

Breast Biopsies Leave Room for Doubt, Study Finds

By DENISE GRADY MARCH 17, 2015



Abby Howell chose to have a biopsy when a mammogram showed some calcification two years ago. Instead of being definitive, the biopsy found atypia — abnormal duct cells that are not cancerous but which some doctors recommend having removed. Credit Kyle Johnson for The New York Times

Breast biopsies are good at telling the difference between healthy tissue and [cancer](#), but less reliable for identifying more subtle abnormalities, a new study finds.

Because of the uncertainty, women whose results fall into the gray zone between normal and malignant — with diagnoses like “atypia” or “[ductal carcinoma in situ](#)” — should seek second opinions on their biopsies, researchers say. Misinterpretation can lead women to have surgery and other treatments they do not need, or to miss out on treatments they do need.

The new findings, [reported Tuesday in JAMA](#), challenge the common belief that a [biopsy](#) is the gold standard and will resolve any questions that might arise from an unclear [mammogram](#) or [ultrasound](#).

In the United States, about 1.6 million women a year have breast biopsies; only about 20 percent of the tests find cancer. Ten percent identify atypia, a finding that cells inside breast ducts are abnormal, but not cancerous. About 60,000 women each year are found to have ductal carcinoma in situ, or D.C.I.S., which also refers to abnormal cells that are confined inside the milk ducts and so are not considered invasive; experts disagree about whether [D.C.I.S.](#) is cancer.

“It is often thought that getting the biopsy will give definitive answers, but our study says maybe it won’t,” said [Dr. Joann G. Elmore](#), a professor at the University of Washington School of Medicine in Seattle and the first author of the new study on the accuracy of breast biopsies.

Her team asked pathologists to examine biopsy slides, then compared their diagnoses with those given by a panel of leading experts who had seen the same slides. There were some important differences, especially in the gray zone.

An [editorial in JAMA](#) said the findings were “disconcerting” and that the study should be a “call to action” for pathologists and breast cancer scientists to improve the accuracy of biopsy readings, by consulting with one another more often on challenging cases and by creating clearer definitions for various abnormalities so that diagnoses will be more consistent and precise. The editorial also recommended second opinions in ambiguous cases.

A second opinion usually does not require another biopsy; it means asking one or more additional pathologists to look at the microscope slides made from the first biopsy. Dr. Elmore said that doctors could help patients find a pathologist for a second opinion.

A surgeon not involved with the study, Dr. Elisa Port, co-director of the Dubin Breast Center and the chief of breast surgery at Mount Sinai Hospital in Manhattan, said the research underlined how important it is that biopsies be interpreted by highly experienced pathologists who specialize in breast disease.

“As a surgeon, I only know what to do based on the guidance of my pathologist,” Dr. Port said. “Those people behind the scenes are actually the ones who dictate care.”

In Dr. Elmore’s study, the panel of three expert pathologists examined biopsy slides from 240 women, one slide per case, and came to a consensus about the diagnosis.

“These were very, very experienced breast pathologists who have written textbooks in the field,” Dr. Elmore said.

Then the slides were divided into four sets, and 60 slides were sent to each of 115 pathologists in eight states who routinely read breast biopsies. The doctors

interpreted the slides and returned them, and the same set was sent to the next pathologist. The study took seven years to complete.

The goal was to find out how the practicing pathologists stacked up against the experts. The task was tougher than actual practice, because in real cases pathologists can consult colleagues about ambiguous findings and ask for additional slides. They could not do so in the study.

There was good news and bad news. When it came to invasive cancer — cancer that has begun growing beyond the layer of tissue in which it started, into nearby healthy tissue — the outside pathologists agreed with the experts in 96 percent of the interpretations, which Dr. Elmore called reassuring. They found the vast majority of the cancers.

For completely benign findings, the outside pathologists matched the experts in 87 percent of the readings, but misdiagnosed 13 percent of healthy ones as abnormal.

The next two categories occupied the gray zone. One was D.C.I.S. For this condition, the pathologists agreed with the experts on 84 percent of the cases. But they missed 13 percent of cases that the experts had found, and diagnosed D.C.I.S. in 3 percent of the readings where the experts had ruled it out.

The finding is of concern, because D.C.I.S. sometimes becomes invasive cancer, and it is often treated like an early-stage cancer, with surgery and radiation. Missing the diagnosis can leave a woman at increased risk for cancer — but calling something D.C.I.S. when it is not can result in needless tests and treatments.

The second finding in the gray zone was atypia, in which abnormal, but not cancerous, cells are found in breast ducts. Women with atypia have an increased risk of breast cancer, and some researchers recommend surgery to remove the abnormal tissue, as well as intensified screening, and drugs to lower the risk of breast cancer.

But in the study, the outside pathologists and the experts agreed on atypia in only 48 percent of the interpretations. The outside pathologists diagnosed atypia in 17 percent of the readings where the experts had not, and missed it in 35 percent where the experts saw it.

“Women with atypia and D.C.I.S. need to stop and realize it’s not the same thing as invasive cancer, and they have time to stop and reflect and think about it, and ask for a second opinion,” Dr. Elmore said.

Abby Howell, 57, who lives in Seattle, had some calcifications show up on a mammogram two years ago, which are sometimes a sign of cancer. She was given the option of just mammograms every six months, or having a biopsy. She chose the biopsy, thinking it would be definitive. But instead, it showed atypia.

Ms. Howell, who has a master's degree in public health, looked up the condition and realized it was unclear whether those odd-looking cells would ever lead to cancer. Surgery was recommended, but she decided to watch and wait instead. So far, her mammograms have been normal, but the experience has shaken her peace of mind.

“If I had to do it all over again, I wouldn't have jumped for the biopsy,” Ms. Howell said. “I really regret it. In a way it's made more anxiety in my life.”



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