A Comparative Study of Volumetric and Area-Based Breast Density Estimation in Digital Mammography: Results from a Screening Population

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Abstract. We compare a volumetric versus an area-based breast density estimation method in digital mammography. Bilateral images from 71 asymptomatic women were analyzed. Volumetric density was measured using *Quantra*^{TM} (*Hologic Inc.*). Area-based density was estimated using *Cumulus* (*Ver. 4.0, Univ. Toronto*). Correlation and regression analysis was performed to determine the association between *i*) density from left versus right breasts and *ii*) volumetric versus the area-based measures. Volumetric breast density measures are strongly correlated but statistically significantly different than the area-based measures (r=0.79, p<0.001). Regression demonstrates a significant non-linear association (R^2=0.70, p<0.001). The density correlation between right and left breasts is also strong for both methods, (r≥0.95, p<0.001). The strong association with the area-based density measures suggests that volumetric breast density could potentially also aid in breast cancer risk estimation. The observed non-linear association between volumetric and area-based estimates may have implications for risk stratification in clinical practice.

Keywords: Volumetric breast density, digital mammography, breast cancer risk.

1 Introduction

Growing evidence suggests that breast density is an independent risk factor for breast cancer, the strongest known attributable risk factor after age [1, 2]. Currently, the most commonly used methods to quantify breast density rely on semi-automated image thresholding techniques to segment the area of the dense tissue in mammograms [3]. Mammographic breast density is then estimated as the percent of dense tissue area within the entire breast [1]. Although useful for breast cancer risk estimation, these methods are highly subjective and difficult to standardize [1, 3-5], a factor limiting their translation for breast cancer risk assessment in the general population. In addition, they do not provide an estimate of true volumetric breast density but a rather rough area-based estimate measured from the mammographic projection image

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of the breast. Methods are now under development to estimate volumetric breast density from mammograms by incorporating image acquisition physics and breast thickness information [6-10]. Knowing that the risk of breast cancer is mainly associated with the total amount of fibroglandular tissue in the breast (where cancer generally originates), volumetric measures of breast density hold the promise to also provide more accurate measures for breast cancer risk estimation [11].

Studies have demonstrated the reproducibility of different volumetric breast density methods and strong associations with known breast cancer risk factors [7, 12]. However, most studies published to date have been performed using digitized screen-film mammograms and have not demonstrated a clear advantage of the volumetric versus the area-based density measures in breast cancer risk estimation [10, 13]. Methods applied directly to digital mammographic images hold the promise to provide more accurate quantitative measures and fully-explore the potential role of using volumetric breast density assessment in breast cancer risk estimation [14, 15].

We performed a study to evaluate a new volumetric method for breast density estimation in digital mammography (DM) in comparison to the commonly used area-based density estimation method for a screening population of women. Our goals were to evaluate the consistency of the volumetric method, compare it to the commonly used area-based approach, and investigate the nature of the association between the volumetric and the corresponding area-based breast density estimates. The results of this investigation could have significant implications on the implementation of density-based breast cancer risk stratification in clinical practice.

2 Methods

Bilateral DM images from 71 asymptomatic women (age 34-75 yrs, mean 54 yrs) presenting for annual screening mammography were retrospectively collected and analyzed under HIPAA and IRB approval from a separate IRB-approved breast cancer screening clinical trial that has been completed in our department[1] [16]. All women were study volunteers who signed informed consent. Digital mammography imaging was performed with a GE DS FFDM system (GE Healthcare, Chalfont St. Giles, UK) at 0.1 mm/pixel resolution and 12 bit gray-levels. Image post-processing was performed with the GE *PremiumView*™ algorithm [17].

Volumetric breast density (VD%) estimation was performed using *Quantra*™ (*Hologic Inc.*), an FDA approved and commercially available fully-automated software based on an extension of the Highnam & Brady method [6] for digital mammography [14]. Briefly, *Quantra*™ estimates the thickness of the fibroglandular breast tissue above each pixel in the image and aggregates these pixel-wise estimates to compute the total volume of fibroglandular tissue in the breast (Fig. 1). Through a similar process, *Quantra*™ considers the entire imaged breast outline, compensating for those portions of the breast that were not uniformly compressed, to estimate the entire volume of the breast. The estimated fibroglandular tissue volume is then divided by the total breast volume to calculate the volumetric percentage of fibroglandular tissue in the breast (*i.e.*, VD%) [18].

[1] GE Healthcare Protocol Number 804380, Penn PI: E.F. Conant.

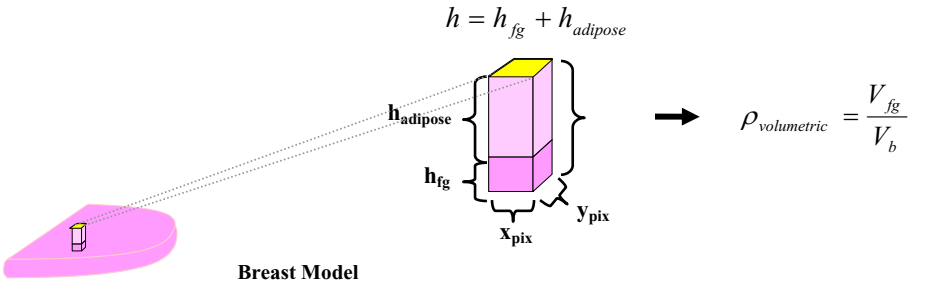

Fig. 1. The main idea of the *Quantra*^{TM} (*Hologic Inc.*) method for estimating pixel-wise breast thickness and deriving a volumetric density measure.

To compare to the commonly used area-based breast density measures, breast percent density (PD%) was estimated in the *PremiumView*^{TM} post-processed DM images by an experienced reader, using the semi-automated image thresholding technique of *Cumulus* (*Ver. 4.0, Univ. Toronto*) [3].

The Student's pair-wise t-test was applied to compare the means of the breast density distributions obtained by the volumetric and the area based methods. The Pearson correlation coefficient (r) was computed and linear regression analysis was performed to determine the degree of association between the density estimates from left and right breasts. In addition, both linear and non-linear regression was performed to model the association between the volumetric and the area-based measures.

3 Results

The volumetric breast density (VD%) measures obtained with *Quantra*^{TM} are strongly correlated (r=0.79, p<0.001) but statistically significantly different than the

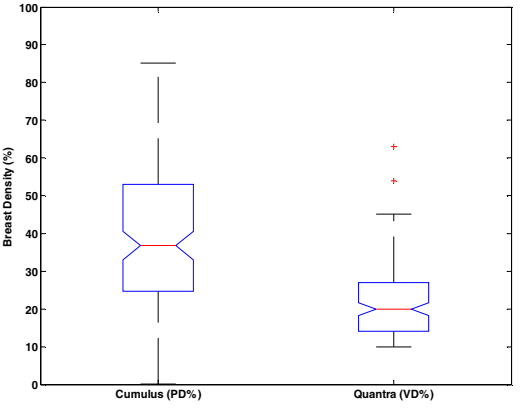

Fig. 2. Box-plots for the distributions of the area-based *Cumulus* percent density (PD%) measures and the *Quantra*^{TM} volumetric density (VD%) measures

corresponding area-based breast percent density (PD%) measures obtained with *Cumulus* ($p<0.001$). As expected, volumetric density estimates (mean=21.94%) are lower than the corresponding area-based estimates (mean=37.97%) (Fig. 2).

When investigating separately for each method the breast density correlations between left and right breasts, both methods are highly consistent, as evidenced by the strong and statistically significant correlations and the linear regression fits (Fig. 3).

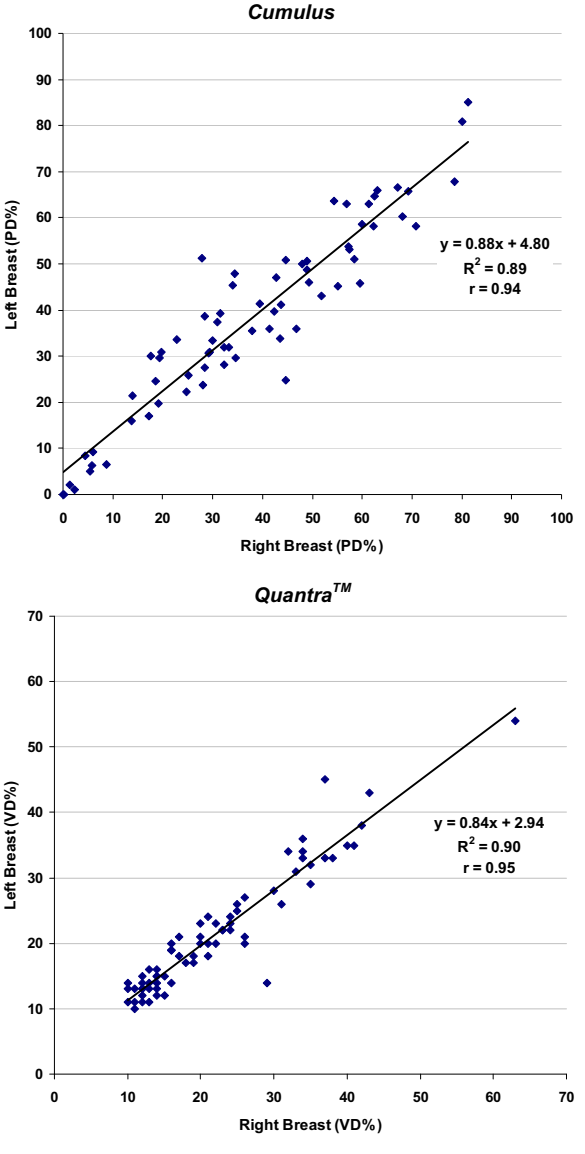

Fig. 3. Linear regression fits between right and left breasts for the *Cumulus* area-based breast percent density (PD%) (up) and the *Quantra*™ volumetric density (VD%) (down)

The *Quantra*™ method had a slightly higher, but significantly different, correlation coefficient than the *Cumulus* method for the volumetric breast density correlation between the right and left breasts ($r = 0.95$, $p<0.001$).

To model the association between the volumetric and the corresponding area-based density measures, both linear and non-linear regression analysis was performed (Fig. 4). Both models show statistically significant associations ($p<0.001$), with the non-linear regression indicating a stronger second-degree polynomial fit ($R^2 =0.70$).

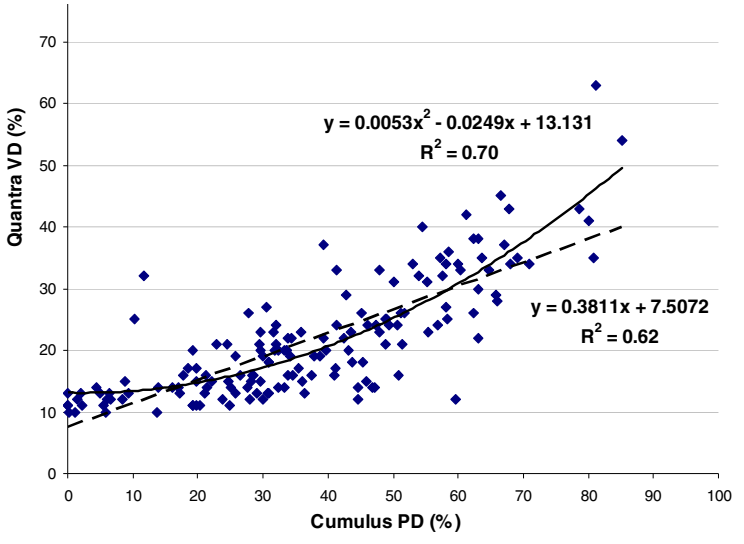

Fig. 4. Linear and non-linear regression fits between the *Quantra*™ volumetric (VD%) breast density measures and the *Cumulus* area-based percent density (PD%) estimates.

4 Discussion and Conclusions

Our study performs a comparative evaluation of the first FDA approved fully-automated software for volumetric breast density estimation in digital mammography (*Quantra*™, *Hologic Inc*.) versus the current gold-standard area-based breast density estimation method (*Cumulus*, *Ver. 4.0, Univ. Toronto*) for a screening population of women. The strong correlation observed between right and left breasts indicates that volumetric breast density measures computed with *Quantra*™ can provide consistent fully-automated measures of breast density for women undergoing mammographic screening. The strong association observed between the volumetric and the corresponding area-based density measures, shown by several studies to correlate with breast cancer risk [1], supports the hypothesis that volumetric breast density measures could also aid in breast cancer risk assessment.

However, the observed non-linear association in our study (Fig. 4) also suggests a potential non-linear relationship between the corresponding volumetric and the area-based risk stratification levels, which could ultimately have implications for risk stratification in clinical practice. This concept is illustrated in Figure 5. Further work is underway to

validate these findings with larger clinical studies and to fully investigate the association between volumetric breast density measures and breast cancer risk. Such larger studies will also help to determine more accurately the risk stratification levels using the volumetric versus the area-based density estimates. Our long term hypothesis is that quantitative methods for measuring volumetric breast density can provide more accurate measures of density and ultimately result in more accurate measures to assess breast cancer risk. In addition, fully-automated methods can alleviate the subjectivity of the currently used semi-automated techniques and accelerate the translation of density-based risk stratification in clinical practice.

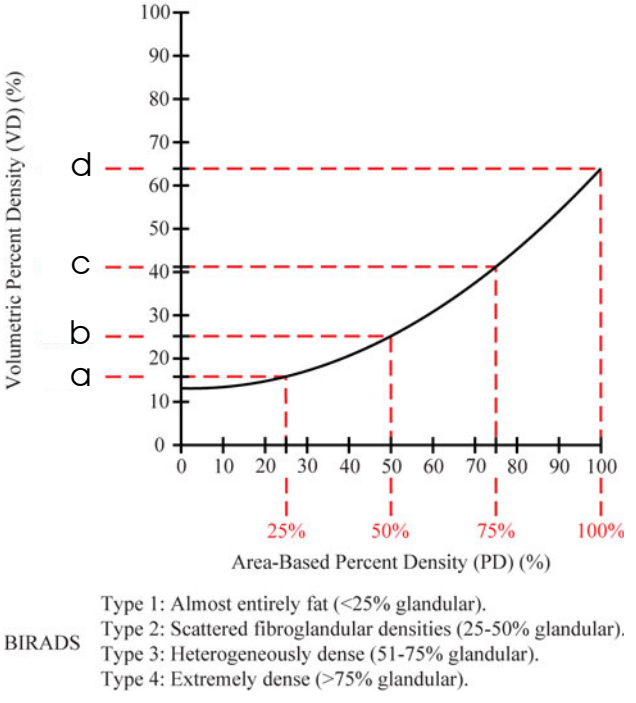

Fig. 5. An illustrative example demonstrating a non-linear association between the established area-based ACR BIRADS density categories for breast cancer risk stratification [19] and the corresponding volumetric density categories based on the specific non-linear trend observed in our study. Larger clinical studies will determine more accurately the corresponding volumetric density risk stratification levels, denoted here for illustration purposes as “a”, “b”, “c”, and “d”.

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