

# Breast density, microcalcifications, and masses may be heritable traits

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An analysis of a large Swedish cohort revealed that breast density, microcalcifications, and masses are heritable features, and that breast density and microcalcifications were positively associated with a genetic predisposition to breast cancer, according to a study published in *Cancer Research*, a journal of the American Association for Cancer Research.

"Breast features identified through mammography are important for identifying women at high risk of developing breast [cancer](#) in the short term," said Natalie Holowko, Ph.D., postdoctoral researcher in the department of Medical Epidemiology and Biostatistics at the Karolinska Institutet in Stockholm. "It is important to understand the genetic determinants of these traits, as the underlying mechanisms for their association with breast cancer is not well understood."

Holowko explained that the heritability of breast cancer is roughly 30 percent, and previous studies have estimated that the heritability of breast density is roughly 60 percent. While breast cancer and breast density have overlapping [single nucleotide polymorphisms](#) (SNPs), the heritability of other mammographic features, such as microcalcifications, masses, or breast density change, have not been previously reported, she noted. "We wanted to study the heritability of these traits, as this could help us identify important loci for breast cancer susceptibility, which could be used to better identify women who are at increased risk for developing breast cancer," Holowko said.

Holowko and colleagues evaluated mammographic screening history and

detailed questionnaire data from the KARMA prospective cohort study in Sweden. Women were enrolled between January 2011 and March 2013; mammograms were continually collected and participants were followed for diagnosis of breast cancer. Women younger than 40 or older than 75 years were excluded, as were women with a prior breast cancer diagnosis, breast enlargement, or breast reduction. The data cutoff was October 2017.

The researchers calculated the heritability of four mammographic features—breast density, average density change per year ( $\text{cm}^2/\text{year}$ ), microcalcifications, and masses—using 1,940 sister pairs. The heritability of breast density was estimated to be 58 percent, similar to previously reported findings. The heritability of microcalcifications and masses were estimated to be 23 percent and 13 percent, respectively. Breast density change was not determined to be an inherited trait.

Holowko and colleagues investigated the associations between mammographic features and [genetic predisposition](#) to breast cancer, as determined by a polygenic risk score (PRS), among 9,365 women in the KARMA cohort. They found statistically significant positive associations between PRS quintiles and [breast density](#) and microcalcifications.

"If we can better understand the mammographic features that are associated with [breast](#) cancer risk, then we can aim to improve how these features are measured and hopefully improve early [breast cancer](#) detection," Holowko said.

"We identified some limitations with modeling assumptions for [density](#) change, however, sensitivity analyses indicated almost no heritability, so we believe the presented results are reliable," noted Holowko. This study was supported by the Swedish Research Council, the Swedish Cancer Society, and the Stockholm County Council. Holowko declares no

conflicts of interest.

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