

News from Volpara Science

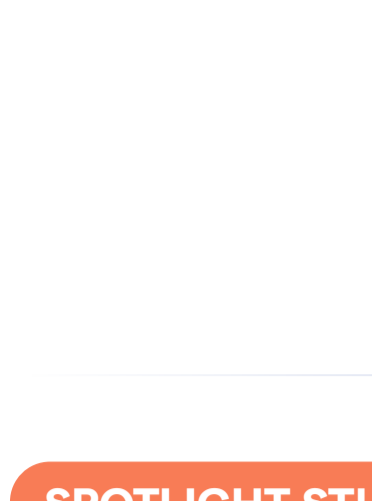
Volume 3: November/December 2021

Research Brief

Volpara's Research Brief is a regular update about the latest from Volpara Science and other industry leaders around the world.

This edition features a recap of Volpara's research presented at RSNA 2021, and an overview of five newly published peer-reviewed publications involving the use of Volpara software.

MEET A MEMBER OF OUR TEAM



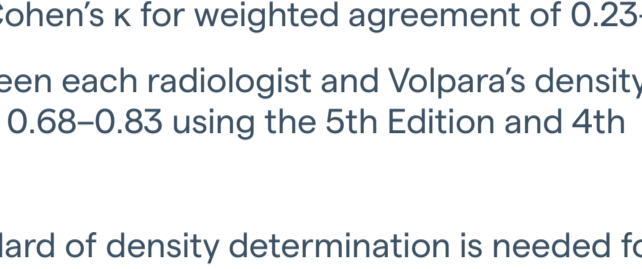
Brian Drohan, PhD
Chief Clinical Scientist (Boston, Massachusetts, USA)

Brian is an expert in the science of breast cancer risk assessment and advises Volpara product and management teams, as well as the clinical community, on the value of integrated risk assessment programs like Volpara® Risk Pathways™. Before joining Volpara, he earned a PhD in Medical/Biomedical Engineering, worked as a software engineer, and eventually joined the risk assessment collaboration between the University of Massachusetts and Massachusetts General Hospital. Brian, along with Dr. Kevin S. Hughes and others, founded CRA Health, which was recently merged with Volpara Health.

During RSNA 2021, Brian presented a PGMI poster and was co-investigator on the Elizabeth Wende Breast Care risk presentation, and presented at the Innovation Theater on the need for early breast cancer risk assessment, emphasizing the importance of a comprehensive risk pathway. [Access the Innovation Theater presentation.](#)

SPOTLIGHT STUDY

Persistent inter-observer variability of breast density assessment using BI-RADS® 5th Edition guidelines




This study from Brigham and Women's Hospital and Boston University investigated the effect of BI-RADS 5th Edition versus 4th Edition guidelines on reader agreement regarding breast density assessment. Persistent subjectivity of visually assessed breast density using BI-RADS 5th Edition guidelines was observed, regardless of the radiologist's experience level. Moreover, more mammograms were interpreted as "dense" using BI-RADS 5th Edition than 4th Edition guidelines, which has implications for breast density laws, risk stratification, and supplemental screening.

Using the 5th Edition guidelines, six radiologists assessed the density of 200 mammograms, and these results were then compared to 2016 data from the same readers using the 4th Edition guidelines, as well as automated/objective density measures obtained from Volpara's density software. Agreement was measured using Cohen's κ and Nelson et al.'s κ s, including κ_w , the weighted κ for ordinal data.

- Inter-reader weighted agreement using the 5th Edition guidelines resulted in a κ_w of 0.73, and a κ of 0.71 for 4th Edition guidelines.
- Intra-reader agreement comparing each radiologists' 5th versus 4th Edition readings ranged from 26% to 47%, resulting in a Cohen's κ for weighted agreement of 0.23–0.34.
- Cohen's κ for weighted agreement between each radiologist and Volpara's density assessments ranged from 0.76–0.85 and 0.68–0.83 using the 5th Edition and 4th Edition guidelines, respectively.

Portnow et al. concluded that "a gold standard of density determination is needed for reliable, reproducible, and consistent quantitative methods, potentially using emerging artificial intelligence technologies."


 DENSITY

Portnow, L., et al. *Clinical Imaging*. 2021. <https://doi.org/10.1016/j.clinimag.2021.11.034>.

BITE-SIZED STUDY SUMMARIES

Automated breast lesion detection and characterization with the Wavelia Microwave Breast Imaging System: methodological proof-of-concept on first-in-human patient data


Wavelia™ is a microwave breast imaging prototype system that does not rely on ionizing x-rays. This study presented methodology for breast lesion detection and characterization in the first-in-human clinical investigation of the Wavelia semi-automated Quantitative Imaging Function (QIF), based on 25 patients. Results indicated the potential to detect and discriminate between malignant and benign palpable breast lumps. The authors presented case examples demonstrating Wavelia's QIF performance across a range of breast densities, as measured using Volpara's density software.

 DENSITY

Fasoula, A., et al. *Applied Sciences*. 2021. <https://doi.org/10.3390/app11219998>.

Coffee, tea, and mammographic breast density in premenopausal women


This study investigated the associations between coffee and tea with mammographic density (MD) in 375 premenopausal women. Patients self-reported their consumption of coffee, and caffeinated and decaffeinated teas, and Volpara's density software was used to determine volumetric percent density (VPD), dense volume (DV), and non-dense volume (NDV). Results show that coffee and caffeinated tea intake are not associated with VPD; however, positive associations were found between decaffeinated tea and VPD.

 DENSITY

Odama, A., et al. *Nutrients*. 2021. doi: [10.3390/nu13113852](https://doi.org/10.3390/nu13113852).

Optimal breast density characterization using a three-dimensional automated breast densitometry system


This study examined objective selection criteria for identifying which women should be screened using supplemental ultrasonography (US). In a population of 441 breast cancer surgery patients in Japan, mammographic density was measured using Volpara's density software. The diagnostic accuracy of mammography decreased with increasing Volpara Density Grade (VDG), with sensitivities of 84.2%, 84.2% and 77.3% for VDG a, b, c and d, respectively; whereas, diagnostic accuracy of US was not associated with VDG. The authors further indicated that supplementary US could benefit patients without suspicious calcifications and volumetric breast density $\geq 25.5\%$ and, if those selection criteria had been applied, the sensitivities of supplemental US would have increased to 95.8% compared with 25% with mammography alone.

 DENSITY

Yoshida, R., et al. *Current Oncology*. 2021. <https://doi.org/10.3390/curronc12080448>

Does circulating progesterone mediate the associations of single nucleotide polymorphisms in progesterone receptor (PGR)-related genes with mammographic breast density in premenopausal women?

This study aimed to identify the associations of genetic variations in progesterone-regulated pathways with mammographic breast density (MD) in premenopausal women, and to identify whether these associations are mediated through circulating progesterone. Researchers sequenced 179 progesterone receptor (PGR)-related single nucleotide polymorphisms (SNPs) and then used Volpara's density software to measure volumetric percent density (VPD) and non-dense volume (NDV). Results indicated that only PGR rs657516 had a direct effect on VPD, but this was not statistically significant. Additionally, five SNPs were associated with circulating progesterone, but these results were also not statistically significant. Taken together, these results suggest that the effects, if any, of SNPs on MD are independent of circulating progesterone.

 DENSITY

Akinjayan, F., et al. *Discover Oncology*. 2021. doi: [10.1007/s12672-021-00438-1](https://doi.org/10.1007/s12672-021-00438-1).

Radiological Society of North America (RSNA) 2021 Annual Meeting & San Antonio Breast Cancer Symposium (SABCS) 2021 research recap

Access to the accepted scientific abstracts below is through RSNA or SABCS login only. Click [here](#) for access to full author lists and affiliations.

Impact on risk categorization with inclusion of mammographic density in the Tyrer-Cuzick model



This retrospective study identified 59,257 patients who had a risk assessment performed at the Elizabeth Wende Breast Care (New York), using the Tyrer-Cuzick version 7 (TC7) risk model (with no breast density input) and recalculated their lifetime risk score using Tyrer-Cuzick version 8 (TC8) with either automated BI-RADS or volumetric breast density (VBD) as the density input, as assessed by Volpara's density software. Using TC7 with no density input, 8.3% of patients were considered high risk (>20% lifetime risk), and using TC8 with automated BI-RADS as the density input, 6.9% of patients were considered high risk. Using TC8 with VBD as the density input, 11.4% of patients were considered high risk. Overall, younger, pre-menopausal women are more affected by the addition of mammographic density to the TC risk model. Of the women who fall into low or intermediate risk categories, 36% have dense breasts and may still benefit from supplemental imaging.

 DENSITY

Destounis, S., et al. *RSNA*. 2021.

Association of automated breast positioning assessment with technical repeats and recalls in the nationalized UK screening program


Breast Screening Programme), the OPTIMAM study looked at the association between images that were repeated due to inadequate positioning and automated PGMI (Perfect/Good/Moderate/Inadequate) scoring for breast positioning. In total, there were 1340 accepted exams with no repeated views, 2134 technical repeats, and 144 technical recalls. Volpara density was used to evaluate breast volume (BV), volumetric breast density (VBD), and breast positioning. Automated breast positioning assessment showed significant differences in PGMI scores between the accepted exams, technical repeats, and technical recalls—for instance, comparing PGMI scores for technical recalls or repeats and accepted exams, there were significantly more images scored as Inadequate and fewer scored as Perfect. Automated image quality assessment algorithms can provide objective and timely feedback, with the potential to reduce technical recalls and help facilities continually improve image quality to meet MQSA standards.

 DENSITY  POSITIONING

Gilroy, H., et al. *RSNA*. 2021.

Denser or thinner? Mammographic breast density characterization around the world

This study compared volumetric breast density (VBD), as calculated by Volpara's density software, across 780,648 patients from the United States, Netherlands, Norway, Brazil, Malaysia, and Greece. The distributions of VBD were compared at equal compressed breast thicknesses. Results show that there were significant differences in VBD within each of the breast thickness bins and when compared to the worldwide average. These international variations in the prevalence of dense breasts suggest that a single model may not be broadly representative, though a single model of VBD as a function of breast thickness may be appropriate for various applications, such as radiation dose estimates or risk modeling.

 DENSITY

Sanderink, W., et al. *RSNA*. 2021.

Breast density associations with tumor characteristics among screen-detected and interval breast cancers diagnosed in a US screening setting

This retrospective study investigated the associations of automated mammographic density (MD) and breast tumor characteristics (TCs) for 318 screen-detected breast cancers and 100 interval cancers diagnosed at Elizabeth Wende Breast Care (New York). TCs were extracted from the clinical records and MD was measured by both BI-RADS™ and Volpara's density software, using volumetric breast density (VBD) and the Volpara Density Grade (VDG). VDG had stronger associations with TCs than BI-RADS—for all cancers, VDG was associated with HER2 status and tumor size ≥ 2 cm, whereas, after splitting data by mode of detection, BI-RADS showed an association with tumor size for screen-detected cancers only. Additionally, VBD had stronger associations with TCs associated with poorer outcomes than both VDG and BI-RADS.

 DENSITY

Destounis, S., et al. *RSNA*. 2021.

Volumetric breast density is a strong predictor of breast tumor size in a US screening population

This retrospective study used linear regression to determine tumor size associations with mammographic density (MD) and tumor characteristics (TCs) in 406 breast cancers diagnosed at Elizabeth Wende Breast Care (New York). MD was assessed using BI-RADS™ as well as Volpara's density software, using volumetric breast density (VBD) and the Volpara Density Grade (VDG). VBD had the strongest associations with tumor size, and women with VDG 4 breasts had 3.8 times the risk of being diagnosed with tumor sizes greater than 2 cm compared to VDG 1 and 2 combined.

 DENSITY

Destounis, S., et al. *RSNA*. 2021.

Deep learning predicts interval and screening-detected cancer from screening mammograms: a case-case-control study in 6369 women

This case-case-control study trained a deep learning model on negative mammograms prior to cancer diagnoses, where 4409 women remained cancer free, 1609 women had screen-detected breast cancer, and 351 had interval invasive breast cancer. The model classified women as either not having developed cancer, having developed screen-detected cancer, or having developed interval invasive cancer. The model was benchmarked against other models using clinical risk factors, including breast density (from Volpara's density software and BI-RADS). The deep learning model underperformed for interval cancer risk when compared to clinical risk factors, including BI-RADS density, but outperformed in predicting screen-detected cancer risk.

 DENSITY

Leong, L., et al. *RSNA*. 2021.

Triaging women from MRI to mammography to adapt screening to changes in breast density using artificial intelligence

This study used data from the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial, which used Volpara's density software to identify patients with extremely dense breasts and triaged them to MRI screening. Based on data from the first two screening rounds of the DENSE trial, a regression convolutional neural network (CNN) was trained to predict volumetric breast density from MRI alone. The correlation between the density predicted by artificial intelligence (AI) and the density determined by Volpara software showed potential for AI to correctly triage more than half (58%) the number of women with decreased breast density from MRI-only screening back to mammographic screening.

 DENSITY

van der Velden, B., et al. *RSNA*. 2021.

AI-triaging of breast MRI for radiological review in the screening of women with extremely dense breasts

This study was a re-analysis of data from the DENSE trial, which used Volpara's density software to identify patients with extremely dense breasts and triaged them to MRI screening. Using exams from the first screening round of the DENSE trial, a CNN was trained to identify breasts with lesions and normal breasts without lesions. Results showed that the AI-triaging of women with dense breasts to MRI screening could dismiss 20% of normal exams from radiological review without dismissing malignant disease.

 DENSITY

Verburg, E., et al. *RSNA*. 2021.

Replacing a radiologist by AI in Dutch population based breast cancer screening and the impact of breast density on performance

This study reviewed the performance of commercially available AI systems as a second reader to assess breast cancers. Volpara® Density Grade™ (VDG®) scores were obtained from Volpara's density software to examine the effect of density on cancers identified by human reading versus AI. Results showed that AI offers higher sensitivity than a single human reader, showing its potential as a second reader. These results were independent of breast density, though a large number of additional cancers were detected in the highest and lowest density categories. It was ultimately concluded that an effective arbitration process is necessary.

 DENSITY

van Winkel, S., et al. *RSNA*. 2021.

Commercially available AI system for breast cancer detection shows promise for risk prediction, including women with dense breasts

This study aimed to determine whether AI algorithms can accurately assist in breast cancer risk prediction. Volumetric breast density (VBD) assessments were obtained from Volpara's density software and malignancy risk score was provided by Transpara®. At the conclusion of the study, it was determined that AI imaging-based measures combined with VBD from Volpara improved discrimination of invasive breast cancer, especially for interval breast cancers, where the AUC increased from 0.66 to 0.72. Therefore, including these measures in risk models could better inform personalized screening.

 DENSITY

Vachon, C., et al. *RSNA*. 2021.

Mammographic density in relation to breast cancer risk factors among Chinese women

This study aimed to investigate the association of breast cancer risk factors on mammographic density (MD) among Chinese women, who often have higher MD compared to European women but a lower overall breast cancer incidence rate. Volpara's density software was used to obtain quantitative MD measures, including absolute dense breast volume and percent breast density. Most risk factors examined showed similar associations with dense volume (DV) and volumetric percent density (VPD)—with age at menopause being positively associated, and age, parity, longer breastfeeding duration, and postmenopausal status all being inversely associated.

 DENSITY

Koka, H., et al. *SABCS*. 2021.

OTHER SCIENCE-RELATED NEWS

[Mammography Educators and Volpara launch customized training for technologists](#)

[Volpara highlights risk assessment research at RSNA 2021](#)

[Volpara's RSNA presence emphasizes rise of AI-driven breast software tools](#)

[Volpara's RSNA research highlights focus on breast density software in action](#)

[Learn how to build trust in use of AI in breast imaging](#)

[Volpara wins Microsoft New Zealand Partner Award](#)

[Takeaways from the Breast Density Twitter Chat with My Density Matters](#)

[Breast cancer previvor Keri Stephens talks patient advocacy with Volpara](#)

[RevealDX CEO writes about lung screening challenges and solutions](#)

If you would like to discuss using Volpara's software for your personalized breast care or early detection research, please contact research@volparahealth.com and we'll be in touch!