

# Mode of Detection and Secular Time for Ductal Carcinoma In Situ

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In this article, the published literature on the role of screening mammography in the detection of ductal carcinoma in situ (DCIS) is reviewed. This includes what is known about the detection of DCIS in different demographic groups. Finally the author describes her views on how the field might be advanced.

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## Detection of Clinically Occult DCIS Through Screening Mammography

Based on Surveillance, Epidemiology, and End Results data, incidence rates of carcinoma in situ, both ductal and lobular, have increased enormously since the widespread adoption of screening mammography, with age-adjusted incidence rates increasing by 660%, from 4.3 to 32.7 per 100 000 woman-years (1) during the years 1973 through 2000. During the same period, the age-specific incidence rate for invasive breast cancer increased only 36% (1), from 99 to 135 per 100 000 woman-years. The diagnosis of DCIS was the primary driver of the increase in CIS incidence.

A 2002 article from the National Cancer Institute's Breast Cancer Surveillance Consortium reviewed the cancers diagnosed in a screening population of 540 738 women aged 40 through 84 years who underwent 653 833 mammograms. Of the 3266 cases of breast cancer diagnosed between 1996 and 1997, 591 (18.1%) were DCIS, with the percentage of DCIS decreasing with age with 28.2% (95% confidence interval [CI] 23.9% to 32.5%) for women aged 40–49 years vs 16.0% (95% CI 13.3% to 18.7%) for women aged 70–84 years. The rate of DCIS per 1000 mammograms increased with age, from 0.56 (95% CI 0.41 to 0.70) for women aged 40–49 years vs 1.07 (95% CI 0.87 to 1.27) for women aged 70–84 years. Sensitivity for detecting DCIS was higher than for invasive breast cancer—86.0% (95% CI 83.2% to 88.8%) vs 75.1% (95% CI 73.5% to 76.8%). These authors concluded that one in 1300 screening mammograms leads to the diagnosis of DCIS (2).

Perhaps somewhat surprisingly, 14% of the DCIS cases detected in this study (83 of 591) were among those with negative screening mammograms, but 21 of those 83 (25.3%) were coded as BI-RADS 3, indicating findings by mammography. Even eliminating those 21, the rate of interval (and presumably symptomatic or detectable on physical examination) DCIS in this large population-based study was 10.5% (2). Dershaw et al. have reported a similar rate (14.6%) of symptomatic cases in a report of a single-center series of 51 women with DCIS (3).

Rates of detection of DCIS from other large-scale 1970s through 1990s screening mammography programs have varied

from 18% to 25.3% (4–10), with one study reporting a DCIS detection rate of 32.8% in non-initial screening rounds (8,10). In contrast, the 1960s Health Insurance Plan Trial had a DCIS detection rate of 12% (11).

Sojourn times or mean duration of preclinical disease has been estimated for DCIS to be 4.8 years through evaluation of the data from the Swedish Two-County Trial (12–14), which is shorter than for all other tumor types evaluated. Annual screening mammography has been associated with smaller tumors, less comedo histology, and lower nuclear grade for DCIS lesions identified (15).

Although the UK National Health Service Breast Screening Programme (NHSBSP) has placed limits on the target rate of DCIS detection range (16), and the percentage of mammograms judged to be abnormal at screening is positively and significantly associated with the frequency of DCIS cases diagnosed (17), there is evidence from the UK NHSBSP that screening units with the highest DCIS detection rates ( $\geq 1.3/1000$ ) detected over 20% more small invasive cancers than did units with DCIS detection rates within the recommended guidelines (18).

Not much has been published about the variability of the detection of DCIS in assorted demographic groups. Surveillance, Epidemiology, and End Results data reveal that age-adjusted incidence rates for DCIS in Hispanics were 50% lower than for non-Hispanic whites between 1973 and 1994, and American Indians had the lowest rate overall. Starting in 1985, rates for all groups increased steadily, averaging 17% per year overall (from 2.9 to 11.8 per 100 000 women) (19). This increase corresponded to more widespread adoption of screening mammography. A report of the DCIS detection rate using New Mexico Tumor registry described DCIS incidence rates between 1973 and 1994 and showed nonsignificant differences in DCIS rates between non-Hispanic whites (11%), Hispanic whites (9%), and American Indians (6%) in that state (20). 1994 Surveillance, Epidemiology, and End Results data reveal that DCIS comprised 14.0% of the breast cancers diagnosed in white women and 13.8% of those diagnosed in African American women, with 18.2% vs 19.7% reported in 1998 (21,22).

More recent data from the National Breast and Cervical Cancer Early Detection Program (from July 1991 through March 1998)

reveal an overall DCIS detection rate of 0.9 per 1000 mammograms (95% CI 0.8 to 1.0), with no significant differences between different ethnic and racial groups (non-Hispanic whites 1.0 [95% CI 0.8 to 1.1], African Americans 0.7 [95% CI 0.4 to 0.9], American Indians/Alaskan Natives 0.6 [95% CI 0.3–0.9], and Hispanics 0.8 [95% CI 0.5 to 1.0]) (8).

## Future Research Directions

As has been recommended by the Institute of Medicine in their 2004 report *Saving Women's Lives: Strategies for Improving Breast Cancer Detection and Diagnosis* (23), a very important goal for improved breast cancer detection is to develop and test individualized screening strategies that allow women at high risk to undergo more vigilant surveillance for breast cancer and possibly to reduce screening frequency in women at low risk. In order for screening strategies to be evidence based, it is quite important for clinical trials to be conducted, with attention both to the frequency of screening events and the type of technologies used. These should be focused primarily on high-risk women, both for invasive tumors and DCIS.

Such trials have been conducted under the auspices of the American College of Radiology Imaging Network (23–25), but more research is needed. Work must be continued with attention to newer imaging technologies, such as tomosynthesis (26), breast computed tomography (27,28), breast PET (29), breast-specific gamma imaging (30,31), and others still in earlier phases of development (32–36).

In addition, we should develop new mechanisms for distinguishing between breast cancer subtypes, both invasive and DCIS, that are at higher risk for becoming invasive and metastatic tumors. This work will most likely involve the application of imaging technologies, including the development of new contrast agents (molecular and otherwise) that can label the biomarkers (eg, p53 mutations, erbB2, or other more specific markers of triple negative and basal breast cancer) that increase the risk for lethal outcomes.

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