Sponzorski članek

DIGITAL BREAST TOMOSYNTHESIS

A clinical assessment based on literature

WHY BREAST TOMOSYNTHESIS?

Breast cancer is one of the most common cancers in women in the Northern Hemisphere. More than 10% of all women can expect to have some manifestation of the disease during their lifetime. Although earlier detection and better treatment may have reduced mortality in recent years, 30% of women with breast cancer will die from the disease. X-ray mammography is still the golden standard of investigational procedures. Digital mammography has improved diagnostics, especially in younger women and in denser breasts, and CAD can be of some help. However, every effort is necessary to raise the early cancer detection rate and thereby reduce the mortality rate. The sensitivity of mammography alone decreases with increasing parenchymal density. Numbers of missed cancers in very dense breasts have been reported to be as high as 52% – 76% (1, 2); in analog screening programs, up to 30% of detectable cancers were not detected. There are numerous reasons for this, the most important being the "structured" or anatomical noise produced by the overlapping tissue structures in the 2D imaging of a 3D object. Misinterpretation of architectural distortion and asymmetrical density, fibroglandular tissue overlapping the cancer and obscuring the margins of the cancer lead to false negative results. False positive findings which may mimic cancer can also be a result of these summation artefacts. The diffuse growth pattern of some tumors with ill-defined borders presents a special problem. Early detection of breast cancer is mandatory. Treatment will be less invasive and prognosis much better for the small noninvasive tumors or clusters of microcalcifications associated with DCIS. Any procedure which can reduce the anatomical noise has the potential of improving early breast cancer detection.

Background

Tomography is a well known procedure in radiography. Analog tomography of the female breast is not feasible (moving table, dose). With digital breast tomography (DBT) came new possibilities. The procedure was first described approximately 25 years ago. In later years an increasing number of reports and studies have discussed the difficulties and possible benefits of DBT. Still, a search in April 2010 in the public literature databases of PubMed and Embase revealed only a hundred papers and communications on the topic for the last 2 years. DBT is a three-dimensional imaging technique which provides an arbitrary set of reconstruction planes in the breast from a limited angle series of projection images acquired while the X-ray tube moves through an arc above the stationary detector (3, 4). The result is a 3D data set of the entire breast volume. The individual "planes of interest" of a chosen slice separation/slice distance, usually 1 mm, can be viewed separately from the rest of the image, thereby reducing the impact of anatomical noise. The individual slice shows enhancement of a lesion, while there is a blurring of the out-of-focus information of the breast tissue. The angular span of the tube is up to 50 degrees (20-60) and the number of projections is usually 25 or less. Expanding the angle and number of slices does not seem to give any further diagnostic information and may prolong the examination time and patient motion noise as well as raise the dose (5, 6). As an adjunct, 1 cm thick slices may provide additional information because of a better delineation of lesions, especially tumors (7). It may also facilitate a quicker look through the whole breast before turning to the 1 mm slices. This is under evaluation. Reconstruction of slices is still done parallel to the detector plane. Future developments which allow you to choose different reconstruction planes in the 3D volume set may expand the diagnostic value of the procedure. Due to the limited acquisition angle the possibilities cannot be compared to computed tomography.

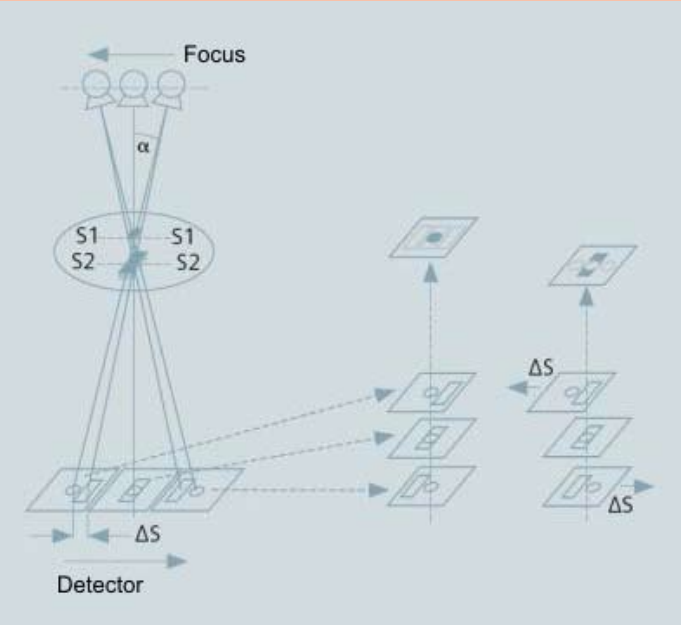

Figure 1: The Principle of Tomosynthesis

CLINICAL CONSIDERATIONS

Dose

The radiation dose for one DBT procedure in the CC or MLO projection is generally comparable to the dose of a two-view screening mammogram: 1–2 mGy in average glandular dose (AGD). The beam quality is similar to that of mammography (4). European Guidelines suggest that the AGD for one mammography exposure to a standard breast of 4.5 cm thickness should be kept below 2.5 mGy (8). Andersson et al. found the mean absorbed dose (exposure angle range 50 degrees, 25 projections, scan time 20 seconds) to be double the dose of a one-view digital mammogram: approx.1.6 mGy (9). Teertstra et al. (22) found an AGD of 1.74 mGy. One DBT procedure is well below the guideline dose. Further investigations will show whether a dose reduction is possible

without losing important diagnostic information. If DBT is used in a screening setting, at least one of the screening mammograms could be replaced by the DBT procedure. For the individual woman this indicates a larger dose. If DBT can replace all screening projections, dose will be the same as today provided one-view tomosynthesis is sufficient from a diagnostic point of view. In a clinical follow-up DBT will replace at least one and may be all additional projections. For the total population DBT, if used in screening, should lead to a lower acquired dose if many recalls and further mammographic examinations can be avoided.

Acquisition Time/Clinical Throughput

Currently the through-put of one tomosynthesis system can be up to 8–10 patients per hour if performing FFDM with DBT. Correct positioning is essential. The scan time can be up to 25 seconds depending on the angular range and the number of projections. As mentioned above, scan time and dose have to be considered under the aspect of obtaining better image quality and more clinical information. Therefore a longer examination (scan) time is feasible in the clinical follow-up situation where usually only a few patients are scheduled per hour. It would, however, never fulfill the requirements in the screening room if all women were scheduled to have one or two DBT per breast. The discussion of whether to use DBT in one projection (MLO) or both will be solved by coming screening trials. Performing DBT on all women may not be justified since 25% of screening participants have fatty breasts. Offering DBT in general for most screening participants would mean a huge investment in equipment, rooms and personnel. At the moment, a better way of performing the DBT examination seems to be to reserve DBT for clinical examinations of both first-timer and follow-up patients, and for women who still want to participate in the screening program but are at high risk and/or have very dense breast tissue as found during an earlier screening procedure, or for those who present with new clinical symptoms. These topics will be addressed in further studies.

Compression

Mammography can be unpleasant, because the compression of the breast is painful. Some women may even refrain from further mammographic procedures. DBT requires a scan time of 20 seconds (see above) which may cause further discomfort and thus create motion artefacts. In a phantom study, Saunders et al. (10) found that for a constant glandular dose, mass and microcalcification conspicuity remained almost constant with decreasing compression, up to 12%. Förnvik et al. (11) found that compression could be performed using only half of the force automatically proposed by the equipment before exposure without losing any important diagnostic information. There was a tendency to more noise in the thickest part of the breast (oblique projection, pectoral area) but this presented no difficulties for the readers. Reduced compression is also of value in contrast-enhanced tomosynthesis (CE-DBT) for ensuring appropriate blood flow in the breast (12, 27).

Reading Time

Of course, adding any tool to the diagnostic process of reading screening mammograms will prolong the reading time. A very recent study (13) concludes that when adding DBT to FFDM the time to review and evaluate an examination increases by 33% compared to reading the FFDM images alone in a previous setting. Good et al. (14) found, in a small study, that reading of DBT studies took almost double the time of reading FFDM studies alone. There were significant differences between the reading radiologists, but in general malignant cases took a little longer to finish than benign cases. Gur et al. (15) report a 50% longer reading time for FFDM + DBT studies compared to FFDM alone. In a personal communication (16), Ingvar Andersson, Malmö, Sweden, who experienced a 50% increase in reading DBT v. FFDM, declares that the goal is to achieve a speed of 50 read DBT cases per hour in a coming large-scale screening trial. But much depends on the training of the radiologists and on the performance and facilities of the reporting workstation

CLINICAL BENEFITS OF TOMOSYNTHESIS?

Recall Rate

There seems to be a general agreement that DBT has an effect on the recall rate. The overlap of structures can be reduced with DBT. Equivocal lesions on 2D images, i.e.: tumor or not, can be disproved. Rafferty (17) reports from an early pilot study that radiologists could reduce the false positive recall rate by 83% (!) with DBT compared to conventional mammography without any significant difference in the cancer detection rate. Poplack et al. (18) found a 40% reduction in recalls in a study comparing DBT with FFDM screening mammography. The type of the finding, masses and architectural distortions in the images influenced the recall rate. Poplack used DBT in suspicious cases referred from screening (recalls), a highly select population. The result of DBT will vary according to the percentage of recalled women (19, comment on Poplack). In the United States more than 10% are recalled, in some of the screening programs in Denmark less than 3%. The greatest effect of DBT on the recall rate can be seen in the United States. It seems difficult to lower the recall rate much with DBT in a Danish screening program. But, of course, some patients with benign findings from DBT will not undergo an otherwise planned biopsy or further investigations. Gur et al (15) comparing FFDM + DBT with DBT alone in a retrospective study of mixed malignant and benign cases found a 30% reduction in the recall rate for cancer-free examinations.Using DBT alone would have reduced the recall rate by 10%.

Sensitivity and Specificity

Gur (15) and Gennaro (20) found no significant improvement in sensitivity or specificity. The latter found that even if DBT improves the image quality and lesion conspicuity (specificity) this has no influence on the clinical performance (sensitivity). The number of detected lesions did not change when DBT was introduced, but the radiologist could be more confident in making decisions. Most authors, though,

find that DBT increases the number of cancers detected and improves the characterization of the lesions compared to one-view or two-view FFDM. In 2007, Rafferty reported (17) from an earlier study, DBT v. two-view screening mammography, that in 89% of cases radiologists found DBT to be equal or better in defining masses and architectural distortions. In 88% of cases microcalcifications were visualized better with DBT. In a small study of subtle cancers, Andersson et al. (9) found that 3/4 of detected cancers were rated more visible with DBT and half of them were upgraded in the BI-RADS classification. In FFDM, of course, the two-view examinations performed better than one-view examinations, but still not as good as one-view DBT. The distribution of clusters of microcalcifications was seen easily enough although the morphologic details of individual calcifications were blurred. 10% of cancers (4 patients) were not found with either examination and one was missed with DBT because of its closeness to the thoracic wall, i.e. mispositioning. Svahn (21) from the same group found that one-view DBT + one-view FFDM, usually the CC projection, had superior specificity to two-view FFDM. Teertstra et al. (22) found the sensitivity in cancer detection to be 93% and the specificity to be 84/86% (BI-RADS 4+5 cases) for both DBT and FFDM.3% of cancers, all invasive lobular carcinomas, were not visible with either modality. 7% of cancers were false negatives with DBT, and these would, of course, have been missed in a screening setting with DBT alone, as well as with FFDM. Pathology revealed an overrepresentation of ILCs, the rest being IDCs and DCISs. The majority of biopsy-proven benign cases, where DBT had initially classified the lesion as BI-RADS 4 or 5 (false positives), were benign microcalcifications, a few cysts and some benign architectural distortions. One third in this false-positive group were suspected masses or densities, but all with negative biopsies and follow-ups.

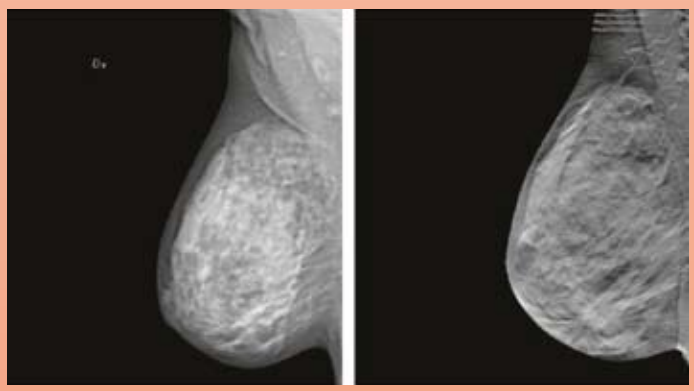

Figure 2: Tomosynthesis slice 25 (right), 2.8 cm ductal carcinoma, grade 3; Patient with a 2.8 cm, grade 3, invasive ductal carcinoma in the right breast imaged with digital mammography and breast tomosynthesis. The MLO digital mammography view shows dense breast tissue with subtle distortion in the lower breast. The MLO tomosynthesis slice shows a spiculated mass in the lower breast, much more evident than the corresponding mammogram.

OUTLOOK

DBT and CAD

CAD (computer aided detection or diagnosis), which has been found to be useful for radiologists in the detection of breast cancer in screening mammography (23), can be implemented with DBT. Some American groups have found a sensitivity of 85% in the detection of masses as well as a reduced false-positive marking rate compared to FFDM + CAD (24-26). DBT + CAD would certainly be helpful when having to scroll through the many reconstructed slices from one DBT exposure.

Contrast-Enhanced DBT

CE-DBT seems an easy way to obtain better information about a mass in the breast. Abnormal blood flow in the breast, tumor uptake and tumor border delineation can be visualized. The X-ray dose can still be held at an acceptable level and only a slight compression of the breast is necessary to avoid patient motion artefacts (27).

Breast Cancer Risk Estimation

DBT may play a role in this field in the near future. Risk assessment is a tool in planning further investigations, treatment and preventive strategies for high-risk women. Hereditary factors, number of childbirths, environmental factors and hormone treatment are known today as potential risk factors. The density and texture structure of the breast parenchyma especially in the retroareolar area can also be indicative of a woman's risk of developing breast cancer. DBT reduces the anatomical noise of skin and subcutaneous fat and offers superior texture visualization. One central DBT projection taken with 20% of the dose of an FFDM exposure correlates better to breast percent density than FFDM (28, 29). DBT can therefore help decide which of the women participating in the screening program should be offered a DBT scan in forthcoming screening rounds, either as an additional procedure or as the only procedure. It is still an open question whether some of the high-risk women who today are offered periodical MRI scans would benefit equally from DBT. Compared to MRI, the sensitivity in detecting small lesions (not necessarily demanding immediate treatment) may decrease slightly, but economic savings would be substantial.

CONCLUSION

Digital Breast Tomosynthesis (DBT) has so far proved to be a helpful tool in the portfolio of diagnostic radiologic procedures in the field of early breast cancer detection. DBT addresses one of the major problems of conventional 2D imaging of the breast: the structural or anatomical noise of overlapping tissue components. An improvement in both sensitivity and specificity in lesion detection and characterization is found in many of the newer publications and reports. Dose is acceptable. Breast compression can be reduced. Because acquisition time and diagnostic work-up for DBT take substantially longer than the fast screening procedure, it seems not feasible today to implement DBT in the screening room as a routine. Although the screening recall rate can be expected to decrease considerably, i.e. 30% or more, if DBT were used as an adjunct to screening, today's DBT must be reserved for the clinical follow-up of screening recalls, for symptomatic women and for women who have a high-risk history of breast cancer. After DBT the biopsy rate is expected to decrease. Some MRIs may not need to be performed. DBT may be combined with CAD (computer aided detection), which should

speed up the decision-making process when reading DBT images. Coming large-scale screening trials will clarify if it is possible to integrate DBT as one of the screening procedures, alone or with FFDM.

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