LEARNING OBJECTIVES

- Explain synthetic mammograms
- Review current literature
- Review accreditation requirements
CLINICAL USE OF DIGITAL BREAST TOMOSYNTHESIS (DBT)

- The first commercial DBT system in the U.S., the Hologic Dimensions, was approved in February 2011.
- GE received approval in August 2014 and Siemens in April 2015.
- FDA definition of an approved screening exam:
  - Hologic and Siemens: a 2D image set, or a 2D + 3D image set.
  - GE: a 2D image set (CC + MLO), or a 2D CC and 3D MLO.

WHAT ARE SYNTHETIC MAMMOGRAMS?

- Synthetic mammograms (SM) seek to replace the conventional 2D mammogram (FFDM) using a 2D image that is generated from the tomosynthesis (DBT) image set.
- This eliminates approximately ½ of the radiation dose, making total exam dose comparable to a typical FFDM mammogram (conventional 2D alone).
- Also shortens time spent under compression and total exam time.

WHY DO WE NEED THE 2D AT ALL?

- Some things are difficult to assess in 1-mm slices:
  - Assessment of side-to-side symmetry
  - Comparison to priors and assessment of interval change
  - Detection of calcifications
  - See more easily how features are distributed
- Provide a “roadmap” or global picture

REGULATORY STATUS OF SYNTHETIC MAMMOGRAMS

- Hologic received FDA approval for C-View in May 2013
  - It may replace the conventional 2D image
  - Approval was based on a Hologic study showing that 3D + C-View is non-inferior to conventional 2D FFDM
- GE has a synthetic mammogram called V-View, but it is not approved to replace the FFDM view
- Siemens has the Insight 2D, but it is not yet commercially available
THE C-VIEW PROCESS

- Perform a standard DBT scan
- Reconstruct tomo slices as normal
- Tomo slices are stacked, summed, and filtered in a method similar to generating a weighted maximum intensity projection (MIP)
- The Hologic C-View software allows adjustment to the default contrast (low, medium, high) and the appearance of the skin line (more or less prominent).
  - These settings are adjustable only by the service engineer.
  - Default used for FDA approval was medium contrast with more prominent skin line.


RECONSTRUCTION AND IMAGE PROCESSING

“For processing” projection
“For presentation” projection
Sample tomo slice
C-View image
HOLOGIC C-View Images

Same Patient
ANOTHER PATIENT

WHAT ARE LIMITATIONS OF C-VIEW?

- Limited by the quality of the tomo images
  - Acquired without a grid
  - Larger pixel size (binning)
  - Higher kV and Al filter
  - Longer exposures can lead to more motion artifact

- Proprietary image processing is used to compensate for these effects

- Some artifacts related to dense objects
**Related to tomo artifacts?**

- Conventional 2D
- Peripheral tomo slice

**What does a phantom look like?**

- FFDM
- SM
WHAT DOES A PHANTOM LOOK LIKE?

FFDM

SM

WHAT DOES A PHANTOM LOOK LIKE?

FFDM

SM
LITERATURE


STUDY 1 (GUR ET AL)

- Retrospective study.
- 10 radiologists interpreted images from 114 women (228 breasts) consisting of a FFDM, SM, and DBT image set.
- Study was conducted before FDA approval of C-View
- All had verified positive, benign, or negative findings.
- Exams were excluded if the findings of interest were too obvious or not visible on both image sets, as determined by 2 radiologists who were aware of the actual findings and were not readers.
- In one session the DBT images were paired with the FFDM image. In a second session, the DBT images were paired with a SM image. The sessions were conducted one month apart and the order randomized.
- Readers rated studies as “recall” or “no recall”.
STUDY 1 (GUR ET AL)

- FFDM + DBT:
  - Average sensitivity was 82.6%
  - Average false-positive recall rate: 29.8%
- SM + DBT:
  - Average sensitivity was 77.2%
  - Average false-positive recall rate: 29.7%
- Difference in sensitivity was significant (p<0.05)
- Increase in sensitivity using FFDM was observed for 9/10 radiologists
- Increase in specificity using FFDM was observed for 5/10 radiologists
- There were 16 microcalcification-related abnormalities that were missed or interpreted incorrectly using the SM images compared to the FFDM images

STUDY 2 (ZULEY ET AL)

- Similar study design to Gur et al (same institution and many of the same authors), with 8 readers and 123 patients.
- This time they assessed:
  - FFDM alone
  - FFDM + DBT
  - SM alone
  - SM + DBT
- They had the readers report full BI-RADS scores and give probability of malignancy from 0-100 if the score was > 3
STUDY 2 (ZULEY ET AL)

- SM alone: AUC = 0.894
- FFDM alone: AUC = 0.889
- SM + DBT: AUC = 0.916
- FFDM + DBT: AEC = 0.939

Not significant

STUDY 2 (ZULEY ET AL)

- 5 readers performed somewhat better with SM over FFDM
- All 8 readers performed marginally better with FFDM + DBT
- Using SM, readers tended to give a higher BI-RADS score to the breast in question when a biopsy-proven cancer was present
- No difference in recall rates
- No significant difference in identification of microcalcifications or masses
STUDY 3 (SKAANE ET AL)

- Prospective study of 24901 women participating in biennial Oslo screening program
  - 12631 from Nov 22, 2010 – Dec 21, 2011 (period 1)
  - 12270 from Jan 20, 2012 – Dec 19, 2012 (period 2)
  - Period 2 had a new version of the synthesized 2D image software
- In each period, compared FFDM + DBT with SM + DBT
- 8 radiologists participated; each included exam was interpreted independently by 4 radiologists
- Findings rated per-breast with a 5-point rating scale of increasing probability of malignancy
- All patients whose images received 1+ score of 2 or greater were discussed by at least 2 radiologists (standard of practice)
  - A consensus-based decision to dismiss or recall a patient was made for exams with ratings of 2 or 3
  - An exam rated 4 or 5 must be recalled

STUDY 3 (SKAANE ET AL)

- Compared: false-positive rates prior to arbitration, cancer detection rates, PPVs
  - Cancer “detected”: score of >1
  - False-positive: score >1 without a verified cancer (dismissed at arbitration, or benign during diagnostic work-up)
- False-positives:
  - FFDM + DBT: 5.3% period 1, 4.6% period 2
  - SM + DBT: 4.6% period 1, 4.5% period 2
- Cancer detection (per 1000 screening exams):
  - FFDM + DBT: 8.0 period 1, 7.8 period 2
  - SM + DBT: 7.4 period 1, 7.7 period 2
- PPVs:
  - FFDM + DBT: 28.5% period 1, 32.1% period 2
  - SM + DBT: 30.3% period 1, 34.9% period 2
STUDY 4 (GILBERT ET AL)

- Compared (1) FFDM alone, (2) FFDM + DBT, and (3) SM+ DBT
- 7060 cases
- Women aged 40-73
- 6 UK facilities and 31 readers
- Recorded location of abnormality on a 9-square grid (and slice number on 3D), suspicion on 5-point scale, and recall/no recall
- Rated lesion visibility, lesion extent, discrimination and overall opinion of DBT vs 2D on 5-point scale
- Sensitivity and specificity calculated for each image set

Sensitivity:
- 87% 2D alone
- 89% 2D + 3D
- 88% synthetic 2D + 3D

Specificity:
- 58% 2D alone
- 69% 2D + 3D
- 71% synthetic 2D + 3D

Significant for all densities, radiologic features, and age groups
**STUDY 4 (GILBERT ET AL)**

- Included 107 patients with T1-stage (≤ 2 cm) invasive breast cancer
  - 20 were not visible on either FFDM or SM (detected by ultrasound)
- Matched to 107 negative cases (BI-RADS 1 or 2) with 1-year negative follow-up
- 3 radiologists compared FFDM and SM images without DBT
- They rated lesions on a 4-point visibility scale, and recorded size, anatomic location, morphological finding type, and BI-RADS score
- Results were analyzed as a whole and separated by fatty/dense breasts, tumor size, calcifications, and non-calcified cancers

---

**STUDY 5 (CHOI ET AL)**

- Included 107 patients with T1-stage (≤ 2 cm) invasive breast cancer
  - 20 were not visible on either FFDM or SM (detected by ultrasound)
- Matched to 107 negative cases (BI-RADS 1 or 2) with 1-year negative follow-up
- 3 radiologists compared FFDM and SM images without DBT
- They rated lesions on a 4-point visibility scale, and recorded size, anatomic location, morphological finding type, and BI-RADS score
- Results were analyzed as a whole and separated by fatty/dense breasts, tumor size, calcifications, and non-calcified cancers
STUDY 5 (CHOI ET AL)

- No significant difference in sensitivity between FFDM and SM, either overall or for fatty/dense subgroups
- For calcification group, no significant differences in performance, although specificities and PPVs of all observers tended to be higher with SM than FFDM
- When analyzed by tumor size and calcification presence, no difference in percentage detected cancers or visibility scores

COMMENTS FROM RADIOLOGISTS

- Impression of image quality?
  - Looks crisper, less noise, edges of tissue very well-defined, calcs not as good
  - Noticed decreased resolution “a bit”, but not bothered
  - Architectural distortion more apparent
  - Calcifications more apparent
  - But... one resident described the images as a “blurry mess”

- Do you see any benefits of conventional 2D image over C-View?
  - Just the calcs right now
  - Comparison to priors
  - No
COMMENETS FROM RADIOLOGISTS

○ Using C-View exclusively?
  • 3 facilities yes, 2 facilities no
  • One started out using FFDM and C-View simultaneously for a few months to increase comfort level before using C-View exclusively; 2 jumped right in
  • No, because CAD system does not work with C-View images
  • No, it is one more thing in the arsenal – an adjunct to conventional image
    ○ Hanging protocol with conventional 2D on the left, C-View on the right – scroll through the C-View to get to the tomo images

○ Other comments
  • Likes the images, but just needs more experience with it (after 2 ½ months)
  • No noticeable differences in call-backs
  • Much prefer C-View images
  • Need to get used to increased conspicuity of architectural distortion to not over-call normal variation

ACCREDITATION

○ Accreditation/Certification Options for Facilities Utilizing a 3D System with either 2D FFDM Images or 2D Images Generated from the 3D Image Set (i.e., 2D Synthesized Images)

○ Currently, the FDA-approved accreditation bodies are not prepared to accredit 3D tomography, as standards have not been developed for this imaging modality. This situation is similar to when FDA approved FFDM for marketing, but the accreditation bodies had not yet developed standards and could not accredit FFDM when it first came on the market. FDA developed the certificate extension program to cover situations where a mammography device has been approved for marketing but where accreditation standards have not yet been established. The certificate extension program that is currently in effect so that facilities can legally use 3D tomography requires that an FDA-approved accreditation body accredit the 2D imaging component of the 3D tomography unit.

○ For MQSA facilities utilizing a 3D system in clinical practice, your accreditation/certification options are as follows:
  • If your facility's practice routinely utilizes 3D imaging with acquired 2D FFDM images, then you may submit those 2D FFDM images to your accreditation body for accreditation of the 2D component of your unit.
  • If your facility's practice routinely utilizes 3D imaging with 2D images generated from the 3D image set (i.e., synthesized 2D images), then you may submit those synthesized 2D images to your accreditation body for accreditation of the 2D component of your unit.

○ http://www.fda.gov/Radiation- EmittingProducts/MammographyQualityStandardsActandProgram/FacilityCertificationan dInspection/ucm114148.htm
○ Accessed 9/7/16