Radiopathological features predictive of involved margins in ductal carcinoma in situ

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ABSTRACT

INTRODUCTION Ductal carcinoma in situ (DCIS) usually manifests as microcalcification on mammography but may be uncalci-fied. Consequently, a quarter of patients undergoing excision of a presumed pure DCIS require further surgery to re-excite mar-gins. Patients at highest risk of margin involvement may benefit from additional preoperative assessment.

METHODS A retrospective review was carried out of patients treated for screen detected, biopsy proven DCIS in a single centre over a ten-year period (1999–2009). Logistic regression analysis identified factors predictive of need for further surgery to clear margins.

RESULTS Overall, 248 patients underwent surgery for DCIS (low/intermediate grade: 82, high grade: 155) and 49 (19.8%) required further surgery. High grade disease was associated with greater mammographic extent (mean: 32mm [range: 5–120mm] vs 25mm [range: 2–100mm]), $p=0.009$) and higher incidence of mastectomy (38% vs 24%, $p=0.034$). Factors pre-dictive of involvement of surgical margins necessitating further surgery included negative oestrogen receptor status (OR: 5.2, 95% CI: 2.1–12.8, $p<0.001$) and mammographic extent (odds ratio [OR]: 1.6, 95% confidence interval [CI]: 1.2–2.1, $p=0.004$). Once size exceeded 30mm, more than 50% of patients required secondary breast surgery for margins.

CONCLUSIONS Reoperation rates for DCIS increase with preoperative size on mammography and negative oestrogen receptor status on core biopsy. Patients with these risk features should be counselled accordingly and consideration should be given to the role of additional preoperative imaging.

KEYWORDS

Breast – Ductal carcinoma in situ – Revision surgery – Margin – Screening

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Ductal carcinoma in situ (DCIS) accounts for 22% of can-cers detected through the National Health Service (NHS) breast screening programme¹ and 75% of DCIS is treated with breast conserving surgery (BCS).² Successful local control of DCIS is dependent on the achievement of clear margins since involvement predicts local recurrence of either DCIS or invasive disease.^{3–5} Presence of disease at or close to margins on formal histological examination therefore necessitates additional surgery if residual disease is suspected.^{6–8}

A quarter (24%) of patients undergoing BCS for non-invasive disease require additional surgery to breast and/or axilla while for those undergoing surgery for invasive disease, the proportion is similar (23%).² Identification of factors predictive of failure of BCS in patients treated for DCIS might identify a subgroup of cases that would benefit from additional preoperative investigation to optimise sur-gical planning.

Our unit has previously described predictors of require-ment of re-excision in patients treated for screen detected, high grade (HG) DCIS.⁹ Negative oestrogen receptor (ER)

status and disease extent were identified as positive predic-tors for requirement of re-excision. However, low/inter-mediate grade (LIG) tumours were not included in the study. As a result, it remained unclear whether these same predictors were relevant across the broader spectrum of DCIS and whether grade itself was relevant in predicting need for re-excision. The aim of the present study was therefore to identify factors predictive of involved margins following BCS across all grades of screen detected, biopsy proven DCIS and to clarify the significance of grade as a predictor.

Methods

Patients treated for biopsy proven DCIS without preopera-tive evidence of an invasive component over a ten-year period (1999–2009) were identified from the Southampton and Salisbury breast screening unit database. All cases with available information were included; 144 patients with HG disease from previous analysis by our unit⁹ were incorporated with data from an additional 104 patients

with any grade of DCIS. Patients having surgery for a preoperative diagnosis other than DCIS and those found to have neither DCIS nor invasive breast carcinoma following surgical excision were excluded. Data were collated retrospectively from case notes, electronically stored patient health records and histopathological reports. All work was performed in accordance with institutional ethical guidelines.

Patient management

Patient management followed the standard unit protocol in place at the time of presentation, which was based on the concurrent best practice guidelines. Patients recalled following screening mammography underwent further mammography and ultrasonography assessment. Core needle biopsy was used for acquisition of tissue for histological assessment; areas of calcification, stromal abnormality or mass-like density were targeted. Either ultrasonography guidance or stereotactic guidance or both were employed according to the judgement of the assessing radiologist.

Patients noted to have DCIS on core biopsy were advised to undergo either a mastectomy or wide local excision (WLE) depending on the size and position of the lesion. Choice of surgery was dictated by consensus opinion following multidisciplinary team discussion, taking into account patient preference. WLE was carried out following preoperative localisation with stereotactic wire insertion. Specimen radiography was performed intraoperatively to assess excision margin and guide cavity biopsy. Following initial WLE, re-excision was considered in patients who were found to have involved margins on histology consistent with National Institute for Health and Clinical Excellence guidelines (target minimum radial margin of excision of 2mm),⁸ and following multidisciplinary team discussion and consensus.

Pathological assessment

Data were collated from historic records of histopathological assessment of both preoperative and postoperative tissue specimens. Histopathological examinations and reports were compliant with contemporaneous NHS breast screening programme standards.¹⁰ Size estimation from histopathological specimens was reported as maximal extent measured from formalin fixed, paraffin embedded slides. The presence of microinvasion was classified as invasive disease.

Radiological assessment

Mediolateral oblique and craniocaudal mammography from all cases was reassessed for study purposes by a consultant radiologist. DCIS extent was estimated by measuring the maximal span of calcifications; multiple discrete areas of calcification were considered to be part of a single lesion and size was recorded as the maximal length encompassing all areas of change. BI-RADS® (Breast Imaging Reporting and Data System; American College of Radiology) breast density score,¹¹ distribution (cluster/segmental/diffuse) and appearance (indeterminate vs probably malignant) of calcification were recorded, as was the presence of stromal deformity or asymmetric density.

Outcome measures and statistical analysis

Continuous datasets were tested for normal distribution and data were analysed using the non-parametric Mann-Whitney U test. Discontinuous datasets were analysed using Pearson's chi-squared test or Fisher's exact test as appropriate. Univariate analysis of factors associated with incidence of occult invasive foci and the need for secondary surgery was performed. Stepwise forward selection logistic regression analysis was used to screen predictors prior to entering associated variables into binary logistic regression analysis; selection of variables was based on goodness of fit (as assessed by Nagelkerke's R^2) and significance in forward selection. Statistical analysis was performed using SPSS® version 21.0 (IBM, New York, US) and Prism® version 6.0 (GraphPad Software, La Jolla, CA, US).

Results

A total of 248 patients underwent surgery for presumed isolated DCIS during the study period (high grade: 155 [62.5%], intermediate grade: 56 [22.6%], low grade: 26 [10.5%], ungraded preoperatively: 11). Of these, 240 (96.8%) were diagnosed following core needle biopsy with or without fine needle aspiration under either ultrasonography ($n=48$) or stereotactic ($n=192$) guidance; one patient required wire guided excision biopsy to confirm diagnosis of suspected DCIS. In seven cases, the biopsy method was not recorded.

The mean patient age was 59.6 years (range: 49–84 years). The mean extent of disease was 29.4mm (range: 2–120mm). All patients presented through screening services following recall; of those with calcification on mammography, 12% had calcifications described as indeterminate in appearance and 88% had changes typical for malignant calcification (variable, casting, linear or branching). In addition to calcifications, 31 patients (12.5%) had associated asymmetric density, 14 (5.6%) had stromal deformity and 29 (11.7%) had associated mass-like density on imaging.

Disease grade, extent and oestrogen receptor status

HG DCIS was associated with a greater mean extent according to preoperative mammography (LIG: 25.0mm, range: 2–100mm, 95% confidence interval [CI]: 20.1–30.0mm; HG: 31.8mm, range: 5–120mm, 95% CI: 28.0–35.8mm; $p=0.009$). Furthermore, a greater proportion of patients with HG disease were treated initially with mastectomy (LIG: 20/82 (24.4%); HG: 59/155 (38.1%); $p=0.034$).

HG tumours were less frequently associated with asymmetric density (LIG: 17/82 [20.7%]; HG: 13/155 [8.4%]; $p=0.019$) and stromal deformity (LIG: 10/82 [12.2%]; HG: 4/155 [2.6%]; $p=0.014$). Incidence of associated mass-like density on imaging was equivalent for both groups (LIG: 11/82 [13.4%]; HG: 17/155 [11.0%]; $p=0.2$).

Negative ER status was demonstrably more prevalent in HG disease (LIG: 0/75 [0%]; HG: 46/147 [31.3%]; ER status unrecorded for 21 cases; $p<0.001$). Human epidermal growth factor receptor 2 status was not assessed routinely.

Surgical management, margins and incidence of invasion

Of the 248 patients in this study, 159 underwent WLE and 80 underwent mastectomy as their primary breast

operation (9 cases unrecorded). Histological reporting of specimens taken at primary surgery identified 90 WLE specimens (56.6%) as having clear margins, 55 (34.6%) had involved margins and 10 (6.3%) had uncertain margins (4 unrecorded). Following corroboration with operative findings during subsequent multidisciplinary team meetings, a third ($n=49$, 30.8%) of the patients who underwent WLE were identified as requiring a second breast operation to remove residual disease; 14 underwent cavity re-excision whereas 35 patients underwent mastectomy. Following repeat excision, the margins of 4 of the 14 patients remained positive and these patients were then treated definitively with mastectomy. In total, among the 239 patients for whom the primary breast operation was recorded, 119 were treated with mastectomy and 120 with WLE.

Forty-six patients were noted to have invasive disease following histological analysis. The mean size of the invasive component was 8.7mm (range: 1–55mm, 95% CI: 5.4–12.0mm). Thirty-three (71.7%) of these were invasive ductal carcinoma, four (8.7%) were invasive lobular carcinoma and the remainder were tubular, mucinous or heterogeneous. Five (10.9%) were grade I, twenty-five (54.3%) were grade II and ten (21.7%) were grade III (6 unrecorded). All grade III invasive tumours were associated with HG DCIS.

Discordance between preoperative and postoperative assessment

For 236 patients, both preoperative grading of DCIS according to core biopsy and final histological grading was available. The vast majority (95.3%) of cases were assigned correctly to either LIG or HG by core biopsy.

The mean discrepancy between estimated size on preoperative mammography and final pathological size was 12.7mm (range: 0–70mm, 95% CI: 10.9–14.4mm). There was no significant difference in mean discrepancy between LIG and HG disease (LIG: 11.5mm, range: 0–55mm, 95% CI: 8.6–14.5mm; HG: 13.3mm, range: 0–70mm, 95% CI: 8.6–14.5mm; $p=0.1$). Discrepancy between preoperative and postoperative sizing became greater with increasing DCIS extent for both LIG and HG cases (Fig 1).

HG disease extent was significantly more likely to be underestimated by more than 10mm on preoperative mammography than the extent of LIG tumours ($p=0.02$) (Table 1). There was no statistically significant increase in underestimation for ER negative DCIS (ER positive: 28/180 [15.6%]; ER negative: 12/47 [25.5%]; $p=0.1$). The mean discrepancy between preoperative mammographic sizing and postoperative histological measurement in both ER positive and negative disease was equivalent (ER positive: 12.3mm, range: 0–70mm, 95% CI: 10.2–14.4mm; ER negative: 12.7mm range: 1–50mm, 95% CI: 9.1–16.4mm; $p=0.3$).

Preoperative mammographic extent, tumour grade and ER status were entered into binary logistic regression analysis to determine predictors of underestimation of size of DCIS on histology; neither extent nor ER status were significant predictors. Presence of HG disease increased the likelihood of size underestimation by >10mm on

Figure 1 Bland–Altman plot demonstrating increasing discordance between estimated preoperative sizing of ductal carcinoma in situ (DCIS) on mammography and final postoperative sizing (taken from histological sections) for both low/intermediate grade and high grade disease. The relatively even spread of data points around the $y=0$ line for smaller lesions implies both under and overestimation of size on preoperative imaging. The average discrepancy was 2.83mm underestimation.

preoperative mammography (odds ratio [OR]: 3.0, 95% CI: 1.3–7.1, $p=0.01$).

Predictors of occult invasive disease

Forty-six patients (18.5%) were found to have invasive disease following histological examination (Table 2). Patients with invasive foci tended to have larger lesions on mammography (mean: 35.7mm vs 28.3mm, $p=0.02$). However, there was no significant difference in age, BI-RADS® score, or the incidence of asymmetric density or stromal deformity.

The difference between the incidence of invasion in ER negative disease (8/47, 17.0%) and in ER positive disease (37/180, 20.6%) was not statistically significant ($p=0.6$). On the other hand, patients with an associated mass-like density on mammography were more likely to have occult invasive disease (10/29 [34.5%] vs 36/209 [17.2%]; relative risk [RR]: 2.0, 95% CI: 1.1–3.6, $p=0.03$), as were those with HG DCIS (36/154 [23.4%] vs 9/77 [11.7%]; RR: 2.0, 95% CI: 1.0–3.9, $p=0.04$).

Binary logistic regression analysis was performed for mammographic extent, grade, presence of mass-like density and ER status to identify independent predictors of an invasive component (Table 3). Both HG disease (OR: 2.8)

Table 1 Discrepancy between estimated preoperative mammographic sizing and final histological measurement of DCIS by disease grade and ER status. Influence of lesion size on discrepancy is illustrated in Figure 1.

		Discrepancy (pre vs postoperative)			p-value
		Underestimated by >10mm	Overestimated by >10mm	Within 10mm	
DCIS grade*	Low / intermediate	7 (8.5%)	19 (23.2%)	56 (68.3%)	0.02
	High	34 (21.9%)	39 (25.2%)	82 (52.9%)	
Total		41	58	138	237
ER status**	Positive	28 (15.6%)	43 (23.9%)	109 (60.6%)	0.1
	Negative	12 (25.5%)	12 (25.5%)	23 (48.9%)	
Total		40	55	132	227

DCIS = ductal carcinoma in situ; ER = oestrogen receptor

*11 cases had unrecorded DCIS grade; **21 cases had unrecorded ER status

and presence of mass-like density (OR: 3.4) independently predicted occult invasive disease. Mammographic extent and ER status were not significant predictors on multivariate analysis.

Predictors of need for further surgery

A third of the 159 patients initially treated with WLE ($n=49$, 30.8%) required a second breast operation. Cases requiring secondary surgery had significantly greater discordance between mean preoperative and postoperative sizing (15.4mm [95% CI: 11.5–19.3mm] vs 7.0mm [95% CI: 5.5–8.4mm], $p<0.0001$). Almost half of the patients requiring secondary surgery (21/49, 42.9%) had extent underestimated by >10mm preoperatively whereas for those who required no further breast surgery, the proportion was much smaller (9/110, 8.2%) ($p<0.0001$).

Cases that required secondary breast surgery had a significantly greater mean extent of disease on preoperative mammography (23.9mm vs 15.9mm, $p=0.002$). Figure 2 illustrates the requirement for further breast surgery according to DCIS extent; although the majority of patients undergoing WLE for lesions measuring <20mm were treated successfully with a single operation (77/88 [87.5%]), the need for additional surgery increased sharply with larger lesions. Secondary surgery rates increased to 45.9% (17/37) with lesions measuring 20.0–29.9mm, 73.3% (11/15) with lesions measuring 30.0–39.9mm and 91.7% (11/12) for lesions measuring ≥ 40 mm. A greater proportion of patients with higher density breasts required more than one breast operation (BI-RADS® 1–2: 22/87 [25.3%], BI-RADS® 3–4: 27/68 [39.7%]) although this difference narrowly failed to achieve statistical significance ($p=0.053$).

Almost two-thirds of patients undergoing WLE for ER negative DCIS required secondary breast surgery (17/28, 60.7%). Grade alone was not indicative of the need for further surgery (LIG: 16/57 [28.1%]; HG: 33/95 [34.7%]; $p=0.5$). However, the combination of HG with ER negative status was associated with a greater number of cases with margin involvement and HG was associated with a greater incidence of size underestimation by >10mm. Almost half

of the patients with diffuse or segmental calcification required secondary surgery compared with only a fifth of those with clustered calcifications (28/58 [48.3%] vs 12/60 [20.0%], $p=0.01$). There was no association between the requirement for further surgery and the presence of asymmetry, stromal deformity or mass-like density.

Binary logistic regression analysis was performed for tumour grade, mammographic extent, ER status, BI-RADS® score and distribution of calcification to identify independent preoperative predictors of the requirement of secondary surgery after attempted WLE (Table 4). Following stepwise forward logistic regression analysis, grade was removed as it was highly non-significant ($p=0.5$). Of the remaining four variables, both ER negative status (OR: 5.2, $p<0.001$) and greater mammographic extent (OR: 1.6, $p=0.004$) independently predicted need for secondary breast surgery, with distribution of calcification ($p=0.1$) and BI-RADS® score ($p=0.1$) failing to achieve statistical significance when multivariate analysis was performed.

Discussion

Previously identified factors predictive of occult invasive disease in DCIS cases include grade,^{12,15} extent,^{15–17} number of calcifications¹² and other mammographic features (architectural distortion, mass, increased density).¹⁵ Few studies have attempted to investigate factors associated with failure of BCS. Dillon *et al* found lesion size to be the only independent predictor of treatment outcome.¹⁶ Nevertheless, the incidence of margin compromise in their cohort was 72% and their study may therefore be unrepresentative of wider practice. Data from the Sloane Project identified bidimensional product as a preoperative predictor of successful BCS in DCIS.¹⁷ Although grade and calcification individually were not significant predictors, stratification of cut-off of bidimensional product according to these factors did improve prediction.

Intuitively, one would expect inaccuracy in preoperative size estimation to result in failure of BCS. Accuracy of mammography in predicting DCIS extent has previously

Table 2 Predictors of occult invasion					
	<i>n</i>	Presence of occult invasion			<i>p</i> -value
		Yes	No	Unknown	
Total	248 (100%)	46 (18.5%)	190 (76.6%)	12 (4.8%)	
Age (years)					0.3
Mean	59.6	58.5	60.0		
Range	49–84	49–72	49–84		
95% CI	58.7–60.5	56.6–60.4	58.9–61.0		
Preoperative mammographic extent (mm)					0.02
Mean	29.4	35.7	28.3		
Range	2–120	5–110	3–120		
95% CI	26.3–32.4	28.6–42.8	24.9–31.7		
Associated mass-like density on imaging					0.03
Yes	29 (11.7%)	10 (21.7%)	19 (10.0%)	0	
No	209 (84.3%)	36 (78.3%)	170 (89.5%)	3	
Unknown	10 (4.0%)	0 (0%)	1 (0.5%)	9	
Preoperative grade on core biopsy					0.04
Low/intermediate	82 (33.1%)	9 (19.6%)	68 (35.8%)	5	
High	155 (62.5%)	36 (78.3%)	118 (62.1%)	1	
Unknown	11 (4.4%)	1 (2.2%)	4 (2.1%)	6	
Appearance of microcalcification					0.1
Indeterminate	22 (8.9%)	1 (2.2%)	21 (11.1%)	0	
Classic malignant (variable, casting, linear, branching)	156 (62.9%)	30 (65.2%)	123 (64.7%)	3	
Not present / unknown	70 (28.2%)	15 (32.6%)	46 (24.2%)	9	
Stromal deformity					0.5
Yes	14 (5.6%)	1 (2.2%)	13 (6.8%)	0	
No	220 (88.7%)	42 (91.3%)	175 (92.1%)	3	
Unknown	14 (5.6%)	3 (6.5%)	2 (1.1%)	9	
ER status					0.6
Positive	180 (72.6%)	37 (80.4%)	140 (73.7%)	3	
Negative	47 (19.0%)	8 (17.4%)	38 (20.0%)	1	
Unknown	21 (8.5%)	1 (2.2%)	12 (6.3%)	8	
Asymmetric density					0.6
Yes	31 (12.5%)	5 (10.9%)	26 (13.7%)	0	
No	202 (81.5%)	38 (82.6%)	161 (84.7%)	3	
Unknown	15 (6.0%)	3 (6.5%)	3 (1.6%)	9	
BI-RADS® score					0.8
1	22 (8.9%)	3 (6.5%)	19 (10.0%)	0	
2	110 (44.4%)	21 (45.7%)	86 (45.3%)	3	
3	85 (34.3%)	19 (41.3%)	66 (34.7%)	0	
4	20 (8.1%)	3 (6.5%)	17 (8.9%)	0	
Unknown	11 (4.4%)	0 (0%)	2 (1.1%)	9	
BI-RADS® = Breast Imaging Reporting and Data System; CI = confidence interval; ER = oestrogen receptor					

Table 3 Binary logistic regression analysis to determine factors predictive of underlying invasive disease according to preoperative radiopathological features

Factor	Univariate analysis	Binary logistic regression analysis			
	p-value	OR	SE	95% CI	p-value
Associated mass-like density on imaging	0.03	3.4	0.5	1.4–8.5	0.009
Grade (low/intermediate vs high)	0.04	2.8	0.4	1.2–6.7	0.017
Mammographic extent of DCIS*	0.02	1.1	0.1	1.0–1.3	0.08
Negative ER status	0.6	2.2	0.5	0.9–5.5	0.1

CI = confidence interval; DCIS = ductal carcinoma in situ; ER = oestrogen receptor; OR = odds ratio; SE = standard error
*OR expressed as odds associated with additional 10mm size increase

Figure 2 Requirement for further breast surgery following initial wide local excision (WLE) for ductal carcinoma in situ

been associated with grade;^{17,18} LIG lesions were less accurately sized mammographically and this has been attributed to less calcification and necrosis in LIG DCIS¹⁸ making size estimation problematic.^{17,19} However, more frequent size underestimation in low compared with HG disease was only significantly demonstrated in patients undergoing mastectomy.¹⁸ Furthermore, the reported relationship between grade and mammographic size discrepancy is inconsistent, and other authors have failed to demonstrate any correlation.²⁰

Our institution has previously identified ER status and extent as predictors of need for further breast surgery following attempted BCS for HG DCIS.⁹ The current paper builds on this by including the wider spectrum of tumour

grades as well as by establishing the relevance of grade in terms of risk of invasion and margin involvement.

Our results show radiopathological differences between grades of DCIS including a higher proportion of ER negative disease and greater extent in HG lesions. In contrast, LIG tumours are more commonly associated with asymmetric density and stromal deformity. Our findings therefore correlate with previous studies demonstrating a strong link between HG and ER expression.^{21–23} Our data also indicate that grade independently predicts presence of invasion (Tables 2 and 3), which is in line with previous publications. Conversely, in our cohort, extent narrowly failed to retain significance on multivariate analysis, contrary to previous findings.^{15–15} This is likely to be due to our smaller sample size. Furthermore, our data suggest mass-like density on mammography is also predictive of occult invasion despite our policy of targeting such lesions for biopsy in addition to areas of calcification preoperatively. This correlates with a meta-analysis from 2011 that identified mass-like density on mammography as predictive of invasion.²⁴

Given the importance of grade in prediction of invasion, this study assessed its relevance in predicting size discrepancy and need for further surgery. Contrary to work published previously,^{17,18,20} our study indicates that HG independently predicts underestimation of DCIS extent preoperatively (Table 1); however, there was no difference in the mean discrepancy for HG and LIG disease. This suggests that HG DCIS is prone to being both under and overestimated to an equal extent (as demonstrated in Fig 1), which may explain conflicting results in the literature. It is unclear why this might be the case.

Despite the association between HG and underestimation of extent, and the concordance between underestimation and need for further surgery, grade did not predict failure of BCS to clear margins. Factors that proved significant predictors of the need for further surgery were ER status and extent (Table 4).

Interestingly, the association between ER negative status and the high incidence of secondary surgery is not easy to explain. Previous publications have demonstrated that ER negative DCIS is more readily visible with ultrasonography and less frequently seen on mammography than ER

Table 4 Binary logistic regression analysis to determine factors predictive of need for secondary breast surgery in patients undergoing wide local excision for DCIS based on preoperative radiopathological features

Factor	Univariate analysis	Binary logistic regression analysis			
	p-value	OR	SE	95% CI	p-value
Negative ER status	0.001	5.2	0.5	2.1–12.8	<0.001
Mammographic extent of DCIS*	0.002	1.6	0.2	1.2–2.1	0.004
Distribution of calcification (cluster vs diffuse/segmental)	0.01	2.4	0.5	0.9–6.6	0.09
BI-RADS® score (1–2 vs 3–4)	0.053	2.1	0.5	0.9–5.1	0.10

BI-RADS® = Breast Imaging Reporting and Data System; CI = confidence interval; DCIS = ductal carcinoma in situ;
ER = oestrogen receptor; OR = odds ratio; SE = standard error
*OR expressed as odds associated with additional 10mm size increase

positive disease.²⁵ Although there was an increase in underestimation of extent in ER negative cases, this failed to achieve significance (Table 1). Nevertheless, ER negative status was strongly predictive of the need for more than one breast operation to clear disease. It follows that additional factors (other than size discrepancy) would seem to be contributory.

Other associations with ER negative DCIS include HG,^{21–23} multifocality/multicentricity, comedonecrosis and presence of mass-like density on mammography.²⁵ However, ER status has not been demonstrated to influence the manifestation of calcification on mammography.²⁵ Similarly, in our study, there was no association between ER status and morphology of calcification (incidence of diffuse/segmental calcification: ER positive 47/98 [48.0%] vs ER negative 9/16 [56.3%]; $p=0.5$). The reasons for an association between ER negative status and failure of BCS therefore merit further investigation.

With regard to lesion size, Figure 1 illustrates the widening disparity between radiographic and histological lesion extents with increasing tumour size. This explains, at least partially, the association between larger size and the need for further surgery following attempted BCS. It also mirrors our previously published findings for HG DCIS⁹ and demonstrates this trend is consistent across all grades of DCIS. Among our cohort of 248 patients, the majority with disease measuring <30mm in extent were treated successfully at the first attempt (Fig 2). Conversely, re-excision rates increased markedly with lesions of ≥30mm.

Our data indicate that extent of DCIS appears to be a common predictor of both BCS failure and occult invasion. Brennan *et al* carried out a meta-analysis in which 20mm was identified as the size cut-off for increased risk of invasive disease.²⁴ Consequently, additional preoperative assessment of cases with larger lesions may improve the success rate of primary surgery by better defining extent^{25–30} while also theoretically increasing diagnosis of occult invasion.³¹ Furthermore, our results suggest that patients with ER negative status might also benefit from additional imaging preoperatively to improve extent estimation. For that reason, although the role of magnetic resonance imaging^{32,33} and emergent diagnostic technologies such as

breast tomosynthesis in the preoperative evaluation of DCIS remains poorly defined, future study selecting cases with such risk factors for augmented preoperative imaging assessment may prove beneficial.

Conclusions

Reoperation for screen detected DCIS is more frequent with greater preoperative size on mammography and ER negative status on core biopsy but not with higher tumour grade. Better understanding of factors that predict repeat surgery may help identify patients in whom additional pre-operative workup or counselling regarding the probability of further surgery may be indicated.

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