

E6. Ductal carcinoma in situ (DCIS); current treatment strategies

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Ductal carcinoma *in situ* is becoming more frequent since the implementation of mammographic screening programmes. It occurs in nearly 25% of all breast cancer diagnoses and approximately 20% to 30% of the breast cancers detected by mammography are carcinoma *in situ*. Most cases present with non-palpable microcalcifications [1].

Some doctors called DCIS a pre-cancerous condition. In fact, 99% of women with this disease will survive their breast cancer after appropriate therapy. Despite recent advances in the diagnosis, evaluation and treatment of breast cancer, the optimal treatment for DCIS is not yet well defined and some of the new therapies are associated with additional morbidity and high costs for perhaps unnecessary treatments.

Although mammography can detect up to 83% of DCIS, this method has been shown to consistently underestimate the extent of disease. Magnetic resonance imaging (MRI) was better at predicting multifocality. It is interesting to note that surgical biopsies taken before undergoing MRI do not reduce the diagnostic accuracy with regard to the tumour extent [2]. Stereotactic core-needle biopsy should be performed in cases of suspicious abnormalities, in order to make a preoperative diagnosis. Core biopsy is able to achieve a positive diagnosis for screen-detected DCIS in 90% of cases. This facilitates the planning of one-step surgery and leads to negative surgical margins in more than 70% of cases when a wide excision is performed. When the lesion is completely removed, the biopsy site should be marked in order to accurately locate the site for definitive excision. DCIS is a heterogeneous disease, but (principally) there are two categories: non-comedo and comedo. The most common, non-comedo types of DCIS are solid, cribriform, papillary and micropapillary. DCIS is generally unifocal, but may be extensive. The growth pattern has been related to nuclear grade and poorly differentiated tumours tend to have a continuous growth pattern, whereas well-differentiated DCIS tend to have a discontinuous growth pattern [3].

The goal of the surgical approach is to completely remove the mammographic abnormality with acceptable cosmetic results. Oncoplastic surgery has becoming the standard treatment for breast cancer patients. Conservative treatment should have the objective of obtaining as big a margin as possible. This concept is completely

different to the objective of obtaining clear margins. What does clear mean? At this point, we can state that a margin of less than 1 mm is positive and more than 10 mm is negative. There is insufficient data existing to define margins between 1 and 9 mm [4]. But why are free margins of 20 mm or more not achievable? Of course the principles of oncological surgery should be combined with plastic surgery techniques in order to obtain a good cosmetic result.

Clearly, the best margins are obtained following a mastectomy. This treatment is very effective for DCIS. Following mastectomy, local recurrence rates are very low, in order of 1%; but mastectomy results in the worst cosmesis. Therefore, a new concept, a "breast-preserving mastectomy" has been introduced. This operation is defined by the width of skin removed around the nipple-areola complex. The purpose of a skin-sparing mastectomy is to allow a better cosmetic result and a natural ptosis after breast reconstruction procedures [5]. Many studies have now clearly demonstrated an almost 50% reduction in local recurrence when radiotherapy is used with surgical excision. The results of the National Surgical Adjuvant Breast Project (NSABP) B-17 trial, after 12 years of follow-up showed a statistically significant decrease in local recurrence of both DCIS and invasive breast cancer in patients treated with radiation therapy: 16% vs. 32% in the patients with excision alone [6].

The European Organisation for Research and Treatment of Cancer (EORTC) (protocol 10853) trial with an identical design to B-17 obtained similar results [7]. Both studies failed to show a difference in breast cancer mortality between the two treatment arms. If there is currently no survival advantage, we must be sure that the benefits of radiation therapy significantly outweigh the additional side-effects and costs. Radiation therapy is accompanied by serious side effects, of a cardiac and pulmonary nature, in a small percentage of patients [8]. There might be some identifiable subgroups of patients for whom radiation therapy doesn't offer any real advantage. The Van-Nuys prognostic Index includes three significant predictors of local recurrence; margin width, tumour size and pathological classification [9]. Margin width reflects the completeness of the excision and therefore the percentage of residual disease to be treated by radiotherapy. The Van-Nuys Breast Center revealed that there is no significant

advantage from radiation therapy if the margins are greater than 10 mm, regardless of the nuclear grade of the tumour or the histological subtype. Axillary lymph-node dissection is not considered necessary in the treatment of DCIS as the risk of nodal metastases is less than 4% [10,11]. A sentinel lymph-node biopsy, with its minimal morbidity, has completely modified the treatment of patients in some centres. Because more than 20% of patients diagnosed as having DCIS in a core biopsy alone will have identifiable invasive carcinoma when the whole tumour is removed, some surgeons have started to extensively employ a sentinel lymph-node biopsy in DCIS patients, forgetting that the chance of axillary metastases is rare. A sentinel node biopsy should be considered when the breast surgical procedure can rule out its subsequent employment [12]. In fact, sentinel node biopsy cannot be performed after mastectomy or very extensive resections, especially when plastic procedures are used. There is no evidence to support the routine use of hormonal treatment for DCIS. Tamoxifen was able to significantly reduce the number of invasive recurrences in patients on the NSABP protocol B24, but this was more evident in the group with positive margins, emphasising the importance of a complete surgical excision [13]. In conclusion, the present treatment modalities may be too aggressive because many DCIS patients neither recur nor progress to invasive cancer. The next fundamental goal will be to understand the biological behaviour of DCIS lesions.

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