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Tomosynthesis as a screening tool for breast cancer: A systematic review

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ABSTRACT

Background: Mammography is an important screening tool for reducing breast cancer mortality. Digital breast tomosynthesis (DBT) can potentially be integrated with mammography to aid in cancer detection.
Method: Using the PRISMA guidelines, a systematic review of current literature was conducted to identify issues relating to the use of tomosynthesis as a screening tool together with mammography.
Findings: Using tomosynthesis with digital mammography (DM) increases breast cancer detection, reduces recall rates and increases the positive predictive value of those cases recalled. Invasive cancer detection is significantly improved in tomosynthesis compared to mammography, and has improved success for women with heterogeneous or extremely dense breasts.
Conclusion: Tomosynthesis reduces some limitations of mammography at the time of screening that until recently were most often addressed by ultrasound at later work-up. Tomosynthesis can potentially be adopted alongside mammography as a screening tool.

Introduction

Breast cancer is the most common cancer affecting women worldwide. One in eight Australian women are diagnosed before they are 85, and across the world 1.7 million new cases were diagnosed in 2012, with the highest incidence in Western Europe.[1] To reduce morbidity and mortality from breast cancer, screening programs have been set up across the world with the understanding that early detection and treatment of cancer will provide a brighter future for these women, and it has been proven to do so, reducing mortality by 22% in women over 50 years and 15% for women aged 40–49.[2–4]

Mammography is the current standard of care for the screening programs internationally. It has very high detection rates, is affordable in developed countries and well tolerated by women. Although it is the modality of choice, mammography has significant limitations, including a low sensitivity and high false positive recall rate, and has limited capability for women with dense breast tissue and under 50 years of age.[2,3,5–11] Other modalities have been employed in the past and are still used now to overcome the limitations of mammography for women with moderate to high risk of cancer, including MRI and breast ultrasound. In the future, breast imaging may move into CT phase contrast imaging. Experimental trials have found dose levels as low as mammography, with no tissue overlap or need for compression and may have better uses for surgical planning, however it has not yet been approved for clinical use.[12]

Tomosynthesis is the most recent modality to be investigated for routine breast screening practices on women. It involves the creation of a pseudo 3D digital image of the breast and was approved by the Food and Drug Administration (FDA) to be used clinically in 2011.[13] Since then many studies have investigated its use diagnostically.[8,9,14–18] Several population-based studies found that digital breast tomosynthesis (DBT) as a screening tool improves the limitations shown by digital mammography (DM) alone.[2,3,5–7] These studies used two-view tomosynthesis and mammography together as a full screening examination. DBT when used in conjunction with mammography has been found to increase sensitivity or detection rate compared with that of mammography alone. It can reduce the number of false positive recall rates; increase positive predictive values and reduces superimposition of tissues.[2,5,6,19] The importance of reducing false positives is not only to reduce the number of tests completed in a radiology department, but also to lower the emotional and financial burden women are subjected to. Tomosynthesis also increases the conspicuity of lesions and has the potential to introduce depth localization, a

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feature not possible with conventional mammography.[20] However, tomosynthesis increases breast compression time by an average of ten seconds per view.[3]

This systematic review assesses the efficacy of tomosynthesis as a screening tool for breast cancer. In 2014, BreastScreen Australia[21] released a statement affirming that until further trials are completed for the benefits of tomosynthesis as a screening tool, they will continue to use two view bilateral mammography as the standard screening tool for BreastScreen.

Digital mammography and tomosynthesis

Mammography screening programs, although slightly different across the world, include similar basic principles. In Australia for example, women are separated into groups based on their relative risk of cancer: baseline risk, elevated risk and high risk. Risk factors include personal history, family history, age, breast density, and women who carry the BRCA1, BRCA2 or p53 genetic mutations.[22] Women with higher risk factors may be invited more frequently for screening, or recommended for other modalities such as MRI or ultrasound. These women are generally asymptomatic and well when they present for their screening mammogram. Four digital images, two of each breast, are taken in a 2-dimensional (2D) screening mammogram: each breast in the craniocaudal (CC) plane, and mediolateral oblique (MLO). The images taken are assessed either by single or double reading by a radiologist depending on the country, who then makes a decision whether to recall the woman or not, and what period of time should elapse before follow-up appointments or tests. The universal goal of mammography screening programs is to detect breast cancer as early as possible and achieve low recall rates.

Tomosynthesis creates a pseudo-3D digital image of the breast, obtained in the CC and MLO planes under compression like mammography. The breast is compressed under the paddles of the tomosynthesis unit, and the radiation source spins in a 15–60° arc over the breast, depending on clinical preference, taking between 10 and 25 low-dose digital images.[16,17,23] There is an increased breast compression time of an average of 10 s per view compared to digital mammography.[3] The images are then reconstructed using a "shift and add" algorithm.[24] Units that use tomosynthesis and mammography integrated together acquire tomosynthesis first, and under the same breast compression the unit moves back to the "central slice", and acquires the 2D mammographic image. The images acquired by tomosynthesis are then viewed alongside the 2D mammogram as a source of reference, scrolled through by a radiologist on a mammography workstation.[19] When tomosynthesis was first clinically introduced, many studies investigated that diagnostic value of using one-plane view of tomosynthesis in the MLO alongside both CC and MLO mammography.[14,17,24,25] This was due to dose concerns, however dose is now similar to acquisitions of conventional mammography,[24] and two-view DBT has been shown to greatly improve the sensitivity of mammography alone and is the preferred method presently under investigation for screening.[2,3,5–7,14]

Methods

A systematic review is an academically rigorous literature review that follows established steps to address a research problem. The systematic review allows conclusions to be drawn from examination of the literature by relevance, quality and methodology.[26] Systematic reviews are suited to problems for which there is an existing body of research but limited consolidation of findings; or where research methodology has been inconsistently applied causing uncertainty in results. The systematic review allows the research question to be rigorously framed, with results presented by themes so further or additional research is targeted and valid. There are a number of recognised approaches to conducting systematic reviews.[27–29] In this case, the PRISMA guidelines for conducting systematic reviews[30] have been adopted.

An initial literature search was performed using the databases Scopus and Academic One File using keywords including "tomosynthesis" and "screening", as well as "digital breast tomosynthesis". Boolean terms were used to further refine results. Articles were included if they considered tomosynthesis as either a diagnostic or a screening method since tomosynthesis is also used as a diagnostic tool and such articles may provide contextual information relating to screening. References from relevant articles were also used to generate further results. This initial search resulted in 226 articles. Articles were excluded if they were not in English, as well as any published before 2005 due to tomosynthesis only becoming clinically available after this point. Studies were also excluded if they compared DBT to film-screen mammography, since current screening standards use digital breast mammography. This resulted in 33 credible articles, which were read in detail. Of these, a further 12 were excluded because they were not predominately about tomosynthesis – six studies compared MRI and mammography, four compared ultrasound and mammography and two investigated the future of CT in breast imaging.

Twenty-one articles were analysed for this systematic review. The majority of articles published were from Europe, the UK, Canada and the USA, and Australia. Of the articles used, five large screening trial studies specifically compared results of mammography to mammography combined with tomosynthesis. Nine compared mammography and tomosynthesis diagnostically; two studies investigated breast density and tomosynthesis; two articles investigated microcalcifications and coned compression views with tomosynthesis; and three studies investigated more efficient methods of reading tomosynthesis data.

Broad themes identified during this review included cancer detection, breast density and dose. Much of the research argues whether tomosynthesis should be used as a screening tool, diagnostic tool, or both; and whether it could potentially replace 2D mammography or be used alongside it.[14]

Results

Using tomosynthesis for cancer detection

Five of the largest cohort studies, which investigated the use of tomosynthesis as a screening tool, have been compared (see Table 1). These studies were conducted across Italy, Norway and the United States of America (USA) from 2011 to 2013, and published from early 2013 to 2014. Some trials were multi-centered, others single. Amongst them are the Oslo Tomosynthesis Screening Trial,[3] part of the Norwegian Breast Cancer Screening Program, and the Screening with Tomosynthesis OR standard Mammography (STORM) trial.[2] Hologic systems were the only FDA-Approved tomosynthesis units at the time of these trials so all studies used the same brand of equipment.[2,3,5–7] All studies found that there was an increase in the cancer detection rate when using digital mammography plus tomosynthesis, compared to conventional mammography alone.[31] In four studies there was also an increase in positive predictive value and a reduction in recall rate.

Also, mammography has higher sensitivity for detection of DCIS than invasive cancers, because microcalcifications that typically occur in DCIS are easily detectable on mammography.[9] If detected before invasion occurs the cure rate is 100%,[11] but it is difficult to detect if invasion has occurred with mammography alone. Studies