

Tissue Biomarker That May Indicate Higher Risk of Aggressive Breast Cancer Development and Death

Stromal disruption, could potentially be used to identify women at increased risk of recurrence or death.

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Researchers at the National Institutes of Health (NIH) have identified a series of changes in the architecture and cell composition of connective tissues of the breast, known as stromal tissue, that is associated with an increased risk of developing aggressive breast cancer among women with benign breast disease, and poorer rates of survival among women with invasive breast cancer. [The research was published May 14, 2025, in the [Journal of the National Cancer Institute](#).]

This process, which they call stromal disruption, could potentially be used as a biomarker to identify women with benign breast disease who are at high risk of developing aggressive breast cancers, as well as those with breast cancer who may be at increased risk of recurrence or death.

Such insights could help inform the development of cancer prevention and treatment strategies that target the stromal microenvironment. In addition, stromal disruption is inexpensive to assess and could be widely adopted, particularly in low-resource settings where molecular analysis is impractical or very expensive.

In the study, the researchers used machine learning to detect subtle changes in the stroma of 4,023 donated samples of healthy breast tissue, 974 biopsies of tissue with benign breast disease, and 4,223 biopsies of tissue with invasive breast cancer.

- In women who donated healthy breast tissue, the same risk factors associated with aggressive breast cancer—including younger age, having two or more children, being self-reported as Black, obesity, and family history—were also associated with increased stromal disruption, suggesting that those risk factors may act via a common stromal tissue pathway.
- In women with benign breast disease, having substantial stromal disruption on biopsy was associated with a higher risk of developing aggressive breast cancer and more rapid onset of

breast cancer than having minimal or no stromal disruption.

- In women with invasive breast cancer, increased stromal disruption was associated with more aggressive disease phenotypes and poorer survival outcomes, particularly for women with estrogen receptor-positive breast cancer, the most common subtype.

The researchers noted that factors such as chronic inflammation and wound healing play a role in stromal disruption. They emphasized the need for additional studies to determine whether strategies to prevent these tissue changes from occurring, such as lifestyle changes and anti-inflammatory medications, might be beneficial to reduce aggressive breast cancer risk, particularly among high-risk women.

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