Comparison of indications, reading time, and workflow of FDA approved supplemental screening automated whole breast ultrasound tomography in women with dense breasts

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Disclosures

Mary Yamashita, MD: a consultant for Delphinus Medical Technologies, Inc

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Supplemental whole breast screening ultrasound for women with dense breasts
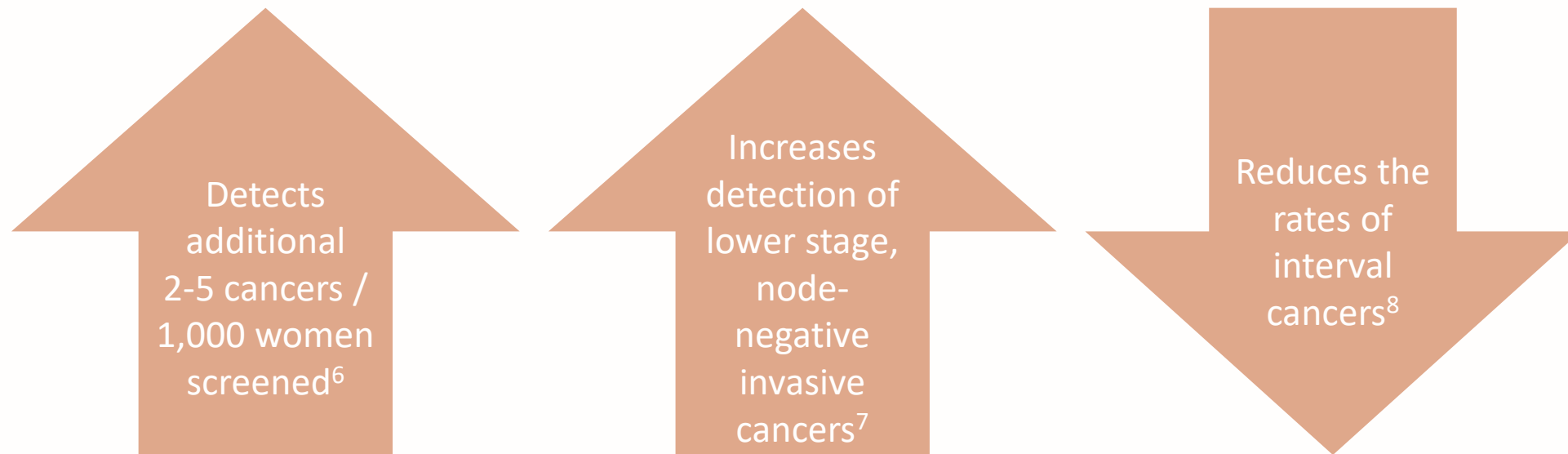
Dense breasts are prevalent in the United States

- Over 40% of women ages 40-74 in the US have dense breasts[1]

- Dense breasts are associated with a masking effect which decreases sensitivity of mammography[2]

- Women with heterogeneously dense and extremely dense breasts have increased risk compared with women with fatty breasts[3]:
  - 2.9 and 4.6 -fold increase in the risk for developing breast cancer[2]
  - 16 and 31-fold increase in the likelihood for interval cancer diagnosis[4]

- Mortality reduction from annual screening mammography is less effective in women with dense breasts[5]

| 13% Mortality reduction Dense Breasts | < | 41% Mortality reduction Non-dense breasts |
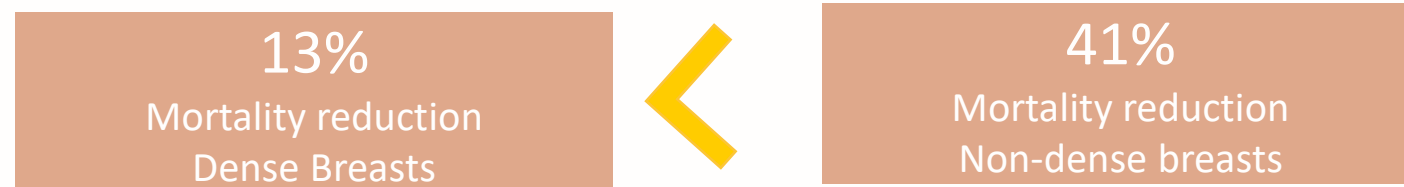
Whole breast ultrasound is important in screening women with dense breasts

- Mammography with supplemental ultrasound in women with dense breasts improves cancer detection[6]

Detects additional 2-5 cancers / 1,000 women screened[6]

Increases detection of lower stage, node-negative invasive cancers[7]

Reduces the rates of interval cancers[8]

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Overview of whole breast ultrasound available for dense breast screening

Two automated whole breast ultrasounds received premarket approval (PMA) for **screening** indication

Approvals	Product / Company		Indication for use
SCREENING & Diagnostic Indication (PMA)	SoftVue Automated Whole Breast Ultrasound Delphinus Medical Technologies		…indicated as an adjunct to mammography for breast cancer screening in asymptomatic women with dense breast parenchyma after confirmation that the breast density composition is BI-RADS c or d at the time of screening mammography. The device is intended to increase breast cancer detection in the described patient population relative to mammography alone. The device is not intended to be used as a replacement for screening mammography. The device can be used at the same visit as screening mammography and SoftVue images are intended to be interpreted with the mammogram results to enhance screening.[9]
SCREENING & Diagnostic Indication (PMA)	Invenia ABUS Automated Breast Ultrasound GE Healthcare		…indicated as an adjunct to mammography for breast cancer screening in asymptomatic women for whom screening mammography findings are normal or benign (BI-RADS Assessment Category I or 2), with dense breast parenchyma (BI-RADS Composition/Density 3 or 4) and have not had previous clinical breast intervention. The device is intended to increase breast cancer detection in the described patient population.[10]

Whole breast ultrasound cleared by FDA for **diagnostic** indications only

Approvals	Product/ Company	
DIAGNOSTIC Indication Only Cleared by 510(k)	ACUSON Siemens Healthineers[12]	
DIAGNOSTIC Indication Only Cleared by 510(k)	QT Scan QT Imaging[13]	
DIAGNOSTIC Indication Only Cleared by 510(k)	SOFIA 3D Breast Ultrasound System FUJIFILM Healthcare America's Corporation[14]	

Comparison of FDA-approved SoftVue and Invenia ABUS automated whole breast ultrasounds

	Delphinus SoftVue[9]	GE Invenia ABUS[10]
Sensitivity & Specificity	Improved sensitivity and specificity[11]	Improved sensitivity
Breast Density	BI-RADS c or d (assessed by radiologist or technologist)	BI-RADS c or d (assessed by radiologist)
FDA Approved Workflow	Mammogram and ultrasound can be performed together in one visit and are interpreted together by Radiologist	Mammogram is performed first and interpreted as negative or benign, BI-RADS 1 or 2, by Radiologist before ABUS can be performed
FDA Approved Indications	Performed in all women with dense breasts, including with history of breast cancer, needle biopsies, implants, or surgery	Performed in women with dense breasts with no previous breast interventions

Comparison of FDA-approved SoftVue and Invenia ABUS automated whole breast ultrasounds

	Delphinus SoftVue[9]	GE Invenia ABUS[10]
Image Acquisition	Reflection, Sound Speed, Attenuation	Reflection
Acquisition Mode	Coronal plane	Transverse plane
Interface	Water (does not require gel)	Ultrasound lotion or gel
Operator	Any staff member, no licensures or credentials required	Not specified
Reconstruction Mode	3D Volume	3D Volume
Image Presentation	4 coronal view sequences: Wafer, Sound Speed, Reflection, and Stiffness Fusion	Coronal, axial, and sagittal

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Workflow benefits and challenges with integrating whole breast screening ultrasound in clinical practice

Workflow : integrating ultrasound into clinical practice for adjunct screening in women with dense breasts

	Handheld ultrasound (HHUS)	Automated breast ultrasound (ABUS)
Workflow Benefits	Familiar modality	Automated
Workflow Challenges		
Indications	No restrictions	Negative/ Benign mammogram interpretation by radiologist required prior to ABUS[10]
Time to perform[7]	13-17 min to perform by radiologist; 20 min to perform by technologist	10-15 min image acquisition time
Net added increase in recalls[7]	7.5%	10.6%
False positive biopsies[7]	Avg 9-11% of biopsies prompted by prevalent screening HHUS were malignant	Avg 8.5% of biopsies prompted by prevalent screening ABUS were malignant
Training for acquisition[7,15]	Shortage of trained technologists; High operator dependence	Dependent on patient positioning, breast compression, even application of lotion
Requires additional imaging[15]	Targeted HHUS needed for final assessment for a lesion	Targeted HHUS needed for final assessment for a lesion

Reading time challenges in clinical practice

|	HHUS	ABUS
Training for interpretation	Radiologist: • Minimal training	Radiologist: • Learning curve (25% recall rate in 1st month)[7]
Number of images	Not standardized, minimum 4 quadrants and retroareolar region[15]	1800-3000 images[7]
Reported reading time[7]	~3 minutes per patient	~9 minutes per patient for normal case; Greater with abnormal findings
Image quality and artifacts[7,15]	Small field of view; Shadowing at interface of fat lobules and Cooper's ligaments	Refractive edge shadowing from fat lobules, fibrous tissue; Image loss due to poor contact at the edge of the sweep

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Overview of automated whole breast ultrasound tomography

Overview of automated whole breast ultrasound tomography

- Prone automated ultrasound system
- Water filled imaging chamber to couple the sound energy between the transducer and the breast tissue
- Single circular transducer surrounds the entire breast
- Vertical motion of the transducer allows scanning from the nipple to chest wall
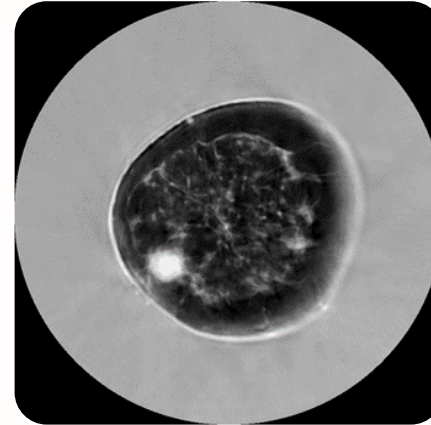- 2-4 minutes to scan each breast
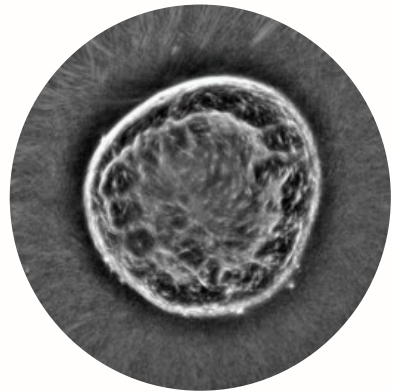
SoftVue displays 4 unique image sequences
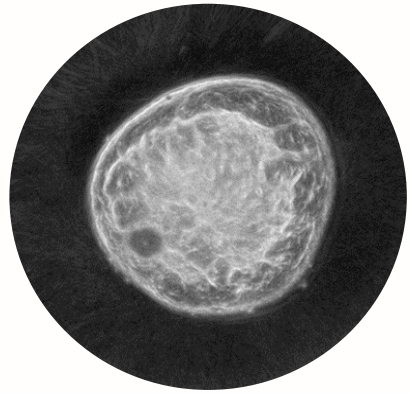
WAFER

WAve**F**orm **E**nhanced **R**eflection. Suppresses fat signals to boost the visibility of masses

Sound Speed

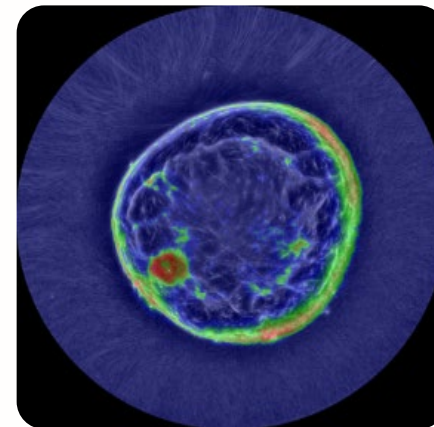Direct output of image acquisition. Measures change in the speed of sound moving through breast tissue/masses.

Reflection

Direct output of image acquisition. Analogous to B-mode.

Stiffness Fusion

Transmission properties of Sound Speed and attenuation, fused with Reflection. Uses color to show stiffness of tissue/masses.

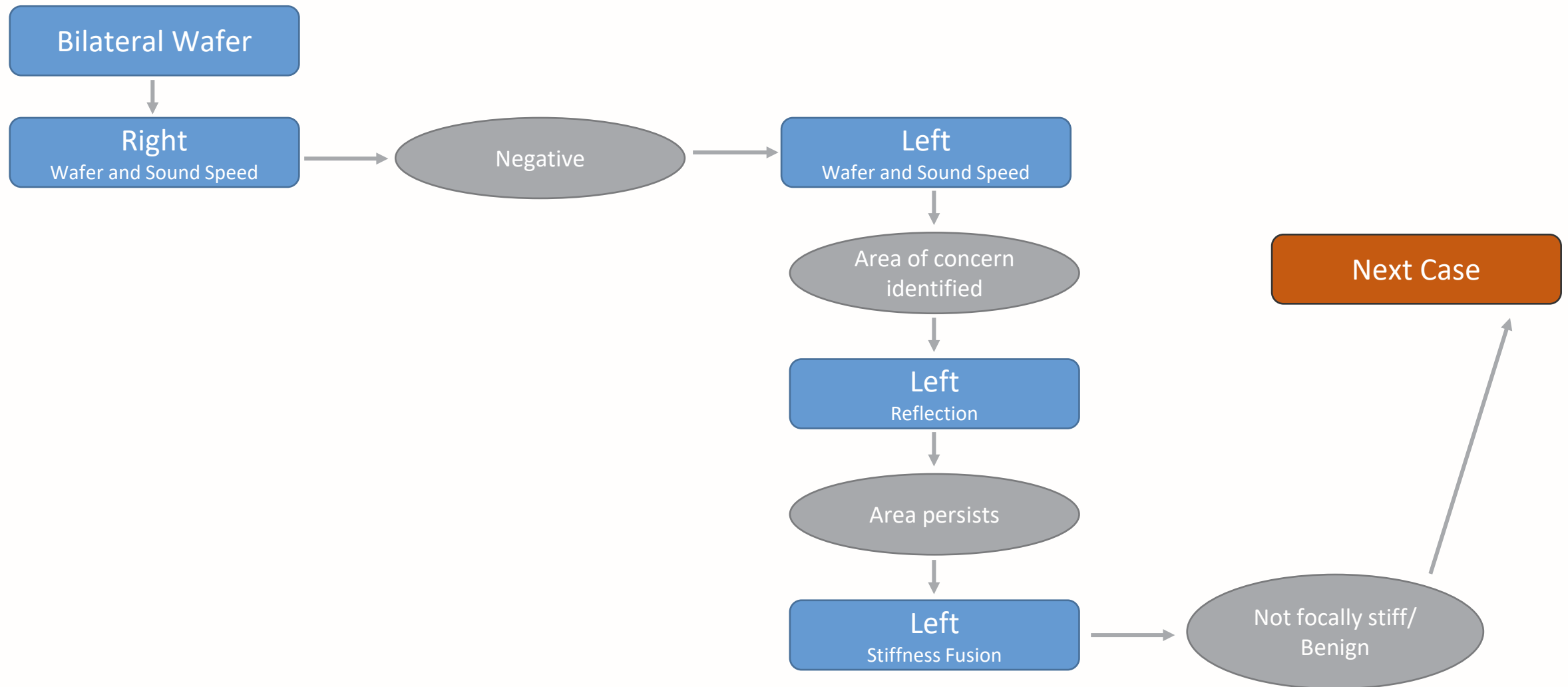Keck School of Medicine of USC

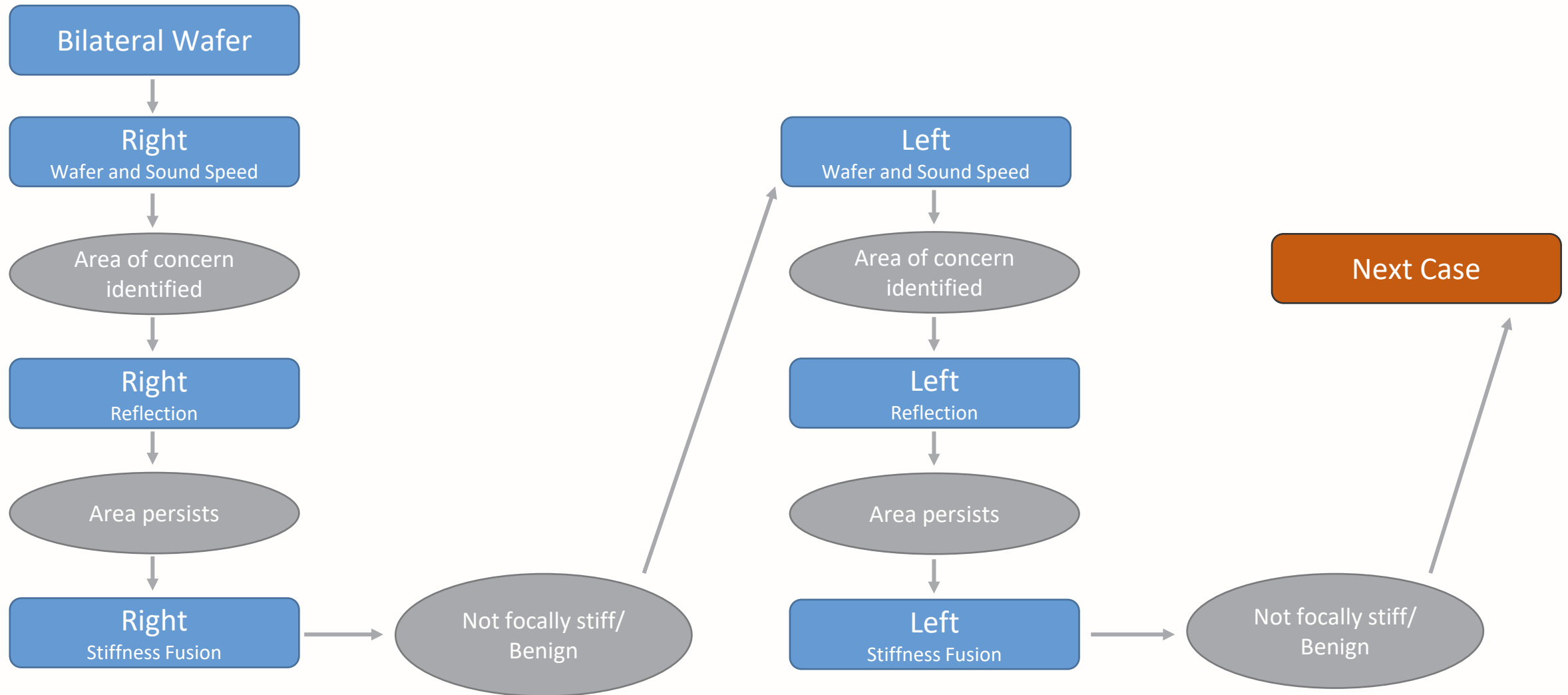# SV reading protocol optimizes review time
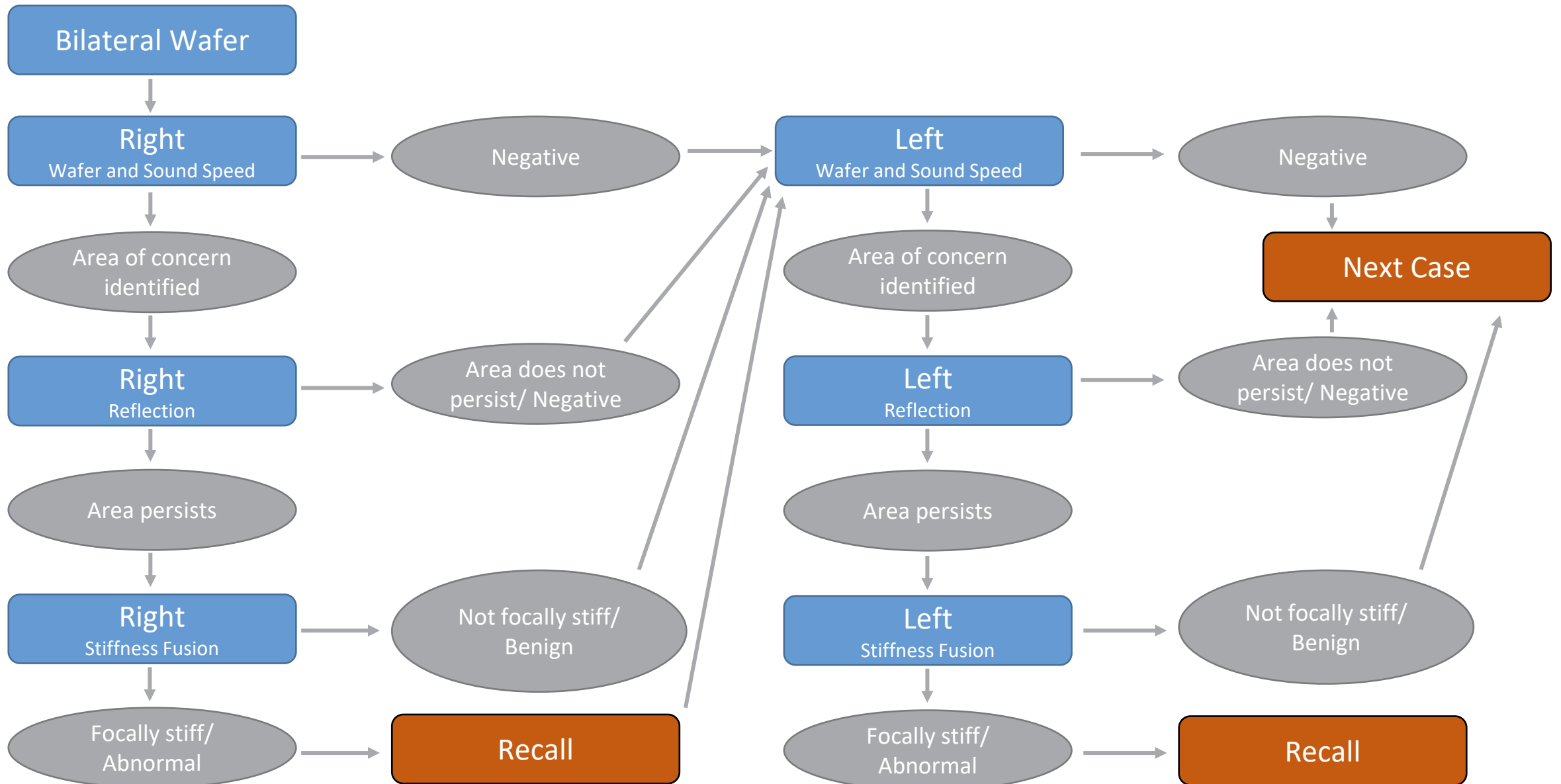
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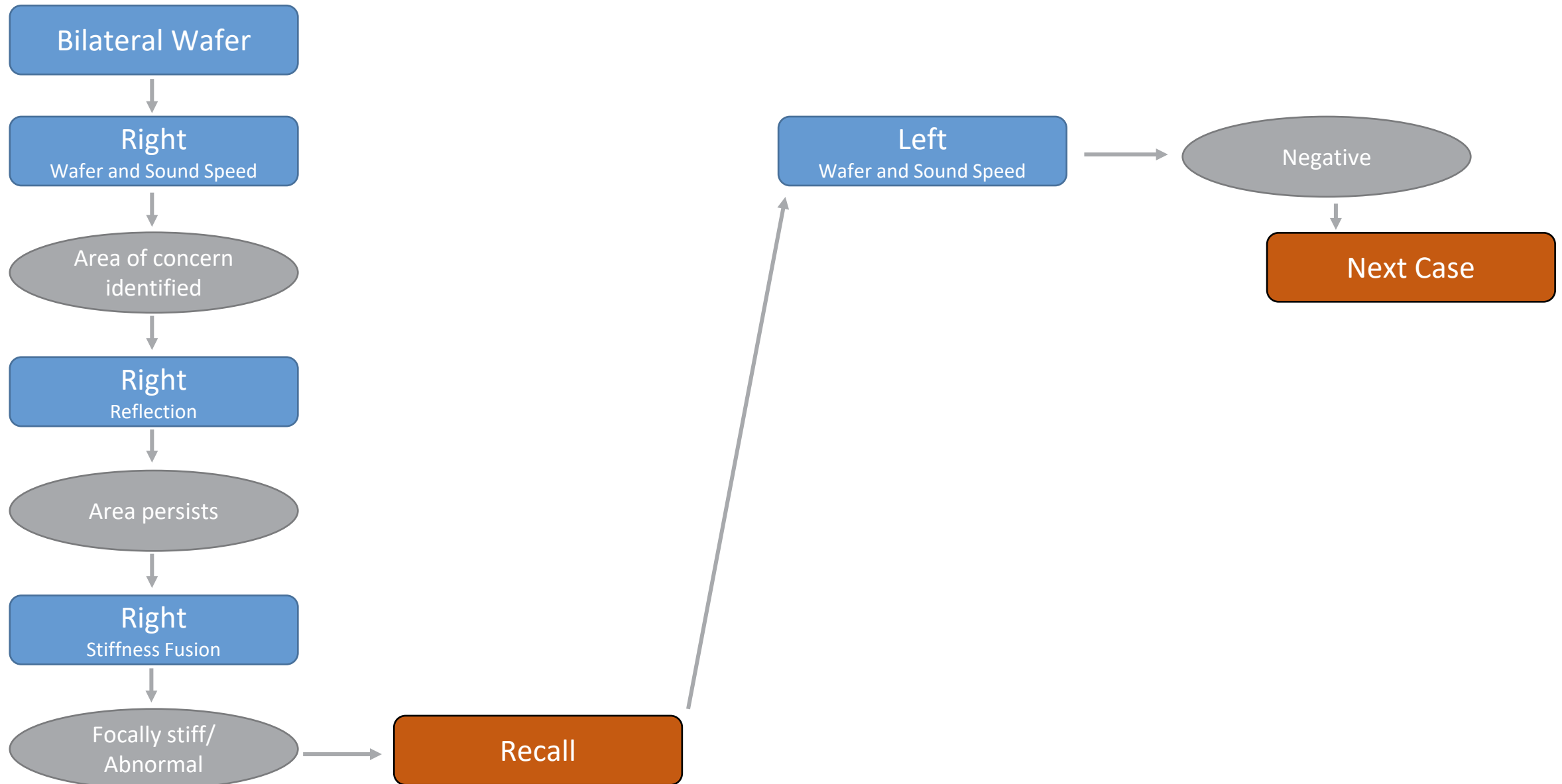SV reading protocol, case examples, and reading time

SV reading protocol : right negative and left benign (fibroadenoma)

SV reading protocol: bilateral simple cysts

SV reading protocol: saline implants with right IDC and left negative

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┌─────────────────────┐
│   Bilateral Wafer   │
└─────────────────────┘
          │
          ▼
┌─────────────────────┐                    ┌─────────────────────┐              ╭───────────────╮
│       Right         │                    │       Left          │   ────────▶  │   Negative    │
│ Wafer and Sound Speed│                    │ Wafer and Sound Speed│              ╰───────────────╯
└─────────────────────┘                    └─────────────────────┘                      │
          │                                                                              ▼
          ▼                                                                      ┌───────────────┐
   ╭───────────────╮                                                            │   Next Case   │
   │ Area of concern│                                                           └───────────────┘
   │   identified   │
   ╰───────────────╯
          │
          ▼
┌─────────────────────┐
│       Right         │
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└─────────────────────┘
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   ╭───────────────╮
   │ Area persists │
   ╰───────────────╯
          │
          ▼
┌─────────────────────┐
│       Right         │
│  Stiffness Fusion   │
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   ╭───────────────╮            ┌───────────────┐
   │ Focally stiff/ │  ───────▶ │    Recall     │
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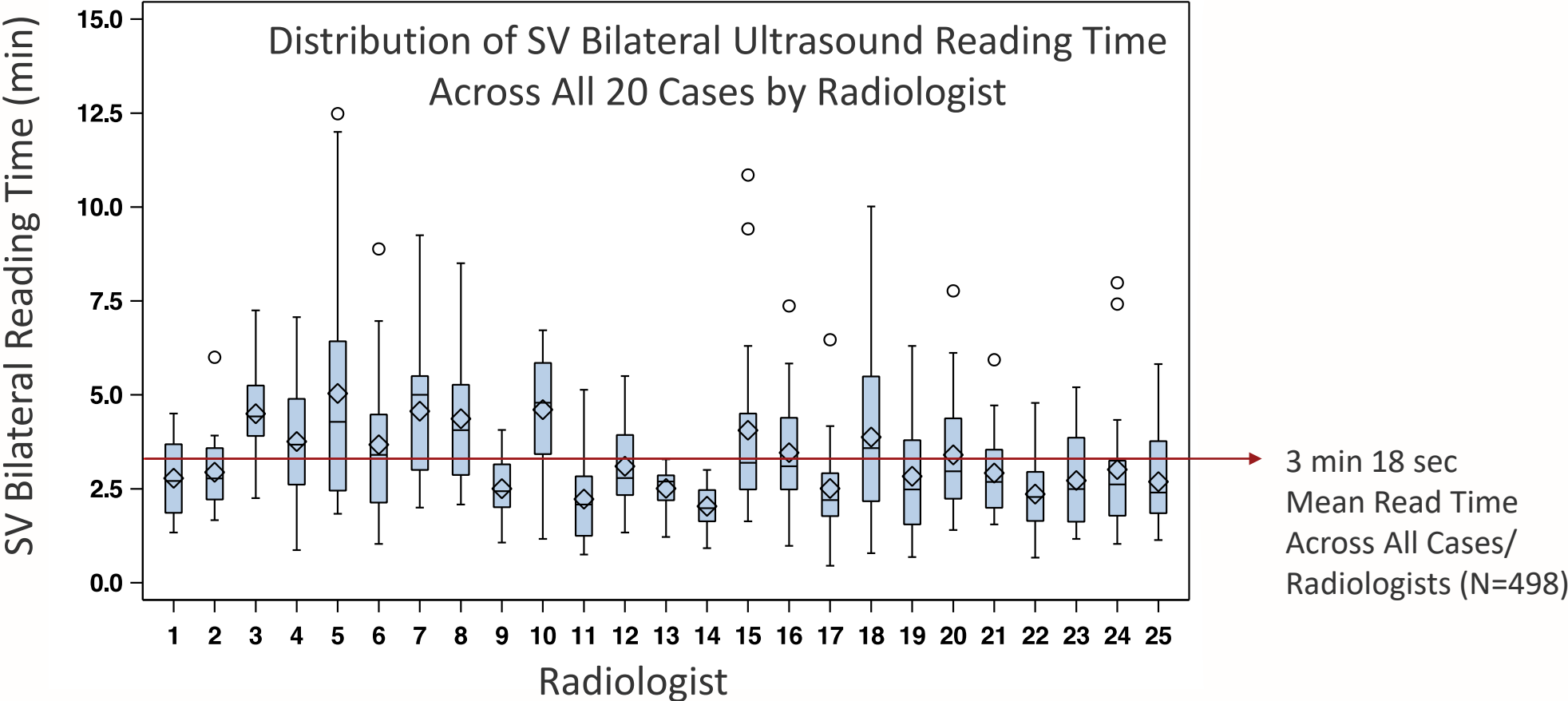
SoftVue reading time study

Study design

- Multi-reader, multi-case design for training radiologists on new technology
- 25 MSQA-certified radiologists from 9 sites across the United States with limited experience with SV
- 20 cases were selected from a case collection registry including cancers, benign masses, cysts, and negative exams
- Times were recorded for reading of SoftVue only

Results: SoftVue reading times

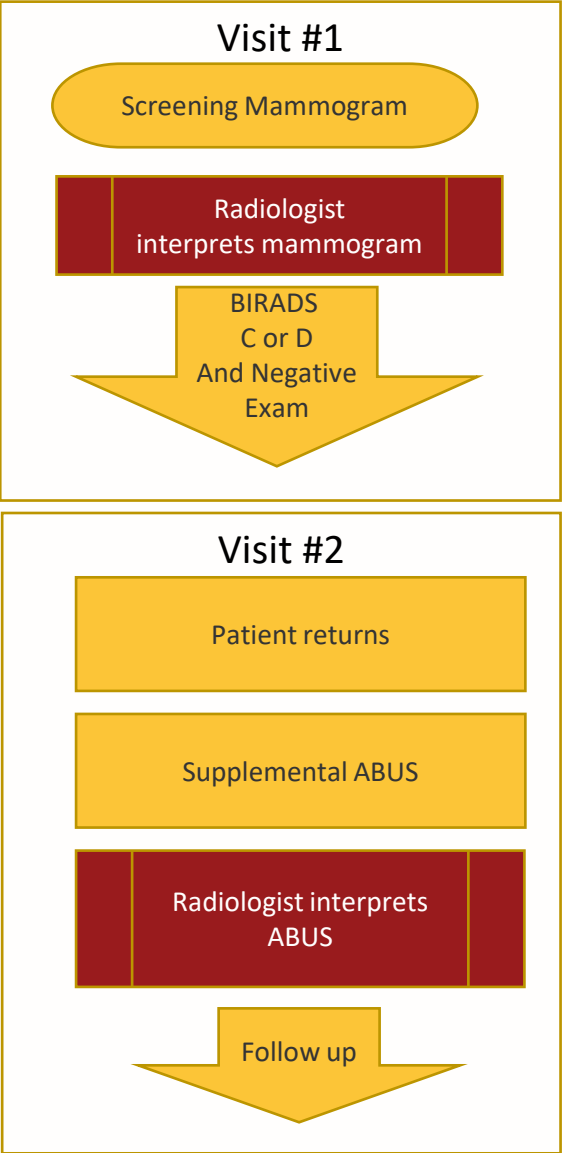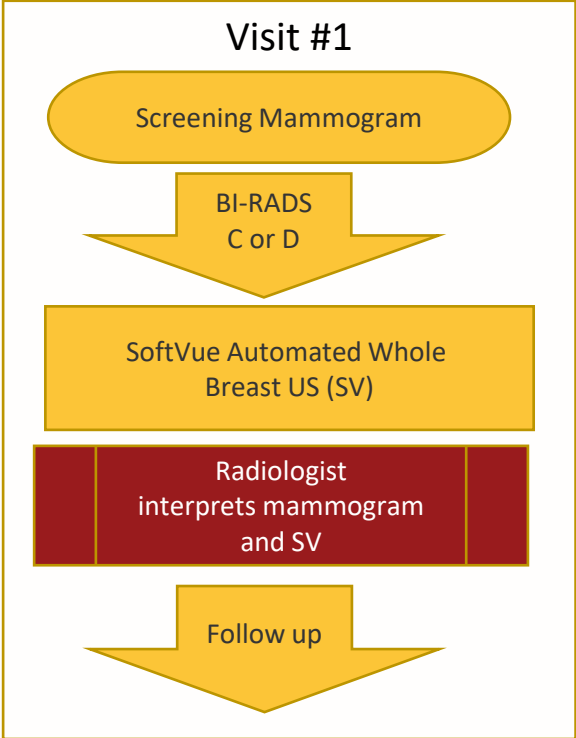- Average bilateral ultrasound reading time was 3 min 18 seconds

Distribution of SV Bilateral Ultrasound Reading Time Across All 20 Cases by Radiologist

3 min 18 sec Mean Read Time Across All Cases/ Radiologists (N=498)

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Workflow comparison

Automated whole breast screening ultrasound workflow comparison[16]

ABUS workflow

Visit #1
- Screening Mammogram
- Radiologist interprets mammogram
- BIRADS C or D And Negative Exam

Visit #2
- Patient returns
- Supplemental ABUS
- Radiologist interprets ABUS
- Follow up

VS

SV workflow

Visit #1
- Screening Mammogram
- BI-RADS C or D
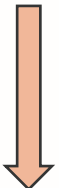- SoftVue Automated Whole Breast US (SV)
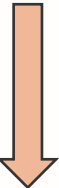- Radiologist interprets mammogram and SV
- Follow up

Radiology workload decreases; Non-physician triages dense breasts

Radiologist workflow optimized Radiologist interprets mammogram and SV together

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Conclusion

Summary: Comparison of indications, workflow and reading time

	Automated whole breast ultrasound tomography (SV)	ABUS
Indications	Performed in all women with dense breasts, including prior history of breast cancer, needle biopsies, implants, or surgery	Performed in women with dense breasts with no previous breast intervention
Workflow	Mammogram and ultrasound can be performed together in one visit and are interpreted together by radiologist	Mammogram is performed first and interpreted as negative or benign, BI-RADS 1 or 2, by radiologist before ABUS can be performed
Reading time	Average per case 3-4 minutes	Greater than 9 minutes per case

Conclusion

- Automated whole breast ultrasound offers benefits of being fully automated and not operator dependent.

- There are only 2 automated whole breast ultrasound technologies approved by the FDA for screening in women with dense breasts with important differences in indications, workflow and reading time.

Limitations

- This presentation reviews published literature on HHUS and ABUS and includes preliminary results from automated whole breast ultrasound tomography.

- More experience in clinical setting is needed for future comparisons.

Video Case Review Examples

- Cyst - https://vimeo.com/882445845/164203cad5?share=copy
- IDC - https://vimeo.com/882445845/164203cad5?share=copy
- Fibroadenoma - https://vimeo.com/882272831/2db3b96daa?share=copy

Thank you

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References

1. Sprague BL, Gangnon RE, Burt V, et al. Prevalence of mammographically dense breasts in the United States. JNCI: Journal of the National Cancer Institute. 2014;106(10).
2. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev. 2006;15(6):1159-1169.
3. Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med. 2007;356(3):227-236.
4. Strand F, Azavedo E, Hellgren R, et al. Localized mammographic density is associated with interval cancer and large breast cancer: a nested case-control study. Breast Cancer Res. 2019;21(1):8.
5. van der Waal D, Ripping TM, Verbeek ALM, Broeders MJM. Breast cancer screening effect across breast density strata: A case-control study. Int J Cancer. 2017;140(1):41-49.
6. Vourtsis A, Berg WA. Breast density implications and supplemental screening. Eur Radiol. 2019;29(4):1762-1777.
7. Berg WA, Vourtsis A. Screening breast ultrasound using handheld or automated technique in women with dense breasts. J Breast Imaging. 2019;1(4):283-296.
8. Ohuchi N, Suzuki A, Sobue T, et al. Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-cancer Randomized Trial (J-START): a randomised controlled trial. Lancet. 2016;387(10016):341-348.
9. https://delphinusmt.com/women/the-softvue-experience/ (FDA PMA P200040B)
10. https://www.gehealthcare.com/about/newsroom/press-releases/setting-new-standard-breast-care-ge-healthcare-introduces-invenia-abus-20 (FDA PMA P110006)
11. Jiang, Y. (2023, May) Innovation to Breast Cancer Detection: A Study of Adjunct SoftVue™ Automated Whole Breast Ultrasound Tomography (SV) to Digital Mammography on Enhancing Lesion Localization and Characterization, Paper presented at the meeting of SBI, MD.
12. https://www.siemens-healthineers.com/en-us/ultrasound/general-imaging/acuson-s2000-ultrasound-machine
13. https://www.qtimaging.com/
14. https://social-innovation.hitachi/en-us/solutions/life_economy/sofia-3d/
15. Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, Pisano ED, Jong RA, Evans WP, Morton MJ, Mahoney MC, Larsen LH, Barr RG, Farria DM, Marques HS, Boparai K; ACRIN 6666 Investigators. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. JAMA. 2008 May 14;299(18):2151-63.
16. Yamashita, M. (2023, March) Innovative workflow for a new technology: A multicenter study examining agreement between radiologists and non-physicians in the assessment of BI-RADS breast density to determine eligibility for SoftVueTM automated whole breast ultrasound tomography screening at the same visit as annual mammogram , Paper presented at the meeting of NCoBC, Las Vegas NV.