Canadian Association of Radiologists/Canadian Society of Breast Imaging Position Statement on the Utilization of Digital Breast Tomosynthesis in Mammography Screening

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Digital breast tomosynthesis (DBT) is a form of serial sectioning created by digital reconstruction of multiple low-dose mammographic projections into contiguous slices. It is often referred to as "tomo" or "three-dimensional" (3D) mammography, although it is not a truly multiplanar form of 3D[1]. Slice thickness may be adjusted depending on the vendor and/or software used for display. Images are obtained in the same plane as the original compression plane and are read as planar images. Tomosynthesis images can be acquired with ("combo-mode") or without standard two dimensional (2D) digital mammography (DM). Synthetic 2D mammograms (SM) are 2D projection images reconstructed from the information acquired during DBT data acquisition (post processing). The DBT slices or "stack" must be interpreted alongside the 2D imaging, either standard 2D DM or SM images[2, 3].

Studies comparing DBT with 2D DM have consistently demonstrated superior performance of DBT including many performance indicators crucial to a successful screening program[2-7]. In North America, where abnormal recall rates are higher than European countries, DBT significantly improves specificity by decreasing false-positive recall rates by 30-40%, with a pooled absolute reduction of 2.9%[8], reducing unnecessary follow-ups (BI-RADS 3) by 50% and increasing the positive predictive value (PPV3) for lesions undergoing biopsy from 30% with 2D DM to 50% with DBT ($p<0.0001$) [9]. This reduces the burden of unnecessary testing and costs of screening programs. In addition, DBT increases the cancer detection rate by 1 to 2/1000 screening exams (average 1.6 per 1000) above 2D DM[8]. A meta-analysis showed that DBT improved CDR in screening and diagnostic settings in dense breasts[10]. DBT's greatest major benefit is its preferential increase in the detection rate of invasive cancers. Studies have shown preferential diagnosis of DBT over 2D DM screening for early detection of lobular carcinomas, and biologically active invasive cancers with fewer nodal and distant metastases[11, 12]. Ductal carcinoma in situ (DCIS) detection remains similar compared with 2D DM. Although there is an increased detection of architectural distortion related to radial scars, PPV3 for detection of malignancy related to this finding remains high at 34%[13]. The potential impact on overtreatment is under active evaluation[14]. The improved clinical performance of DBT is related to its ability to diminish the effects of overlapping tissue by displaying one thin section of tissue at a time, resulting in improved detection and evaluation of focal asymmetries, architectural distortion and some apparent masses. Calcifications can also be easily detected on DBT and/or the accompanying SM or 2D DM images. Recent studies[15, 16] have demonstrated SM to be comparable to 2D DM for the detection of calcifications, although 2D magnification views remain the standard for the workup of calcifications requiring characterization, regardless of how they were detected. The application of Artificial Intelligence (AI) tools may improve workflow by decreasing DBT reading times and increasing the accuracy of interpretation [17]. To date, several DBT machines are approved by Health Canada as stand-alone screening and diagnostic systems.

The radiation dose for a single DBT projection is equivalent to that of a single view 2D DM image[18, 19]. The dose for 2D DM + DBT ("combo mode") single image and projection is therefore approximately double to just over double but remains within acceptable dose limits. There is no additional radiation required for SM as this is simply a post processed image and hence the dose of an SM + DBT projection is equivalent to the single DBT projection dose. Many observational studies[3, 4, 20] have confirmed the SM + DBT have an equivalent accuracy as 2D DM + DBT (combo mode). Data regarding the diagnostic performance of single use of SM+DBT in the screening setting are scarce and several large randomized breast DBT screening trials are underway, such as TMIST [13], the PROSPECTS trial in the United Kingdom, the TOSYMA trial in Germany, the Proteus Donna and RE-Tomo trials in Italy[21]. SM + DBT are increasingly replacing the "combo mode" thereby addressing the concern of radiation dose.

Current Clinical Indications

Screening

Screening outcome benchmarks are improved with the use of DBT. DBT can improve recall rate and PPV for recall[22], which is of strong interest to Canadian screening programs[23]. Interval cancers, which are cancers diagnosed in between normal screening intervals, have been demonstrated at reduced rates in women screened with DBT[24-26]. In the Malmo Breast Tomosynthesis Screening Trial of women screened with DBT and digital mammography, the interval cancer rate (ICR) was 1.6 per 1,000 screened, significantly lower than 2.8 per 1000 in the group screened with digital mammography[25]. However, the To-Be trial from Norway recently published their results of a non significantly lower ICR of 1.4/1000 with DBT vs 2/1000 for DM (p=0.20)[27] and a meta-analysis showed no significant difference in pooled ICR, with heterogeneity of data and few datasets[28]. Likely more studies will be needed for conclusive evidence of reduction in ICR with DBT.

DBT is increasingly being used for screening worldwide. Results of large prospective and retrospective screening trials have demonstrated consistently improved cancer detection rates and PPVs and decreased recall rates. American College of Radiology [29] and European guidelines [30] concluded that DBT may be recommended for screening. Recent European guidelines suggest that women with dense breasts may benefit the most from DBT screening[30].

A large randomized control trial is currently underway, with the intention of enrolling 165,000 patients at over 90 sites (TMIST), comparing 2D-DM+DBT with 2D-DM alone[14]. The study is designed primarily to investigate if 2D-DM+DBT detects lethal cancers (advanced cancers or small aggressive cancers). Many secondary aims including recall rates are being addressed.

Diagnostic

DBT is very useful in diagnostic breast imaging. DBT has been found to be better than coned compression views for investigating 2D mammographically detected abnormalities. It improves the radiologist's confidence for diagnosis, reduces unnecessary additional tests such as breast ultrasound and additional mammographic views, and identifies additional disease if full view DBT is used. It has been shown to improve workflow; non-contributory ultrasound and BI-RADS 3 call-backs are reduced by 50%[9] with an absolute reduction of 2.4 per 1000[31] and an overall (20%) increase in the PPV3 for biopsy[9].

In addition to full view DBT, spot tomosynthesis uses the same radiation dose and can be helpful to distinguish true findings from summation artifact. When working up DBT findings, ultrasound is often the first choice for many asymmetries, masses and architectural distortion. Tomosynthesis-guided biopsy can be performed for calcifications and for suspicious DBT findings that are occult on ultrasound. This technique has been shown to reduce the biopsy time by as much as 50%. The characterization of microcalcifications still requires 2D true lateral and cranio-caudal magnification views. Greater availability of contrast-enhanced tomosynthesis may further improve the specificity of DBT in future [32, 33]. When tomosynthesis-guided biopsy is not available, MRI may be required to investigate DBT-only findings.

CSBI Recommendations for Tomosynthesis in Canada

1. Recommend using screening with DBT to reduce abnormal recall rates, increase cancer detection rates, reduce interval cancer rates and increase PPV for recalled lesions. DBT is predicted to be the future for screening mammography and replace 2D DM.

2. Recommend switching or upgrading to a DBT unit when it is time to replace end of life mammography units. The Mammography Accreditation Program (MAP) Standard including SM views allows accreditation of SM+ tomosynthesis data, as mandated by the screening programs.

3. There is strong evidence that SM may be used instead of 2D images. If synthetic views are used without 2D imaging, it is mandatory to review the tomosynthesis stack. Tomosynthesis slices or synthetic views must not be used independently.

4. Where DBT is employed for screening and diagnosis, there must be access to advanced breast imaging, which may include tomosynthesis-guided biopsy, "second look" ultrasound and/or breast MRI. This is required to aid biopsy of subtle lesions which may not be visible on standard 2D mammography.

5. SM is comparable to 2D DM for microcalcification detection, but true magnification views are required for microcalcification characterization.

6. While tomosynthesis may be considered a supplemental screening tool to 2D mammography, it does not replace the need for supplemental screening with other imaging modalities in patients with dense breast tissue, or who are at high risk for breast cancer. Other supplemental screening modalities such as Breast MRI, contrast-enhanced mammography and breast ultrasound should be used in these patients[34, 35].

Challenges to implementation of DBT include, but are not limited to:

1. Workflow considerations: Interpretation time is higher but less than double of that of routine 2D DM [4, 36]. This is also dependent on the number of images (breast thickness) to be reviewed and more importantly, the network speed. With experience, reader interpretation time may increase by 25-30% over 2D DM[37]. However, reduced recall rate, fewer benign biopsies and fewer BI-RADS 3 findings requiring follow-up will improve the workflow.

2. PACS considerations: DBT has large digital storage requirements over and above 2D DM. It is required that the tomosynthesis stack be stored in addition to the 2D DM and synthetic images for the required retention time. Advances in data compression, storage costs, synthetic view image quality and evidence to support synthetic-view-only comparison may address this concern. Providing high network speed and updated reporting workstations is also an ongoing cost consideration for facilities.

3. Reimbursement: Fee code reimbursement must be adjusted for DBT above 2D DM for both screening and diagnostic in some Canadian provinces and new fee codes may need to be established in others[38]. This is to account for the increased radiologists' reading time as well as the higher equipment and storage costs. Despite increased costs to individual facilities, implementation of DBT allows cost savings to the entire medical system[38, 39]. The literature indicates that the cost savings are related to fewer workups, biopsies and unnecessary follow up testing, and importantly, less aggressive treatments required due to earlier detection. With reduced call backs and follow ups, additional out-of-pocket costs to patients for the added travel and parking, time from work, child or family care will also be reduced. Cost effectiveness studies have shown that it is cost effective to screen with DBT, particularly in women with dense breasts[39-42].

Personnel Requirements

In addition to standard mammography requirements, it is strongly recommended that radiologists willing to initiate reporting DBT participate in an initial 8 hours of training specific to DBT as per the ACR requirement to reduce the learning curve and avoid an increased recall rate[43]. If radiologists had regular DBT training in residency or fellowship, or have been using it in regular practice, an extra 8 hours of dedicated DBT training is not required if appropriate ongoing practice maintenance is achieved. Technologists and medical physicists should obtain appropriate training as available.

Contraindications

Like digital mammography there are no known absolute contraindications specific to DBT, and should follow recommendations for use of 2D mammography as per CAR guidelines[43].

References:

1. Sechopoulos I. A review of breast tomosynthesis. Part I. The image acquisition process. *Med Phys* 2013; 40:014301

2. 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; 200:1401-1408

3. Friedewald SM, Rafferty EA, Rose SL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA* 2014; 311:2499-2507

4. Skaane P, Bandos AI, Gullien R, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology* 2013; 267:47-56

5. Ciatto S, Houssami N, Bernardi D, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. *The lancet oncology* 2013; 14:583-589

6. Durand MA, Haas BM, Yao X, et al. Early clinical experience with digital breast tomosynthesis for screening mammography. *Radiology* 2015; 274:85-92

7. 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; 274:337-342

8. Marinovich ML, Hunter KE, Macaskill P, Houssami N. Breast Cancer Screening Using Tomosynthesis or Mammography: A Meta-analysis of Cancer Detection and Recall. *J Natl Cancer Inst* 2018; 110:942-949

9. Raghu M, Durand MA, Andrejeva L, et al. Tomosynthesis in the Diagnostic Setting: Changing Rates of BI-RADS Final Assessment over Time. *Radiology* 2016; 281:54-61

10. Phi XA, Tagliafico A, Houssami N, Greuter MJW, de Bock GH. Digital breast tomosynthesis for breast cancer screening and diagnosis in women with dense breasts - a systematic review and meta-analysis. *BMC cancer* 2018; 18:380

11. Yun SJ, Ryu CW, Rhee SJ, Ryu JK, Oh JY. Benefit of adding digital breast tomosynthesis to digital mammography for breast cancer screening focused on cancer characteristics: a meta-analysis. *Breast Cancer Res Treat* 2017; 164:557-569

12. Durand MA, Friedewald SM, Plecha DM, et al. False-Negative Rates of Breast Cancer Screening with and without Digital Breast Tomosynthesis. *Radiology* 2021; 298:296-305

13. Choudhery S, Johnson M, Larson NB, Anderson T. Malignant Outcomes of Architectural Distortion on Tomosynthesis: A Systematic Review and Meta-analysis. *AJR Am J Roentgenol* 2020;

14. TMIST (Tomosynthesis Mammographic Imaging Screening Trial). In: National Cancer Institute, 2018. Available from: https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/tmist#trial

15. Lai YC, Ray KM, Lee AY, et al. Microcalcifications Detected at Screening Mammography: Synthetic Mammography and Digital Breast Tomosynthesis versus Digital Mammography. *Radiology* 2018; 289:630-638

16. Wahab RA, Lee SJ, Zhang B, Sobel L, Mahoney MC. A comparison of full-field digital mammograms versus 2D synthesized mammograms for detection of microcalcifications on screening. *Eur J Radiol* 2018; 107:14-19

17. Conant EF, Toledano AY, Periaswamy S, et al. Improving Accuracy and Efficiency with Concurrent Use of Artificial Intelligence for Digital Breast Tomosynthesis. *Radiol Artif Intell* 2019; 1:e180096

18. 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* 2015; 24:93-99

19. Gennaro G, Bernardi D, Houssami N. Radiation dose with digital breast tomosynthesis compared to digital mammography: per-view analysis. *Eur Radiol* 2018; 28:573-581

20.Skaane P, Bandos AI, Eben EB, et al. Two-view digital breast tomosynthesis screening with synthetically reconstructed projection images: comparison with digital breast tomosynthesis with full-field digital mammographic images. *Radiology* 2014; 271:655-663

21. Lang K. The Coming of Age of Breast Tomosynthesis in Screening. *Radiology* 2019; 291:31-33

22. Giess CS, Pourjabbar S, Ip IK, Lacson R, Alper E, Khorasani R. Comparing Diagnostic Performance of Digital Breast Tomosynthesis and Full-Field Digital Mammography in a Hybrid Screening Environment. *AJR Am J Roentgenol* 2017; 209:929-934

23. Canadian Partnership Against Cancer. Pan-Canadian Framework for Action to Address Abnromal Call Rates in Breast Cancer Screening. Toronto, Canada: Canadian Partnership Against Cancer, 2020. Available from: https://s22457.pcdn.co/wp-content/uploads/2020/07/Framework-for-action-ACR-breast-screening-EN.pdf

24. McDonald ES, Oustimov A, Weinstein SP, Synnestvedt MB, Schnall M, Conant EF. Effectiveness of Digital Breast Tomosynthesis Compared With Digital Mammography: Outcomes Analysis From 3 Years of Breast Cancer Screening. *JAMA Oncol* 2016; 2:737-743

25. Johnson K, Lang K, Ikeda DM, Akesson A, Andersson I, Zackrisson S. Interval Breast Cancer Rates and Tumor Characteristics in the Prospective Population-based Malmo Breast Tomosynthesis Screening Trial. *Radiology* 2021:204106

26. Houssami N, Bernardi D, Caumo F, et al. Interval breast cancers in the 'screening with tomosynthesis or standard mammography' (STORM) population-based trial. *Breast (Edinburgh, Scotland)* 2018; 38:150-153

27. Hofvind S, Moshina N, Holen AS, et al. Interval and Subsequent Round Breast Cancer in a Randomized Controlled Trial Comparing Digital Breast Tomosynthesis and Digital Mammography Screening. *Radiology* 2021:203936

28. Houssami N, Hofvind S, Soerensen AL, et al. Interval breast cancer rates for digital breast tomosynthesis versus digital mammography population screening: An individual participant data meta-analysis. *EClinicalMedicine* 2021; 34:100804

29. American College of Radiology. ACR Statement on Breast Tomosynthesis. 2014. Available from: https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Breast-Tomosynthesis

30. European Commission Initiative on Breast Cancer. Tomosynthesis use in screening. March 12, 2021. Available from: https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines/screening-tests/DBT-or-DM

31. McDonald ES, McCarthy AM, Weinstein SP, Schnall MD, Conant EF. BI-RADS Category 3 Comparison: Probably Benign Category after Recall from Screening before and after Implementation of Digital Breast Tomosynthesis. *Radiology* 2017; 285:778-787

32. Chou CP, Lewin J, Pan HB. Contrast-enhanced tomosynthesis: The best of both worlds or more of the same? *Eur J Radiol* 2016; 85:509

33. Chou CP, Lewin JM, Chiang CL, et al. Clinical evaluation of contrast-enhanced digital mammography and contrast enhanced tomosynthesis--Comparison to contrast-enhanced breast MRI. *Eur J Radiol* 2015; 84:2501-2508

34. Tagliafico AS, Mariscotti G, Valdora F, et al. A prospective comparative trial of adjunct screening with tomosynthesis or ultrasound in women with mammography-negative dense breasts (ASTOUND-2). *Eur J Cancer* 2018; 104:39-46

35. Comstock CE, Gatsonis C, Newstead GM, et al. Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening. *JAMA* 2020; 323:746-756

36. Bahl M, Gaffney S, McCarthy AM, Lowry KP, Dang PA, Lehman CD. Breast Cancer Characteristics Associated with 2D Digital Mammography versus Digital Breast Tomosynthesis for Screening-detected and Interval Cancers. *Radiology* 2018; 287:49-57

37. 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; 270:49-56

38. Cressman S, Mar C, Sam J, Kan L, Lohrisch C, Spinelli JJ. The cost-effectiveness of adding tomosynthesis to mammography-based breast cancer screening: an economic analysis. *CMAJ Open* 2021; 9:E443-E450

39. Fleming MM, Hughes DR, Golding LP, McGinty GB, MacFarlane D, Duszak R, Jr. Digital Breast Tomosynthesis Implementation: Considerations for Emerging Breast Cancer Screening Bundled Payment Models. *J Am Coll Radiol* 2019; 16:902-907

40. Wang J, Phi XA, Greuter MJW, et al. The cost-effectiveness of digital breast tomosynthesis in a population breast cancer screening program. *Eur Radiol* 2020; 30:5437-5445

41. Sankatsing VDV, Juraniec K, Grimm SE, et al. Cost-effectiveness of Digital Breast Tomosynthesis in Population-based Breast Cancer Screening: A Probabilistic Sensitivity Analysis. *Radiology* 2020; 297:40-48

42. Kalra VB, Wu X, Haas BM, Forman HP, Philpotts LE. Cost-Effectiveness of Tomosynthesis in Annual Screening Mammography. *AJR Am J Roentgenol* 2016; 207:1152-1155

43. Appavoo S AA, Causer P; Crystal P, Kornecki A; Mundt Y, Seely JM, Wadden N. Canadian Association of Radiologists (CAR) Practice Guidelines and Technical Standards for Breast Imaging and Intervention 2016. https://car.ca/wp-content/uploads/car_breastimagingguidelines_2016_en.pdf