Comparison of quantitative volumetric and subjective BI-RADS density classification in women with dense breasts

Authors & Disclosures

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Background

- Increased breast density is an independent risk factor for developing breast cancer.
- Women with heterogeneously dense and extremely dense breasts have increased risk compared with women with fatty breasts:
  - 2.9 and 4.6 -fold increase in the risk for developing breast cancer
  - 16 and 31-fold increase in the likelihood for interval cancer diagnosis

References:
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.
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.
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.

Background

- Personalized breast cancer risk assessment has become an important part of comprehensive breast cancer screening programs
- Many risk prediction models are more accurate when breast density is included (BCSC, Tyrer–Cuzick/IBIS, BOADICEA)
- But…
  - Standard of care uses the mammogram to determine breast density
  - ACR recommends all women have breast cancer risk evaluation by age 25.
- A radiation-free objective tool for breast density assessment would be advantageous, especially for women under 40.

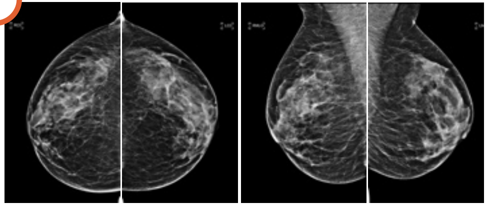
References:
Kim G, Bahl M. Assessing Risk of Breast Cancer: A Review of Risk Prediction Models. J Breast Imaging. 2021 Feb 19;3(2):144-155.
Vilmun BM, Vejborg I, Lynge E, Lillholm M, Nielsen M, Nielsen MB, Carlsen JF. Impact of adding breast density to breast cancer risk models: A systematic review. Eur J Radiol. 2020 Jun;127:109019

Purpose

In women with dense breasts, we compared the level of agreement between 4 methods of density assessment:

Quantitative automated density assessments

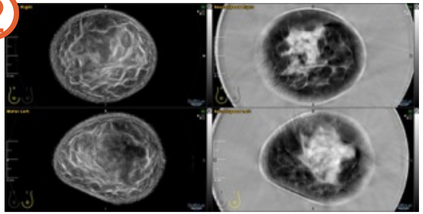
1



+ Volpara

By 3D mammography and volumetric data

2



SoftVue

By whole breast ultrasound tomography volumetric data

Subjective density assessments

3

By technologist

4

By Radiologist

Materials and Methods

448 women with heterogeneously or extremely dense breasts enrolled in a prospective case collection registry between December 2016 and October 2019 who had both DBT with Volpara and SV.

Quantitative density assessments

Participants had annual screening mammogram with 3D digital breast tomosynthesis (DBT) (Hologic) and same or next-day SoftVue (SV) automated whole breast ultrasound tomography

Subjective density assessments

Technologist assessed breast density at the time of the mammogram using the BI-RADS density composition scale

Radiologist interpreted the mammogram and reported the BI-RADS density assessment

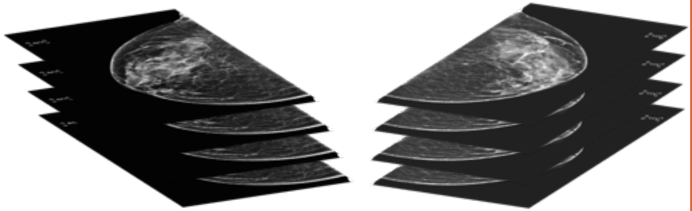
How is quantitative density calculated?

Image data is acquired for each case from
1 mammogram with digital breast tomosynthesis or
2 whole breast ultrasound tomography

Images analyzed as voxels (3D)

Full breast density is calculated

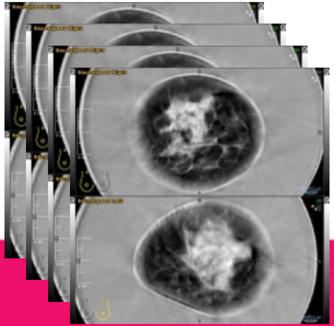
1 ~50 tomo slices per breast



Voxel is fatty tissue (black)
or
Voxel is fibroglandular tissue (white)

$$\text{Volumetric breast density (\%)} = \frac{\text{Volume of fibroglandular tissue (cm}^3\text{)}}{\text{Volume of breast (cm}^3\text{)}}$$

2 ~60 coronal slices per breast
Sound Speed right
Sound Speed left



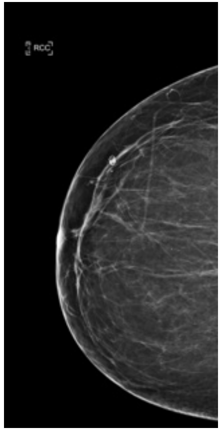
Sound Speed calculated for each voxel (m/s)

$$\text{Volume averaged Sound Speed (m/s)} = \frac{\sum \text{Sound Speed per voxel (m/s)}}{\text{Total number of voxels in breast}}$$

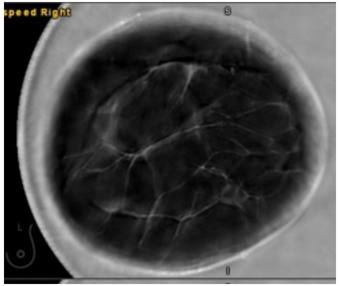
How are the quantitative methods different?

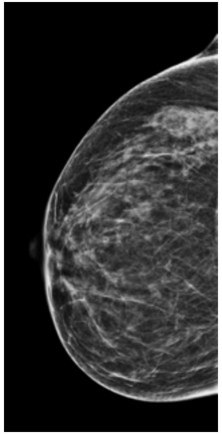
	Volpara method	SV method
Image data	DBT	Whole breast Sound Speed
Base unit	Mammogram voxels (3D)	Sound Speed voxels (3D)
Measurement	Voxel intensity classified as dense or fatty tissue	Voxel Sound Speed value is averaged (in meters/ sec)
Modeling	Uses modeling to convert DBT layers into 3D volume of dense and fatty tissue	Uses mapping function to convert the volume averaged Sound Speed (typically 1400-1600 m/s) into the SoftVue Density Index (unitless number 0-100)
Quantitative density value	Percent of total breast volume that is dense tissue	Density index based on the volume averaged Sound Speed
BI-RADS display value	Displayed as a/b/c/d	Displayed as estimated a/b/c/d

Examples of mammograms and Sound Speed slices corresponding to the 4 BI-RADS density categories

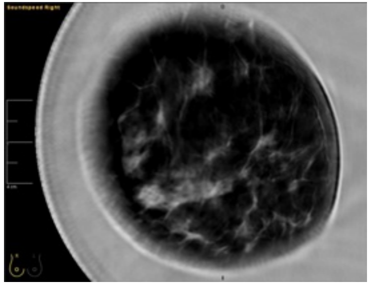


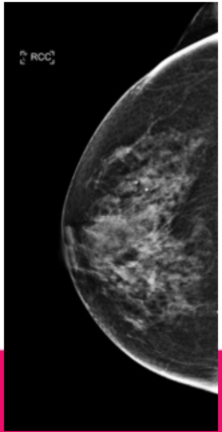
BI-RADS a: fatty



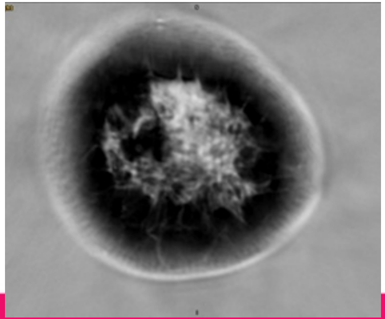


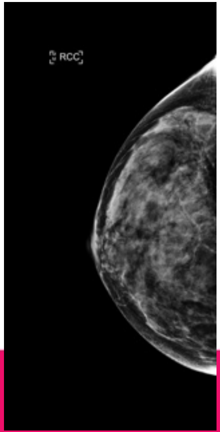
BI-RADS b: scattered



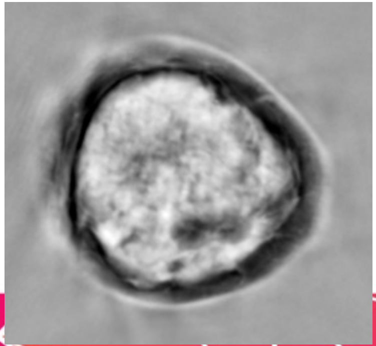


BI-RADS c: heterogeneous





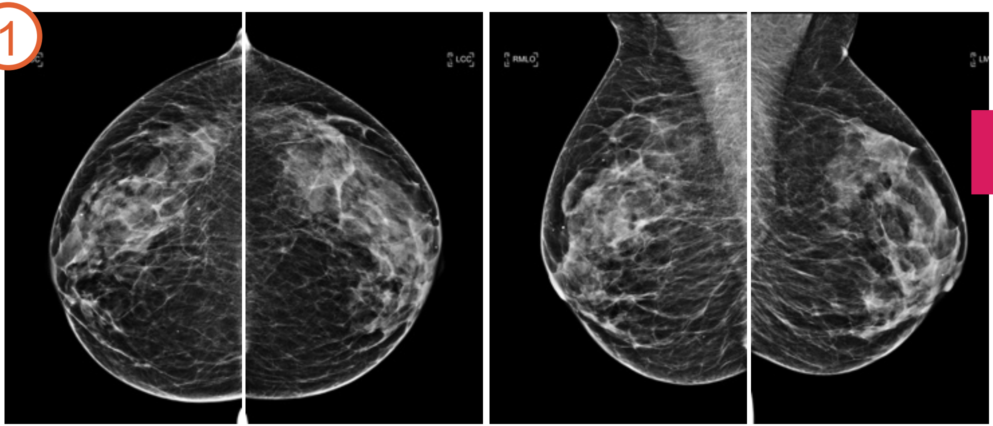
BI-RADS d: extremely dense

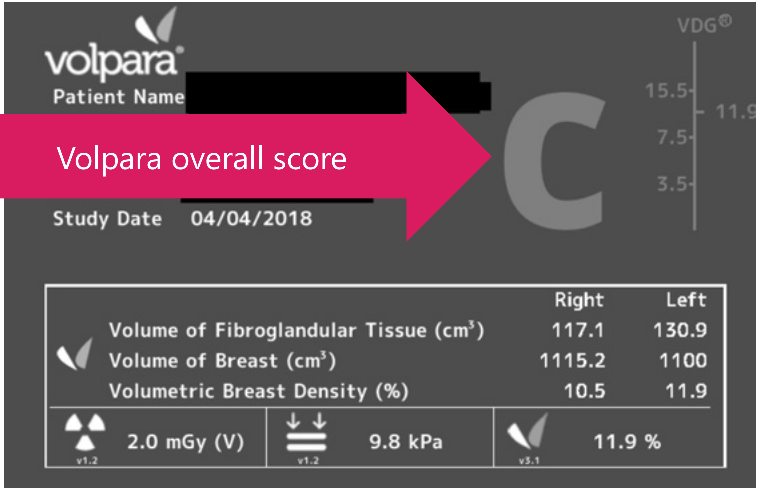


Materials and Methods: DBT + Volpara

The Volpara overall score from mammography was used for agreement analysis

1

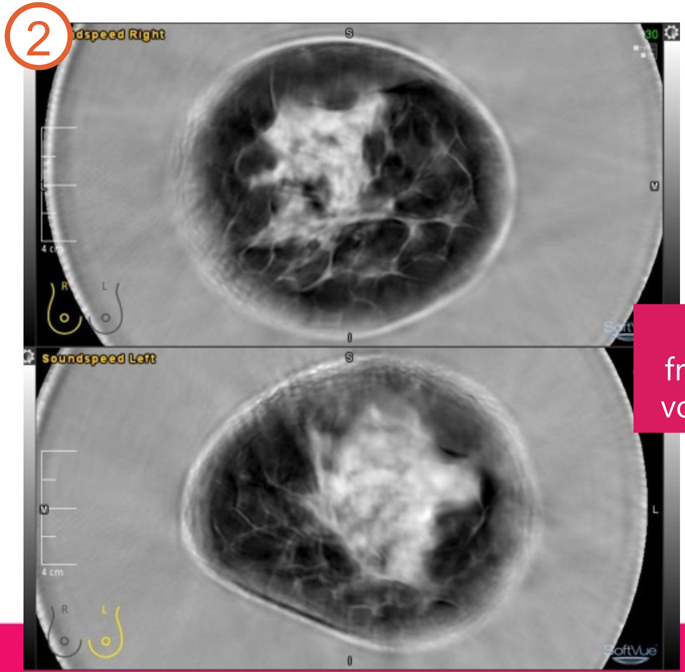




Volpara overall score

Materials and Methods: SV

SV category estimate based on the highest SV density index from 2 breasts was used for agreement analysis



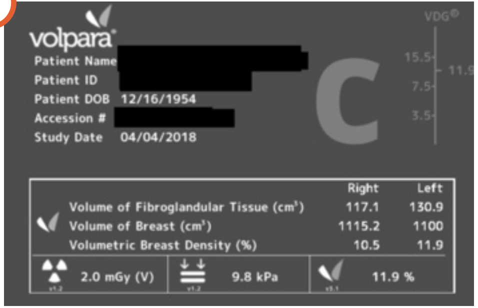
SV density index, a number from 0 to 100 derived from the volume-averaged Sound Speed

SV densest rating from 2 breasts used

Materials and Methods: Comparison

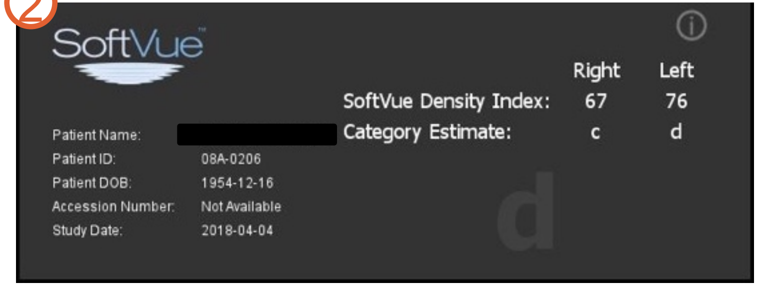
The Volpara overall score from mammography was compared with the SV category estimate based on the highest SV density index

1



BI-RADS between 2 quantitative methods were compared

2



Results: Overall agreement

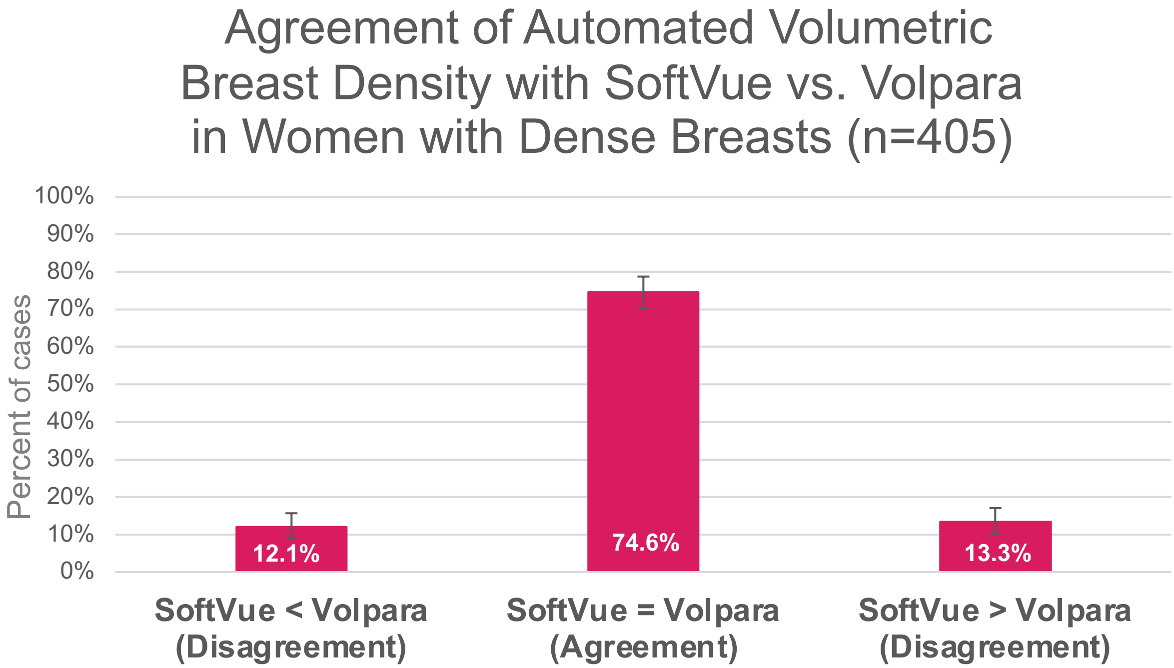
Agreement between SV and Volpara was the highest of the 4-way and pairwise tests and statistically significant

Agreement Analysis of BI-RADS Breast Density in Women with Dense Breasts			
	N	**Kendall's Coefficient of Concordance**	**95% CI for Kendall's Coefficient of Concordance**
4-Way Agreement between SoftVue, Volpara, Radiologist, Technologist	403	0.69 "good agreement"	(0.651, 0.728)
2-Way Agreement between SoftVue & Volpara	405	0.81	(0.776, 0.851)
2-Way Agreement between SoftVue & Radiologist	446	0.71	(0.669, 0.749)
2-Way Agreement between Volpara & Radiologist	421	0.78	(0.746, 0.822)

Notes: Four- way and pairwise agreement was tested using Kendall's coefficient of concordance (W). Kendall's Coefficient of Concordance is used due to the endpoint being an ordinal variable (a/b/c/d). A concordance value of 1 indicates perfect agreement and above 0.60 indicates "good" agreement.

Results: Agreement between SV and Volpara

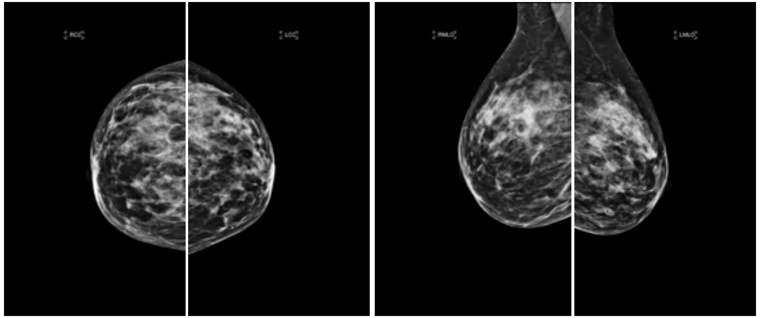
In 74.6% of cases, the SV and Volpara BI-RADS ratings were the same

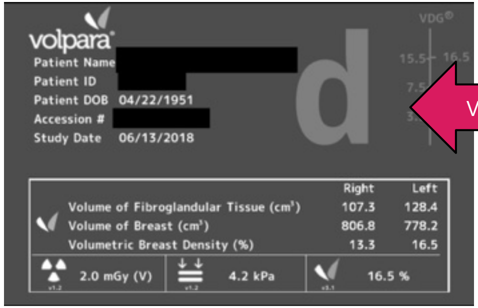


Notes: SV Volumetric density recorded as BI-RADS a/b/c/d.
95% confidence intervals are calculated using the binomial exact method.

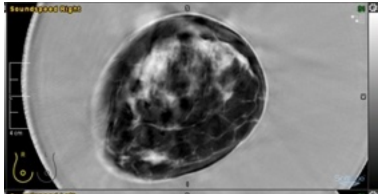
Disagreement example : SV < Volpara

The difference in the SV and Volpara rating is not clinically relevant because both are dense. SV rating agreed with radiologist rating BI-RADS c.

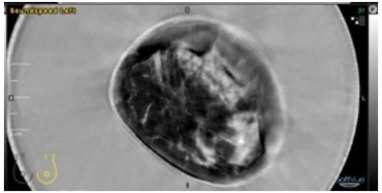




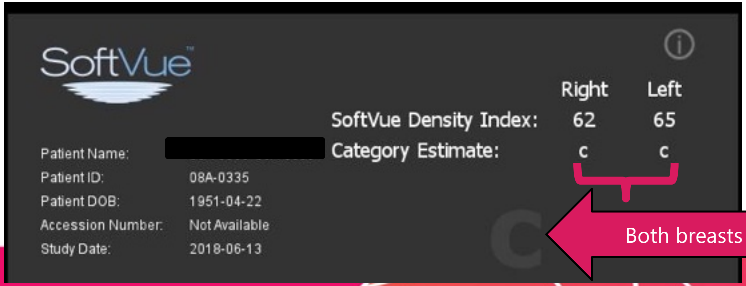
Volpara overall score used



Sound Speed Right



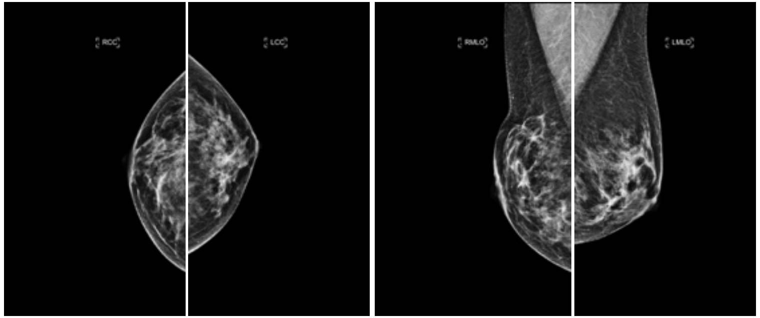
Sound Speed Left

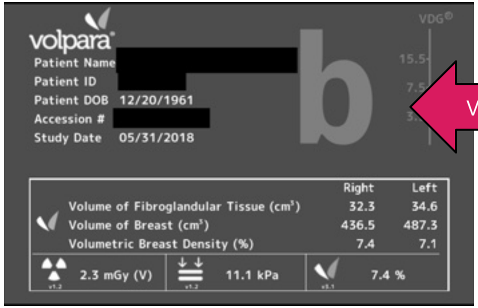


Both breasts rated c

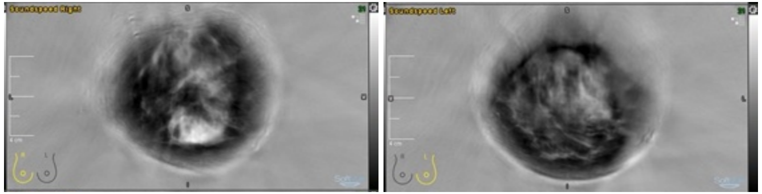
Disagreement example: SV > Volpara

SV rating BI-RADS c would have categorized this patient as having heterogeneously dense breasts and changed the clinical risk assessment. SV rating agreed with radiologist rating BI-RADS c.



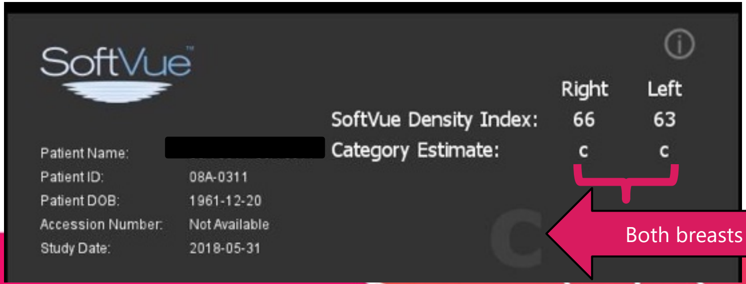


Volpara overall score used



Sound Speed Right

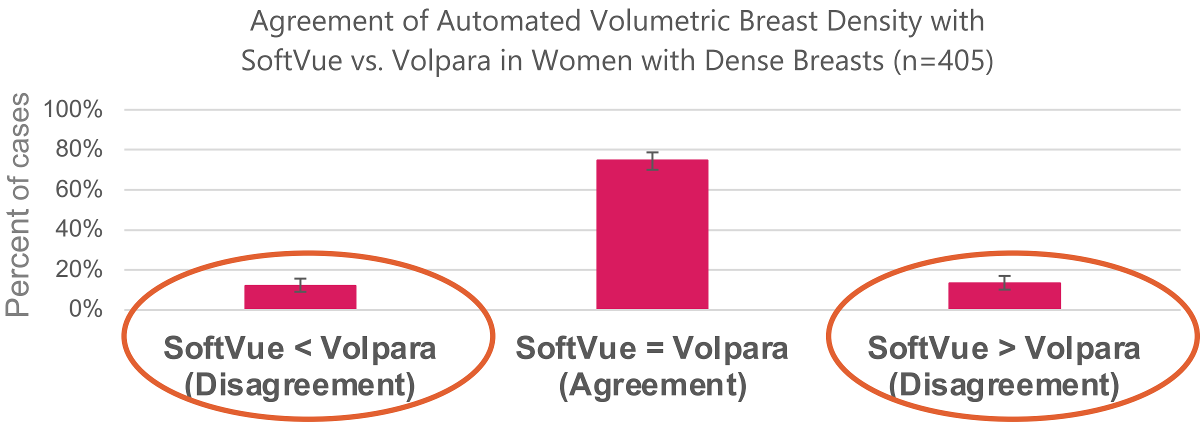
Sound Speed Left



Both breasts rated c

Results: Analysis of 103 disagreement cases

Disagreement groups had a high prevalence of breast implants



Prevalence of breast implants (implant cases/ total cases)		
SV < Volpara N=49	SV = Volpara N=302	SV > Volpara N=54
57% (28/49)	17% (50/302)	26% (14/54)

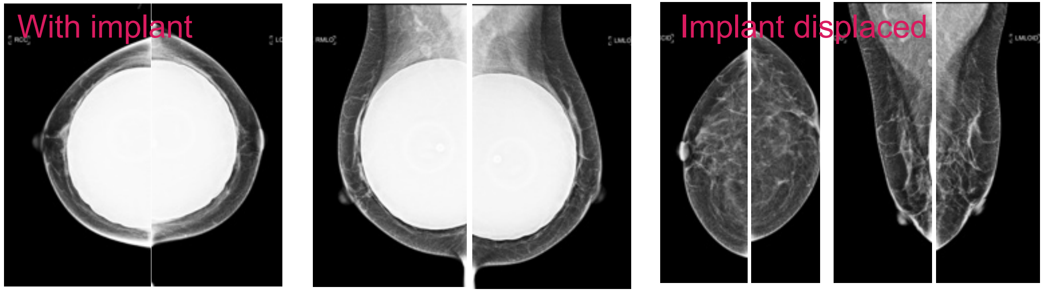
Results: Impact of breast implants

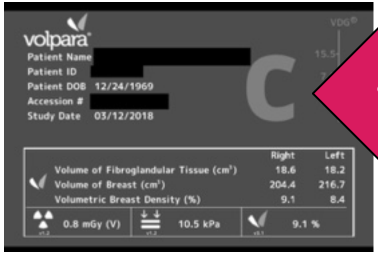
- With saline implants, SV overestimated the density, Volpara was similar to the radiologist.
- With silicone implants, SV equal to or underestimated the density and Vopara equal to or overestimated the density compared to the radiologist

Disagreement based on implant type		
	SV < Volpara	SV > Volpara
Saline implants (implant cases/ total cases)	7% (2/28)	93% (13/14)
Silicone implants (implant cases/ total cases)	93% (26/28)	7% (1/14)

Disagreement example : SV>Volpara with saline implant

- For SV density calculations, saline implants are light gray (example slice 41) with a higher Sound Speed than fatty tissue but lower SS than dense tissue. Some of the slices (example slice 18) did not have the implant so the Sound Speed was still calculated for those voxels. Because the Sound Speed is averaged over the whole breast volume, the SV density index is most likely overestimated due to the saline implant. The breast tissue visible in both imaging modalities is heterogeneously dense. Radiologist rated the case as BI-RADS c.




volpara

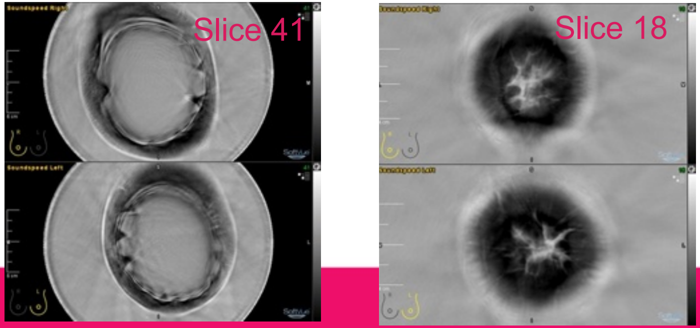
Patient Name [redacted]
Patient ID [redacted]
Patient DOB 12/24/1969
Accession # [redacted]
Study Date 03/12/2018

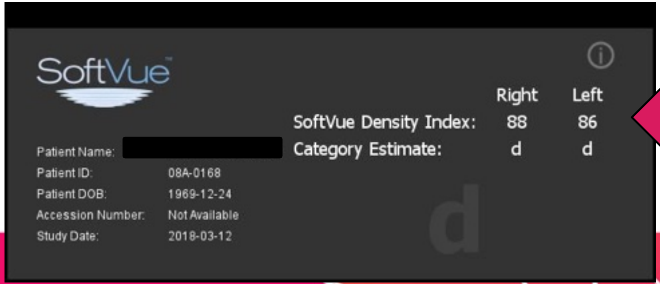
C

	Right	Left
Volume of Fibroglandular Tissue (cm³)	18.6	18.2
Volume of Breast (cm³)	204.4	216.7
Volumetric Breast Density (%)	9.1	8.4

0.8 mGy (V) 10.5 kPa 9.1 %

Volumetric breast density % calculated from implant displaced images




SoftVue

	Right	Left
SoftVue Density Index:	88	86
Category Estimate:	d	d

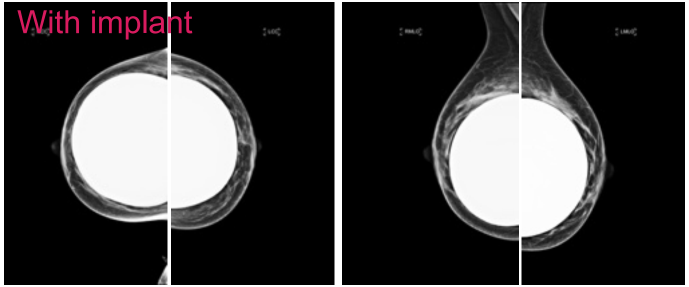
Patient Name: [redacted]
Patient ID: 08A-0168
Patient DOB: 1969-12-24
Accession Number: Not Available
Study Date: 2018-03-12

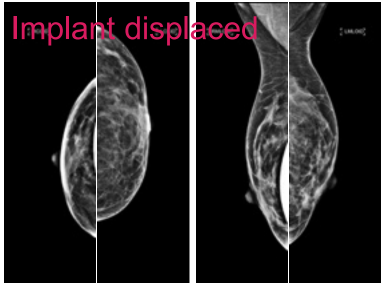
d

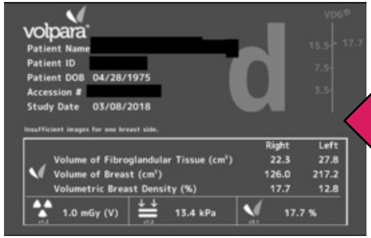
Density indices high due to saline implants

Disagreement example : SV<Volpara with silicone implant

- For Volpara density calculations, white voxels are fibroglandular tissue. If the silicone implants are not displaced, Volpara density is overestimated. Volpara is most often calculated from the implant displaced images.
- For SV density calculations, the silicone implants show up as black artifact because ultrasound doesn’t penetrate silicone (example slice 38). Some of the slices (example slice 17) did not have the implant so the Sound Speed was still calculated for those voxels. Because the Sound Speed is averaged over the whole breast volume, the SV density index is most likely underestimated due to the silicone implant.






volpara

Patient Name [redacted]
Patient ID [redacted]
Patient DOB 04/28/1975
Accession # [redacted]
Study Date 03/08/2018

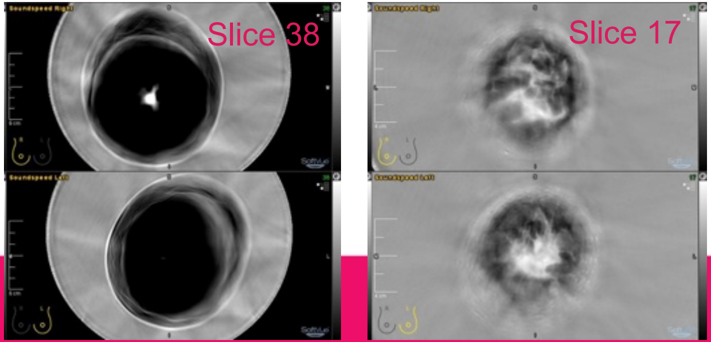
d

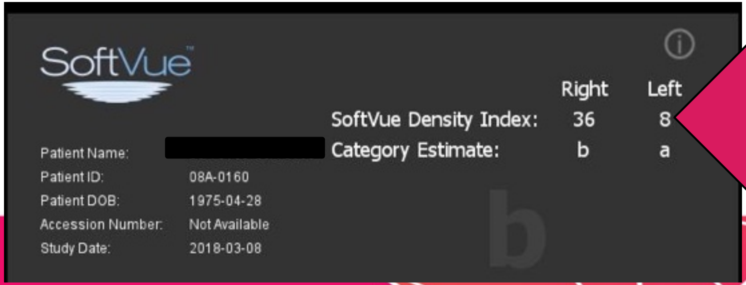
Insufficient images for one breast side.

	Right	Left
Volume of Fibroglandular Tissue (cm³)	22.3	27.8
Volume of Breast (cm³)	126.0	217.2
Volumetric Breast Density (%)	17.7	12.8

1.0 mGy (V) 13.4 kPa 17.7 %

Volumetric breast density % calculated from implant displaced images




SoftVue™

	Right	Left
SoftVue Density Index:	36	8
Category Estimate:	b	a

Patient Name: [redacted]
Patient ID: 08A-0160
Patient DOB: 1975-04-28
Accession Number: Not Available
Study Date: 2018-03-08

b

Density indices low due to silicone implants

Results: Agreement (implants excluded)

4-way and pairwise agreement improves when cases with breast implants are excluded

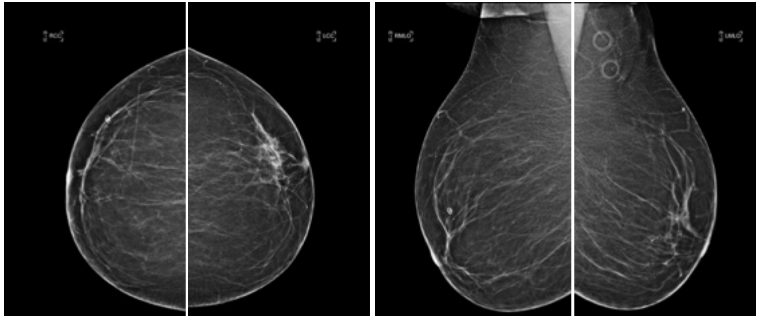
Agreement Analysis of BI-RADS Breast Density in Women with Dense Breasts						
	N (Full Sample)	Kendall's Coefficient of Concordance	95% CI	N (Cases with implants excluded)	Kendall's Coefficient of Concordance	95% CI
4-Way Agreement between SoftVue, Volpara, Radiologist, Technologist	403	0.69	(0.651, 0.728)	310	0.74	(0.697, 0.778)
2-Way Agreement between SoftVue & Volpara	405	0.81	(0.776, 0.851)	312	0.88	(0.850, 0.911)
2-Way Agreement between SoftVue & Radiologist	446	0.71	(0.669, 0.749)	346	0.75	(0.708, 0.793)

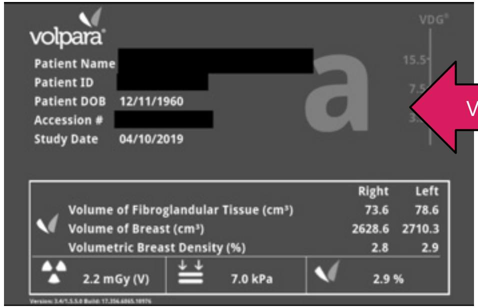
Agreement improves

Notes: 4-way & pairwise agreement was tested using Kendall's coefficient of concordance (W). Kendall's Coefficient of Concordance is used due to the endpoint being an ordinal variable (a/b/c/d). A concordance value of 1 indicates perfect agreement and above 0.60 indicates "good" agreement.

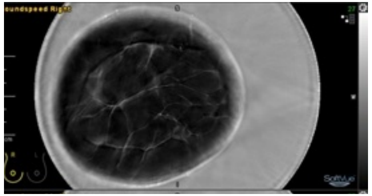
Disagreement example: Within ± 5 of quartile threshold

This case was in the disagreement group but the results of the two methods were very close to agreement. SV rating BI-RADS b was chosen due to the highest value (Right 26, Left 25)

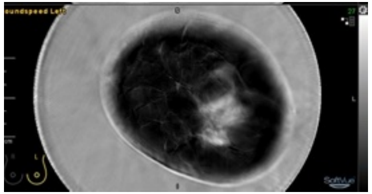




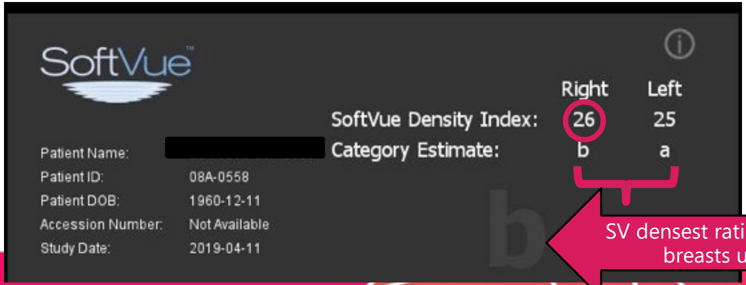
Volpara overall score used



Sound Speed Right



Sound Speed Left



SV densest rating from 2 breasts used

Results: Analysis of 103 disagreement cases

Disagreement groups had:

- Approx. half of cases with SV density indices within 5 points of quartile thresholds for a/b/c/d conversion

	SV < Volpara N=49	**SV > Volpara N=54**
SV density index ± 5 points of a/b/c/d quartile thresholds	55% (27/ 49)	44% (24/ 54)
Crossed threshold of BI-RADS b ↔ c (implants excluded)	20% (10/ 49)	15% (8/ 54)

Study limitations

- Study population was dense breasts; does not represent population distribution of women presenting for annual screening
- Study population had 23% (92/405) prevalence of breast implants. Automated density values are not reliable unless implants are excluded (manually or by software masking).
- Quantitative values calculated by SV and Volpara were not directly compared. Comparisons were made using ordinal variables (a/b/c/d) from the overall Volpara score and the estimated category for SV.

Conclusion

- SoftVue breast density index, algorithmically calculated from whole breast ultrasound transmission data, has good agreement with Volpara automated breast density assessments using 3D mammography for women with dense breasts.
- SoftVue breast density index is comparable with radiologists' subjective BI-RADS assessments from mammography.
- SoftVue breast density assessment performance improved when breast implants were excluded from analysis.

Clinical Relevance

- SoftVue ultrasound tomography offers objective, accurate breast density comparable with DBT-based tools or subjective ratings by radiologists.
- The density analysis is built into the SV image interpretation software and requires no additional hardware or software.
- The ability to characterize dense breast tissue with a volume averaged Sound Speed numerical index may be used to measure smaller changes in density before larger BI-RADS category changes are noticed. Use of numerical indices may improve risk stratification in clinical risk assessments
- Clinical risk assessment using breast density may be applied, especially to women under age 40, without unnecessary radiation.

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LEADING THROUGH CHANGE

THANK YOU