



Editorial

Ductal Carcinoma In-Situ: An Editorial

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Ductal carcinoma in-situ (DCIS) is an increasingly common pre-invasive form of breast-cancer. 27% of all new breast cancer diagnoses in 2008 in the United States were DCIS as opposed to less than 1% before the introduction of national mammographic screening programmes [1].

It is probably the pre-cursor of most invasive breast-cancer but not all DCIS will progress to this stage. So the challenge in the modern treatment of DCIS is to avoid over-treatment.

Historically, DCIS presented incidentally or with a breast mass or nipple discharge. Post introduction of screening it now more commonly presents as asymptomatic calcifications seen on mammography. We know that this latter group have lower rates of local-recurrence after treatment [2,3] and so a proportion of these cases may be less clinically relevant [4]. The question of over-treatment in screening cases has been brought into sharp focus recently by a significant analysis published in the Lancet [5].

Integral to the successful management of DCIS, is surgery to remove the disease with clear margins [6] (this may involve breast conservation or mastectomy with or without reconstructive techniques). Breast radiotherapy and hormonal treatments are also given as adjuvants where appropriate but can these be safely omitted in certain cases?

Treated DCIS has an excellent overall prognosis and so differences in survival have been difficult to demonstrate even in large trials. Differences in local-recurrence rates have been used as a surrogate marker for survival. Radiotherapy was shown to reduce local recurrence in early breast-cancer in 1995 [7] and to be indirectly associated with improved survival in 2005, in that one death was prevented for every four local-recurrences avoided [8]. A direct improvement in overall survival in early breast-cancer attributable to radiotherapy of around one sixth has since been demonstrated [9].

An analysis of long term data on patients treated for DCIS from the NSABP B-17 and NSABP B-24 trials [10] showed that at 15 years, the radiotherapy treated patients had significantly fewer local-recurrences and that this effect increased over time. Of those that did recur 54% were invasive, and for these patients overall survival was lower (HR of death = 1.75, 95% CI = 1.45 to 2.96, P<0.001).

An analysis of the major DCIS trials from the nineties showed that radiotherapy halves the local recurrence rate, producing an

absolute reduction in local recurrence at 5 years of 10% and of 15% at 10 years and this benefit is preserved for lower risk cases [11].

The UK/ANZ DCIS trial assessed the effect of adjuvant treatment with Tamoxifen after breast conserving surgery and radiotherapy for DCIS. After a median of 12.7 years follow-up [12], a significant reduction in local recurrence and contra-lateral tumours in Tamoxifen treated patients was seen (HR 0.71, 95% CI 0.58–0.88;p=0.002). Trials are ongoing to determine if Aromatase inhibitors are superior to Tamoxifen in the adjuvant setting after breast conserving surgery for DCIS (NSABP B-35 and IBIS II).

So, there is significant potential benefit overall for patients with DCIS from adjuvant treatments, but given the very good overall prognosis of this condition, patients with a low risk of local-recurrence are likely to be those in which adjuvant treatments could be omitted. Tumour size and grade, the presence or absence of inflammatory changes or necrosis and the 'comedo' sub-type (high-grade, central confluent necrosis and solid architectural pattern in >50% of the duct spaces) have been found to be statistically associated with the risk of local recurrence in an independent pathological review of cases from the UKCCCR/ANZ DCIS trial [13]. Margin width was the most significant factor associated with local-recurrence in a large meta-analysis [6]. These factors in isolation are not enough to safely omit adjuvant treatments or to validate less extensive surgery but in combination may be useful.

The Van Nuys index uses a combination of factors that are known to influence local-recurrence rates (size of tumour, grade and margin width at operation) to generate a score. Low recurrence rates have been reported after breast conserving surgery even in the absence of radiotherapy with the lowest Van Nuys scores [14] and this index is being used to guide treatment decisions.

Oncotype-DX-DCISTM is a genomic assay that aims to guide radiotherapy decisions in DCIS by generating a score which predicts the likelihood of local-recurrence [15]. This score was validated using tissue and recurrence outcomes from the ECOG 5194 study which included patients treated with BCS alone [16].

It is regrettable that a common condition with such a good general prognosis is so variable in its clinical implications. Thankfully, ongoing research (such as that outlined above) will continue to help us answer the uncertainty that remains in trying to best treat patients with DCIS while minimising harm.

References

1. Jemal A, Siegel R, Ward E, et al. (2008) Cancer Statistics 2008. *Cancer J Clin* 58: 71-96.
2. Kerlikowske K, Molinaro A, Cha I, Ljung BM, Ernster VL, et al. (2003) Characteristics Associated with Recurrence among Women with Ductal Carcinoma In-situ Treated by Lumpectomy. *J Natl Cancer Inst* 95: 1692-1702.
3. Bijker N, Peterse JL, Duchateau L, Julien JP, Fentiman IS, et al. (2001) Risk factors for recurrence and metastasis after breast conserving therapy for ductal carcinoma in-situ: analysis of European Organisation for Research and Treatment of Cancer trial 10853. *J Clin Oncol* 19: 2263-2271.
4. Virnig B, Tuttle T, Shamiyan T, Kane R (2010) Ductal Carcinoma in Situ of the Breast: A Systematic Review of Incidence, Treatment, and Outcomes. *J Natl Cancer Inst* 102: 170-178.

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5. Independent UK Panel on Breast Cancer Screening (2012) The benefits and harms of breast cancer screening: an independent review. *The Lancet* 380: 1778-1786.
6. Wang S, Shamlivan T, Virnig B, Kane R (2011) Tumor characteristics as predictors of local recurrence after treatment of ductal carcinoma in situ: a meta-analysis. *Breast Cancer Res Treat* 127: 1–14.
7. Early Breast Cancer Trialists' Collaborative Group (1995) Effects of Radiotherapy and Surgery in Early Breast Cancer — An Overview of the Randomized Trials. *N Engl J Med* 333: 1444-1456.
8. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, et al. (2005) Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and on 15-year survival: an overview of the randomised trials. *The Lancet*. 366: 2087-2106.
9. Early Breast Cancer Trialists' Collaborative Group (2011) Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *The Lancet* 378: 1707-1716.
10. Wapnir I, Dignam J, Fisher B, Mamounas E, Anderson S, et al. (2011) Long-Term Outcomes of Invasive Ipsilateral Breast Tumor Recurrences After Lumpectomy in NSABP B-17 and B-24 Randomized Clinical Trials for DCIS. *J Natl Cancer Inst* 103: 478–488.
11. Early Breast Cancer Trialists' Collaborative Group (2010) Overview of the randomised trials of radiotherapy in ductal carcinoma in situ (DCIS) of the breast. *J Natl Cancer Inst Monogr* 41: 162-177.
12. Cuzick J, Sestak I, Pinder S, Ellis I, Forsyth S, et al. (2011) Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. *Lancet Oncol* 12: 21–29.
13. Pinder S, Duggan C, Ellis I, Cuzick J, Forbes J, et al. (2010) A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial. *British Journal of Cancer* 103: 94 – 100.
14. Silverstein MJ (2003) The University of Southern California/Van Nuys prognostic index for ductal carcinoma in-situ of the breast. *Am J Surg* 186: 337-343.
15. Solin L, Gray R, Baehner F, et al. (2011) A quantitative multigene RT-PCR assay for predicting recurrence risk after surgical excision alone without irradiation for ductal carcinoma in situ (DCIS): a prospective validation study of the DCIS Score from ECOG E5194. 34th Annual San Antonio Breast Cancer Symposium, San Antonio, TX.
16. Motwani SB, Goyal S, Moran MS, Chhabra A, Haffty BG (2011) Ductal carcinoma in situ treated with breast-conserving surgery and radiotherapy: a comparison with ECOG study 5194. *Cancer* 117: 1156-1162.

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