Issues in Emerging Health Technologies

Tomosynthesis (3D Mammography) for Breast Cancer Screening

Summary

✓ **Digital breast tomosynthesis (DBT) is a novel imaging technology that captures three-dimensional (3D) images of the breast.**

✓ **DBT can be used for screening or diagnosis.**

✓ **Seven recent, large screening studies that each enrolled more than 10,000 women showed that DBT can reduce the need to recall women for further testing compared with current two-dimensional (2D) screening. Three of the studies showed that DBT improves cancer detection rates.**

✓ **A budget impact analysis found DBT to be cost-saving compared with current 2D screening due to lower recall rates and the reduced treatment costs that result from early cancer detection.**

✓ **Implementation issues include the significant cost to purchase the technology, training requirements for radiologists and technologists, increased radiologist interpretation time, and greater data storage requirements.**

The Technology

Traditional two-dimensional (2D) mammography captures two static images of the breast. One particular shortcoming of 2D technology is the overlapping of breast images that can decrease accuracy of interpretation. With digital breast tomosynthesis (DBT), an X-ray beam sweeps in an arc of 15 to 50 degrees (depending on the manufacturer) across the breast, and an electronic detector digitally captures between nine and 25 X-ray projection images.[1-6] These images are generally captured in two views: craniocaudal (head-to-toe direction) and mediolateral oblique (angled side-view).[2,3,5] The data from these projections are used in computer algorithms to reconstruct a series of parallel thin "slices" (tomographic images) corresponding to 0.5 mm to 1 mm intervals through the breast. The slices create a three-dimensional (3D) volume of data that represents the breast's tissue structures.

The objective of DBT is to improve detection of breast cancer compared with 2D mammography screening by:

- decreasing the tissue overlap that occurs from projection of X-rays through the different structures in the breast
- reducing suspicious presentations of normal tissues
- facilitating differentiation of lesion types.[6]

Regulatory Status

Mammography systems are designated as Class III medical devices by Health Canada. In Canada and the United States (US), DBT screening must include both 2D and 3D image sets (2D plus 3D)[10,11] (Health Canada, Ottawa, Ontario: personal communication, 28 Feb 2015); however, this is not the case in Europe.[2]

In 2009, Health Canada licensed the Selenia Dimensions 2D/3D Mammography System (device licence #79158, Hologic Inc., Danbury, Connecticut),[7] which is marketed in Canada by Christie Innomed.[8,9] Selenia Dimensions received US Food and Drug Administration (FDA) approval in February 2011 for routine clinical use in screening or diagnostic work-up.

The SenoClaire Breast Tomosynthesis System by GE Medical Systems (Buc, France) was licensed for use in Canada in May 2014 (device licence #93289)[7] and in the US in August 2014.[13]

In April 2015, Siemens Healthcare (Erlangen, Germany) received US FDA approval for its True 3D Breast Tomosynthesis option for the MAMMOMAT Inspiration digital mammography system.[12]

Selenia Dimensions and SenoClaire received CE (Conformité Européene) clearance in the European Union (EU) in 2008[14] and 2013,[15] respectively.

Other manufacturers are seeking regulatory approval for DBT systems, including the Giotto Tomo system (IMS, Bologna, Italy) (currently approved in the EU)[16] and the AMULET Innovality (Fujifilm Europe, Düsseldorf, Germany).[17]

Patient Group

Breast cancer is the most common cancer among Canadian women (excluding non-melanoma skin cancers) and the second leading cause of cancer death in this group. Canadian estimates for 2014 predicted that 24,400 women would be diagnosed with breast cancer (26% of all new cancer cases in women) and 5,000 would die from the disease (14% of all cancer deaths in women).[18] Challenges with breast cancer are not only its incidence rate but also the lack of proven preventive strategies — early detection and treatment are currently the main approaches.[19]

Screening mammography is often credited with significantly reducing the number of deaths from breast cancer.[20] The Canadian Breast Cancer Foundation states that over the past three decades, mammography has helped to reduce deaths from breast cancer by more than 35%.[21] However, a lack of consensus remains about the benefits of breast screening as well as its potential harms, shortcomings, and indications.[2,22-24]

The Canadian Task Force on Preventive Health Care recommends that women aged 50 to 74 at average risk of breast cancer have mammography screening every two to three years, with mammography not generally recommended for those aged 40 to 49.[25] In contrast, the US Preventive Services Task Force recommends that average-risk women aged 50 to 74 be screened every two years and that screening decisions for women under age 50 be individualized based on context and patient values.[26]

Current Practice

The main screening tool for breast cancer is 2D screening mammography, but its 75% to 80% sensitivity is not ideal.[4,27] This means that, of 100 women who truly have breast cancer, only 75 to 80 will have their cancers detected through a screening mammogram. Sensitivity decreases to 50% for women with dense breasts[27] because their lesions may be hidden, and some breast cancers may be missed as a result.[4,28] False-positive test results lead to recalls for 12% to 16% of women undergoing their first screens and 4% to 6% of women undergoing subsequent screens.[29] These women are subjected to further radiation exposure and biopsies.[6] Recent attention has focused on a number of mammography issues, including the rate of false-positives (in part due to the fact that normal breast tissue, when overlapping, can

appear abnormal with 2D technology); issues related to false-positive recalls; and the fact that many biopsies after screening are unnecessary, as they turn out to be negative for cancer.[28,30,31]

There are several options for follow-up after screening mammography. The most common are diagnostic mammograms and ultrasound. An ultrasound can differentiate cysts from solid masses and may increase the accuracy of cancer detection by 50% compared with mammography alone, particularly in high-risk women and those with dense breasts.[6] However, ultrasounds also result in false-negative and false-positive findings, with benign diagnoses in 70% to 90% of cases.[6] Magnetic resonance imaging (MRI) has higher sensitivity than 2D mammography, but it has a number of limitations. For example, the positive predictive value and specificity are low, tumour diameter can be overestimated, the cost is high, and some patients cannot undergo MRI, such as those with metallic implants or claustrophobia.[6,27]

The Canadian Association of Radiologists (CAR) published guidance on breast imaging and intervention in late 2013,[32] including a description of DBT and its applications and limitations.

At that time, DBT was in the active stages of testing and early stages of clinical use, and the CAR guidance noted that it was unclear what the role of DBT would be in general population screening, subgroup screening, and diagnosis.

Methods

Literature Search Strategy
A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, PubMed, Embase, and the Cochrane Library (2015, Issue 1). Grey literature was identified by searching relevant sections of the CADTH Grey Matters checklist (http://www.cadth.ca/resources/grey-matters). No methodological filters were applied. The search was limited to English language documents published between January 1, 2012 and January 21, 2015. Regular alerts were established to update the search until April 1, 2015. Conference abstracts were excluded from the search results.

The Evidence

A number of studies of DBT for breast screening were identified. The seven largest studies (each enrolling more than 10,000 women)[28,31,33-38] were selected for detailed review in this report (Table 1). All studies were based on established breast screening programs using Hologic Selenia Dimensions technology for 3D screening, with six studies conducted in the US[28,31,33-35,38] and the seventh in Norway.[36] The Norwegian study was prospective (women received both types of imaging and served as their own controls), while the American studies were retrospective (four were before-and-after studies of outcomes once the new technology was installed[33-35,38] and two enrolled groups of women who received the older and newer technologies at different sites over the same time period).[28,31] The Norwegian study involved double reading with arbitration: all images in the study were interpreted by two independent radiologists who had to reach a consensus for the need for recall before a woman was asked to return for more imaging.[36] Study sizes ranged from approximately 13,000 to approximately 450,000 women. Of the six studies that reported sources of research support and conflicts of interest, three noted ties to Hologic.[35,36,38] Additional study details are presented in Appendix A.

The seven studies collectively examined recall rates and cancer detection outcomes for more than 600,000 women, primarily in the US. Each of the six American studies showed a statistically significant reduction in the rates of women recalled for further investigations, ranging from 15% to 37%, but the Norwegian study did not — possibly because its methodology, which included arbitration through double reading of test results, led to a higher chance that a test result would be flagged for recall.

Differences between 2D and 2D plus 3D screening in cancer detection rates were statistically significant in only three of the seven studies: the prospective Norwegian study[36] and two American before-and-after retrospective reviews.[28,35] The other four studies found no significant difference in rates of cancer detection per 1,000 women screened,[31,33,34,38] although one of the US studies[38] found a trend toward lower invasive cancer detection rates of 2.8 versus 4.3 per 1,000 women for 2D versus 2D plus 3D, respectively ($P = 0.07$.) In addition, of the three studies that looked at biopsy rates after screening (Appendix A),[33,35,38] only one found a statistically significant result — 18.1 versus 19.3 per 1,000 women for 2D versus 2D plus 3D, respectively ($P = 0.004$).[35] Two studies assessed the positive predictive value of biopsy, and neither found a significant result.[28,34]

Adverse Effects

Radiation dose is an important concern, due to the radiosensitivity of breast tissue. Dose of radiation varies depending on number of views, exposure controls, and other factors.[6,39] With DBT, each exposure is only a fraction of a 2D dose, but many images are captured and the overall dose generated by combined 2D plus 3D units can be twice that of 2D alone.[1,4,5,39-42] However, this higher dose is still below the limit accepted by the US *Mammography Quality Standards Act* for a single screening mammography exam.[38,43] A recent innovation is to replace the 2D step in combined imaging with "synthetic" 2D views reconstructed from the DBT acquisitions. This can potentially eliminate the requirement for 2D imaging altogether and halve the overall radiation dose compared with that of 2D alone.[1,4,9,40,41] Another concern with 2D mammography is the pain of breast compression, which can affect screening compliance; patient discomfort may be reduced with DBT as there is less need to maximize breast compression to eliminate tissue overlap.[6,10]

Table 1: Summary of Included Studies			
First Author (Year), Study Design	**N**	**Outcomes**	
		Recall Rate After Screening (2D vs. 2D+3D)	**Cancer Detection Rate per 1,000 Screened (2D vs. 2D+3D)**
Friedewald (2014),[35] Before-and-after retrospective review	454,850	10.7% vs. 9.1% ($P < 0.001$); 15% reduction	4.2 vs. 5.4 ($P < 0.001$)
Greenberg (2014),[28] Retrospective review	59,617	16.2% vs. 13.6% ($P < 0.0001$); 16% reduction	4.9 vs. 6.3 ($P = 0.035$)
Haas (2013),[31] Retrospective review	13,158	12.0% vs. 8.4% ($P < 0.01$); 30% reduction	5.2 vs. 5.7 ($P = 0.70$)
Lourenco (2015),[34] Before-and-after retrospective review	25,498	9.3% vs. 6.4% ($P < 0.00001$); 31% reduction	5.4 vs. 4.6 ($P = 0.44$)
McCarthy (2014),[33] Before-and-after retrospective review	26,299	10.4% vs. 8.8% ($P < 0.001$); 15% reduction	4.6 vs. 5.5 ($P = 0.32$)
Rose (2013),[38] Before-and-after retrospective review	23,355	8.7% vs. 5.5% ($P < 0.001$); 37% reduction	4.0 vs. 5.4 ($P = 0.18$)
Skaane (2013),[36] Prospective study	12,621	2.9% vs. 3.7% ($P = 0.005$); 27% increase for 2D+3D (but double reading with arbitration was used)	7.1 vs. 9.4 ($P < 0.001$)

2D = two-dimensional; 2D+3D = two-dimensional plus three-dimensional (combined); 3D = three-dimensional; N = number of patients; vs. = versus.

Administration and Cost

The technology cost of newer digital mammographic units is high, with DBT capability costing about US$750,000.[20,40] In the US, DBT is still considered investigational and there is no fee item to facilitate billing by providers. This is also the case in Canada; for example, the British Columbia, Alberta, and Ontario physicians' fee guides do not include DBT.[44-46] According to the literature, including some of the studies cited here, the current paradigm in the US is for the provider to either absorb the increased cost or charge patients an extra US$50 on top of the fee for 2D mammography for this imaging step.[5,20,28,43,47] One US report describes a range of additional charges for DBT from US$25 to US$250.[48]

A US cost-effectiveness analysis[43] of biennial screening of women aged 50 to 74 with dense breasts calculated an incremental cost per life-year gained of US$70,500 for 2D plus 3D screening versus 2D alone. Clinical data were obtained from the Norwegian trial[36] and the base case cost of additional DBT was set at US$50 (US data were not available at the time of the analysis). The calculated incremental cost per quality-adjusted life-year (QALY) was about US$54,000 (neither cost per cancer detected nor impact on mortality rates were reported). Assuming that DBT led to moderate improvements in sensitivity and specificity, 405 false-positive results were avoided per 1,000 women after 12 screening rounds and 0.5 breast cancer-related deaths per 1,000 women were averted. The cost-effectiveness was most sensitive to the additional cost of tomosynthesis; increasing the cost of adjunct tomosynthesis did not affect the relative cost-effectiveness of combined screening until the added cost of tomosynthesis exceeded US$87, for a total screening cost of US$226.[43]

Concurrent Developments

A number of breast imaging technologies are under development, including breast MRI, contrast-enhanced mammography, ultrasound with elastography or microbubbles, and dual-energy mammography (spectral mammography). Other breast imaging technologies being explored include breast computed tomography (CT) scanning (a dedicated CT system that provides 3D images without compression), 3D ultrasound, radionuclide breast imaging, and positron emission tomography (PET).[27,39,49]

Rate of Technology Diffusion

In Canada, a 2014 article reported the installation of three Selenia Dimensions DBT units at Toronto's Princess Margaret Cancer Centre, with plans for further expansion.[8] News items report that other breast tomosynthesis units have been installed at a British

Columbia centre and at the Women's Breast Health Centre in Ottawa.[50,51]

A 2012 survey of 1,800 physician members of the US Society of Breast Imaging explored the extent of DBT diffusion.[48] The survey response rate was 30%, and results showed that 30% of respondents reported using DBT. At the extremes, 51% of respondents had a single DBT unit, whereas for 6% of respondents, all units were DBT. About 80% of respondents used DBT for screening, although only 20% of these offered it to all screening patients. The use of DBT was twice as common in academic practices as it was in private practices.

Implementation Issues

Experts have identified a number of implementation issues:

- Reading DBT image sets (approximately 200 images versus four for 2D) can double the time required for interpretation of mammograms.[5,41] For example, the reading time per patient was reported to have increased from 33 to 77 seconds in an Italian study,[52] from 45 to 91 seconds in a Norwegian study,[53] and from 114 to 168 seconds in an American study.[54] Increased radiologist experience with DBT does not seem to significantly decrease interpretation times.[20] However, it was noted that longer interpretation times may be offset by decreases in recall rates and a reduced need for additional views.[40]
- No Canadian training requirements for DBT were identified; however, the US requires mandatory eight-hour training for interpreting radiologists to comply with the US *Mammography Quality Standards Act*.[42] This training is offered by several continuing medical education companies (radiologists who undergo the training are not authorized to provide training for other radiologists).[55] Technologists are also required by the US *Mammography Quality Standards Act* to undergo eight hours of training, although this is offered by technology vendors at the time of device installation.[55]
- DBT data storage requirements are large and IT resources may need expansion.[5,20] The data can be stored at 4:1 lossless compression to decrease the total size of the dataset, although this is more than 10 times greater than the size of a compressed four-view digital mammography set.[2] One reference noted that required DBT storage

space can be 100 times that of 2D, and if every tomographic image that is taken is preserved, this increases to 200 times.[55]

- Images can be interpreted using only a vendor-specific workstation, and sending them to patients or health care providers in other institutions is difficult.[42]
- In addition to the cost of purchasing DBT equipment, additional space and funding are needed for the dedicated workstations used to interpret DBT images.[20]

References

1. Svahn TM, Houssami N, Sechopoulos I, Mattsson S. Review of radiation dose estimates in digital breast tomosynthesis relative to those in two-view full-field digital mammography. Breast. 2014 Dec 29;24(2):93-9.

2. Roth RG, Maidment AD, Weinstein SP, Roth SO, Conant EF. Digital breast tomosynthesis: lessons learned from early clinical implementation. Radiographics. 2014 Jul;34(4):E89-102.

3. Tejerina BA, Tejerina BA, Rabadan DF, De Lara GA, Rosello Llerena JA, Tejerina GA. Breast imaging: how we manage diagnostic technology at a multidisciplinary breast center. J Oncol [Internet]. 2012 [cited 2015 Jan 26];2012:213421. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3398658/pdf/JO2012-213421.pdf

4. Geisel JL, Philpotts LE. Breast tomosynthesis: A replacement or an adjunct to conventional diagnostic mammography? Current Breast Cancer Reports. 2014;6(2):132-7.

5. Conant EF. Clinical implementation of digital breast tomosynthesis. Radiol Clin North Am. 2014 May;52(3):499-518.

6. Alakhras M, Bourne R, Rickard M, Ng KH, Pietrzyk M, Brennan PC. Digital tomosynthesis: a new future for breast imaging? Clin Radiol. 2013 May;68(5):e225-e236.

7. Medical devices active licences search [Internet]. Ottawa: Health Canada [cited 2015 Feb 19]. Available from: http://webprod5.hc-sc.gc.ca/mdll-limh/start-debuter.do?lang=eng

8. Zeidenberg J. Trailblazers use tomosynthesis to improve the diagnosis of breast cancer [Toronto]. Canadian Healthcare Technology [Internet]. 2014 Nov [cited 2015 Feb 24];19(8):14. Available from: http://www.canhealth.com/wordpress/wp-content/uploads/2014/10/Canadian-Healthcare-Technology-2014-08.pdf

9. Christie Innomed. [Internet]. Sainte-Eustache (QC). HOLOGIC® Selenia dimensions; [cited 2015 Feb 24]. Available from: http://www.christieinnomed.com/en/selenia-dimension

10. Uematsu T. The emerging role of breast tomosynthesis. Breast Cancer. 2013 Jul;20(3):204-12.

11. Selenia Dimensions 3D System - P080003 [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2013 Jun 9. [cited 2015 Feb 19]. (Medical devices). Available from: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm246400.htm

12. Perriello B. FDA approves Sienens 3D breast tomo device. MassDevice [Internet]. 2015 Apr 23 [cited 2015 Apr 24]. Available from: http://www.massdevice.com/news/fda-approves-siemens-3d-breast-tomo-device

13. SenoClaire - P130020 [Internet]. Silver Spring (MD): U.S.Food and Drug Administration; 2014 Aug 26. [cited 2015 Feb 19]. Available from: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/pma/pma.cfm?num=p130020

14. Hologic to showcase award winning 3D mammography and other advanced imaging technologies at RSNA 2012 [Internet]. Bedford (MA): PRNewswire; 2012 Nov 19. [cited 2015 Feb 19]. Available from: http://www.prnewswire.com/news-releases/hologic-to-showcase-award-winning-3d-mammography-and-other-advanced-imaging-technologies-at-rsna-2012-179972121.html

15. GE Healthcare announces CE marking for its breast tomosynthesis solution, SenoClaire [Internet]. San Francisco: Business Wire; 2013 Jul 16. [cited 2015 Feb 19]. Available from: http://www.businesswire.com/news/home/20130716005842/en/GE-Healthcare-Announces-CE-Marking-Breast-Tomosynthesis%20-%20.VOIRXy5jfaQ#.VOYs7Z2EhD-

16. DBT (Digital Breast Tomosynthesis) [Internet]. Bologna (Italy): IMS; 2015. [cited 2015 Feb 19]. Available from: http://www.imsitaly.eu/19/ims%2c-giotto-tomo%2c-dbt-digital-breast-tomosynthesis

17. AMULET innovality. Innovation and quality in mammography [Internet]. Tokyo: FujiFilm; 2015. [cited 2015 Feb 19]. Available from: http://www.fujifilm.com/products/medical/products/digital_mammography/innovality/index.html

18. Canadian Cancer Society. [Internet]. Toronto. Breast cancer statistics; [cited 2015 Feb 24]. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/breast/statistics/?region=bc

19. Lei J, Yang P, Zhang L, Wang Y, Yang K. Diagnostic accuracy of digital breast tomosynthesis versus digital mammography for benign and malignant lesions in breasts: a meta-analysis. Eur Radiol. 2014 Mar;24(3):595-602.

20. Lee CI, Lehman CD. Digital breast tomosynthesis and the challenges of implementing an emerging breast cancer screening technology into clinical practice. J Am Coll Cardiol. 2013 Dec;10(12):913-7.

21. Canadian Breast Cancer Foundation. Screening by mammography [Internet]. Toronto: The Foundation; 2011. [cited 2015 Mar 10]. Available from: http://www.cbcf.org/central/AboutBreastHealth/EarlyDetection/Mammography/Pages/default.aspx

22. Apesteguia Ciriza L, Pina Insausti LJ. Population-based breast cancer screening: Certainties, controversies, and future perspectives. Radiologia. 2014 Nov;56(6):479-84. In Spanish.

23. Kopans DB. Digital breast tomosynthesis from concept to clinical care. AJR Am J Roentgenol. 2014 Feb;202(2):299-308.

24. Drukteinis JS, Mooney BP, Flowers CI, Gatenby RA. Beyond mammography: new frontiers in breast cancer screening. Am J Med [Internet]. 2013 Jun [cited 2015 Jan 26];126(6):472-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4010151/pdf/nihms571320.pdf

25. CMAJ [Internet]. Ottawa: Canadian Medical Association. New breast cancer screening guidelines released: Canadian task force on preventive health care issues updated guidelines; 2011 Nov 21 [cited 2015 Feb 24]. Available from: http://www.cmaj.ca/site/misc/pr/21nov11_pr.xhtml

26. U.S. Preventative Services Task Force [Internet]. Final recommendation statement: breast cancer: screening; 2014 Dec [cited 2015 Feb 24]. Available from: http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/breast-cancer-screening#clinical-considerations

27. Jochelson M. Advanced imaging techniques for the detection of breast cancer. Am Soc Clin Oncol Educ Book [Internet]. 2012 [cited 2015 Jan 26];65-9. Available from: http://meetinglibrary.asco.org/content/223-114

28. Greenberg JS, Javitt MC, Katzen J, Michael S, Holland AE. Clinical performance metrics of 3D digital breast tomosynthesis compared with 2D digital mammography for breast cancer screening in community practice. AJR Am J Roentgenol. 2014 Sep;203(3):687-93.

29. Coldman AJ, Phillips N. False-positive screening mammograms and biopsies among women participating in a Canadian provincial breast screening program. Can J Public Health. 2012;103(6):e420-e424.

30. Margolies L, Cohen A, Sonnenblick E, Mandeli J, Schmidt PH, Szabo J, et al. Digital breast tomosynthesis changes management in patients seen at a tertiary care breast center. ISRN Radiol [Internet]. 2014 [cited 2015 Jan 26];2014:658929. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4045465/pdf/ISRN.RADIOLOGY2014-658929.pdf

31. Haas BM, Kalra V, Geisel J, Raghu M, Durand M, Philpotts LE. Comparison of tomosynthesis plus digital mammography and digital mammography alone for breast cancer screening. Radiology. 2013 Dec;269(3):694-700.

32. Canadian Association of Radiologists. CAR practice guidelines and technical standards for breast imaging and intervention. Ottawa: CAR; 2013. 45 p. [cited 2015 Feb 26]. Available from: http://www.car.ca/uploads/standards%20guidelines/20131024_en_breast_imaging_practice_guidelines.pdf

33. McCarthy AM, Kontos D, Synnestvedt M, Tan KS, Heitjan DF, Schnall M, et al. Screening outcomes following implementation of digital breast tomosynthesis in a general-population screening program. J Natl Cancer Inst. 2014 Nov;106(11).

34. Lourenco AP, Barry-Brooks M, Baird GL, Tuttle A, Mainiero MB. Changes in recall type and patient treatment following implementation of screening digital breast tomosynthesis. Radiology. 2015 Feb;274(2):337-42.

35. Friedewald SM, Rafferty EA, Rose SL, Durand MA, Plecha DM, Greenberg JS, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. JAMA. 2014 Jun 25;311(24):2499-507.

36. Skaane P, Bandos AI, Gullien R, Eben EB, Ekseth U, Haakenaasen U, et al. Prospective trial comparing full-field digital mammography (FFDM) versus combined FFDM and tomosynthesis in a population-based screening programme using independent double reading with arbitration. Eur Radiol [Internet]. 2013 Aug [cited 2015 Jan 26];23(8):2061-71. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3701792/pdf/330_2013_Article_2820.pdf

37. Ciatto S, Houssami N, Bernardi D, Caumo F, Pellegrini M, Brunelli S, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. Lancet Oncol. 2013 Jun;14(7):583-9.

38. Rose SL, Tidwell AL, Bujnoch LJ, Kushwaha AC, Nordmann AS, Sexton R, Jr. Implementation of breast tomosynthesis in a routine screening practice: an observational study. AJR Am J Roentgenol. 2013 Jun;200(6):1401-8.

39. Kilburn-Toppin F, Barter SJ. New horizons in breast imaging. Clin Oncol (R Coll Radiol). 2013 Feb;25(2):93-100.

40. Patterson SK, Roubidoux MA. Update on new technologies in digital mammography. Int J Womens Health [Internet]. 2014 [cited 2015 Jan 26];6:781-8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4140703/pdf/ijwh-6-781.pdf

41. Houssami N, Skaane P. Overview of the evidence on digital breast tomosynthesis in breast cancer detection. Breast. 2013 Apr;22(2):101-8.

42. Holland K. Taking a breast center one step further: implementing breast tomosynthesis. Radiol Manage. 2012 Jan;34(1):40-2.

43. Lee CI, Cevik M, Alagoz O, Sprague BL, Tosteson AN, Miglioretti DL, et al. Comparative effectiveness of combined digital mammography and tomosynthesis screening for women with dense breasts. Radiology. 2015 Mar;274(3):772-80.

44. Medical Services Commission. Diagnostic radiology [Internet]. Vancouver: BC Ministry of Health; 2013 Apr. 13 p. [cited 2015 Feb 26]. (MSC Payment Schedule). Available from: http://www.health.gov.bc.ca/msp/infoprac/physbilling/payschedule/pdf/37-diagnostic-radiology.pdf

45. Government of Alberta. Alberta Health Care insurance plan: medical procedure list as of 01 October 2014. Edmonton: Alberta Health; 2014. 260 p. [cited 2015 Feb 26]. (Schedule of Medical Benefits (SOMB)). Available from: http://www.health.alberta.ca/documents/SOMB-Medical-Procedures-2014-10.pdf

46. Ontario Ministry of Health and Long-Term Care. [Internet]. Toronto. Schedule of benefits for physician services under the health insurance act; 2014 May 1 [cited 2015 Feb 24]. Available from: http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html

47. Bonafede MM, Kalra VB, Miller JD, Fajardo LL. Value analysis of digital breast tomosynthesis for breast cancer screening in a commercially-insured US population. Clinicoecon Outcomes Res [Internet]. 2015 [cited 2015 Feb 5];7:53-63. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296908

48. Hardesty LA, Kreidler SM, Glueck DH. Digital breast tomosynthesis utilization in the United States: a survey of physician members of the Society of Breast Imaging. J am coll radiol. 2014 Jun;11(6):594-9.

49. 3D technologies poised to change how doctors diagnose cancers [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2014 Sep 30. [cited 2015 Feb 19]. Available from: http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm416312.htm

50. Goomansingh C. 3D mammograms may increase early detection of breast cancer: study [Internet]. Toronto (ON): Global News; 2014 Jun 24. [cited 2015 Apr 15]. Available from: http://globalnews.ca/news/1413016/3d-mammograms-may-increase-early-detection-of-breast-cancer-study/

51. Women's Breast Health Centre annual review April 2011-March 2012 [Internet]. Ottawa (ON): The Ottawa Hospital Women's Breast Health Centre; 2012. [cited 2015 Apr 15]. Available from: https://www.ottawahospital.on.ca/wps/wcm/connect/971248804b9dc8269192dd56b8a72a08/WBHC+Annual+Review+11-12.pdf?MOD=AJPERES

52. Bernardi D, Ciatto S, Pellegrini M, Anesi V, Burlon S, Cauli E, et al. Application of breast tomosynthesis in screening: incremental effect on mammography acquisition and reading time. Br J Radiol [Internet]. 2012 Dec [cited 2015 Jan 26];85(1020):e1174-e1178. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3611720/pdf/bjr-85-e1174.pdf

53. Skaane P, Bandos AI, Gullien R, Eben EB, Ekseth U, Haakenaasen U, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. Radiology. 2013 Apr;267(1):47-56.

54. Dang PA, Freer PE, Humphrey KL, Halpern EF, Rafferty EA. Addition of tomosynthesis to conventional digital mammography: effect on image interpretation time of screening examinations. Radiology. 2014 Jan;270(1):49-56.

55. Hardesty LA. Issues to consider before implementing digital breast tomosynthesis into a breast imaging practice. AJR Am J Roentgenol. 2015 Mar;204(3):681-4.

BREAST CANCER SCREENING — 2D ALONE VERSUS 2D PLUS 3D MAMMOGRAPHY

Author (Year); Country; Study Years and Type	Population	Intervention (All 2D and 3D)	Comparator	Outcomes
Friedewald et al. (2014);[35] US; before-and-after retrospective review of 2D cohort (2010-2011) vs. 2D+3D cohort (2011-2012) at 13 centres	N = 454,850: 62% had 2D and 38% had 3D as well as 2D	Hologic Selenia Dimensions	2D DM (devices NR)	• *Recall rate after screening mammogram:* 10.7% vs. 9.1%; absolute difference 1.6% ($P < 0.001$) • *Cancer detection rates per 1,000 screens:* 4.2 for 2D vs. 5.4 for 2D+3D; absolute difference 1.2 (95% CI, 0.8 to 1.6; $P < 0.001$) • *Invasive cancer detection rates per 1,000 screens:* 2.9 for 2D vs. 4.1 for 2D+3D; difference 1.2 (95% CI, 0.8 to 1.6; $P < 0.001$) • *Biopsy rates per 1,000 screens:* 18.1 for 2D vs. 19.3 for 2D+3D; absolute difference 1.3 (95% CI, 0.4 to 2.1; $P = 0.004$)
Greenberg et al. (2014);[28] US; retrospective review of 2 cohorts screened over the same time span (2011-2012) at different sites (2D or 2D+3D)	N = 59,617 (mean age 60 years): 65% chose 2D and 35% chose 3D (most paid an extra fee of US$50)	Hologic Selenia Dimensions	2D DM mammogram (Hologic Selenia)	• *Recall rate after screening mammogram:* 16.2% for 2D vs. 13.6% for 2D+3D; absolute difference 2.6% ($P < 0.0001$); relative reduction 16.1% ($P < 0.0001$) • *Cancer detection rates per 1,000 screens:* 4.9 for 2D vs. 6.3 for 2D+3D; cancer detection rate 28.6% greater for 3D vs. 2D ($P = 0.035$) • *Invasive cancer detection rates per 1,000 screens:* 3.2 for 2D vs. 4.6 for 2D+3D; cancer detection rate 43.8% higher for 3D vs. 2D ($P = 0.0056$) • *PPV (detected cancer patients per 100 recalls):* 3.0 for 2D vs. 4.6 for 2D+3D ($P = 0.0003$); a 53% advantage for 3D • *PPV for biopsy:* 23.8% for 2D vs. 22.8% for 2D+3D ($P = 0.696$)
Haas et al. (2013);[31] US; 2011-2012; retrospective review of 2 cohorts screened over the same time span at different sites (2D or 2D+3D)	N = 13,158: 54% had 2D and 46% had 3D as well as 2D	Hologic Selenia Dimensions	2D DM (Hologic Selenia)	• *Recall rate after screening mammogram:* 12% for 2D vs. 8.4% for 2D+3D ($P < 0.01$); this corresponds to a 30% reduction in recall rates with the addition of 3D • *Cancer detection rates per 1,000 screens:* 5.2 for 2D vs. 5.7 for 2D+3D ($P = 0.70$); 9.5% increase in cancer detection rate with the addition of 3D or a need to screen 2,018 women with 3D to detect one additional cancer; subgroup analysis: detection rates for women at high risk and baseline risk were NSD between groups
Lourenco et al. (2015);[34] US; before-and-after retrospective review of 2D cohort (2011-	N = 25,498 (mean age 55 years; range 25 to 90): 49% had 2D and 51% had 3D	Hologic Selenia Dimensions	2D DR mammogram (Senographe, GE Medical)	• *Recall rate after screening mammogram:* 9.3% (CI 8.8% to 9.9%) for 2D vs. 6.4% (CI 6.0% to 6.8%) for 3D; absolute difference 2.9%; relative reduction 31% ($P < 0.00001$); recall rate lower with 3D for asymmetries but lower with 2D for

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2012) vs. 2D+3D cohort (2012-2013)				masses, distortions, and calcifications • *Cancer detection rates per 1,000 screens*: 5.4 for 2D vs. 4.6 for 2D+3D (*P* = 0.44); cancer detection rate 28.6% greater for 2D+3D vs. 2D (*P* = 0.035) • *PPV for biopsy*: 30.2% for 2D vs. 23.8% for 2D+3D (*P* = 0.21)
McCarthy et al. (2014);[33] US; before-and-after retrospective review of 2D cohort (2010-2011) vs. 2D+3D cohort (2011-2013)	N = 26,299: 41% had 2D and 59% had 3D as well as 2D	Hologic Selenia Dimensions	2D DM (devices NR)	• *Recall rate after screening mammogram*: 10.4% for 2D vs. 8.8% for 2D+3D (adjusted OR = 0.80, 95% CI, 0.74 to 0.88; *P* < 0.001); this corresponds to a 15% reduction or 16 fewer recalls per 1,000 screened with DBT • *Cancer detection rates per 1,000 screens:* similar for DM and DBT (4.6 vs. 5.5; *P* = 0.32) • *Biopsy rates per 1,000 screens*: similar for DM and DBT (18 vs. 20; *P* = 0.14), as were cancer yields of both biopsies recommended and those actually performed
Rose et al. (2013);[38] US; before-and-after retrospective review of 2D cohort (2010) vs. 2D+3D cohort (2011-2012)	N = 23,355: 59% had 2D and 41% had 3D as well as 2D	Hologic Selenia Dimensions	2D DM (Hologic Selenia)	• *Recall rate after screening mammogram*: 8.7% for 2D vs. 5.5% for 2D+3D (*P* < 0.001); this corresponds to a 15% reduction or 16 fewer recalls per 1,000 screened with DBT • *Cancer detection rates per 1,000 screens:* similar for DM and DBT (4.0 vs. 5.4; *P* = 0.18) • *Invasive cancer detection rates per 1,000 screens*: 2.8 for 2D vs. 4.3 for 2D+3D (*P* = 0.07) • *PPV (detected cancer patients per 100 recalls)*: 4.7% for 2D vs. 10.1% for 2D+3D (*P* < 0.001) • *Biopsy rates per 1,000 screens*: similar for DM and DBT (15.2 vs. 13.5; *P* = 0.59)
Skaane et al. (2013);[36] Norway; prospective study with women serving as their own controls (4 exams done using one compression), 2011-2012, DOUBLE READING with arbitration	N = 12,621 women aged 50 to 69	Hologic Selenia Dimensions Unit (2D/3D + synthesized 2D/3D)	Hologic Selenia Dimensions Unit (2D + 2D with CAD)	• *Recall rate after screening mammogram*: 2.9% for 2D vs. 3.7% for 2D+3D (*P* = 0.005) • *Cancer detection rates per 1,000 screens:* 7.1 for 2D vs. 9.4 for 2D+3D (*P* < 0.001); 30% increase for 2D+3D • *PPV (detected cancer patients per 100 recalls):* similar at 24.7% for 2D and 25.5% for 2D+3D (*P* = 0.97) • *Pre-arbitration false-positive scores:* 10.3% for 2D vs. 8.5% for 2D+3D (*P* < 0.001)

2D = two-dimensional; 2D+3D = two-dimensional plus three-dimensional (combined); 3D = three-dimensional; CAD = computer-aided detection; CI = confidence interval; DBT = digital breast tomosynthesis; DM = digital mammography; NR = not reported; NSD = not significantly different; OR = odds ratio; PPV = positive predictive value; vs. = versus.