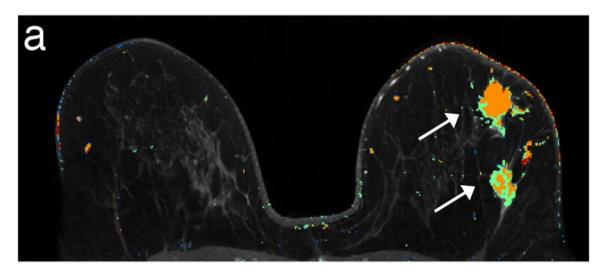
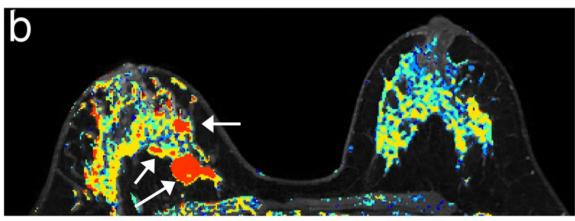


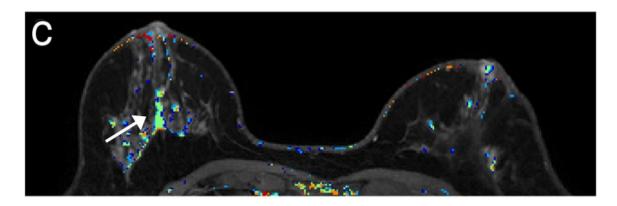
## For women with genetic risk, twice-a-year MRI beats mammograms

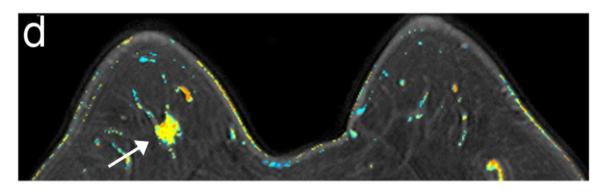
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DCE-MRI every six months performed well for early detection of invasive breast cancer in genomically stratified high-risk women. Credit: Fred Pineda, postdoctoral fellow, the University of Chicago Medicine

Getting magnetic resonance imaging (MRI) scans twice a year instead of one annual mammogram is far more effective at detecting early breast cancers in young women with a high-risk genetic profile than mammograms alone, according to a research team based at the University of Chicago Medicine and the University of Washington, Seattle.

The results, first presented Dec. 8, 2017 at the annual San Antonio Breast Cancer Symposium and now available online in *Clinical Cancer Research*, suggest that for women with high-risk genetic <u>mutations</u>, intensive efforts to find small early cancers can be crucial to improving outcomes.

"This study demonstrates for the first time that aggressive breast cancers can be caught early, without excessive recalls or biopsies," said Olufunmilayo Olopade, MD, the Walter L. Palmer Distinguished Service Professor and Associate Dean for Global Health at the University of Chicago Medical Center.

Because of intensive surveillance and high-quality care, the majority of high-risk women in this study did not develop <u>breast cancer</u>, despite the fact that most of these women had genetic mutations such as BRCA1.

For their study, "Intensive surveillance with bi-annual dynamic contrastenhanced magnetic resonance imaging downstages breast <u>cancer</u> in



BRCA1 mutation carriers," the researchers enrolled 295 women into a clinical trial. The mean age at entry was 43.3 years.

To join the trial, volunteers had to have a lifetime risk for breast-cancer greater than 20 percent. More than half (53%) of the women who enrolled had one of 11 known breast-cancer related genetic abnormalities. Seventy-five of those 157 women had BRCA1 mutations, and 61 had BRCA2 mutations.

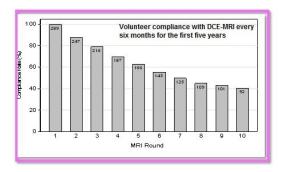
The study also included women who had been diagnosed with breast cancer or ductal carcinoma in situ before age 35, or had a mother or sister diagnosed with breast cancer before age 50 (before 40 for those of African ancestry). All study subjects had a panel of genetic tests looking for genes associated with a predisposition to breast cancer.

After evaluation by a physician and a genetic counselor, participants were scheduled to undergo a clinical breast examination and a dynamic contrast-enhanced <u>magnetic resonance imaging</u> scan (DCE-MRI) every six months, plus a digital mammogram every 12 months. Those with high-risk mutations who completed five years of the study protocol were offered continued screening.

Over the course of the study, the researchers performed 2,111 DCE-MRIs (on average, about seven for each participant) and 1,223 mammograms (four per participant). They found 17 cancers: four ductal carcinoma in situ and 13 early stage breast cancers.

Fifteen of those cancers occurred in participants with pathogenic mutations. Eleven involved BRCA1, three involved BRCA2, and one involved CDH1. None of the cancers had spread to the lymph nodes. The mean tumor size was 0.61 centimeter (about 1/4 of an inch). All cancers detected during the study were smaller than a centimeter.





Their primary reasons for leaving the study were the cost of health insurance, prophylactic mastectomy, and moved away or changed healthcare provider. Credit: The study authors

The 17 patients who developed a cancer were followed continuously for a median of 5.3 years (range 0.5 to 11 years). All are alive and free of systemic disease. Patient anxiety levels decreased over time and patient-reported quality of life improved. The study authors recommend "further interventional studies evaluating this novel screening approach to personalize breast cancer risk assessment and prevention."



In this study, DCE-MRI every 6 months "performed well for early detection of <u>invasive breast cancer</u> in genomically stratified high-risk women," said Gregory Karczmar, Ph.D., professor of radiology at the University of Chicago. "This is the ultimate goal of breast cancer screening," he added, "detecting node-negative, invasive tumors less than 1 centimeter."

"For these patients, annual mammography did not provide any additional benefit to bi-annual dynamic contrast-enhanced MRI scans," the authors agreed.

Mammograms are routinely used to screen for breast cancer, but they are "not the best option for about 40 percent of women," Karczmar said.
"This includes those with dense breasts as well as those with significant genetic risks."

"MRI is much more sensitive than mammography," he added. "It can find invasive breast cancers sooner than mammograms and it can rule out abnormalities that appear suspicious on a mammogram. Unfortunately, MRI is much too expensive for routine screening."

Mammograms will remain important for most women, but for women at high risk who are getting a DCE-MRI every six months, "annual mammograms can be eliminated," Olopade said.

"The central goal of our study was to understand the needs of the highestrisk women," said study co-author Mary Claire King, Ph.D., professor of genome sciences and of medicine at the University of Washington and the American Cancer Society Research Professor for Breast Cancer.

King has advocated for all women to be offered testing for BRCA1 and BRCA2 at about age 30, regardless of personal or family history of cancer, so that women with mutations can take action to prevent cancer



in their futures.

"My hope is that mammography and MRI will be used in ways that make sense given a woman's personal genetics," she said. "Women with mutations in BRCA1 or BRCA2 have very different needs for surveillance for <a href="mailto:breast">breast</a> disease than women with no mutations in these genes. This is particularly true for healthy young women with mutations. It's truly critical to offer intensive surveillance to still-healthy women with BRCA1 or BRCA2 mutations."

A number of patients withdrew from the study within five years. Their primary reasons for leaving were the cost of health insurance or other payment issues, 27 percent; prophylactic mastectomy, 16 percent; and moved away or changed healthcare provider, 11 percent.

The American Cancer Society (ACS) currently recommends an annual DCE-MRI as well as an annual mammogram for <u>women</u> who are at high risk, typically starting at age 30.

**More information:** Rodrigo Santa Guindalini et al, Intensive surveillance with bi-annual dynamic contrast-enhanced magnetic resonance imaging downstages breast cancer in BRCA1 mutation carriers, *Clinical Cancer Research* (2018). <u>DOI:</u> 10.1158/1078-0432.CCR-18-0200

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