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T e breast consists mainly of two tissue components: f broglandular tissue and fat. Fibroglandular tissue is a mixture of f brous stroma and epithelial cells that line the ducts of the breast. In mammography, f broglandular tissue appearing bright is referred to as 'mammographic density (MD)'. Evidence from many studies has established the role of MD as an independent risk factor of breast cancer [1-9]. Change (increase or decrease) in MD overtime is also linked to change in cancer risk [10,11]. Additionally, breast morphology is also associated with breast cancer risk [12,13].

MD can be measured qualitatively or quantitatively. Qualitative methods include Wolfe criteria [14] and the Breast Imaging and Reporting Data System (BI-RADS) criteria [15]. More sophisticated methods assign di f erent scores, such as the six categories developed

of percent dense tissue area on mammograms, and most of studies were done using a Cumulus thresholding segmentation method [17-19]. Overall, two-dimensional (2D) MD su f ers from the problem of tissue overlap. T e woman's position and degree of compression may also lead to di f erent projection views, and thus di f erent measured densities. Limitations of 2D area-based measures have led research groups to develop volumetric measures of breast density [20-25]. However, researchers have found that volume density did not provide a better cancer risk predictor compared with the 2D MD measured by thresholding method [22]. In recent years, two automated volumetric density quantif cation tools (Quantra™ (http://www.hologic.com/en/breast-screening/volumetric-assessment/) and Volpara™ (http://www.volparadensity.com/)) have been developed and approved by the FDA. Whether those new analysis methods can provide stronger breast cancer risk estimates is being investigated.

In the breast densitometry community, there is a strong urgency to develop reliable quantitative density measurement methods that can predict individual patients' risks. Magnetic Resonance Imaging (MRI)-based analysis has received great attention [24,26-33], but its clinical role has not been proven yet. MRI provides a detailed three-dimensional (3D) distribution of f broglandular tissue that is not subject to the tissue overlap problem in mammography. It also allows for slice-by-slice segmentation of f broglandular and fatty tissues. A f er adequate segmentation procedures, the entire f broglandular tissue can be included without contamination with fatty tissue. E f orts in past years have led to the development of a novel computer-aided segmentation method for quantitative analysis of whole breast volume and breast density with 3-D MRI [34,35] and ref ned methods for evaluating the density morphological distribution pattern [36]. Several studies have compared the density measured by MRI and mammography. A study by Khazen et al. showed high correlation between MD and the density calculated from MRI (r=0.78); mammography, on the other hand, overestimated density by almost a factor of two [27]. Such results were expected given the nature of tissue projection on mammograms. It is therefore believed that the claims of risk and density changes based on 2-D images should be reevaluated [37]. 3-D MRI has been applied to study age- and race-related breast density di f erences [38] as well as breast density changes in patients receiving chemotherapy [39] and tamoxifen [40]. Although mammograms are less expensive than breast MRI, a recent article by Eng-Wong et al. [26] examining high-risk

premenopausal women receiving raloxifene found that MD did not show changes while MR breast density showed signi f cant reduction. Based on their f ndings, they suggested that MR breast density is more sensitive for detecting small changes, may provide a promising surrogate biomarker, and should be investigated further in breast cancer prevention trials.

In addition to MRI, emerging new technologies including optical imaging [41-46], ultrasound [47-49], digital breast tomosynthesis [50], dual energy imaging [51-53], and dedicated breast Computed Tomography (CT) [54-56] are being developed for assessing f broglandular tissue volume, percent breast density, and breast tissue compositions. Using optical imaging, researchers noted that dense breasts tend to contain a greater proportion of water, lipid, and total hemoglobin concentration, and therefore have greater scattering than fatty breasts [41-44]. A strong correlation was noted between MD and an optical index based on tissue composition and scattering parameters derived from optical measurements [45]. A study comparing the measurements of breast density using 3D automated whole breast ultrasound and MRI showed high correlation between breast density and breast volume quantif cation [48]. Digital Breast Tomosynthesis (DBT) is increasingly being used in clinical practice. A high correlation between percent density estimated by digital mammograms and central DBT projections was noted [50]. Another study, however, found that digital mammography overestimated breast density by 15.1% in comparison to DBT [57]. Another technology, dual energy imaging, expahiautomalogynomparing oheir f nd9b0 -537autoatp:7 images should be r

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