiculations (thin, low contrast, fiber-like structures) radiating outwards. Irregular shape, ill-defined margins, presence of spiculations, and other features are markers of malignancy.
- Architectural distortions: Distortions in the normal parenchymal pattern of the breast, with no associated visible mass. These include radiating spiculations, which are fine fiber-like tissues of low contrast.
- Microcalcifications: Specks (usually high contrast) that could be as small as 100 μm in size, usually grouped in clusters. Their size and shape, and more importantly the shape and distribution of the cluster, are determinants of the probability of malignancy present.
- Asymmetries: Fibroglandular tissue patterns tend to be symmetric between the left and right breasts. Deviations from this, i.e., presence of asymmetry, can be markers of malignant development.

Although other signs of pathologic processes exist, these are the main features of breast cancer in mammograms, and, importantly, the ones that define the capabilities that a mammography system must possess. As can be seen, soft-tissue lesions (masses and architectural distortions, especially) require high contrast, while depiction of calcifications requires very high spatial resolution. Mammography systems are optimized to

deliver these two demanding capabilities in the same image, a challenging feat.

2.2 Digital Mammography

Until the turn of the century, mammography was performed using screen-film. However, the development of digital detectors allowed for the introduction of digital mammography. The benefits of digital over screen-film mammography are numerous, the most important being the following:

- Linear response with high dynamic range: Digital detectors cannot be under- or overexposed (until saturated), in terms of resulting contrast. Whereas films had a narrow exposure range in which an image had adequate contrast, changes in the overall exposure in digital mammography will only affect the level of noise, but not the contrast between tissues. This reduces the number of retakes.
- Lower dose: Especially in more recent generation of digital mammography, the dose required per acquisition has been substantially reduced (Hendrick et al. 2010; Bouwman et al. 2015).
- Easy transmission and archiving: Of course, a digital signal is much easier to transmit and archive than a film.
- Improved workflow: Images can be checked immediately after acquisition at the acquisition workstation, resulting in a faster check of the need for a retake.
- Production of a digital image: This might be the most important advantage, since it allows for easy post-processing of the image to optimize its display, and, perhaps even more importantly, for more advanced imaging methods, such as contrast-enhanced spectral mammography and digital breast tomosynthesis.

Of course, screen-film mammography is cheaper and was the established technology, so there was a significant cost in upgrading to digital mammography. Finally, the spatial resolution of screen-film mammography is superior to that of digital mammography.

Even though the DMIST trial showed only a detection performance improvement with digital mammography over screen-film for specific subgroups of the general population it did not show an overall detection performance improvement with digital mammography over screen-film (Pisano et al. 2005). However, the other benefits of digital mammography beyond clinical performance, as listed above, have resulted in screen-film mammography being completely phased out in the developed world.

2.3 Digital Breast Tomosynthesis

Digital mammography, however, is not without limitations. Chief among them is its 2D nature, which results in the need to represent the 3D breast tissue distribution information onto a single 2D plane. This results in tissue superposition, where two features of the breast that are actually separated in the vertical direction coincide in the mammographic image. If one of these features is a malignant lesion, it could be rendered undetectable due to it being superimposed by the other, resulting in a loss of sensitivity. In addition, if both of these tissues are normal, they could project in such a way that they appear to be something suspicious, resulting in a loss of specificity. Therefore, the ability to represent the breast in its true 3D form, or at least in a form that approximates it, held great promise in improving clinical performance.

With the introduction of digital detectors for breast imaging, Niklason et al. introduced in 1997 the first practical study on digital breast tomosynthesis (Niklason et al. 1997). One of the major advantages of digital breast tomosynthesis, also called *limited-angle tomography*, is its similarity to mammography. As can be seen in Fig. 2, in its simplest implementation, breast tomosynthesis involves the acquisition of several mammography-like images, *projections*, while the X-ray source rotates around the compressed breast. By acquiring a number of such projections over a certain angular range, enough information about the

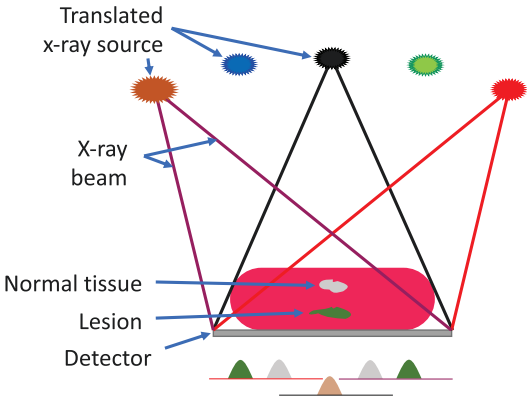

Fig. 2 Diagram of the acquisition of a digital breast tomosynthesis image. The breast is positioned in the same manner as for mammography. The X-ray source rotates over a limited angle around the breast, acquiring several low-dose mammography-like images at each preset acquisition angle. Depending on the vertical location of the features inside the breast, these shift differently in their location in each projection. This provides enough information to the reconstruction algorithm to generate a pseudo-3D image of the breast volume

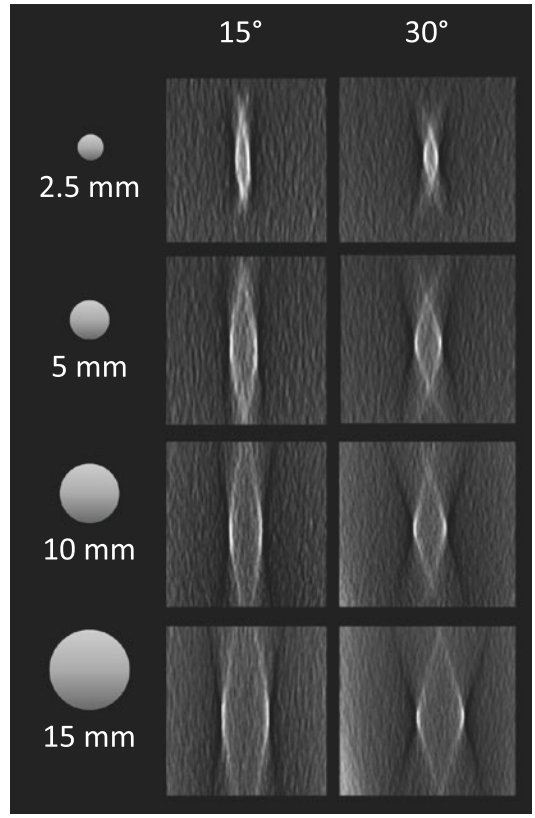

Fig. 3 Simulated digital breast tomosynthesis images of a circular disk of various sizes for two different total angular ranges, shown from the side. The size of the disk affects over how many slices, beyond the ones it actually occupies, the signal can still be seen. As can be seen, therefore, being a pseudo-3D modality, the effective vertical resolution in DBT is size and contrast dependent. (Image courtesy of Dr. John Boone, from Nosratieh et al., "Comprehensive assessment of the slice sensitivity profiles in breast tomosynthesis and breast CT," *Medical Physics*. 39(12), 7254–7261 (2012). © American Association of Physicists in Medicine)

relative position of the different tissues in the breast is obtained that a *pseudo*-3D image of the breast can be reconstructed.

As a result of the reconstruction process, the imaged breast is represented as a stack of slices parallel to the detector entrance (and therefore to the breast support table). It is important to note that tomosynthesis is not a true 3D modality, given that the limited angle covered during projection acquisition does not allow for a full recovery of the vertical (direction perpendicular to the detector surface) distribution of tissue. Rather, the tissues that are actually located above and below the currently viewed tomosynthesis slice are preferentially blurred out from the image, but not necessarily completely removed.

The visibility of these out-of-plane structures depends on their contrast and on the angular range of the acquisition (Sechopoulos and Ghetti 2009). A large or very bright signal, e.g., a large calcification, might be visible in many or all tomosynthesis slices, while a small or faint mass might be well constrained to only appearing in a few slices, even if beyond the ones that it actually occupies (Fig. 3). Therefore, strictly speaking the reconstructed tomosynthesis slices do not have a specific thickness, since what is depicted in them depends on the nature of the signal. As done by Niklason et al. in their original paper, most tomosynthesis systems today still reconstruct one slice every 1 mm in the vertical direction. This does not mean that the slices are 1 mm thick, but rather that they are separated by 1 mm.

Even though tomosynthesis results in a limited vertical spatial resolution, its ability to partially suppress the effect of tissue superposition is enough to have an important impact on the sensitivity and specificity for breast cancer detection,

compared to standard digital mammography, as will be discussed in Sects. 5 and 6.

After the advent of tomosynthesis, which was at first introduced in the clinic as an adjunct to mammography, the vendors introduced the concept of the *synthetic mammogram*. The intent of this image was to generate a mammogram-like 2D image from the tomosynthesis data that would replace and avoid the acquisition of a real mammogram. For this, computer algorithms were developed that would summarize the information in the reconstructed tomosynthesis stack of slices into one 2D image, with the aim of replicating, as closely as possible, what a mammogram of that same breast would look like (Gur et al. 2012). Although initial attempts of generating these synthetic mammograms resulted in a loss of performance compared to the use of real digital mammograms, even when used together with the tomosynthesis stacks, subsequent generations of synthetic mammograms have been shown to result in equivalent performance as digital mammograms, again, when in combination with the tomosynthesis stacks (Gur et al. 2012; Skaane et al. 2014).

Synthetic mammogram-generating algorithms have continued to evolve, including even introducing a rotating synthetic for easier visibility of feature depth (Tani et al. 2014). However, although it is still not recommended to be used without the corresponding tomosynthesis stack for detection, early comparisons of the performance of synthetic mammograms compared to digital mammography and tomosynthesis stack have been performed, yielding disparate results (Murphy et al. 2018; Rodriguez-Ruiz et al. 2018c). In addition, currently it is thought that the synthetic mammogram should not attempt to replicate a mammogram as closely as possible, but rather should attempt to summarize the interesting features found in the tomosynthesis stack onto one 2D image. This is an important change in the thinking behind the synthetic mammogram. Given the original intent of the synthetic mammogram, its generation involved the attempting to replicate the projection of the 3D tissue information onto one plane. The newer role of the synthetic requires the analysis of the 3D image content from a diagnostic point of view, similar to that of a computer-aided detection or diagnosis algorithm.

2.4 Mammographic Views

For both mammographic and breast tomosynthesis acquisitions the breast is positioned, and compressed, in specific orientations. There are a number of possible views, some for imaging the whole breast (or as much tissue as possible), while others, such as spot or magnification views, involve special equipment and are aimed at imaging only a specific portion of the breast. In the former set are included the two most common views, which are the ones used for screening: the craniocaudal (CC) and the mediolateral oblique (MLO) views.

The CC view is acquired with the breast compression paddle and the breast support table horizontal (parallel to the floor), with the breast laid on the latter. For compression, the breast is compressed downward by the paddle until the appropriate level of compression is achieved. The MLO view involves rotating the mammography gantry to approximately 45°, positioning the support table on the lateral side of the patient, below the axilla, and compressing from the medial side. In the MLO view the pectoralis muscle should be included in the field of view. There are various guidelines that determine what is an appropriate positioning for these and the other mammographic views (e.g., Kopans 2007; European Commission 2006).

3 Imaging Systems

To acquire mammography (and digital breast tomosynthesis) images, mammography systems are adaptations of radiography systems optimized for the requirements of breast imaging. The main components of a (digital) mammography/tomosynthesis system are the X-ray source, the compression paddle, the breast support table, the anti-scatter grid, and the (digital) detector (Fig. 4). Of course, there are many other

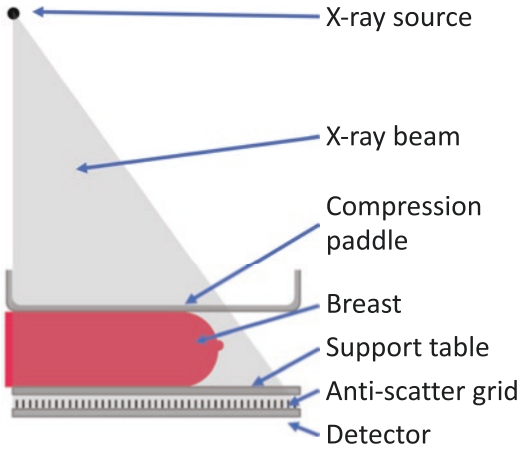

Fig. 4 Diagram showing the main components of a (digital) mammography/tomosynthesis system: X-ray source, compression paddle, breast support table, anti-scatter grid, and (digital) detector

components that make the acquisition of an image possible, but these, in addition to the acquisition workstation, form the main components of the image acquisition chain.

3.1 X-Ray Source

Although some alternative X-ray sources are being investigated, especially for digital breast tomosynthesis (Qian et al. 2012), currently all mammography systems use a traditional X-ray tube as the source of X-rays. X-ray tubes do not emit X-rays of a single energy, but rather a spectrum of X-rays, which include a range of X-ray energies, with a varying number of X-rays at each energy. The energy range of these X-rays and the number of X-rays at each energy level are important determinants in the trade-off among the resulting image contrast, image noise, and dose to the breast.

To obtain the high contrast required for breast imaging, the mammographic X-ray tube uses lower tube voltages than those used in any other radiographic application. For mammography, voltages between 25 and 32 kV are the most commonly used, while for tomosynthesis higher voltages, up to ~38 kV, may be used (Feng and Sechopoulos 2012). Using such low tube voltages has the benefit of increasing tissue contrast, but results in the need for higher tube currents and/or exposure times; in mammography and tomosynthesis, exposures at anywhere between ~60 and ~200 mAs are commonplace, while general radiography values are typically below 10 mAs.

In addition to using lower voltages, mammographic X-ray tubes have traditionally used anodes of materials other than tungsten, the commonly used material in radiographic X-ray tubes. Tubes with anodes made of molybdenum and rhodium were common. However, current state-of-the-art mammography systems mostly use tungsten-anode X-ray tubes.

To further optimize the shape of the X-ray spectrum used to acquire the images, additional filtration is added to mammographic X-ray tubes. These filters are intended to preferentially absorb X-rays of specific energy ranges, for different purposes. In the first place, one fundamental requirement is to remove the X-rays of very low energy from the beam. These X-rays, if allowed to reach the breast, would all be absorbed in the first few mm of tissue, increasing the dose to the breast without providing any additional information to the resulting image. Depending on the X-ray tube anode, filtration is also used to absorb the higher energy X-rays emitted by the X-ray source. Allowing too many of these X-rays in the beam would, due to their high energy, reduce the contrast in the image. However, a balance needs to be achieved, since more X-rays being detected result in a lower image noise.

The motion of the X-ray source during digital breast tomosynthesis projection acquisition varies across commercial systems. In most tomosynthesis systems, the X-ray tube continues to rotate during acquisition of each projection. This decreases acquisition time and simplifies the motion mechanism, but introduces a loss of spatial resolution (Zhou et al. 2007). Currently one tomosynthesis vendor uses a stop-and-shoot method, in which the X-ray tube stops completely at each projection acquisition position before performing the projection acquisition. This has the benefit of avoiding the loss of spatial resolution due to the effective increase in the size of the

focal spot, while needing to ensure that no overt vibration in the system due to the sudden stop in motion is present during acquisition.

3.2 Compression Paddle

During acquisition of a mammographic or breast tomosynthesis image, the breast is mechanically compressed against the breast support table by a compression paddle. Compression paddles are composed of different types of transparent plastic, a few mm thick. They can be of different sizes, some being as large as the active detector area (usually 24 cm × 30 cm), while others are specific for diagnostic spot views, and therefore could be as small as 7.5 cm in diameter.

Compression paddles are designed to remain relatively horizontal and therefore parallel to the breast support, while some incorporate a flexible attachment to their holder, therefore tilting upwards towards the posterior of the breast as compression force is increased (Mawdsley et al. 2009; Tyson et al. 2009). Although this adjustment to the natural breast anatomy is proposed to result in decreased pain, in a study of 288 women undergoing screening no difference in perceived pain was detected, while the flexible paddle resulted in a reduction in the amount of fibroglandular tissue in the posterior section of the breast and a reduction in contrast (Broeders et al. 2015).

Other innovations aiming at reducing discomfort or pain and/or increasing tissue coverage have been introduced by several manufacturers, such as curved compression paddles, breast cushioning pads, and positioning sheets. In general, there have been few independent studies on the effectiveness of these devices in reducing discomfort or improving image quality, and the studies that have been performed report equivocal results (Timmers et al. 2015; Markle et al. 2004). Another option aimed at reducing patient discomfort is giving the women the option of performing the breast compression themselves (Kornguth et al. 1993; Balleyguier et al. 2018). This alternative has yielded very promising results, with no loss of image quality and with the women expressing a willingness to repeat the experience. The more recent study included a quantitative comparison on compression level, breast thickness, and average glandular dose between technologist compression and self-compression (Balleyguier et al. 2018). Perhaps surprisingly, the women applied a higher final compression force to themselves than that used by the technologist, resulting in statistically, though probably not clinically, significant reductions in compressed breast thickness and dose (Balleyguier et al. 2018).

3.3 Anti-scatter Grid

The most important component to the imaging chain in the breast support table, aside from the detector itself, is the anti-scatter grid. The inclusion of the signal from scattered X-rays in the image results in a reduction of contrast. To reduce this effect, a grid is located between the breast support and the detector entrance surface that preferentially absorbs scattered X-rays while transmitting through non-scattered (also called *primary*) X-rays. To accomplish this, anti-scatter grids consist of a series of very fine walls, called *septa*, closely spaced, that are either parallel to each other or focused so that they are parallel to the expected incident primary X-rays. Since scattered X-rays tend to travel at other, larger, angles, these are more probable to encounter one of these septa. Since the septa are composed of highly attenuating material, these X-rays are absorbed, while the primary X-rays that traverse the grid parallel to the septa continue straight through (Fig. 5).

Of course, since the septa has some thickness to them, they are not perfect in transmitting all primary X-rays. Therefore, in a high-spatial-resolution application like mammography, the shadows of the septa would be visible if this is not accounted for. To avoid this, the anti-scatter grid is moved during acquisition of the mammogram, so as to blur out the shadow of the septa. This, unfortunately, results in an added complexity to the system, since a motion system needs to be added within the detector housing to perform

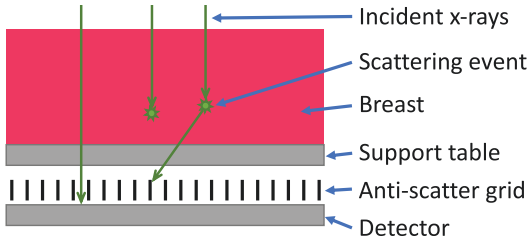

Fig. 5 Diagram showing how an anti-scatter grid works. X-rays that are incident on the breast may travel straight through (leftmost X-ray), be absorbed in the breast (center X-ray), or scatter in the breast (rightmost X-ray). The X-rays that do not undergo any interaction with the breast tissue travel through the anti-scatter grid parallel to the septa, so most of them are transmitted through. The X-rays that undergo a scattering event change direction, and are therefore more likely to be absorbed by the septa of the grid

this movement. In general, inadequate motion of the anti-scatter grid is the main source of artifacts when any grid-related problem arises in the images.

Two types of anti-scatter grid are common in mammography systems: linear and cellular. Linear grids have septa in one direction, and therefore need to be separated, for structural reasons, with a solid material, which is commonly carbon fiber. Cellular grids are composed of septa in both perpendicular directions, so they result in improved scatter rejection. The honeycomb-like structure of the septa eliminates the need for a solid material in between, so the space simply consists of the ambient air. Due to these factors, cellular grids result in a somewhat better contrast improvement compared to linear grids (Rezentes et al. 1999). However, cellular grids require a more complex motion path to blur out the septa shadow, and therefore are more prone to malfunctioning.

Given the varying incident angle of primary X-rays due to the rotating X-ray source, in general the anti-scatter grid is not used during acquisition of tomosynthesis projections. This results in the signal from the scattered X-rays being included in the acquired projections, which has been found to reduce contrast and signal-to-noise ratio (Liu et al. 2006; Wu et al. 2009). The digital breast tomosynthesis systems from one commercial vendor do use the anti-scatter grid during tomosynthesis, however.

Recently, one manufacturer has, for breast thicknesses up to 69 mm, replaced the use of the anti-scatter grid with a software-based post-acquisition correction for the effects of X-ray scatter (Fieselmann et al. 2013; Monserrat et al. 2018; Abdi et al. 2018). Removal of the anti-scatter grid avoids its (unwanted) attenuation of the primary X-rays. After evaluation of screening outcomes of over 70,000 patients, Abdi et al. found an equivalent performance with the software-based solution but with a reduction in the dose of 13–36%, depending on breast thickness.

3.4 Digital Detector

Currently two main types of digital detectors are used in commercial digital mammography/digital breast tomosynthesis systems, the indirect and the direct detectors.

Indirect detectors, only used by one system vendor, involve a two-stage detection process, in which the incident X-rays are first absorbed in a crystal layer that, upon absorption of each X-ray, emits light. This light is the one that is then actually detected and quantified by the digital detector, resulting in a digital signal that corresponds with the amount of X-ray energy arriving at the detector. This two-stage behavior is similar to that used in screen-film.

Direct detectors rely on a detection layer in which the incident and absorbed X-rays directly result in an electrical charge, which is then quantified by the electronics of the detector.

Both types of detectors result in digital images composed of ~2400–3500 pixels × 3000–4500 pixels, depending on their pixel size, to cover the current standard full field size of ~24 cm × 30 cm. Although previous-generation digital mammography systems included detectors of the order of 24 cm × 20 cm, the current larger area detectors minimize the number of tiled acquisitions that were needed to fully image a larger compressed breast. For tomosynthesis, it is also common, to decrease acquisition time, for the pixels to be

binned (combined) during readout by 2 × 2 pixels. This results in pixels in tomosynthesis projections being double the size of those in mammography images, with a consequent loss of spatial resolution (Zhou et al. 2007). Newer and upcoming digital breast tomosynthesis systems do not perform this pixel binning, and count with newer electronics that still allows them to have fast image acquisitions.

During tomosynthesis acquisition, some imaging systems also rotate the detector with the X-ray source, while in others the detector remains stationary. To date, there do not seem to be any reports on if there is any benefit to either approach.

4 Breast Compression

There are many reasons why the breast is compressed during acquisition:

- Dose reduction: The thinner the breast, the lower the dose needed to acquire an adequate image.
- X-ray scatter reduction: Breast thickness is the largest factor in the amount of X-ray scatter generated in the breast, which reduces image contrast. Therefore, a thinner breast is important to reduce this effect.
- Tissue immobilization: To minimize the possibility of motion blur in the images, especially important for sharp depiction of calcifications, it is important to achieve good breast compression.
- Tissue coverage increase: During breast compression, additional posterior tissue is brought into the field of view.
- Exposure time reduction: A thinner breast, resulting in the need for lower exposure, allows for a faster acquisition, reducing the chances for tissue motion.
- Thickness equalization: Constant breast thickness results in a more consistent signal throughout the image, decreasing the requirements of dynamic range and post-processing.
- Geometric distortion reduction: Features farther away from the detector are magnified differently from those close to the detector, seeming larger even if of the same size. Breast compression minimizes this effect.

For all these reasons, adequate breast compression is important, allowing for the acquisition of adequate images at the lowest dose possible. Unfortunately, there are too many factors involved in determining what is an "appropriate" compression for each breast, with perhaps some of them unknown (e.g., overall breast density). Therefore, it is impossible to prospectively give appropriate, breast-specific guidelines of what level of compression should be achieved per acquisition. In some screening protocols, a minimum compression force is set, but these are general, not evidence based (Waade et al. 2017a, b), and probably result in many cases in over-compression of the breast (Agasthya et al. 2017; Lau et al. 2017).

It is obvious that not achieving an appropriate compression level, and therefore under-compressing the breast, can affect clinical performance due to increased tissue superposition, in addition to increase in dose, scatter, risk of motion blur, etc., resulting in a loss in sensitivity and a need for repeated acquisitions. However, it has also been found that over-compression may also affect clinical performance, resulting in lower sensitivity during screening (Holland et al. 2017b). Therefore, avoiding over-compression not only is important to not subject the woman to unnecessary pain or discomfort beyond what is truly necessary, but might also be important to optimize screening performance. The mechanisms involved as to why over-compressing might lead to a loss of detectability of some lesions is not yet understood.

In an effort to optimize the level of compression used for each patient, it has also been suggested that compression pressure as opposed to compression force should be the metric of choice to determine and set compression level. Pressure is defined as the amount of force divided by the area over which it is applied. Therefore, the same amount of compression force applied on a smaller breast results in a higher compression pressure. Some reports show that monitoring and setting

pressure level result in a more consistent level of compression compared to using force (de Groot et al. 2013).

5 Clinical Performance of Digital Breast Tomosynthesis

There have been a large number of studies comparing digital breast tomosynthesis compared to digital mammography both for detection and for diagnosis. These have included side-by-side comparative studies; multi-reader multi-case receiver operating characteristic retrospective interpretation studies; retrospective evaluation of performance in both the screening and diagnostic setting; and prospective population screening studies, among others. In addition, some review articles have already comprehensively evaluated the available literature (Baker and Lo 2011; Gilbert et al. 2016; Houssami and Skaane 2013; Vedantham et al. 2015; Hodgson et al. 2016; Yun et al. 2017). Here we will discuss some of the findings of these studies, although a comprehensive review of all such literature is beyond the scope of this chapter.

5.1 Lesion Visibility

Some early studies before and upon introduction of digital breast tomosynthesis to the clinical realm compared the depiction of lesions between this modality and that in mammography. In one of the earliest such studies, Poplack et al. compared the conspicuity of recalled lesions with breast tomosynthesis to that of diagnostic screen-film mammography (Poplack et al. 2007), finding that the former yielded superior lesion conspicuity more often than the latter. However, calcifications were judged better visualized with mammography in 8 out of the 14 available lesions.

Andersson et al. compared the visibility of 40 cancers in single-view tomosynthesis to single- and two-view digital mammography (Andersson et al. 2008). Interestingly, all lesions were chosen due to their subtlety or non-visibility in digital mammography, and the tomosynthesis view acquired was the one that depicted the lesion in mammography the least. Even in these conditions, breast tomosynthesis showed an improvement in visibility for 22 cancers vs. one-view mammography and 11 cancers vs. two-view mammography. The authors reported equal calcification detectability, with the distribution of the clusters well depicted but the morphology of the individual calcifications not as well visualized in tomosynthesis.

In a second study from the same group, Lång et al. (2014) investigated the visibility and the reasons behind discrepant interpretations of a subset of lesions from a previously performed observer study (Svahn et al. 2012). Breast tomosynthesis again depicted the lesions more clearly, with only 1 lesion out of 26 being assessed as more clearly visible in mammography. Lång et al. also performed a very interesting evaluation of these discrepant lesions, using the opinions of three expert radiologists to evaluate why the discrepant lesions were missed by each modality. The reason for each false negative was deemed to be as either due to a lack of visibility (is the lesion visible?), a lack in the radiographic visibility of lesion characteristics (does the lesion look malignant?), or an interpretative error by the reader (did the radiologist decide incorrectly?). All lesions were visible in tomosynthesis, and in only one case were its features not suggestive enough of malignancy to be recalled. In other words, the information to (correctly) detect the lesion was there in the vast majority of cases. This was not the case for digital mammography, for which the vast majority of lesions were deemed not visible or their features of malignancy not being sufficiently clear. These findings suggest a potential radical change in the conduct and performance of screening for breast cancer.

5.2 Detection

In the same study by Poplack et al. referred above, the addition of digital breast tomosynthesis to the digital mammography screening exam

would have reduced the recall rate by approximately 40% (Poplack et al. 2007). However, the acquisition of tomosynthesis images was not performed during the same compression event as that of the mammographic image. Therefore, the effect of repositioning on the ability to resolve a substantial number of overlapping tissue-mimicking lesions is unknown.

Various multi-reader multi-case observer studies compared the detection performance of digital breast tomosynthesis to mammography (Rafferty et al. 2013, 2014; Gur et al. 2009; Clauser et al. 2016; Gennaro et al. 2010; Spangler et al. 2011; Wallis et al. 2012; Rodriguez-Ruiz et al. 2018b). In general, breast tomosynthesis, especially with two views, outperformed mammography for all types of lesions. The use of single-view tomosynthesis resulted in different conclusions, ranging from no benefit over two-view mammography to a substantial benefit. In one study, the increase in performance of single-view tomosynthesis was half of that of two-view tomosynthesis (Rafferty et al. 2014). Two studies specifically compared the performance in detecting calcifications, failing to detect a difference in the overall calcification detection (Clauser et al. 2016; Spangler et al. 2011), even though Spangler et al. did detect an increased sensitivity for calcification detection with mammography. These studies were important due to the early studies that showed a decrease in conspicuity of calcifications with tomosynthesis.

Retrospective studies on the impact of screening with digital breast tomosynthesis have reported, in general, an important decrease in the recall rate, and mostly an increase in the cancer detection rate (Destounis et al. 2014; Lourenco et al. 2015; Friedewald et al. 2014; Rose et al. 2013; McCarthy et al. 2014; Greenberg et al. 2014; Durand et al. 2015; Sharpe et al. 2016; Powell et al. 2017). It should be noted that, as is standard in the USA, the recall rate before introduction of breast tomosynthesis was in the vicinity of 10% for all studies. In addition, standard screening practice in the USA is the single reading of exams.

In Europe, meanwhile, investigators have performed large prospective screening trials to estimate the potential impact of breast tomosynthesis on screening performance (Skaane et al. 2013; Bernardi et al. 2016; Ciatto et al. 2013; Zackrisson et al. 2018; Romero Martin et al. 2018; Gilbert et al. 2015; Lång et al. 2016). Given some major differences in the way that screening is performed in these European programs compared to the institutional screening performed in the USA, the impact of this new modality was expected to be different. These trials show an important increase in the cancer detection rate, in the order of 30–40%, while the effect of tomosynthesis on recall rate seems to depend on the baseline (mammography) recall rate. Specifically, the effect of using breast tomosynthesis for screening is to tend to homogenize the recall rate, with higher baseline values decreasing, while low recall rates increasing, resulting in a recall rate approaching 3.5–5.0%.

All these observational studies and, especially, the prospective screening trials were performed with different tomosynthesis systems, and with a variability of acquisition and reading strategies. The use of two- and single-view tomosynthesis, tomosynthesis as an adjunct or a replacement of mammography, single-reading tomosynthesis while double-reading mammography, or single or double reading of both are all parameters that have been varied in these studies. In any case, overall it does appear that tomosynthesis increases the sensitivity of screening, with the aforementioned impact on recall rate. The use of single-view tomosynthesis, single-reading tomosynthesis, and/or tomosynthesis as a replacement of mammography seems to be feasible, but, given the variety in characteristics of the systems evaluated and the methods used, it is challenging to provide a single conclusion for what implementation is possible.

Of course, an actual outcome benefit from the introduction of tomosynthesis into screening would be a reduction in interval cancers and, eventually, mortality. Given its relatively new introduction, any impact that screening with breast tomosynthesis has on mortality would be impossible to evaluate for many more years to come. Several studies have compared the interval cancer rates after standard mammographic

screening compared to after screening with digital breast tomosynthesis, the majority of them in the context of the large prospective screening trials performed in Europe. For the most part, interval cancer rates have not been detected to be lower after tomosynthesis screening, or have been marginally lower with no statistical significance (McDonald et al. 2016; Bahl et al. 2017; Houssami et al. 2018; Hovda et al. 2019; Skaane et al. 2018; Bernardi et al. 2020; Conant et al. 2020). It should be noted, however, that these studies have not been powered for this endpoint, and therefore the numbers of interval cancers involved up to now have been low. New larger trials, like the TOSYMA trial in Germany and TMIST in North America, may provide a more definitive answer as to the impact of tomosynthesis screening on interval cancers.

5.3 Diagnosis

The impact of digital breast tomosynthesis in the diagnostic setting has also been evaluated. Brandt et al. compared, using a multi-reader multi-case observer study design, the diagnostic performance of two-view breast tomosynthesis to multiple-view diagnostic mammography for noncalcified lesions (Brandt et al. 2013). The average number of mammographic views acquired for the included cases was three. Tomosynthesis, even with the lower number of views acquired, achieved similar performance as that of diagnostic mammography.

Zuley et al. performed a similar study, comparing two-view breast tomosynthesis to multiple-view diagnostic mammography, again for the diagnosis of noncalcified lesions (Zuley et al. 2013). Zuley et al. did find an increase in performance, with a significant increase in the area under the ROC curve for tomosynthesis compared to that obtained for diagnostic mammography.

In a recent study, Bahl et al. performed a retrospective evaluation of the performance of breast tomosynthesis for the diagnosis of clinical concerns, excluding screening recall cases (Bahl et al. 2019). For these types of cases it was also found that tomosynthesis could outperform mammography, with an equivalent cancer detection rate, and a slightly decreased abnormal interpretation rate. A comparison of the number of views acquired per modality was not provided, however.

Of course, if breast tomosynthesis is used for screening, there would be no benefit in acquiring these images again during workup due to abnormal findings at screening. Therefore, it is expected that the diagnostic workup of screen-detected lesions, especially noncalcified ones, could involve only the use of ultrasound, to discard the presence of cysts.

6 Population Screening with Digital Breast Tomosynthesis

As mentioned previously, population screening with digital breast tomosynthesis has not yet been widely implemented. Even though the observational trials in the USA and the large prospective screening trials in Europe have shown important benefits with this modality, one of the major concerns of transitioning to tomosynthesis for population screening is the increase in reading time with this modality. Therefore, there has been an intense interest in reducing the effort in reading digital breast tomosynthesis exams for the detection of suspicious lesions at screening. It is possible that a combination of time-saving strategies could be the final solution to make breast tomosynthesis feasible for widespread screening. These strategies could include both the reduction of time spent in reviewing each case and reducing the number of cases needing human reading. A number of alternative strategies are being investigated to determine which one, or a combination thereof, could result in tomosynthesis screening requiring similar resources to mammography screening.

In the first place, given the ability of DBT to reduce tissue superposition, the acquisition of only the MLO view for screening could be feasible. The Malmö Tomosynthesis Breast Screening Trial was performed using single-view

tomosynthesis (Lång et al. 2016; Zackrisson et al. 2018), resulting in an important increase in cancer detection rate. As mentioned above, since the baseline recall rate with mammography was low, tomosynthesis did result in an increase in the recall rate. Rodriguez-Ruiz et al. 2018c evaluated and compared the detection performance of single-view DBT to three other combinations of DBT and DM views, and found the former non-inferior to all other strategies (Rodriguez-Ruiz et al. 2018b, c). Single-view DBT resulted in a 25% reading time increase compared to two-view DM, considerably less than the doubling in reading time due to two-view DBT (Skaane et al. 2013). It should be noted that both of these studies were performed with a wide-angle tomosynthesis system, so the generalization of these findings with a tomosynthesis device that covers a narrower angular range remains to be investigated.

Although screening mammography in Europe is mainly performed with double reading (with either consensus or arbitration), the possibility of single-reading breast tomosynthesis images for screening has been investigated. Houssami et al. showed that single-reading tomosynthesis screening during the STORM trial would still result in a 41.5% increase in cancer detection rate (from 5.3 to 7.5 cancers per 1000 women screened) with a reduction in the recall rate of 26.5%, from 4.9% to 3.6% (Houssami et al. 2014). In another large prospective screening trial, Romero Martin et al. also showed substantial improvement in performance with single-reading tomosynthesis, with a 21.3% increase in cancer detection rate (4.7 to 5.7 per 1000) and an almost halving of the recall rate from 5.0% to 2.5%, a 42.0% reduction (Romero Martin et al. 2018).

Due to the limited vertical resolution of DBT, the usual DBT slices separated by 1 mm, resulting in dozens of slices to be read per view, could be reduced without compromising performance by combining the information into thicker (~8 mm) slabs. This was first proposed by Diekmann et al., proposing an advanced method to combine the slices into thicker slabs that is a good compromise between maximizing the visibility of masses and calcifications (Diekmann et al. 2009). This method was evaluated in a retrospective observer study by Agasthya et al. who showed a significant reduction in interpretation time of about 28% with a nonsignificant increase in performance with the 8 mm slabs (Agasthya et al. 2016). Dustler et al. evaluated the quality of depiction of lesions in 2 mm thick slabs, finding no loss in image quality, while interpretation of such images was found to be 20% faster (Dustler et al. 2013). In another study from the same group, combining slices to 10 mm thick slabs was found to hamper lesion detectability, however (Petersson et al. 2016).

In a fraction of *simple* cases, it could be possible that the review of only the synthetic mammography image obtained from the tomosynthesis acquisition information could be enough to discard the case as normal, substantially reducing the reading time. For *difficult* cases, in which the presence of dense glandular tissue results in the potential for false positives or negatives, then the entire tomosynthesis stack would need to be reviewed. The optional review of the stack should not affect the specificity of interpretation, since before recalling based on a synthetic mammography finding, the radiologist would review the stack. To estimate the fraction of *difficult* cases due to tissue masking that would need full stack review, a previous study on quantification of the masking effect could be used (Holland et al. 2017a). Using a very conservative threshold for full tomosynthesis stack review in which 90% of interval cancers are included, about 40% of cases could be defined as *easy*, and therefore possible to only review the synthetic image. In a study evaluating the visibility of cancers in synthetic 2D images alone, Murphy et al. found that all cancers visible in the tomosynthesis stacks were visible in the synthetic mammograms, including all cancers that were not visible in the digital mammography images (Murphy et al. 2018). The review of the synthetic mammogram only for a certain number of cases is an exciting and promising strategy, but one that needs further study before it can be used. Since the creation of the synthetic mammogram is purely based on software algorithms,

it is expected that the quality of these images will continue to evolve as manufacturers improve their algorithms further.

Finally, using artificial intelligence (AI), we should be able to avoid the human interpretation of a substantial portion of screening cases, resulting in a substantial reduction in the case volume to be read. The introduction of deep learning algorithms for computer-aided detection (CAD) has increased CAD performance in mammography to levels equivalent to an average breast radiologist (Rodriguez-Ruiz et al. 2019). Recently, breast tomosynthesis CAD algorithms, also based on AI, have become commercially available, and have shown to result in both an improvement in performance and a substantial reduction in reading time (Conant et al. 2019). Now that these computer algorithms are as good as humans in interpreting digital mammography and breast tomosynthesis images, they could be used as a first reader to triage between the cases that need to be human-read and those that do not. With such a computer-based triaging system, half of the screening cases could be automatically labeled normal, and hence not human-read, with only a 7% of cancer cases being incorrectly included in that category (Rodriguez-Ruiz et al. 2018a). It should be noted that human reading results in ~25% of cancer cases being interpreted as normal (National Evaluation Team for Breast cancer screening in the Netherlands (NETB) 2016). The possibilities to improve performance and/or reduce reading time with AI in screening with tomosynthesis are varied and numerous. Although a full review of this topic is beyond the scope of this chapter, several recent review articles on this fast-evolving topic are available (Sechopoulos et al. 2020; Sechopoulos and Mann 2020; Geras et al. 2019). Of course, double reading of two-view digital breast tomosynthesis examinations (including digital mammography images) for screening would most probably yield the highest performance, as opposed to incorporating any or a combination of the abovementioned strategies. However, in many screening programs, implementation of screening tomosynthesis with this *standard* strategy is not feasible, due to the important increase in radiologist reading time needed. Therefore, it must be realized that the potential of these strategies should be investigated, and eventually they should be implemented, if by doing so a substantial portion of the benefit of tomosynthesis screening is maintained while the increase in reading time is manageable. To achieve this, additional studies on the generalizability of these methods for the different types of tomosynthesis systems and the possible combination of various of these strategies should be undertaken.

7 Radiation Dose

Mammography and digital breast tomosynthesis are low-dose X-ray imaging examinations. However, their use for screening of the general population results in there being an intense interest in the characterization and optimization of the dose involved in these modalities. These are, after all, by far the most commonly performed screening tests on asymptomatic people that use ionizing radiation. Therefore, not only should the level of radiation dose be well understood and minimized, but also its meaning and the current limitations of our methodology and knowledge also need to be communicated.

7.1 Basics of Breast Dosimetry

The metric that quantifies the radiation dose to the breast is the average glandular dose (AGD). The dose is qualified as being the "glandular dose" because, as opposed to the dose to all of the breast tissue, only the dose to the fibroglandular tissues in the breast is of interest. This is because these are the ones most at risk to develop breast cancer. The term "average" is used to reflect that the dose is the average of the dose to all the glandular tissue in the breast. Since breast imaging uses relatively low-energy X-rays, there is a very large variation in the dose deposited throughout the breast during a single acquisition. The dose at the top surface of the compressed breast, closest to the X-ray source, can be an order of magnitude

higher than that at the bottom of the breast, closest to the detector (Sechopoulos et al. 2010). The current models that translate organ dose to risk are based on the average dose to the entire organ, so any large differences in dose within an organ are not taken into account.

The average glandular dose in the breast, just like any other organ dose, cannot be measured, only estimated. This is done by measuring the intensity and characteristics of the X-rays that the breast is exposed to, and then converting this value to an AGD using specific conversion coefficients. These conversion coefficients to obtain AGD were obtained by assuming a simplified model of the breast, in which all the fibroglandular and adipose tissues are perfectly mixed and are spread evenly throughout the breast (Dance 1990; Dance et al. 2000, 2009, 2011).

7.2 Meaning of Breast Dose Estimates

This means that even when we estimate the dose resulting from a mammographic or breast tomosynthesis acquisition, we are not estimating *that patient's breast dose*. Even if we take into account the exposure technique used for that acquisition, we only consider the number and type of X-rays to which we exposed that breast. The dose we calculated estimated on those factors is the dose to a *model breast*, which does not represent that patient's breast characteristics. This model breast could be of the correct thickness, since conversion coefficients are available for different thicknesses of breast. In addition, perhaps some consideration of the density (fraction of glandular tissue) of the breast could be taken into account, since conversion coefficients for different densities are also available. However, the true structure of the fibroglandular tissue inside the breast, i.e., where it is located, is not considered in the current dose estimations. Assuming that the fibroglandular tissue is spread out evenly throughout the whole breast makes our dose estimates not *patient specific* but model estimates. It has been found that using these model dose estimates can overestimate the dose to the actual patient breast by up to a factor of 2 and, on average, overestimates the dose by 30% (Sechopoulos et al. 2012; Hernandez et al. 2015).

Other patient-specific factors, such as the thickness of the skin of that specific breast, and the mammographic view (CC, MLO, etc.), are also not taken into account. As can be expected, the thicker the breast skin, the lower the AGD (Huang et al. 2008), while the dose in the MLO view, for the same acquisition technique, is lower than that in the CC view (Sechopoulos et al. 2007). However, conversion coefficients are not available for different skin thicknesses nor different mammographic views.

Therefore, it must be remembered that our current breast dose methods and estimates are not aimed at estimating the AGD to each specific patient for each specific view acquired. Even if the breast density of the patient is considered, as in some commercial breast dosimetry products, the resulting AGD is not *patient specific*. Rather, these estimates aim to obtain a relative estimate of the dose, useful for controlling the constancy of the behavior of the systems, the appropriateness of their use, and the optimization of techniques and technologies.

7.3 Mammography vs. Tomosynthesis Dose

During the introduction of digital breast tomosynthesis, especially for screening of asymptomatic women, one major concern was how does the dose from tomosynthesis compared to that from mammography. Furthermore, if tomosynthesis were used as an adjunct to rather than a replacement of mammography, would the total dose be doubled, or more?

Early phantom-based characterization and comparison of the dose from mammography and tomosynthesis using the first commercial digital breast tomosynthesis system were performed by Feng and Sechopoulos (2012). Using simple phantoms that represented a range of breast thicknesses and densities, the authors found that the dose ratio between that from breast tomosynthesis to that from mammography varied

considerably. For the traditional "standard" breast, i.e., 5 cm thick and 50% density, the dose from the two modalities was essentially equal, with only an 8% increase with breast tomosynthesis. For a more clinically relevant standard breast, now considered to be about 6 cm thick and ~15% dense, tomosynthesis resulted in almost a doubling of the dose of that of mammography.

In a review paper, Svahn et al. collected all the comparisons of the dose between mammography and tomosynthesis provided in the early clinical performance comparisons between the two modalities (Svahn et al. 2015). Of course, the dose comparison varied greatly, depending on the system used, and, presumably, depending on the characteristics of the breast. However, as expected, the greatest variation in how the dose from mammography compares to that of tomosynthesis depended on how the two modalities would be implemented, that is, if tomosynthesis were used as an adjunct to mammography, and if tomosynthesis would involve the acquisition of one or two views. As a result of this variability, the dose from a tomosynthesis exam could be as low as a third of that of a standard two-view mammographic exam (if single-view tomosynthesis replaces mammography), to resulting in more than doubling of the dose (if two-view tomosynthesis is used in combination with mammography).

Once digital breast tomosynthesis was introduced to normal clinical practice, then more extensive patient-based dose data became available and could be compared, especially on a patient-by-patient basis. In a comprehensive study, Bouwman et al. compared the dose between both modalities for thousands of women imaged with systems of various vendors (Bouwman et al. 2015). Again, the ratios between the modalities varied depending on the breast characteristics, and, especially, depending on the system vendor. Figure 6 shows the resulting AGD values for both modalities with one system, based on the acquisitions of 2500 women. As can be seen, the dose from breast tomosynthesis is less variable for a given compressed breast thickness than that from digital mammography. In addition,

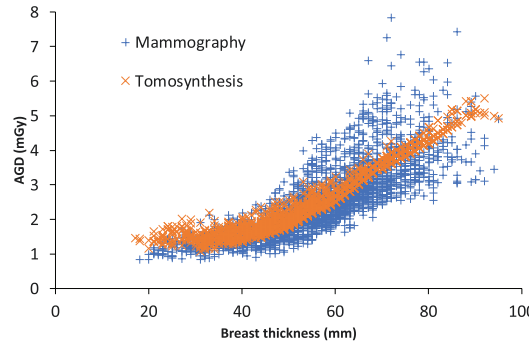

Fig. 6 Comparison of the average glandular dose (AGD) resulting from mammography (DM) and digital breast tomosynthesis (DBT) with one system, based on the acquisitions of 2500 women. The dose from DBT is less variable for a given compressed breast thickness than that from DM. The former tends to be higher than the latter for thin breasts, while for thicker breasts there is a smaller difference, and for many thick breasts DBT results in a lower dose. (Adapted from Bouwman et al. "Average Glandular Dose in Digital Mammography and Digital Breast Tomosynthesis: Comparison of Phantom and Patient Data." *Physics in Medicine and Biology* 60(20): 7893–7907. © Institute of Physics and Engineering in Medicine. Reproduced by permission of IOP Publishing. All rights reserved)

for thin breasts the dose from tomosynthesis is mostly higher than that from mammography, while for thicker breasts there is a smaller difference, and for many thick breasts tomosynthesis results in a lower dose. For the latter, the tomosynthesis dose distribution is well within the range of dose values resulting from mammography. Overall, with this system, the dose from digital breast tomosynthesis is 8% higher, on average, than that from digital mammography. For other systems, Bouwman et al. found varying differences overall for the dose from tomosynthesis compared to that from mammography.

Overall, the dosimetric consequences of moving from mammography to tomosynthesis imaging will be settled, in the big picture, not due to any dose penalty or savings due to physics- or technical-based optimization work on either modality, but by the clinical decision of how many views of each modality will be involved in one complete breast examination. This is because acquiring a single view as opposed to two, and/or replacing the mammographic acquisition with the computation of a synthetic mammogram,

introduces much larger savings in dose than those that can be achieved by optimization of the acquisition technique or the technology involved in the imaging systems.

7.4 Radiation Dose vs. Clinical Performance

Even if, as mentioned above, the dose during X-ray-based breast imaging is of particular interest due to its use for screening, the main focus of concern and interest should still be the optimization of clinical performance.

The amount of radiation used for acquisition of a mammogram or a breast tomosynthesis image has a direct consequence on the level of noise in the image. Lesion detectability, especially of calcifications, is limited by image noise (Burgess et al. 2001). Therefore, it is important that the appropriate levels of dose are used to obtain an adequate, diagnostic, image. Compromising the clinical performance to save some fraction of the dose used, even for screening, should not be considered.

Furthermore, as discussed above, the choice of modality or combination of modalities has a much larger impact on the total dose of a breast exam than image acquisition technique selection. Implementing screening as one-view or two-view tomosynthesis, as a replacement or an adjunct to mammography, has, of course, the largest impact on the level of dose used for screening. The decision as to what modality or combination should be used for screening should be taken based on expected outcomes and other factors that determine feasibility: reading time, human and economic resources, etc.

As discussed in Sects. 5 and 6, digital breast tomosynthesis results in important increases in cancer detection rate, and, in some cases, in an important reduction in recall rate. Even if for widespread screening of the general (asymptomatic) population it is determined that the optimal implementation of tomosynthesis screening results in an increase in dose, then the benefit in outcomes should be considered above any increase in risk due to radiation.

According to the current model of risk based on exposure to ionizing radiation, a mammography-based screening program, even involving annual mammography between 40 and 55 years of age and biennially up to 74 years of age, would potentially result in 10.6 deaths due to radiation-induced breast cancers per 100,000 women (Yaffe and Mainprize 2011). This is in comparison to 2070 breast cancer deaths in that same cohort of women between 40 and 74 years old, of which 497 could be saved by breast cancer screening (Yaffe and Mainprize 2011). Clearly, any discussion on the appropriateness of breast cancer screening with mammography or breast tomosynthesis should not be based on appropriateness of the radiation doses involved, but on clinical, economic, and other factors.

Furthermore, it should be noted that the current model used to relate the dose to risk of cancer development, as also used by Yaffe and Mainprize for the calculations above, assumes that there is no *safe* level of radiation. This means that no matter how low the radiation dose, if enough people are exposed to it, some cancers, and therefore some deaths, will be induced. Especially at the diagnostic imaging dose levels there is a lack of consensus on the effects and risks of this level of radiation, and they might be nonexistent (American Association of Physicists in Medicine (AAPM) 2018). Therefore, as stated by this Position Statement of the AAPM, given the uncertainty in these risk models, the use and recommendations for use of these imaging modalities should be based on their clinical appropriateness, and should be used with the levels of radiation that are needed to achieve the required image quality.

7.5 Total Breast Dose During a Screening Examination

Let us consider a hypothetical scenario of a mammographic screening exam consisting of the usual two views (CC and MLO) of each of the two breasts. For this exercise, let us assume that both breasts are exactly the same size and density, and that all the fibroglandular tissue present in the

imaged breast is exposed during both the CC and the MLO views. However, due to the MLO view compression resulting in the breast being a little thicker, the two views result in a slight difference in AGD; both left and right CC views each result in an AGD of 1.0 mGy while the left and right MLO views each result in an AGD of 1.2 mGy.

What is the total dose to the breasts for this screening exam?

It is tempting to answer that the total dose is simply the sum of the dose of the four acquisitions: 4.4 mGy. However, to obtain the correct answer, the definition of dose needs to be considered:

Dose = Energy deposited in tissue
/Amount of tissue the energy is deposited in

The amount of tissue, in the case of breast imaging, as mentioned, is the mass of fibroglandular tissue.

If we first consider the dose to each individual breast only, e.g., the left breast only, then the total dose to the left breast from the acquisition of both views is 2.2 mGy. This is because whatever X-ray energy was deposited during the acquisition of each of the two views, it was in the same fibroglandular tissue, the one of the left breast. Now, when the right breast is imaged, it also results in a total dose due to acquisition of both views of 2.2 mGy. However, the X-ray energy deposition that resulted in this other dose was deposited in different fibroglandular tissue, that present in the right breast. Therefore, when calculating the total dose to both breasts, we do not only have double the energy deposition, but also have double the amount of tissue it is deposited on. As a result, the total breast dose due to this bilateral two-view screening examination is the average of the total dose received by each breast due to the two views. Since each breast was exposed to an AGD of 2.2 mGy, the total AGD to the breasts from this exam was also 2.2 mGy.

In short, when the dose from multiple views of the same breast is being calculated, the individual dose values are added. However, when the total dose to both breasts is being calculated, then the total dose received by each breast is averaged together.

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