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Editorial

Incidence and Treatment of Ductal Carcinoma *In Situ* of the Breast

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IN 1996, the American Cancer Society estimated that there were 1400 new cases of male breast cancer in the United States. Only approximately 1% of those were thought to be ductal carcinoma *in situ* (DCIS). That translates to approximately 14 new cases of male DCIS during an entire year. While DCIS is a rare problem in men, it is almost epidemic in women with more than 30000 new cases expected in 1996 in the United States [1].

In this issue of the *European Journal of Cancer*, Cutuli and associates (pages 35–38) [2] analyse 31 cases of male breast ductal carcinoma *in situ* (male DCIS). It took 19 medical centres 22 years to accrue that many cases. That translates to 1.4 cases per medical centre per 22 years or 1 case per medical centre every 15.7 years—not very many. I was fascinated to read the paper since I personally had little experience with male DCIS. As I write this, our group has seen and treated almost 600 women with DCIS, one of the largest single facility series in the world. During the 17-year period it took to accrue our series, we have cared for only one man with DCIS—a rate almost exactly the same as the one reported by Cutuli and associates [1].

With my limited experience of one case, it seems clear to me that Cutuli and associates' [2] recommendation of total mastectomy without axillary dissection is the procedure of choice for male DCIS. Breast preservation for men with DCIS would require careful clinical follow-up and would bring with it the potential of local recurrence. If male DCIS is anything like female DCIS, half of these local recurrences would be invasive. Since male breasts are neither functional nor contribute significantly to men's sexuality or self-image, there seems little reason to explore lesser procedures, thereby exposing men to the same dilemma that has become routine for women with DCIS. For most men, little would be gained by breast preservation. For men diagnosed with DCIS, the road ahead is straightforward, clear and simple.

For women with the same disease, the road is cluttered. As the number of cases of female DCIS increase at a dramatic rate, paralleling our increasing use of mammography, there is clinical disagreement, chaos and confusion. The conflict between sexuality, wholeness, self-image and functionality versus curability is dramatically different for women than for men.

Throughout the 1960s, to most physicians, breast cancer was breast cancer. It was all the same, and all forms would have been treated with mastectomy. During the last three decades, there have been tremendous changes in diagnosis, treatment and our understanding of breast cancer biology. Instead of a clinical rarity presenting as a mass or nipple discharge, DCIS is now common and generally non-palpable. Today, it is routinely discovered mammographically rather than clinically. Instead of a single simple treatment, there are now several alternative treatments, all accompanied by a great deal of confusion. Instead of doctors deciding what to do and when to do it, as they did 30 years ago, patients now play a key role in the treatment decision-making process.

It was hoped that the results of National Surgical Adjuvant Breast Project (NSABP) Protocol B-17, published in 1993 [3], would have solved this now complex DCIS treatment controversy. Approximately 800 patients with DCIS excised with clear surgical margins were prospectively randomised into two groups: excision only versus excision plus radiation therapy. Actuarial projections to 5 years revealed a statistically significant decrease in local recurrence of both DCIS and invasive breast cancer in patients treated with radiation therapy. These data led the NSABP to recommend post-excision radiation therapy for all patients with DCIS who chose to preserve their breasts. The study was criticised for a number of reasons [4, 5], the most important being a lack of pathological subset analysis. Consider the following 2 patients, both of whom would receive radiation therapy if NSABP recommendations were followed. Patient 1 has a 5 mm low-grade DCIS widely excised with a minimum of 10 mm margins in all directions. Compare her with patient 2, a woman with a 20 mm high-grade lesion with DCIS approaching to within 0.1 mm of the inked margin but not involving it. According to the NSABP, both of these patients require no additional surgery and should be treated with radiation therapy.

At our facility, the first patient would receive no additional therapy—careful clinical follow-up with physical examination and mammography every 6 months is all that would be prescribed. The second patient would undergo a wide re-excision prior to making a final treatment decision.

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Table 1. The Van Nuys Prognostic Index scoring system

Score	1	2	3
Size (mm)	≤ 15	16–40	≥ 41
Margins (mm)	≥ 10	1–9	< 1
Pathological classification	Non-high-grade Without necrosis	Non-high-grade With necrosis	High-grade With or without necrosis

One to three points are awarded for each of three different predictors of local breast recurrence (tumour size, margin width and pathological classification). Scores for each of the predictors are summated to yield a VNPI score ranging from a low of 3 to a high of 9.

Significant residual disease approaching the new margins would merit a recommendation for mastectomy with immediate reconstruction; widely clear new margins with little or no residual DCIS would merit either a recommendation for careful follow-up without breast irradiation; or if intermediate margins were obtained, radiation therapy would be suggested. While I have great respect for the NSABP and for what they have accomplished, I have difficulty accepting a blanket recommendation for radiation therapy for all patients with DCIS who elect breast preservation.

At our institute, we believe that there are numerous clinical, pathological and laboratory factors that can aid clinicians and patients wrestling with the difficult treatment decision-making process and that these prognostic factors can be quantified. Our research has shown that nuclear grade, the presence of comedo-type necrosis, tumour size, and margin width are all important factors in predicting local recurrence in patients with DCIS [6, 7]. By using a combination of these factors, it may be possible to select subgroups of patients who do not require irradiation, if breast preservation is elected. Alternatively, it may be possible to select patients whose recurrence rate is potentially so high, even with breast irradiation, that mastectomy is preferable.

Our group used the first two of these prognostic factors, i.e. nuclear grade and comedo-type necrosis, to develop a simple reproducible DCIS pathological classification [8]. However, nuclear grade and comedo-type necrosis are inadequate as the sole guidelines in the treatment selection process. Tumour size and margin status are also important independent prognostic factors by multivariate analysis. By combining all of these factors, we have developed the Van Nuys Prognostic Index (VNPI) [9, 10].

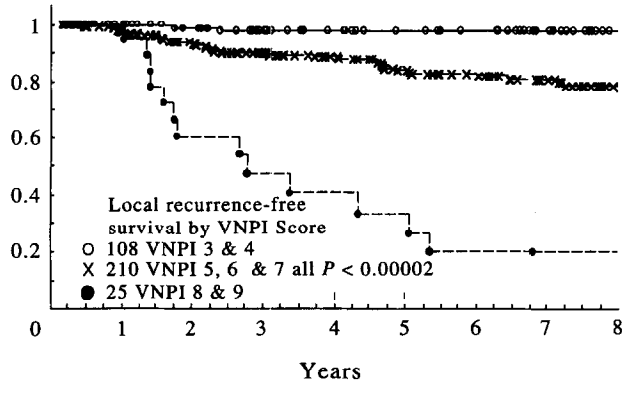

Figure 1. Probability of local recurrence-free survival grouped by Van Nuys Prognostic Index score for 343 patients.

Table 1 shows the VNPI scoring system. Scores from one to three are given for each of the three predictors of local breast recurrence (size, margin width and pathological classification). The scores for each predictor are summated to yield a VNPI score ranging from a low of 3 to a high of 9. Patients with a low VNPI score (3 or 4) show no difference in disease-free survival at 8 years regardless of whether or not they received radiation therapy and can be treated with excision only. Patients with intermediate scores (5, 6 or 7) show a statistically significant decrease in local recurrence rates with radiation therapy. Conservatively treated patients with VNPI scores of 8 or 9 exhibit unacceptably high local recurrence rates, regardless of irradiation, and should be considered for mastectomy (Figure 1).

The VNPI is the first attempt to quantify known important prognostic factors in DCIS, making them clinically useful in the treatment decision-making process. The VNPI needs to be prospectively verified before its routine clinical use is adopted. In the future, other factors, such as molecular markers, may be integrated into the VNPI or into other prognostic indices when they are shown to influence statistically the likelihood of local recurrence after breast preservation therapy for DCIS.

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