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REVIEW

Management of ductal carcinoma *in situ* of the breast

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The advent of mammographic breast screening has increased the detection of ductal carcinoma *in situ* (DCIS), which now accounts for 15–20% of all breast cancer. While symptomatic DCIS has been treated satisfactorily by mastectomy, this may be an over-treatment of smaller screen-detected lesions. Although local excision, with or without radiotherapy, is associated with a significant risk of local recurrence of DCIS or invasive cancer, salvage surgery is usually successful. The long-term breast-specific mortality rate of treatment by mastectomy and local excision are similar. Whereas mastectomy is still appropriate for women with lesions >30 mm in diameter or centrally placed and for those women who demand the best possible disease-free survival, local surgery should otherwise be considered.

Malignant change in the breast has been recognised to have a pre-invasive stage since 1913 *(1)*. This review describes the current dilemmas in the management of ductal carcinoma *in situ* (DCIS). Lobular carcinoma *in situ* will not be considered as it has a different biological behaviour and requires different management *(2,3)*.

DCIS is recognised as the proliferation of malignant epithelial cells within ducts and acini, with no light microscopic evidence of invasion beyond the basement membrane *(4)*. Currently, problems in deciding appropriate management for this condition have arisen because breast screening programmes have led to a much higher proportion of DCIS than was previously the case in the management of symptomatic breast cancer, and screen-detected DCIS is usually smaller than symptomatic disease *(5)*. Thus, it is no longer appropriate to advise mastectomy in all cases.

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Treatment options

The treatment options available for management of DCIS are the same as for invasive carcinoma: wide excision (with or without radiotherapy) and mastectomy (possibly bilateral). In recent years there has been a trend towards less aggressive surgery for invasive breast cancer *(6)* but, paradoxically, surgery for non-invasive disease may be more radical than for invasive cancer *(7)*. Whereas invasive breast cancer is often a systemic disease at the time of presentation and so local measures have little influence on outcome *(8)*, DCIS represents a localised stage of the disease amenable to local therapy *(5)*. Broders acknowledged this in 1932 *(9)*: "if carcinoma *in situ* appears alone, its recognition is necessary, for failure to recognise it may constitute an error of omission fraught with grave danger to the patient; if it goes unrecognised carcinoma is allowed to masquerade as a benign or not more than pre-carcinosis process, with a possibility of its becoming too far advanced to be amenable to treatment".

Obviously mastectomy, ideally bilateral, represents the most effective treatment of *in situ* carcinoma *(10)*. After mastectomy for DCIS, the long-term, risk of death from ipsilateral breast cancer is very low at less than 2% *(3)*. Higher rates of breast-related mortality of up to 10% are only reported with the inclusion of patients who have DCIS on biopsy, but are found to have occult invasion in

the mastectomy specimen *(11–13)*. However, one must question whether the natural history of DCIS and the long-term results of more conservative surgery justify such a radical approach.

Natural history of DCIS

The natural history of DCIS can be determined from studies of patients who underwent biopsy that was initially diagnosed as benign and in whom no further surgery was undertaken. In a study of 28 such patients, Page *et al. (14)* found seven carcinomas (28%) among the 25 patients followed for at least 3 years (range 3–10 years; mean 6.1 years). A similar study reported eight of 30 patients (27%) who developed carcinoma after a mean follow-up of 9.7 years *(15)*. In the latter study only half the patients had complete follow-up and it has been calculated that the risk of developing ipsilateral invasive carcinoma after biopsy alone of DCIS is in the order of 40% at 10 years *(3)*. This figure may be an underestimate as assessment was possible only in those in whom DCIS was initially misdiagnosed and in whom a subsequent correct diagnosis was made. Furthermore, these reports contain almost exclusively patients with non-comedo DCIS; the comedo pattern may behave more aggressively *(16–18)*. The apparent difference in recurrence rates in the different histological subtypes may be explained by later recurrence in patients with the non-comedo pattern *(19)* and can disappear with a longer follow-up *(5)*. It is probable that more sensitive markers of invasive potential than histological subtype, such as aneuploidy of the tumour cells *(20)* and c-erbB-2 expression *(4)*, will be used in the future.

Progression to invasive cancer is not inevitable and there is evidence that DCIS may involute with age *(21)*. The incidence of DCIS at post-mortem in women who have previously diagnosed breast cancer is 23%, while there is a 10% life-time risk of clinical contralateral cancer *(21)*. In contrast, in patients who have contralateral mastectomy at the time of treatment of DCIS or invasive cancer *(10,22)*, the rate of DCIS in the opposite breast is higher, at between 30% and 50%.

Effect of screening

The advent of screening programmes has highlighted the differences between two ends of the spectrum of disease. Symptomatic DCIS has a very different outcome from small screen-detected changes *(23,24)*. In reports which recruited patients before 1980 *(10,11,13,25,26)*, most patients had 'gross' DCIS. In these reports DCIS constituted only 3–5% of cases of breast cancer *(3)*. The clinical features include a palpable mass, nipple discharge or Paget's disease of the nipple. After biopsy for diagnosis followed by mastectomy, occult invasion was found in the mastectomy specimen in up to 20% of patients and nodal metastases were present in up to 10% of cases *(3,11,13,23)*. For these patients who appear to have 'multicentric' disease *(10)* and a significant risk of synchronous invasive breast cancer *(11)*, mastectomy is appropriate management. These patients have a high rate of recurrence after local excision *(22,26)*.

In contrast, mammography and mass screening have increased to 15–20% the proportion of breast carcinoma detected in the *in situ* phase *(24)*. DCIS is not only being diagnosed with greater regularity, there has also been a change in its pattern. Up to 90% of DCIS is now detected by mammography *(5)*, and the lesions are usually impalpable *(7)*. Approximately half of the mammographically detected foci of DCIS are less than 20 mm in diameter on histological assessment *(5,17,19,27)*.

Breast conservation in DCIS

In the era of symptomatic presentation of DCIS, it was believed that this condition was usually multicentric *(10)*, because of the 60–75% incidence of residual DCIS in the mastectomy specimen after diagnostic biopsy *(11,22)*. The careful histological study of Holland *et al. (27)* demonstrated that although DCIS may be extensive it is almost invariably continuous through the duct systems. Although only one of 82 lesions was found to be truly multicentric, in one-third of these patients more than one quadrant of the breast was affected. Recurrent disease after local excision is almost invariably in the same quadrant as was the original lesion *(5,7,17)*. This implies that if adequate local excision can be achieved, then that should be adequate therapy. However, strict criteria must be applied to obtain low local recurrence rates with simple excision *(17)*. These authors stress that local excision is only feasible for lesions less than 25 mm in diameter on histological assessment. The size of mammographic microcalcification is only a guide to histological size and may be an underestimate, particularly in the non-comedo subtypes *(27)*. Clear excision margins must be obtained, but even using specimen-orientated radiography this is possible in the initial biopsy in only 70% of cases *(28)*, while without using this technique only about one-half of lesions are fully excised at guided biopsy *(29,30)*. Finally, the breast must be amenable to clinical and mammographic follow-up and this may exclude those non-comedo lesions (up to 50%) that do not contain microcalcification *(27)*.

Table I shows a comparison of the results of breast conservation and mastectomy for DCIS. This confirms that local excision is associated with a higher local recurrence rate than mastectomy. When interpreting these data one must remember that in all series including both local excision and mastectomy, except for that of Fisher *et al. (31)*, patients with smaller, more favourable lesions were selected for local excision.

The limitations of breast conservation in DCIS are similar to those for invasive tumours. There are several reasons why breast conservation may not be appropriate for larger areas of DCIS. Increasing size makes complete excision incompatible with cosmetic breast conservation. Furthermore, microinvasion becomes increasingly likely

Table I. Results of treatment of ductal carcinoma *in situ*

	Wide excision			*Wide excision and radiotherapy*			*Mastectomy*		
Series (reference)	*Number*	*Recurrence*	*Met/Deaths*	*Number*	*Recurrence*	*Met/Deaths*	*Number*	*Recurrence*	*Met/Deaths*
Carter *et al. (11)*							38	0	3
Fisher *et al.* 1986 *(31)*	22	5	0	29	2	0	27	0	1
Zafrani *et al. (25)*				54	3	1			
Sunshine *et al. (10)*							70	0	3
Carpenter *et al (32)*	28	5	0				10	0	0
Lagios *et al. (17)*	79	8	1				115	0	2
Price *et al. (33)*	35	22	4				19	1	
Graham *et al. (26)*	37	14	1	7	0	0	9	1	0
Schwartz *et al. (34)*	70	11	0						
Silverstein *et al. (5)*	26	2	0	103	10	1	98	1	0
Simpson *et al. (35)*							36	0	0
Fisher *et al.* 1993 *(7)*	391	64	2	399	28	3			
Solin *et al. (19)*				172	16	4			
Southampton*	54	13	0				8	1	0
Total	720	144 (19%)	8 (1%)	681	59 (8%)	9 (1%)	295	4 (1%)	9 (2%)

* Unpublished data Met/Deaths = Those patients with distant metastases or death from breast cancer at the time of reporting

with increasing size. While this change is rare with lesions below 24 mm diameter it is found in half of lesions above 55 mm *(17)*. Finally, larger lesions are more likely to involve the nipple, which is affected in one-quarter of all cases, but in up to 70% of those larger than 40 mm in diameter *(12,27)*. We can confirm that the size of the focus of DCIS is the most important predictor of the success of conservative surgery. In our unit we have found a high rate of local recurrence in patients treated by local excision without radiotherapy (Table I, unpublished data). All recurrences were in patients with lesions >30 mm maximum mammographic diameter and we now advocate mastectomy for these patients.

There is a role for the patient's own choice in the management of DCIS, just as in breast cancer. The decision to opt for conservation or mastectomy is a relative one and a fully informed patient can contribute to this choice. Those who request the highest chance of local disease free and survival rates, in preference to a good cosmetic result will request mastectomy *(5)*.

Adjuvant therapy

The role of radiotherapy in the management of DCIS is not clear. A local recurrence rate of about 10% over a follow-up period of 4–10 years can be achieved with local excision of DCIS followed by radiotherapy *(5,19,25)*. Approximately one-half of these recurrences are invasive *(2)*. Similar results have been obtained without radiotherapy by the application of strict criteria to the management of patients by local excision *(17)*.

Two randomised studies have so far reported the results of local excision with and without radiotherapy *(7,31)* and others are in progress *(4)*. In the more recent study *(7)*, the incidence of recurrent DCIS was only marginally reduced by radiotherapy from 10.4% to 7.5%, after a mean follow-up of 43 months, but the risk of invasive recurrence was greatly reduced from 10.4% to 2.9%. In this study there is a high rate of recurrence in the control group, and in the previous study *(31)* in those patients who were allocated to mastectomy there was a 54% incidence of residual DCIS after local excision, indicating that excision had not been sufficiently radical. In invasive breast cancer with extensive *in situ* changes, which make up about 15% of all breast cancers *(2)*, there is a high incidence of local recurrence. This high incidence may be reduced by radiotherapy *(36)*, but not all authors confirm this *(6,37)*. The increased risk of recurrence appears to be related to residual DCIS *(38)* and suggests that DCIS may be resistant to the effects of radiotherapy.

The role of hormonal therapy in DCIS has not as yet been clarified, but the ongoing UK Co-ordinating Committee on Cancer Research (UKCCCR) DCIS trial will address this issue. There is evidence that oestrogen receptor expression in DCIS is similar to that of invasive cancer *(39,40)* and therefore tamoxifen may well be of some benefit.

Management of recurrence

If local excision is employed in the management of DCIS there will inevitably be local recurrences. The majority of these will be detected by mammographic follow-up *(17)*. These patients will usually undergo successful salvage therapy. Table I shows the number of patients with local recurrence and metastatic disease in several large series of patients with DCIS. If we assume that patients with metastases will eventually die of breast cancer, the cancer-specific death rate of patients with DCIS treated by local excision is about 1%. This compares favourably with similarly derived data from patients treated by mastectomy *(3)*. The most important endpoint in the treatment of DCIS is long-term survival. The argument in favour of local treatment of invasive breast carcinoma is equally applicable to DCIS: for small lesions, although local recurrence is increased in patients undergoing breast-conserving surgery, survival is not materially altered.

Conclusion

In contrast with lobular carcinoma *in situ*, DCIS appears to be a localised condition and does not represent a field change. DCIS may be extensive, but is almost always continuous in a single focus. Small lesions can be completely excised by local excision with a high chance of cure. Large lesions (30 mm or more in diameter) and those situated near and involving the nipple are not suitable for local excision and will require mastectomy. After complete excision of an area of DCIS the risk of tumour in the remaining breast tissue is not greatly elevated.

The role of radiotherapy and tamoxifen as adjuvants to local excision remains unclear. Therefore, the entry of suitable patients into the UKCCCR DCIS trial is to be encouraged.

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