

Genetics may identify breast cancer patients who can safely omit radiation therapy after breast-conserving surgery

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Patients with invasive breast cancer who had low scores on an investigational gene molecular signature had similar rates of local recurrence whether or not they received adjuvant radiation therapy after breast-conserving surgery, according to results of a meta-analysis

presented at the San Antonio Breast Cancer Symposium, held December 6-10, 2022.

Patients with breast cancer who undergo breast-conserving surgery are recommended to receive adjuvant radiation therapy to reduce the risk of local recurrence. "However, many patients will not experience a local recurrence even without radiation therapy," said Per Karlsson, MD, a professor of oncology at the Sahlgrenska Comprehensive Cancer Center and the University of Gothenburg in Sweden.

"Currently, we do not have any reliable predictive classifiers to identify patients who might be able to skip radiation therapy," he added. "Since radiation therapy can be associated with problematic side effects in some patients, it is of clinical importance to identify those patients for whom radiation therapy can be safely omitted."

In this study, Karlsson and colleagues evaluated the predictive potential of POLAR (Profile for the Omission of Local Adjuvant Radiotherapy), an investigational 16-gene molecular signature that was developed based on gene expression differences between patients with and without local recurrence after breast-conserving surgery. Genes included in the signature have known roles in cellular proliferation and the immune response.

The researchers performed a [meta-analysis](#) of 623 patients with lymph node-negative, estrogen receptor-positive, HER2-negative breast cancer who were enrolled in one of three randomized clinical trials examining the efficacy of breast-conserving surgery with and without local breast radiation therapy.

The clinical trials included in the meta-analysis were the Swedish SweBCG91RT trial, the Scottish Conservation Trial (SCT), and a trial from the Princess Margaret Hospital (PMH) in Canada. Among the 623

patients in the meta-analysis, 354 were from SweBCG91RT, 137 from SCT, and 132 from the PMH trial.

To evaluate the predictive capability of POLAR, the researchers analyzed [gene expression](#) in patient breast tumor samples to assign each patient a POLAR score; they then examined the impact of radiation therapy for patients with high and low POLAR scores.

Among the 429 patients with high POLAR scores, those who received adjuvant radiation therapy after breast-conserving surgery had a 63 percent reduction of local recurrence compared with those who did not receive adjuvant radiation therapy, suggesting that adjuvant radiation therapy was beneficial for these patients.

In contrast, for the 194 patients with low POLAR scores, there was no significant difference in local recurrence rate between those who received adjuvant radiation therapy and those who did not. After 10 years, 5 percent of patients who received radiation therapy experienced a local recurrence, compared with 7 percent of those who did not receive radiation therapy.

"In a patient-level meta-analysis of three independent randomized [clinical trials](#), the POLAR gene profile successfully predicted which patients would and would not benefit from local radiation therapy, thereby identifying a group of breast cancer patients where radiation therapy may be safely omitted after breast-conserving surgery," summarized Karlsson.

"Although only a minority of patients experience [severe side effects](#) to breast radiation, this adds up to a fair number of patients once you consider how prevalent [breast cancer](#) is," he added. "The POLAR gene profile may, therefore, help mitigate toxicities and improve quality of life for many patients." Karlsson noted that the POLAR gene profile will

need further validation and additional streamlining before it could be used in the clinic.

Future research from Karlsson and colleagues will examine whether the POLAR gene profile can also identify patients who could safely avoid regional radiation therapy, which is associated with more severe toxicities than local [radiation therapy](#).

A limitation of the study is its retrospective design. Additionally, the POLAR gene profile was developed using samples from patients who did not receive currently available endocrine therapies; however, validation trials included patients who received such therapies.

More information: Conference: www.sabcs.org/

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