

## **Associations of dense and fatty breast-tissue complexity with breast cancer risk: Preliminary evaluation using imaging biomarkers driven by breast morphology**

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**Background** We investigate the potential different contributions of dense versus fatty breast tissue in breast cancer risk assessment, using quantitative imaging phenotypes of tissue complexity driven by breast morphology.

**Methods** Contralateral mediolateral-oblique (MLO) view digital mammograms from 106 women with unilateral invasive breast cancer and 318 age-matched controls were retrospectively analyzed. A previously validated algorithm was used to automatically segment the dense and fatty tissue areas within the breast and to estimate breast percent density (PD%). Parenchymal tissue characterization was performed using an automated framework, in which established tissue-complexity descriptors (i.e., a total of 34 texture features) are estimated in multiple regions defined by an anatomically-oriented breast coordinate, and are then weighted in their contribution by the underlying tissue composition of each region. Summary values of these texture measures over the entire breast region were calculated for two different weighting scenarios, i.e., when the dense tissue is more heavily weighted than the fatty tissue and vice-versa. Associations with breast cancer were evaluated using logistic regression and the area under the curve (AUC) of the receiver operating characteristic (ROC) was used to assess discriminatory capacity, where a baseline model including only PD% and adjusted by body-mass-index (BMI) was compared to a model augmented with our features.

**Results** Associations of tissue-complexity features were significantly higher when dense tissue regions were assigned higher weights than fatty tissue (AUC=0.85), compared to when fatty tissue was weighted more heavily (AUC=0.76,  $p<0.05$ ). Adding our breast-morphology-driven features to the baseline model increased discriminatory capacity (from AUC=0.72 to AUC=0.84,  $p<0.05$ ), which was not significantly different from the performance of texture features alone.

**Conclusions** Innovative imaging biomarkers representing the dense and fatty tissue complexity may hold a promising role in evaluating breast cancer risk profiles more accurately, thus augmenting tailored screening and prevention strategies for breast cancer.