RSNA QUIC Breast Density Quantification – Implementation Roadmap version 06-18-2026

i. Introduction

The RSNA Quantitative Imaging Committee (QUIC) was formed in 2024. The mission statement of QUIC is "to improve patient care, clinical research, and education by guiding and promoting implementation of quantitative imaging biomarkers." QUIC builds on prior work of the Quantitative Imaging Biomarkers Alliance (QIBA), which primarily provided rigorous specifications (Profiles) for individual quantitative imaging biomarkers (QIBs). The vision of QUIC is to move beyond QIBA Profiles to develop broader "Implementation Roadmaps" for collecting and distributing appropriate QIB information to all stakeholders on the information pipeline, including radiologists, referring physicians, patients, researchers, and the healthcare enterprise.

QUIC identified specific Use Cases that are appropriate for quantitative imaging for further development into Implementation Roadmaps. Mammographic breast density quantification was prioritized as one of four initial Use Cases. The focus of the QUIC Breast Cancer Workgroup is on automated mammographic breast density quantification for breast cancer risk stratification and supplemental screening indication within a U.S.-specific practice scope. The purpose of this structured document is to describe the entire process for clinical implementation of breast density quantification including motivation, stakeholders, drivers, challenges, and guidelines.

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1. Specific QIB(s) and Definitions

The breast is a soft tissue organ with a heterogeneous composition. The three main tissue components of the breast include glandular tissue, fibrous connective tissue, and adipose tissue. Glandular tissue (lobules and ducts) is responsible for milk production and milk transport to the nipple. Fibrous tissue (including Cooper's ligaments) provides structural support to the breast. The glandular tissue and fibrous tissue combined are referred to as fibroglandular tissue. Adipose (fatty) tissue fills and surrounds the fibroglandular tissue and contributes to overall breast size.

X-ray-based breast imaging modalities (mammography, digital breast tomosynthesis) rely on the difference in X-ray attenuation between fibroglandular tissue and fatty tissue for image contrast. The X-ray attenuation coefficient of fibroglandular tissue is higher than that of fatty tissue resulting in a more radiopaque (white) appearance on mammography compared to a more radiolucent (black) appearance of fatty tissue (1). Thus, breast composition on digital mammography (DM) and digital breast tomosynthesis (DBT) is modeled as having two components – dense (fibroglandular) tissue and non-dense (fatty) tissue. DM offers two-dimensional (2D)

images of the breast composition, while DBT allows for volumetric breast visualization owing to the acquisition of multiple projection images at different angles, which are then reconstructed into quasi-3D slices (2, 3). DBT is clinically offered either in conjunction with 2D DM or on its own with a 2D composite image constructed from the tomosynthesis projection images referred to as a "synthetic mammographic image" (4).

This document focuses on **mammographic breast density**, which is a measure of the amount of dense tissue (fibroglandular tissue) in the breasts imaged using DM or DBT. Breast composition can also be assessed using direct photon-counting technology (5) (e.g. Philips Spectral Breast Density Measurement Application developed for the MicroDose SI mammography system) as well as with ultrasound and MRI, which are outside the scope of this document.

For clinical radiology reports, mammographic breast density is a **categorical, ordinal variable**. The American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) defines four categories of mammographic breast density (A, B, C, and D) (**Figure 1**) in increasing order (6).

- **Category A –** "The breasts are almost entirely fatty".
- **Category B** – "There are scattered areas of fibroglandular density".
- **Category C** – "The breast are heterogeneously dense, which may obscure small masses".
- **Category D** – "The breasts are extremely dense, which lowers the sensitivity of mammography".

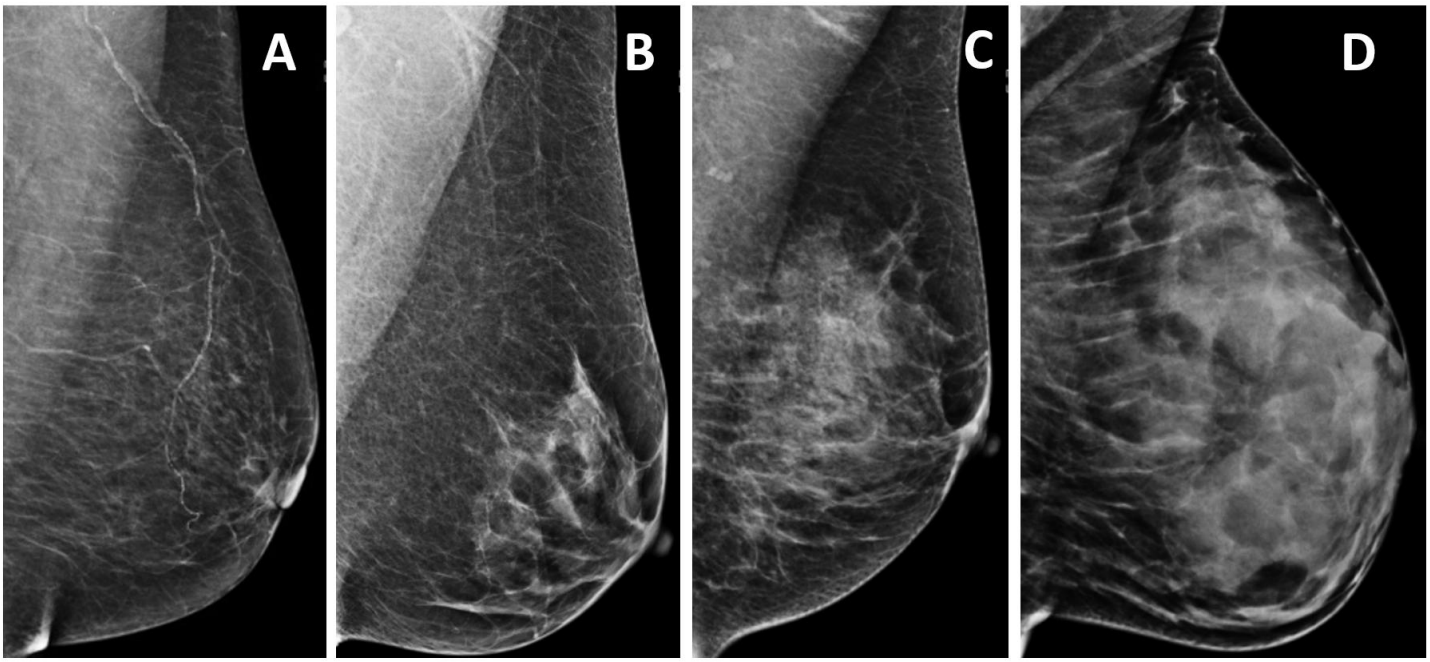

Figure 1: *ACR BI-RADS categories of mammographic breast density based on visual assessment by the interpreting radiologist. MLO views of the left breast in 4 different asymptomatic women undergoing screening mammography. (A) Category A – "The breasts are almost entirely fatty". (B) Category B – "There are scattered areas of fibroglandular density". (C) Category C – "The breast are heterogeneously dense, which may obscure small masses". (D) Category D – "The breasts are extremely dense, which lowers the sensitivity of mammography".*

For breast density notification letters to patients, mammographic breast density is a **dichotomous variable**. Categories A and B are considered "**not dense**". Categories C and D are considered "**dense**".

Mammographic breast density can also be described as a **continuous numerical variable**. Automated software-based quantitative methods have been developed to measure absolute and percent breast density. **Absolute breast density** corresponds to the absolute amount of dense tissue, while **percent density** reflects

the relative amount of dense tissue within the breast. Both mammographic density measures can be quantified using 2D area (cm^2) or 3D volume (cm^3). **Area percent density** (APD, %) is calculated as the area of fibroglandular tissue (cm^2) divided by the overall breast area (cm^2) x 100. **Volumetric percent density** (VPD, %) is calculated as the volume of fibroglandular tissue (cm^3) divided by the overall breast volume (cm^3) x 100 (**Figure 2, Figure 3**).

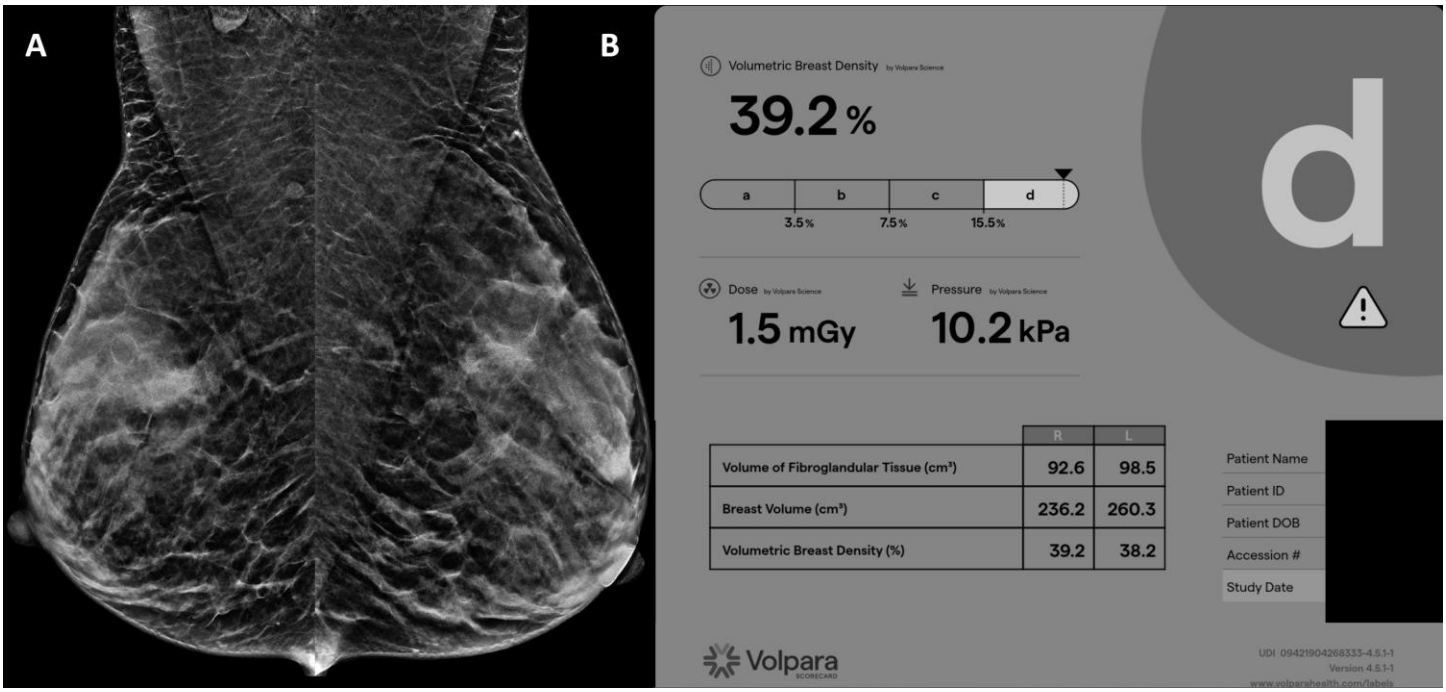

Figure 2: *40-year-old asymptomatic woman undergoing screening digital breast tomosynthesis. (A) Synthesized MLO view of the right breast. (B) Synthesized MLO view of the left breast. Automated breast density software (Volpara) report includes volume of fibroglandular tissue, breast volume, and volumetric breast density for the right and left breasts, an overall volumetric breast density (39.2%), and an overall ACR BI-RADS category assessment (Category D).*

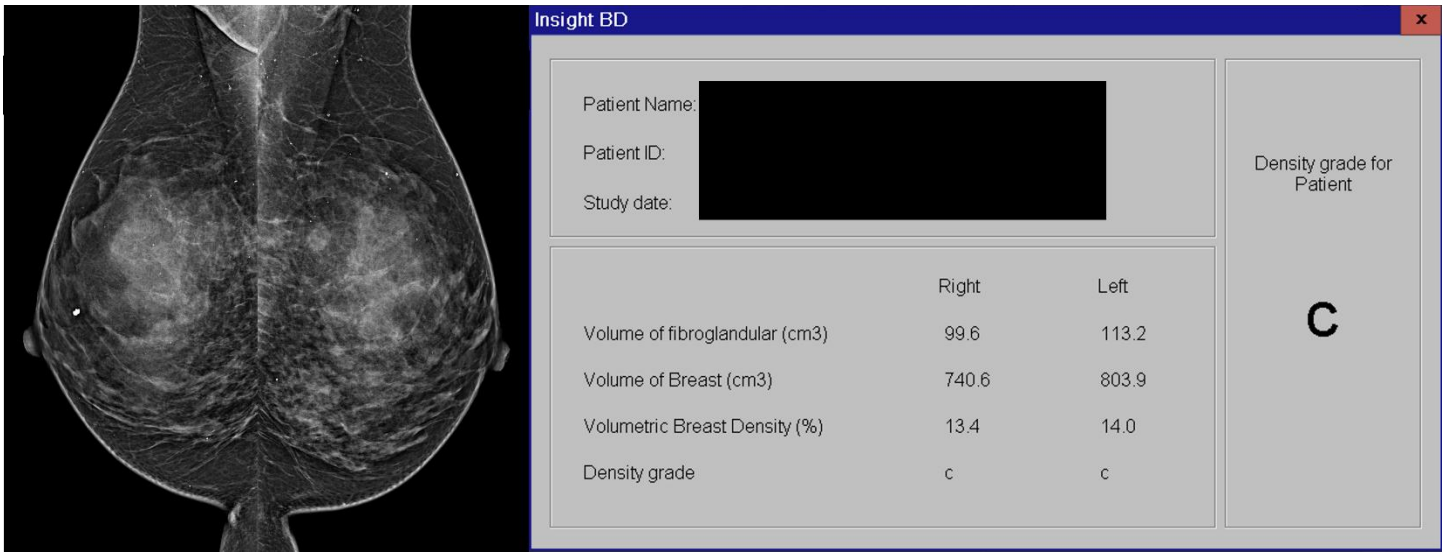

Figure 3: *42-year-old asymptomatic woman undergoing digital breast tomosynthesis. Synthesized MLO view of the right and left breasts. Automated breast density software (Insight BD) report includes volume of fibroglandular tissue, breast volume, volumetric breast density and density grade for the right and left breasts, and an overall ACR BI-RADS category assessment (Category C). Image provided by Siemens Healthineers.*

Artificial intelligence (AI) algorithms using deep learning have been developed to aid radiologists in the assessment of breast tissue composition (7). These software systems can automatically determine continuous area (8) and volumetric (9) breast density measures, and the ACR BI-RADS breast density category (10) from DM and DBT. Some approaches generate quantitative density measurements (e.g., volumetric or area-based density), while others provide categorical classifications based on image features, which may have different implications for reproducibility and longitudinal assessment. An example of a proprietary software algorithm system that analyzes the distribution and texture of the parenchymal tissue to categorize breasts into the 4 breast composition categories is shown in **Figure 4**.

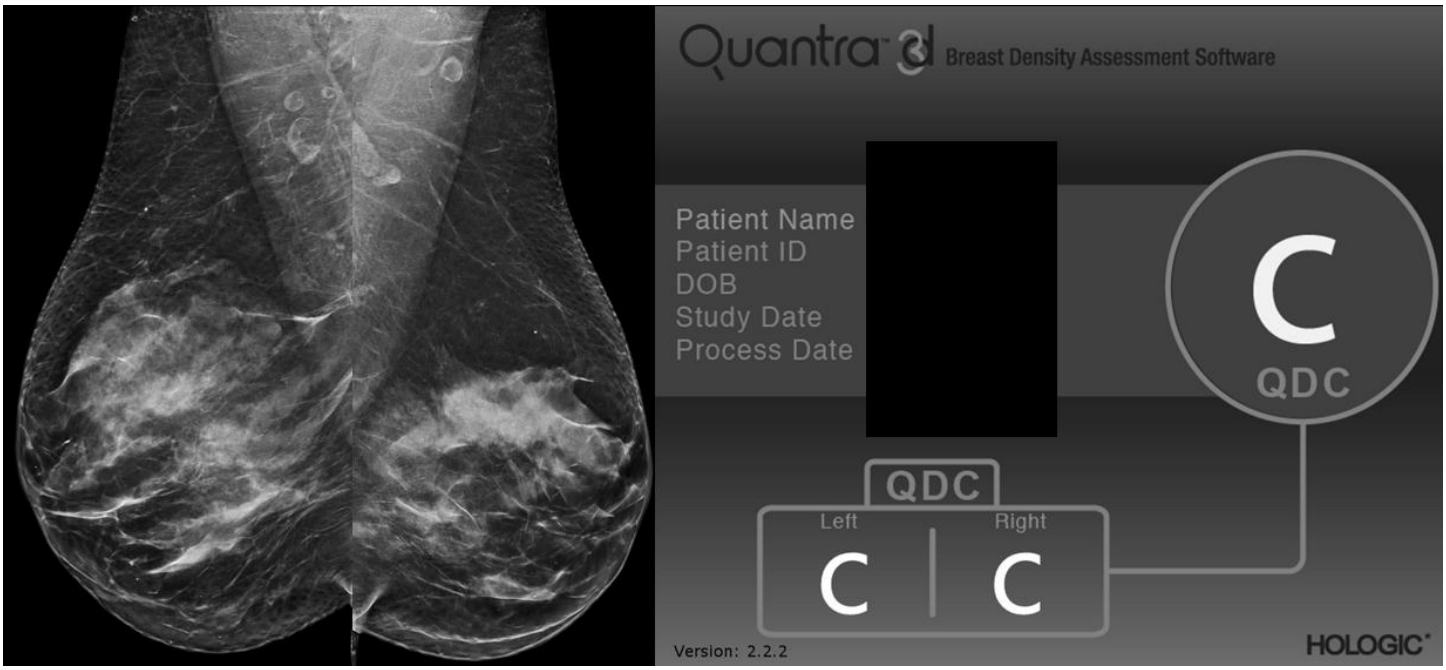

Figure 4: *47-year-old asymptomatic woman undergoing screening digital breast tomosynthesis. Synthesized MLO view of the right and left breasts. Automated breast density software (Quantra) report includes the overall ACR BI-RADS category assessment and the density category for each breast.*

2. Relevant Disease and Patient Populations

The disease focus for this QIB is **breast cancer**. Breast cancer is the most common cancer type for women and is the highest cause of cancer death for women younger than 50 years old (11). Estimates for 2026 indicate there will be 321,910 new cases of breast cancer diagnosed in U.S. women with 42,140 breast-cancer related deaths (12). Screening mammography reduces breast cancer mortality through early detection (13).

The patient population most pertinent to mammographic breast density as a QIB are **asymptomatic patients undergoing screening mammography** for breast cancer early detection. Mammographic breast density is also included in diagnostic mammography reports for patients who are symptomatic or being evaluated for abnormal screening mammogram results.

3. Motivation and State of the Evidence

Over 40% of women aged 40-74 years old in the United States have mammographically dense breasts (14). Mammographically dense breast tissue can mask or obscure noncalcified cancers and reduce the sensitivity for breast cancer detection. For example, the sensitivity of mammography is highest in fatty breasts (approximately 87-98%) and lowest in extremely dense breasts (approximately 30-63%) (15-17). Similarly, the breast cancer

mortality benefit of screening mammography is lower for women with dense breasts compared to those with non-dense breasts (18).

The chance of an interval breast cancer diagnosis after a negative screening mammogram is higher for women with dense breasts (19). In a retrospective study of 652 screen-detected cancers and 119 interval cancers, breast density was the sole risk factor significantly associated with a diagnosis of interval cancers (20). Furthermore, volumetric breast density captured the potential masking risk due to increased breast density more precisely than the visual BI-RADS density categories.

Dense breast tissue is an independent risk factor for breast cancer development in addition to age and genetic factors. Patients with extremely dense breasts have a 4- to 6-fold higher breast cancer risk compared to those with fatty breasts (21). Breast density is included in some breast cancer risk assessment models (Tyrer-Cusick model, Breast Cancer Surveillance Consortium model, Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm) as a variable (22). Incorporation of breast density into these risk models has been shown to improve risk stratification for individualized approaches for breast cancer screening and prevention (23-27). Volumetric measures of breast density (absolute dense volume, percent VPD) have been shown to be a more accurate predictor of breast cancer risk than risk factors alone and than area breast density measures (28-30).

New federal regulation went into effect in 2024, as an amendment to the U.S. Food and Drug Administration Mammography Quality Standards Act (MQSA), requiring that patients be notified of their breast density notification for every mammogram report and also be informed that additional imaging studies may aid cancer detection. Mammographic breast density based on the clinical report determines eligibility and insurance coverage for supplemental breast cancer screening modalities (e.g. ultrasound, MRI, contrast-enhanced mammography, molecular breast imaging). This has the potential to impact a large number of patients estimated at over 25 million based on the prevalence of dense breasts among U.S. screening-age women (14).

Breast density assessment is most commonly performed by qualitative visual estimation by the interpreting radiologist and manually entered into the mammogram report. This process is subjective with inter-reader and intra-reader variability and can be prone to data entry error. Potential consequences of inaccurate breast density assessment include 1) missed benefit of early detection of breast cancer missed by mammography due to dense breasts incorrectly assigned as non-dense, 2) added harms of false positive result from a supplemental screening exam if non-dense breast incorrectly assigned as dense.

Thus, there is a critical need for standardization and automation of mammographic breast density quantification reporting. Accurate breast density assessment is important for determining eligibility for supplemental breast cancer screening tests and for accurate breast cancer risk assessment. Successful implementation would result in correct identification of patients who do and do not qualify for supplemental breast cancer screening. Robust breast density assessments over time are also critical to ensure longitudinal consistency in downstream care for screened women (31).

There are additional applications of breast density quantification beyond current clinical use. Quantitative breast density could be used as a key variable in clinical trials. Use of quantitative methods for breast density assessment could better refine clinical trial eligibility for supplemental screening trials. Furthermore, quantitative breast density has been used as a clinical trial endpoint for assessing the biologic effect of some chemoprevention agents (e.g. tamoxifen) (32).

4. Indications

The intended patient population for automated breast density quantification are individuals who are having a DM or DBT exam. Clinical indications for screening versus diagnostic mammography are detailed in ACR Appropriateness Criteria. Briefly, screening mammography is for asymptomatic women with specific

recommendations based on age and risk factors (33, 34). Diagnostic mammography is for patients who are symptomatic or being evaluated for abnormal screening mammogram results (35-37).

The intended users of automated breast density quantification systems are healthcare professionals involved in breast imaging (e.g., radiologists, technologists, physicists, and informatics team).

5. Pre-Approval and Scheduling

Clinical implementation of automated breast density quantification does not require additional pre-approval or altered scheduling processes. Patients may present for screening mammography without an advance order from a physician or healthcare provider (38). Scheduling can follow the standard scheduling templates for mammography per institutional guidelines.

6. Protocols, Acquisition, and Image Generation

Clinical implementation of automated breast density quantification does not require modifications to the standard protocols for DM or DBT. These exams are performed in accordance with the Mammography Quality Standards Act (MQSA) legislation and regulations published by the Food and Drug Administration (FDA) (39). Standard imaging acquisition is performed following ACR Practice Parameters and Technical Standards (38). For example, standard views for a screening exam include a minimum of craniocaudal (CC) and mediolateral oblique (MLO) views of both breasts.

Breast density quantification is performed as a post-processing step using commercially available, FDA-cleared software. Mammographic or tomosynthesis image data are transmitted to the breast density software system using standard digital imaging and communications in medicine (DICOM) data transfer approaches. Output data from the breast density software system are transmitted to the picture archive and communication system (PACS) and the radiology information system (RIS) (e.g., Epic Radiant). Based on user preferences, the radiologist can review the output data as a DICOM Secondary Capture Image within PACS, or within the RIS by way of DICOM Structured Report information.

7. Extraction of QIB(s), Software Vendors, and Validation Methods

The first breast density software was cleared by the FDA for clinical use in 2008. Currently, several FDA 510k-cleared software systems are commercially available for breast density quantification in clinical practice (examples included in **Table 1; Supplemental Excel file**). Research-based software systems have also been developed (examples included in **Table 2, Figure 5**); however, these are not for clinical use.

Table 1: FDA 510(k) Cleared Automated Breast Density Assessment Software Systems

Software	Vendor	Output Data (in addition to categorical density A-D)
Volpara TruDensity	Lunit International Ltd	Volumetric Breast Density
Quantra Version 2.2	Hologic Inc	
IntelliMammo densityai	Densitas	
Visage Breast Density	Visage Imaging Inc	
Transpara Density 1.0.0	ScreenPoint Medical	Volumetric Breast Density
Saige-Density v.2.5.0	DeepHealth Inc	
PowerLook Density Assessment V4.0	iCAD Inc	
WRDensity	Whiterabbit AI Inc	
DenSeeMammo version 1.2	Statlife	
Insight BD	Siemens	Volumetric Breast Density
MammoScreen BD	Therapixel	

ClariSIGMAM	ClariPi Inc	

Table updated and adapted from references (40) and (41).

Table 2: Research Software for Breast Density Quantification (not for clinical use)

Software	**Developer**
Cumulus	Sunnybrook Health Sciences Centre, Toronto, ON, Canada
Laboratory for Individualized Breast Radiodensity Assessment (LIBRA)	University of Pennsylvania
TomoLIBRA	University of Pennsylvania
TRACE4BDensity	DeepTrace Technologies
MedDensity	University of Genoa, Italy

All software systems provide output data as a 4-category breast density, which fulfills the MQSA requirement. Software systems differ in the methodologies used. Some use physics-based models or deep learning AI algorithms to determine volumetric breast density which is then used to determine the BI-RADS breast density category. Many software systems use machine learning and deep learning algorithms that may incorporate the dispersion and texture pattern of breast tissue to directly determine the BI-RADS breast density category. Deep learning AI algorithms are also used by multiple software vendors to replicate human visual assessment of breast density.

There are additional differences between software vendors to consider when selecting a system for clinical implementation. Some software solutions are compatible only with certain mammographic imaging system manufacturers as imaging sources (e.g., Hologic, GE, Siemens). Most software uses DBT images, however a few require DM. Input image data format can also vary (raw DBT projection images versus processed "for presentation" DM or synthetic 2D images). Output devices and format may differ slightly between vendors; however, most supported output devices are mammography workstations, PACS, and RIS using DICOM structured report and secondary capture. Deployment options may differ slightly such as a standalone computer, virtual machine, or add-on module to PACS. Breast density software systems may also be an integrated product combined with AI-assisted detection (**Figure 6**).

Software validation activities follow the FDA guidance document, "Content of Premarket Submissions for Device Software Functions – Guidance for Industry and Food and Drug Administration Staff" Available at https://www.fda.gov/media/153781/download.

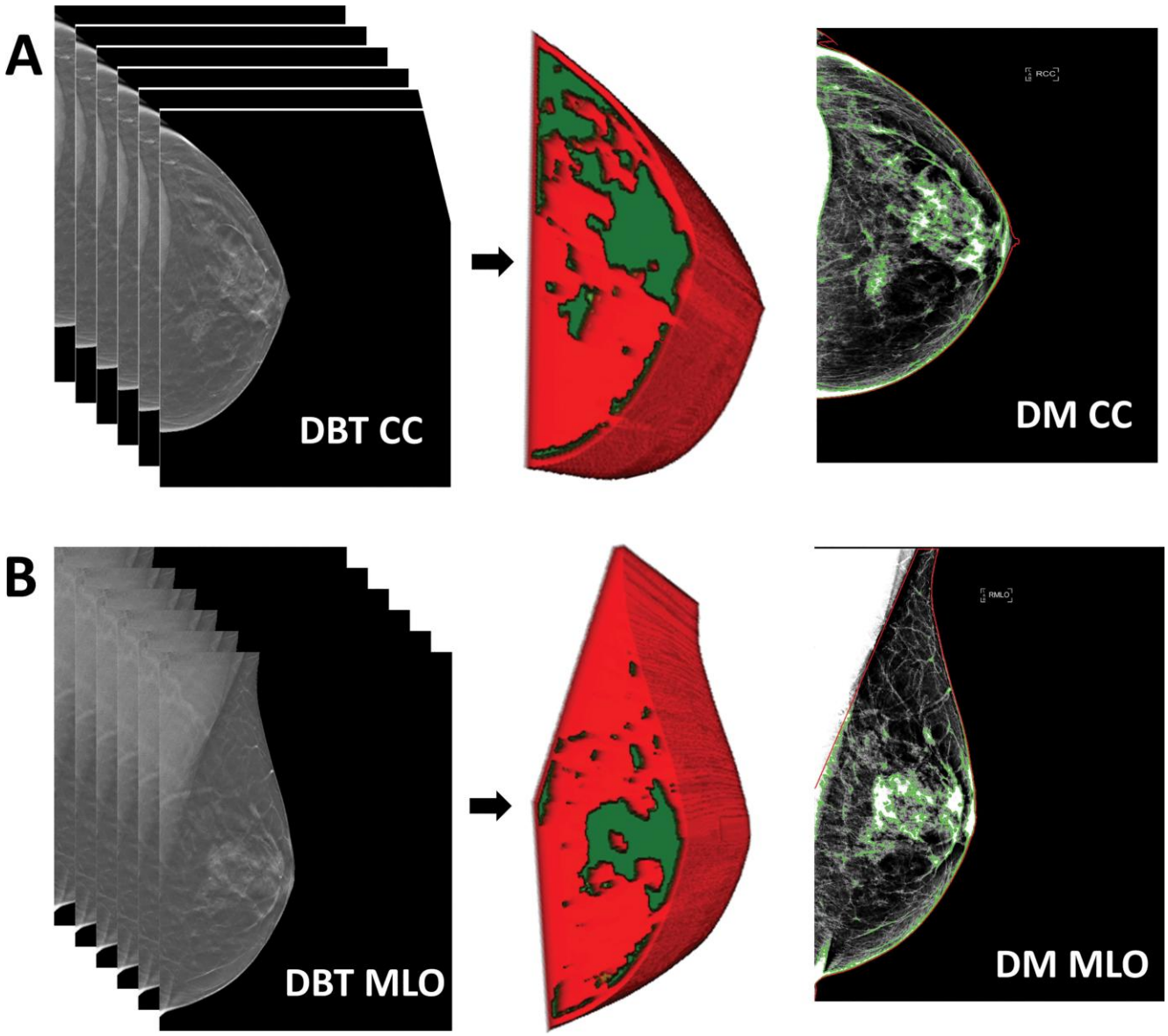

Figure 5: *Examples of volumetric breast density evaluation from digital breast tomosynthesis (DBT) and digital mammography (DM) in* ***(A)*** *craniocaudal (CC) and* ***(B)*** *mediolateral oblique (MLO) breast views, which were obtained in the same woman (aged 56 years) at the same time using publicly available research software systems (TomoLIBRA for DBT and LIBRA for DM). Volumetric measurements of volumetric percent density of 17.1% and density volume of 71.9 cm^3 were obtained from DBT (where dense-tissue regions of the breast are marked in green). Area-based breast measurements obtained from DM were percent density of 19.2% and density area of 17.2 cm^2. Figure is reprinted, with permission, from reference (29).*

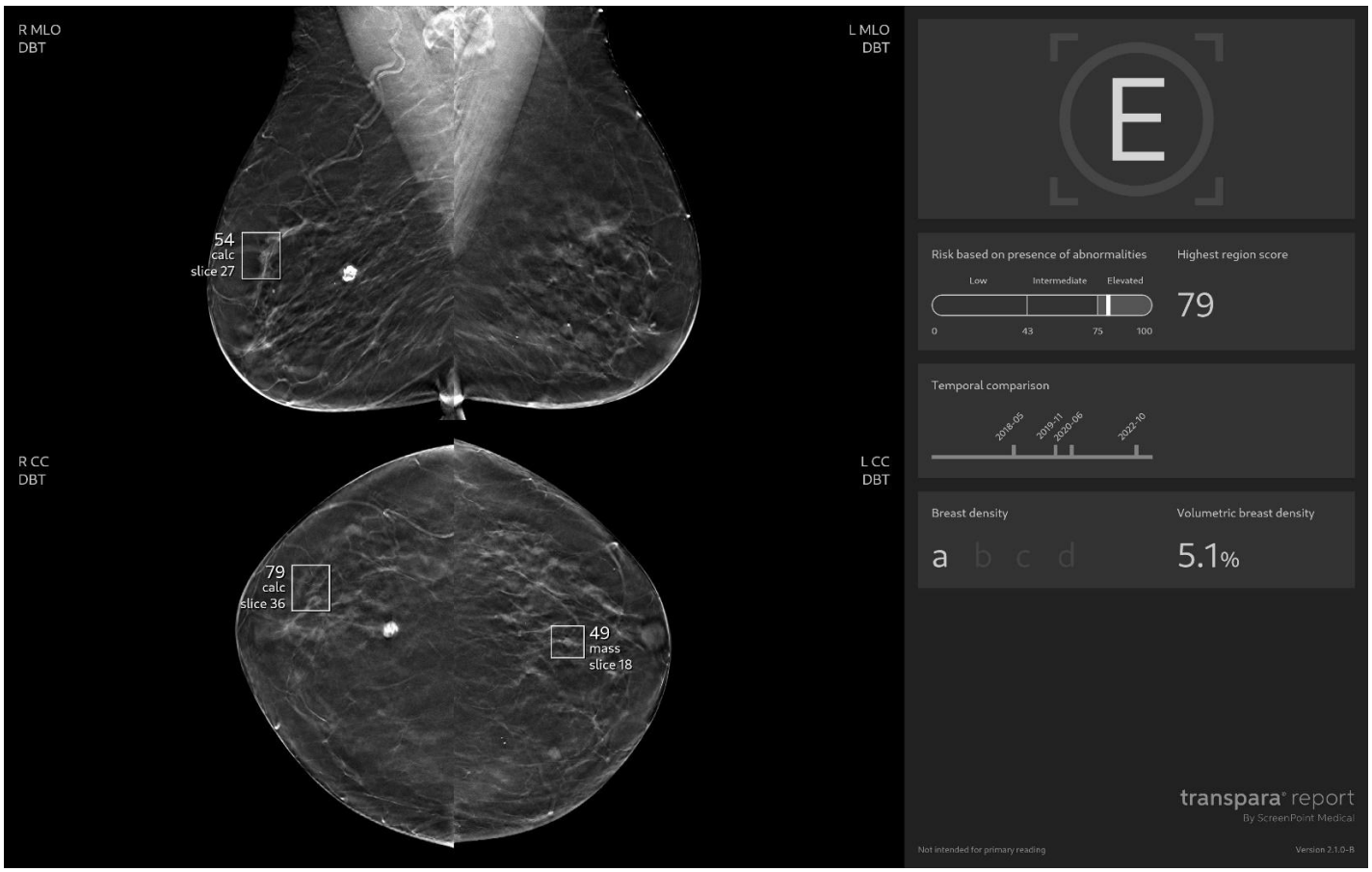

Figure 6: *72-year-old asymptomatic woman undergoing screening digital breast tomosynthesis. CC and MLO DBT views of the right and left breasts. This software provides automated breast density quantification, reporting the overall ACR BI-RADS category (Category A) and volumetric breast density (5.1%). The software also provides AI-assisted lesion detection (elevated risk, E) and incorporates a comparison with prior mammograms (temporal comparison) to detect changes over time and adjust risk scoring accordingly. Image provided by ScreenPoint Medical.*

8. Relevant QIBA Profiles

As of 2026, there is no QIBA profile for breast density quantification. A QIB profile for breast density would lay the foundation for reproducibility benchmarks that can be applied across software vendors. The Quantitative Medical Imaging Coalition (QMIC) is an expert-led group for QIB profile development, separate from RSNA QUIC, and would be an excellent resource for future work in this area.

9. FDA-Qualified Biomarkers

A biomarker is defined as a characteristic that is measured as an indicator of normal biological or pathologic processes, or response to an exposure or intervention. Radiologic phenotypes are types of biomarkers.

An FDA-qualified biomarker is a special designation for a biomarker that has undergone a formal 3-stage review process through the Biomarker Qualification Program (BQP) for a specific context of use (COU) primarily in drug development. There are seven biomarker categories (susceptibility/risk, diagnostic, monitoring, predictive, prognostic, pharmacodynamic/response, and safety). A COU contains two components: 1) the biomarker category and 2) the biomarker's intended use in drug development.

Although mammographic breast density is an indicator of breast cancer risk and cancer detection sensitivity, it is not designated as a qualified biomarker by the FDA. This process is important to distinguish from the FDA MQSA requirement for breast density reporting and from the FDA 510(k) clearance of software programs for breast density assessment and of mammography-based imaging devices.

https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/biomarker-qualification-program

10. Other Data Needed for Clinical Implementation

Automated breast density software systems do not require any additional input data besides the mammogram images. Other data, such as age and risk factors, may be used in conjunction with the breast density results to guide further clinical management.

11. Interpreter Qualifications and Interpretation of Results

DM and DBT examinations must be interpreted by trained physicians who meet MQSA requirements. The Accreditation Council for Graduate Medical Education requires 12 weeks of training in breast imaging during radiology residency. For initial qualification, the FDA MQSA requires that individuals who are board-certified in radiology must 1) be licensed to practice medicine, 2) be certified in diagnostic radiology by the American Board of Radiology (ABR), American Osteopathic Board of Radiology (AOBR) or Royal College of Physicians and Surgeons of Canada (RCPSC), and 3) have interpreted 240 mammograms within the last 2 years of residency. Additionally, 60 hours of Category I CME in mammography is required as well as 8 hours of training in a specific mammographic modality before beginning to use that modality. For continuing qualification, physicians must interpret 960 mammographic examinations over a 24-month period and have 15 category I CME in a 36-month period.

https://accreditationsupport.acr.org/support/solutions/articles/11000049778-interpreting-physician-mammography-revised-05-22-2024-

MQSA requires that breast density is documented in every mammogram report. Specific wording is defined in 21 CFR 900.12(c)(1)(vi). Use of automated breast density quantification software is not required by MQSA. The software results provide standardized, quantitative information to aid the radiologist in the assessment of breast tissue composition but does not replace the final assessment of breast density category made by an MQSA-qualified interpreting physician.

https://www.fda.gov/radiation-emitting-products/regulations-mqsa/mqsa-alternative-standard-26-issuing-report-breast-density-assessment-phrased-singular-or-neither

Software analysis of breast density is performed in the background following imaging acquisition of the mammogram with results displayed for the interpreting radiologist. The radiologist reviews the automated results together with the mammogram images to confirm that the mammogram images are of adequate quality to use as input data and that the density results seem reasonably concordant with the visual assessment. The radiologist can accept the automated software assessment of density or change the category based on their clinical judgement. The availability of quantitative measures may help support this review process by reducing inter-reader variability and promoting more consistent assessment across cases (42). The final breast density category is included in the radiology report for the patient and referring physician and for the patient letter.

12. Path for Interpreter Feedback

Some breast density software systems include analytics to track and monitor performance through aggregate data. This data could be compared with previously published population-based distributions of breast density. This data can also provide feedback to refine the algorithm used by the software and is typically done

intermittently by vendors for algorithm updates. Aggregate reports based on breast density could also be helpful for selecting dense and non-dense cases for the purposes of ACR accreditation.

As required by MQSA, each breast imaging facility must establish and maintain a mammography medical outcomes audit program to calculate key performance metrics such as recall rates and cancer detection rates. Breast density quantification could be included in individual radiologist dashboards and in yearly practice audit information regarding false negatives and interval cancers.

13. Information on Context of QIB: Reliability, Confidence Intervals, Quality Control

a. Reliability and Confidence Intervals

Reproducibility describes the agreement between measurements taken on the same subject but with different imaging methods (e.g. different vendors, analysis software) (43). It is a critical component in a biomarker's technical performance capability, establishing the basis for the biomarker to diagnose, prognose, assess change over time, and in clinical trials for the biomarker to be used for patient selection and treatment monitoring.

The reproducibility coefficient (RDC) is a metric used to describe a biomarker's reproducibility. Differences between two serial measurements in the range of $-RDC_{0.95}$ to $+RDC_{0.95}$ are interpreted as differences expected due to measurement variability with some level of confidence (usually 95%), whereas differences outside the range are likely not due to measurement variability and might represent a biological change (44). RDC is best measured in clinical test-retest studies.

Reproducibility can be assessed by comparing output from an initial processing run and a second processing run on the same subject (e.g. comparison between screening mammography and diagnostic mammography for recalls), although other designs have been reported in the literature (e.g. Left vs Right breast; MLO vs CC view). Agreement between repeat measurements on the same subject can be quantified by the within-subject mean absolute deviation or the within-subject standard deviation, from which the RDC can be derived. Factors that may affect reproducibility include the presence of breast implants and prior surgical procedures.

There is limited literature reporting the RDC of breast density measurements (**Table 3**). Note that measures of correlation (e.g. Pearson's correlation coefficient) do not describe reproducibility.

Table 3: Reproducibility of volumetric breast density measurements

Software	Reported reproducibility of volumetric breast density measurement	Derived $RDC_{0.95}$ estimates
Transpara Density 1.0.0	Mean absolute deviation of 1.1-1.2%[1].	RDC~2.2-2.4%
Volpara TruDensity	Absolute difference in means of 2.7%[2] Within-breast standard deviation of 0.99%[5]	RDC~5.3% RDC~2.7%
Insight BD	Mean absolute deviation of 1.5-2.8%[3].	RDC~2.9-5.5%
Quantra	Mean absolute deviation of 1.91%.[4] Within-breast standard deviation of 1.64%[5]	RDC~3.7% RDC~4.5%
Cumulus ABD Cumulus V	Within-breast standard deviation of 3.32%[5] Within-breast standard deviation of 3.59%[5]	RDC~9.2% RDC~9.9%

[1]Comparison of MLO to CC view of same breast, as well as left vs right breast [Screenpoint Medical B.V. 510(k) premarket summary].
[2]Comparison of DM to DBT acquisitions [Tromans C, Highnam R, Morrish O, Black R, Tucker L, Gilbert FJ. Volumetric breast density estimation on conventional mammography versus digital breast tomosynthesis. Scientific Exhibit, 2014, Poster C-0363].

[3]Comparison of DM to DBT acquisitions, MLO vs CC views, as well as left vs right breast [Siemens' Insight BD white paper].
[4]Comparison of serial DM acquisitions [Ko E, Kim R, Han B. Reproducibility of automated volumetric breast density assessment in short-term digital mammography reimaging. Clinical Imaging 2015; 39:582-586] (45).
[5]Comparison of same-day, different-technologist DM acquisitions [Alonzo-Proulx O, Mawdsley G, Patrie J, Yaffe M, Harvey J. Reliability of automated breast density measurements. Radiology 2015; 275: 366-376] (46).

b. Quality Control

Technical parameters of mammographic imaging may influence breast density which emphasize the importance of good quality control and assurance required by MQSA regulations (47). Key parameters include breast positioning, compression, and motion.

Only the portions of the breast that are included in the images can be utilized by the breast density software system. Adequate breast positioning should maximize anatomic coverage (47). The CC view should include all medial and lateral breast tissue, including the retroglandular fat and often includes a portion of the pectoral muscle on the posterior edge. The MLO view should include the axillary tail, an open inframammary fold, and visualize the pectoralis major muscle as a convex curve or straight line. The length of the posterior nipple line on the CC view should be within 1 cm of the length of the posterior nipple line on the MLO view. The nipple should be in profile in at least one view of each breast. Skin folds should be minimal or absent. There should be no imaging artifacts (e.g. deodorant).

Breast compression is another key technical factor that may affect breast density measurements by automated software (48-51). Compression is important to minimize motion blur and separate overlapping tissue. Motion blur can limit spatial resolution and image sharpness (47). The study by Lau et al found that variations in compressed breast thickness and tube voltage (kVp) can impact volumetric breast density, with compressed breast thickness being the main parameter (49). Other imaging physics parameters, such as tube current-exposure time product (mAs), filter thickness, detector gain, detector offset, and image noise, had limited effect on volumetric breast density estimation (49). The type of compression paddle used may also influence breast thickness. For instance, flexible paddles can tilt when compressed leading to variation of the breast thickness and to errors in volumetric breast density quantification if correction factors are not used (52). Furthermore, increased compressed breast thickness can reduce mammographic sensitivity (53). Thus, it is important to consider quality control factors, particularly breast compression, when evaluating different algorithms for automated breast density quantification and for longitudinal studies tracking accuracy over time.

14. Informatics Considerations

Breast density software systems typically utilize a cloud-based virtual machine to orchestrate the flow of information between the mammography unit, vendor software, and PACS/RIS. The virtual machine is set within institutional firewalls in order to meet security standards and pass institutional governance and utilizes DICOM and HL7 message standards to coordinate the flow of information between systems. Raw DM or DBT projection images are sent from the modality to the virtual machine. Vendor software embedded in the virtual machine processes the images and generates breast density assessment output. The density assessment output is sent by the virtual machine to the RIS and PACS, where healthcare professionals can view the results. Density software can also be contained on the modality workstation with processing of images occurring on the workstation rather than being sent to a cloud-based machine.

15. Stakeholders

Successful implementation of automated breast density quantification in clinical practice requires engagement from a broad network of multidisciplinary stakeholders. Each group brings unique expertise and perspectives that can facilitate standardization and adoption.

a. Patients and Patient Advocacy Groups

Breast density notification started through grass-roots patient efforts led by a women diagnosed with stage 3C breast cancer shortly after a negative mammogram with dense breasts (54). Patient advocacy led to Connecticut becoming the first state to enact a breast density notification law in 2009 and ultimately to the federal legislation that went into effect in 2024. Effective engagement of patients, care givers, and other advocacy groups are important to ensure that the clinical impact of automated breast density quantification meets patient needs and expectations for high value care as well expand access to individualized breast cancer screening and prevention strategies.

Unlike other exams in radiology, screening mammography is unique in that patients who are asymptomatic and over the age of 40 years old can self-refer without requiring a physician order for scheduling. Patients are the initial driver and ultimate stakeholder for which the effect of breast density on breast cancer risk and mammographic sensitivity have the most significant impact. Automated software may provide a more standardized, objective, reproducible assessment for consistent messaging to patients to help them make informed decisions about supplemental screening.

There are several patient advocacy groups focused on breast density. Some of these groups include My Density Matters, Are You Dense Advocacy, DenseBreast-info, and Operation Breast Density. Their goals include raising awareness through public and healthcare provider education, advocating for legislative changes regarding breast density notification and insurance coverage for supplemental screening. Advocacy groups also focus on promoting personalized, risk-based screening to improve early breast cancer detection and patient outcomes.

b. Radiologists

Radiologists who interpret mammography are essential stakeholders for the integration of automated breast density quantification into clinical practice. They are the immediate end-user and are critical for demonstrating how adjunct quantitative measures may improve risk stratification for supplemental screening. Automated population of breast density into the mammography report can facilitate shorter turn-around times for interpretation and reporting and provide an objective method for reducing variability.

Imaging centers and radiology practice groups are also key stakeholders in practice-level decisions to pilot implementation, refine workflows, and provide feedback on software performance.

c. Radiology Residents and Breast Imaging Fellows

Post-graduate trainees in radiology represent the future workforce who are faced with increasing demands of clinical volume with an aging population. With increased longevity and recent change in the U.S. Preventive Services Task Force shifting the start of screening mammography from 50 to 40 years old (55), screening mammography volumes are expected to increase. Consequently, long-term investments to equip the next generation of radiologists with automated tools to improve workflow efficiency that also benefits patient care are paramount.

d. Technologists

Technologists control critical image quality parameters during acquisition that factor into the accuracy of breast density quantification and ensure images are adequate for diagnostic interpretation. Through patient preparation, they explain the imaging exam, answer questions, ensure patient comfort, and reduce patient anxiety to minimize motion artifact. Through patient positioning, technologists ensure proper breast tissue coverage to maximize visualization. Appropriate compression of the breast is essential for image quality as

well as consistent exposure settings. Technologists perform regular quality control testing of mammography equipment, troubleshooting technical issues, and maintaining safety standards. Furthermore, first-hand operational experience and insight from technologists are key for successful rollout of enhancements for workflow efficiency that benefit both patients and radiologists.

e. Medical Physicists and Imaging Scientists

Clinical medical physicists perform quality assurance testing on mammography equipment to ensure high quality images necessary for accurate measurement of breast density. Imaging scientists are essential in technology development and testing for image acquisition, processing, and quantification methods that are robust, reproducible, and clinically meaningful. Innovative tools have been developed by medical physicists and imaging scientists for fully automated breast density quantification using physics-based models to provide objective measures of the volume of dense breast tissue on mammography.

f. Referring Healthcare Providers

Primary care providers (e.g., family medicine, internal medicine, OB/Gyn) play an important role in mammography as they are responsible for discussing screening recommendations with asymptomatic patients. They provide an initial individualized assessment of breast cancer risk, including family history and other risk factors, to determine when to start screening mammography. Furthermore, they evaluate patients with breast symptoms and perform clinical breast exams to determine whether diagnostic mammography is indicated.

In the mammography notification letter following mammography for patients with dense breasts, patients are directed to talk to their healthcare provider about breast density, risks for breast cancer, and their individual situation. Primary care providers will receive breast density information through the standard clinical radiology report and are responsible for additional discussion with the patient regarding formal breast cancer risk assessment and supplemental screening tests in patients with dense breasts.

Multidisciplinary healthcare providers in high-risk breast clinics (e.g., breast surgeons, medical oncologists, nurse practitioners, genetic counselors) collaborate to create enhanced personalized screening plans and risk-reducing strategies. These providers use various risk assessment models, some of which, include breast density as a risk factor.

Breast cancer specialty care teams (e.g., breast surgeons, medical oncologists, radiation oncologists) will also be referring their patients for mammography. These providers may be asked by their patients to explain the clinical significance of breast density and whether additional screening is advised. For example, the American College of Radiology recommends screening breast MRI for patients with a personal history of treated breast cancer who have dense breasts (56).

g. Medical Professional Societies

Radiology professional societies are key stakeholders. The American College of Radiology (ACR) publishes the BI-RADS Manual which includes guidance on overall reporting standards, including breast density (6). The BI-RADS Committee could discuss whether clinical radiology reports should include in the technique section if breast density software was used. Another discussion topic would be if volumetric breast density should be included in addition to the required categorical assessment of breast density. The ACR could also review evidence for the current breast density reporting standard and encourage research where there are gaps (e.g., reporting density from synthetic 2D mammogram images).

RSNA, ARRS, and the Society of Breast Imaging (SBI) could also help educate their members (general radiologists and breast imaging radiologists) regarding breast density quantification and clinical implementation.

Other medical professional societies may help disseminate educational information to their members who are referring healthcare providers. These groups may include the American College of Physicians (ACP), American Academy of Family Physicians (AAFP), American Geriatrics Society (AGS), National Comprehensive Cancer Network (NCCN), American Society of Breast Surgeons (ASBS), and American Society for Radiation Oncology (ASTRO).

The ACR is also responsible for publishing appropriateness criteria for supplemental breast cancer screening based on breast density (34). In addition to the ACR, other professional groups that issue guideline recommendations for breast cancer screening are critical stakeholders. These groups may include the United States Preventive Services Task Force (USPTF) and the American Cancer Society (ACS).

The American Medical Association (AMA) is also an important stakeholder for reimbursement as they appoint the CPT Editorial Panel responsible for maintaining and updating the CPT code set.

h. Informatics Teams

Informatics teams are critical for effectively implementing mammographic breast density quantification into the clinical workflow. They function to integrate the breast density software tools into the clinical interpretation process by the radiologist and ensure seamless transfer of QIB data to the structured radiology reporting system and EHR (see earlier sections). Engagement of informaticists is also key for development and implementation of decision-support tools that could create pending orders for supplemental screening modalities for referring healthcare providers.

i. Insurance

Insurance providers and other payers shape access and reimbursement policies that ultimately dictate affordability and, by extension, access to advanced technologies in patient care. For these reasons, it is essential to convey to insurance providers how broader deployment of quantitative breast density measurement may improve the correct identification of women with dense breasts with indications for supplemental screening. Further research is essential to generate the evidence linking quantitative assessment of breast density to changes in clinical management and patient benefit, which is essential for regulatory and payer acceptance.

j. Industry Vendors

Vendors are key stakeholders in the implementation of quantitative breast density assessment, as they provide the hardware, software, and technical support to enable high-quality, accessible image acquisition and analysis. Their collaboration with clinical teams and other users is essential to ensure compatibility and to facilitate seamless integration into clinical workflows. Vendors also play a crucial role in training users, maintaining equipment, and driving innovation through ongoing product improvement.

- Software developers – create robust quantification pipelines, automate workflows, commit to interoperability
- DM/DBT system manufacturers – ensure input image data compatibility with various breast density software systems
- Phantom manufacturers
- PACS vendors – allow and optimize display of breast density results

- Reporting system vendors – ensure ease of automatic population of breast density data into structured reports and integration with EHR-based risk assessment models.

16. Financial Implications

For patients, screening mammography is considered part of preventive care and is fully covered by insurance without a copay, deductible, or coinsurance. The Current Procedural Terminology (CPT) billing code for standard bilateral screening mammography, including computer-aided detection, is 77067 with an add-on code of 77063 for DBT. This covers the technical fee of image acquisition and professional fee of image interpretation. There is no additional CPT code or separate reimbursement for the use of automated breast density quantification software. To justify reimbursement, supporting evidence is needed of how use of breast density quantification improves inter-reader reliability and ultimately changes clinical management.

The process for a CPT code change involves a formal application to the American Medical Association (AMA) which undergoes review by the CPT Editorial Panel (57). Next steps involve the Relative Value Scale Update Committee (RUC) to determine an accurate relative value recommendation for the service and valuation process and finalization by CMS. Newly approved codes may take up to 2 years to become effective. The most recent CPT Editorial Panel meeting held in September 2025 included an application for establishing Category I code 77X11 for augmentative analysis for volumetric breast density. This application was rejected by the Panel (https://www.ama-assn.org/system/files/sept-2025-summary-of-panel-actions.pdf).

Clinically Meaningful Algorithmic Analyses (CMAA) is a potential new category of CPT codes under development by the AMA. These AI-related codes describe services in which algorithms process clinically relevant data, such as images, to produce actionable results that directly impact patient care and outcomes. If approved, this could be a potential avenue for reimbursing automated breast density quantification.

Downstream financial implications include the potential effect on utilization of supplemental screening modalities based on breast density. For example, some states have laws mandating insurance coverage for supplemental screening for women with dense breast tissue. Other states have introduced similar legislation. At the federal level, the Find It Early Act bill (H.R. 6182, S.1410) has been introduced that would require insurance to cover supplemental screening for women with dense breasts.

Software costs for automated breast density quantification are variable and may be influenced by institutional negotiations. Costs may also be bundled into larger software packages that include other AI tools for breast cancer detection. Options for financing can include a one-time upfront fee or an annual fee based on expected volumes of exams (software as a subscription).

17. Gaps or Barriers and Potential Solutions in Technology

a. Lack of “ground truth” to compare accuracy of different software systems

Automated breast density quantification correlates with measurements made with phantoms, MRI, and radiologist visual assessment (58, 59). However, a physical ground truth is not possible.

b. Limited data comparing breast density measurement across different software systems

Technical differences in the methodology for breast density quantification exist between different software systems. Thus, although correlation exists, the different systems do not produce identical results (58). It is important to be aware that there are different volumetric breast density cutoff values for dense versus non-dense depending on the software (60). Furthermore, the same software system will be required for longitudinal assessments of breast density (61).

c. Limited data comparing breast density measurement obtained using different mammographic imaging systems

Different mammographic imaging systems use vendor-specific technology for image acquisition which may affect breast density quantification. A recent study by Wagner et al demonstrated that volumetric breast density distributions differed between 3 commonly used mammographic devices (Siemens, GE, Hologic) (62). These authors present a solution that use percentile matching to avoid bias between system vendors for identifying women with similar breast density (62). However, this study did not account for patient population differences. An earlier study by Damases et al found that mammographic density measurements are not affected by different manufacturers' mammographic imaging systems (63).

d. Limited data on consistency of breast density quantification over time

Since patients will receive notification of their breast density, it is important to minimize changes in breast density categories from dense to non-dense occurring year-to-year that are due to software variability and not a true biologic change. Studies by Holland et al and Holley at al. compared the consistency of breast density assessment in serial screening mammograms obtained using automated mammographic density measurements with the consistency of radiologist's visual assessment (31, 42). Both studies found that more women stay in the same breast density category over time when the classification was done with an automated density software system (42).

18. Gaps or Barriers and Potential Solutions in Motivation and Resources for Implementation

There is incomplete utilization of currently available commercial breast density software. A key barrier to widespread implementation of automated breast density quantification in the clinical setting in the United States remains the lack of billing codes and reimbursement to offset the added software costs and personnel support. Continued efforts are needed in exploring different reimbursement options as described earlier.

More cost-effectiveness studies of density-based breast cancer screening strategies could also better inform clinicians, patients, and policymakers as they weigh the potential role of breast density in making decisions regarding breast cancer screening (64, 65).

Competing needs and requests for IT support at the local level represent another barrier to implementation. The use of AI software tools in breast imaging and other aspects of radiology continue to increase which add to backlogs of institutional IT requests. Supporting physician champions to partner with IT for implementation guidance and prioritization may facilitate the process. Departmental support is also needed for career development of radiologists to become boarded in medical informatics to serve in physician champion roles.

19. Potential Timeline Needed for Implementation

An individual practice may need 6 to 12 months for clinical implementation of automated breast density quantification. This timeline may vary by practice type and by institution. Initial time is needed for budget planning and financial approval. Institutions may also require a technology and security review by institutional governance groups.

A broader timeline for widespread clinical implementation remains a work in progress and depends on tackling the gaps and barriers described above. To advance along this timeline, all relevant stakeholders identified above must be proactively engaged. These phases will likely overlap, and feedback loops will be critical: lessons from early adopters should inform the overall process, and implementation challenges should feed into future roadmap revisions.

Phase 1 is pilot clinical integration and early adoption. This is the current status of implementation. This phase depends on many factors including radiologist engagement, vendor support, and informatics integration.

Phase 2 is broad clinical adoption and reimbursement. We anticipate this to take 3-5 years. This phase depends on evidence generation including cost-effectiveness, payer engagement, and policy advocacy. Increased clinical implementation of AI-based mammography tools may facilitate this process as automated breast density quantification is frequently part of a larger software package.

Subsequent phases focus on clinical integration with personalized risk assessment tools and supplemental screening referral processes. If supported by strong clinical trial data, another integration phase may involve quantitative breast density in chemoprevention and adjuvant therapy decision algorithms (initiation and longitudinal treatment monitoring). This phase may be dependent on establishment of quantitative mammographic breast density as an FDA-qualified biomarker (see earlier section).

20. Metrics for Tracking Success

Several metrics would be useful to collect for individual practices to internally assess the success of clinical implementation and to share with other practices considering adopting this change. Monitoring these metrics may ensure that the automated software provides reliable, consistent, and clinically actionable data.

Performance accuracy and agreement metrics:

- Reproducibility (See earlier section)
- Quality control pass rates

Clinical workflow and operational efficiency metrics:

- Implementation time which includes the time needed for purchasing, IT approval, installation, and integration into the PACS.
- Processing time needed by the software to generate the density report and auto-populate the mammogram report.
- Percentage of reports in which the radiologist manually changed the automated breast density assessment.

Clinical impact and outcome metrics:

- Supplemental screening referral rates pre and post implementation
- Effect on breast cancer risk assessment models

Information regarding use of automated breast density quantification software could also be added to standard data fields for the ACR National Mammography Database for future studies on utilization and clinical impact.

21. Future research and areas of further work for the QUIC Breast Cancer Group

The current roadmap represents an important initial step toward the clinical integration of automated breast density quantification. The QUIC Group has identified several areas of future work, as outlined below.

Survey on Implementation of Breast Density Quantification
The group aims to conduct a large-scale survey to assess how breast density quantification is being adopted in routine clinical practice. This will include variability in software platforms, workflows, and reporting practices across institutions. Barriers and facilitators to adoption, as discussed earlier, will also be included. This effort will provide real-world data to guide ongoing quality improvement and education initiatives.

Breast Density Quantification in Breast Cancer Risk Assessment Tools

Addition of mammographic breast density measures to conventional risk factors can improve risk stratification (30). In the case-control study by Brentnall et al, VPD was not more informative than visual BI-RADS 4th Edition density assessment but provides a practical advantage of full automation (30). In addition, in a recent study by Kaul et al, use of VPD with Tyrer-Cuzick version 8 resulted in better model calibration for invasive breast cancer and overall breast cancer (invasive + DCIS) than BI-RADS density for 5-yr risk prediction (66). Further work in this area includes:

- Compiling evidence from studies that have used volumetric breast density in risk assessment calculators to establish whether quantitative measures can improve predictive accuracy of risk assessment tools.

Breast Density Quantification in Chemoprevention and Adjuvant Endocrine Therapy Response Assessment

As risk-reducing strategies continue to evolve, there is an urgent need to determine whether breast density quantification can serve as a reliable biomarker for predicting efficacy and assessing early response to treatment, particularly with tamoxifen (67-69). For example, the International Breast Cancer Interventional Study 1 (IBIS-1) for women at elevated risk for breast cancer was a randomized control trial of tamoxifen or placebo for chemoprevention (70, 71). The study found a 63% reduction in breast cancer risk in women who experienced at least a 10% reduction in mammographic density (70, 71). Furthermore, changes in mammographic breast density can also be a biosensor of tamoxifen effectiveness and adherence in the adjuvant setting for patients with a personal history of breast cancer (72). A decrease in mammographic breast density during adjuvant tamoxifen therapy has been shown to be associated with improved long-term survival (73). Future research includes:

- Reviewing evidence from clinical trials that have used quantitative breast density reduction as a surrogate endpoint for 1) a reduction in breast cancer incidence in the chemoprevention setting and 2) a reduction in breast cancer-specific survival in the adjuvant setting.
- Establishing whether quantitative measures can guide treatment continuation or discontinuation decisions.

Breast Density Quantification by Other Imaging Modalities

Breast density can also be quantified using other breast imaging modalities (74). MRI techniques, such as proton density fat fraction, have been studied for breast density measurement (75-77). Ultrasound tomography (UST) can provide whole-breast sound speed as a measure of breast density (78, 79). Automated breast density mapping has also been developed using low-power microwave radiofrequency scanning which detects dielectric differences between fat and glandular tissue (80). Quantification of breast density based on Hounsfield units (HU) using breast CT has also been reported (81, 82). These approaches remain investigational at this time.

Potential Biomarkers of Breast Cancer Risk using Vascular-Based and Molecular Imaging

Research into novel imaging-derived biomarkers in risk assessment, diagnosis, and treatment monitoring of breast cancer continues to evolve (83, 84). Potential areas of expansion for the QUIC Group include automated, quantitative assessment of:

- Background parenchymal enhancement on MRI and contrast-enhanced mammography.
- Background parenchymal uptake on MBI and FDG PET.

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