

## Ductal Carcinoma In Situ: A Rose by Any Other Name

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Until the late 1970s or early 1980s, the treatment of what was then called noninvasive intraductal carcinoma was relatively straightforward. Patients were told they had a very good prognosis, and they were treated with a mastectomy. At some centers, they received a radical mastectomy, “just to be cautious.” What is now called ductal carcinoma in situ (DCIS) was an uncommon breast cancer, representing less than 5% of new cases, and most of these were palpable lesions.

Today, largely as a result of data from clinical trials, patients with newly diagnosed DCIS have the option of breast-conserving surgery, and the majority select that option (1,2). What was once an uncommon finding now represents up to 25% of new breast cancers and as much as 33% of mammographically detected breast cancers (3). Assuming there is no increase in the prevalence of DCIS, the increased incidence is likely due to the use of screening mammograms and of breast magnetic resonance imaging, which provides improved technological ability to detect the disease, along with core needle biopsy, which has made the ability to sample image-detected lesions more feasible and rapid.

With this increase in incidence, new dilemmas in the postsurgical treatment of DCIS have arisen. In this issue of the Journal, Punglia, Schnitt, and Weeks (4) outline the current difficulties associated with the management of DCIS and suggest some steps designed to improve the situation. They ask whether DCIS is really a cancer or a precursor lesion or perhaps a marker of risk. Indirect evidence suggests that this entity is primarily a precursor lesion, although not a “committed” precursor. There is evidence that DCIS does share genetic sequences similar to those of invasive cancer and that it may also be affected by stromal factors that promote invasive development (5–10). The percentage of today’s DCIS patients who will progress to invasive disease if left untreated is not accurately established but is likely to involve the minority of cases. Recent moves to change the term “DCIS” or to delete the word “carcinoma” from this appellation no doubt stem in part from this fact. Although the old adage “sticks and stones may break my bones, but names will never hurt me” may be true on the playground, in the breast clinic it might be nice to avoid the label “breast cancer”—as well as the fear and anxiety that can accompany those words—when speaking of or to DCIS patients. Nevertheless, we do need to inform our patients that DCIS, by any name, is more than a minor medical nuisance.

Although it is true that for the entire population of DCIS patients the risk of breast cancer mortality is very low, for those women who do develop an invasive ipsilateral breast cancer event, there is an increased mortality risk, and most of the deaths are attributed to breast cancer (11). Studies have shown repeatedly that

radiation therapy after breast-conserving surgery for DCIS results in a roughly 50% relative decrease in both the recurrence of DCIS and the occurrence of invasive disease when compared with no radiation (1). However, because most DCIS patients do not have a recurrence/occurrence, the absolute benefit is not large. The use of selective estrogen receptor modulators and perhaps aromatase inhibitors in estrogen receptor–positive DCIS patients can further reduce the number of in-breast tumor events and can substantially reduce the number of new primary cancers of the opposite breast (12,13). Although most of the studies we have referenced used a 5-year duration of therapy, the recent reports of the ATLAS and ATTOM studies demonstrate that the use of tamoxifen for up to 10 years is superior to 5 years of treatment for invasive breast cancer (14,15). A longer duration of selective estrogen receptor modulator therapy or switching to an aromatase inhibitor after 5 years may also improve outcome for patients with DCIS.

Punglia et al. (4) correctly point out that the various postexcision therapies are not truly adjuvant therapy, and they promote a change to a prophylactic or preventative paradigm that focuses attention on the risks and benefits of interventions designed to prevent future invasive cancer risk. This approach has merit but should be addressed in a stepwise fashion that assesses risk factors and treatment benefits in a personalized fashion. At a time when we are beginning to use biologically based assessments in the treatment of patients with invasive breast cancer, we should attempt the same for those with DCIS.

It appears that the best solution for these issues will be to develop the ability to identify each patient’s likely prognosis and to predict response to therapy for that individual. Which DCIS patients will not progress to invasive disease and can therefore be treated effectively by local excision alone or perhaps only a core biopsy with follow-up? Which patients will progress to invasive disease, and among those, who will respond to radiation, selective estrogen receptor modulators, aromatase inhibitors, or perhaps a yet-to-be-developed therapy directed at the “switch” or “switches” that begin the transition to invasive disease? Conventional histological characteristics, tumor size, and margin width have not been fully successful in identifying such patient groups (16,17). Using samples from a subset of women from the ECOG E5194 study, which was a prospective trial of DCIS patients selected for treatment with surgical excision alone, the 12-gene *Oncotype DX* DCIS score predicted the 10-year risk of local recurrence (18). Such results require further validation. Unlike the *Oncotype DX* recurrence score that is performed on estrogen receptor–positive invasive breast cancer blocks, the DCIS score has not yet demonstrated benefit in predicting response to therapy after

excision, which could be far more valuable. But the test is nonetheless a step in the right direction.

It is a platitude to conclude that more research is required, but that is the case with DCIS. Studies into the molecular biology and genetics of breast cancer are primary among the important work still required. Other important studies to conduct include detailed assessments of patients' educational and psychosocial needs to better assist them in making decisions about which therapies are appropriate in their particular case. These issues have been evaluated extensively in patients with invasive breast cancer; similar studies should be conducted in DCIS patients. Making drastic changes in nomenclature with the hope that those changes will improve the situation may be an interesting semantic and sociological exercise, but it is doubtful that they will, at least in the immediate future, result in different decisions being made by women diagnosed with this entity.

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# Prostate Cancer Screening: Biases and the Need for Consensus

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In the 1990s, several studies were published showing that serum prostate specific antigen (PSA) aided in the diagnosis of localized prostate cancer (1,2). Widespread screening was adopted quickly in the United States, where it is dogma that early detection and aggressive treatment saves lives.

This bias toward screening would delay and hinder study to determine whether screening truly saves lives. It would be more

than 20 years before the results of well-designed prospective randomized studies would be published assessing the effectiveness of PSA screening—notably, the Prostate, Lung, Colon and Ovarian Cancer Screening Trial (PLCO)(3,4), which suggested that screening does not reduce mortality at 13 years median follow-up, and the European Randomized Study of Prostate Cancer (ERSPC)(5,6) study and Goteborg (7) trial, which suggested that