Topical Paper

# BREAST DENSITY:
# IT ISN'T JUST DENSITY

## Introduction

As breast density increases, the risk of developing breast cancer increases[1-2], while the sensitivity of mammography decreases[3]. More specifically, mammographic sensitivity decreases by as much as 16% for dense breasts[1] – and 40% of women will have dense breasts at some point in their lives[2]. Additionally, women with a BI-RADS 4 breast density have over four times the relative risk of developing breast cancer as compared to those with BI-RADS 1[3]. Consequently, current guidelines (e.g., NCCN) suggest that additional screening modalities such as ultrasound or magnetic resonance imaging be considered for some women with dense breasts.

In clinical practice, radiologists visually assess breast density, assigning each patient an ACR BI-RADS composition category of a, b, c, or d[4]. Unfortunately, visual assessment is subjective, and thus, suffers from significant intra- and inter-observer variability[5-7]. That is, BI-RADS categories for the same patient assessed by different readers or by the same reader at different times, will vary significantly. To mitigate this variability, several companies have developed automated methods for measuring breast density.

## Automated Breast Density Assessment

Automated approaches for assessing breast density can be stratified into two distinct methodologies.

The first approach measures the physical absorption of X-rays (given by the pixel values in the mammogram) to estimate the percent volume covered by fibroglandular tissue[8]. The percent volume is then mapped to a score from a to d, analogous to the BI-RADS category. Such volumetric methods have inherent limitations. First, pixel values in the mammographic images may not reflect the actual absorption of X-rays[9], decreasing the accuracy of – or completely invalidating – the volumetric assessments. For example, volumetric measurements from mammograms imaged using a Lorad Selenia are less accurate than those from the GE Senographe; the Selenia compression paddle can tilt during compression, whereas the Senographe paddle remains rigid[10]. Furthermore, the pixel values of both standard for-presentation images and synthetic C-view images are not directly related to the X-ray attenuation. Second, since BI-RADS categories are defined not only by the percentage of the breast covered by dense tissue, but also by the dispersion of this tissue throughout the breast, volumetric methods are inherently limited in their ability to accurately reproduce BI-RADS scores.

The second approach assesses breast density by examining the mammographic texture and appearance of the dense tissue, emulating – quantitatively – the approach advocated by the ACR. The advantage of this approach is that in addition to considering the percent breast density, it also analyzes the texture and dispersion pattern of the tissue. To better understand this, consider Figure 1. This figure depicts two mammograms with identical percent breast densities; however, the second mammogram – with its single large focus of density – is more likely to obscure a cancerous mass than is the first mammogram – with its smaller, scattered densities.

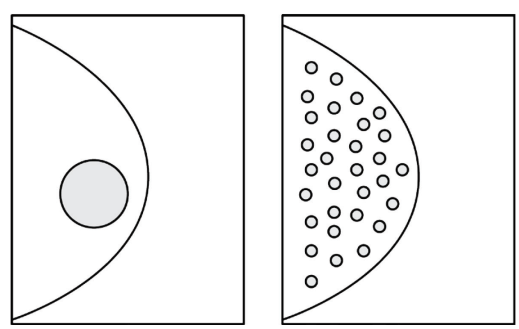

*Figure 1. Mammograms with same density, but with different masking properties.*

Interestingly, in our own study, we noticed that in 4% of all pairs of cases in which the BI-RADS assignments (of the two cases) differed by one category, the difference in breast density (as assessed by radiologists) was inversely proportional to the difference in BI-RADS category. This suggests that percent breast density alone is insufficient to correctly assign BI-RADS categories to mammograms. Currently, the PowerLook® Density Assessment (iCAD Inc.) is the only commercially available, FDA-approved system that analyzes the texture and dispersion pattern of tissue.

## Accurate and Consistent Density Estimates Using Automated Breast Density Assessment

For automated breast density systems to be efficacious in a clinical setting, they must yield accurate and consistent results. Initial studies support such efficacy. Gweon, et al.[11], reported a weighted kappa statistic of 0.54 – indicating moderate agreement[12] – between the Volpara density grade (Matakina Technology) and a consensus of three radiologists' BI-RADS categories. A similar analysis of PowerLook Density Assessment (reported in an FDA clinical study) yielded a weighted kappa statistic of 0.64 – indicating substantial agreement[12] – between the PowerLook Density Assessment density grade and a consensus of 13 expert radiologists' BI-RADS categories. In a different study of 490 patients, the density estimates produced by PowerLook Density Assessment had less than half the variability of those produced by 10 radiologists.

## CONCLUSIONS

The significant intra- and inter-observer variability among radiologists can lead to the same patient receiving two different BI-RADS scores at two different examinations. To mitigate this possibility, researchers have created automated breast density systems, which can yield consistent, accurate density estimates. Unfortunately, all of these density products – with the exception of the PowerLook Density Assessment – do not follow the ACR BI-RADS lexicon. Instead, they assign categories using only percent breast density, disregarding tissue patterns. This limits their ability to accurately reproduce BI-RADS scores.

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