Automated Quantitative Measures of Terminal Duct Lobular Unit Involution and Breast Cancer Risk—Letter

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We read with interest the recent article from Kensler and colleagues (1), "Automated measures of terminal duct lobular unit involution and breast cancer risk." This article represents an important first effort to use computational quantitative methods to assess age-related involution of breast tissue to predict breast cancer risk. However, we are concerned that their conclusion may prematurely limit the development of automated quantitative pathology methods to predict breast cancer risk.

Work in the Mayo Clinic Benign Breast Disease Cohort demonstrated that reduced levels of involution, broadly categorized visually, are associated with increased breast cancer risk, both in initial benign biopsies (2) and in serial biopsies when degree of involution does not increase over time (3). Importantly, a prior study from the Nurses' Health Study also confirmed that visually defined involution levels were associated with breast cancer risk (4). Morphometric measures of terminal duct lobular unit (TDLU) involution have also shown associations with breast cancer risk (5).

Thus, the effort by Kensler and colleagues to apply computational pathology to assess lobular involution in benign breast disease (BBD) biopsies to predict breast cancer risk represents an extension of prior work. Among controls, they found some expected associations between epidemiologic features and measures of TDLU involution, but they did not find the expected relationship between advancing age and increased involution among women ages <50 years nor an association with breast cancer. They concluded that "among Nurses' Health Studies women diagnosed with BBD, TDLU involution is not a biomarker of subsequent breast cancer." This conclusion seems premature, especially in light of their prior report demonstrating an association of breast cancer with visually assessed involution. Inconsistencies between their current and past report may reflect limitations of the measurement approach or the sample, rather than lack of a relationship between TDLU involution and risk.

Measuring TDLU involution is complex, and the use of computational pathology for this purpose is in its infancy. Given that TDLU involution reflects the amount and biological state of epithelium as a plausible marker of risk, we propose that accurate and unbiased methods to measure TDLU involution are important. Computational methods hold promise for transforming pathology diagnosis from an informed subjective activity to one that melds human expertise with objective, standardized, and reproducible measurements. We remain optimistic that work to integrate computational analysis of TDLU involution with molecular assays and radiologic features may enable a breakthrough in risk assessment, in which the tissue provides an integrated measure of risk.

Authors' Disclosures

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