Margins in Breast Conserving Surgery: Could We Have Alternatives

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ABSTRACT

***Background**: For patients with breast cancer, a negative surgical margin at first breast conserving surgery (BCS) minimizes the need for reoperation and likely reduces postoperative anxiety. We assessed margin status after BCS in early-stage breast cancer. **Aim of work**: This study was conducted to evaluate the self-reported practice patterns and perceptions of obtaining free surgical margins in BCS in our university hospital. It is about alternatives of assessment of safe margins (gross, microscopic) and how safe it is not to depend entirely on frozen section intraoperatively, through studying the rate of wider margins after both ways. **Methods:** A prospective, randomized study (card picking by the patient under supervision of the ward nurse) of 103 female patients underwent breast-conserving surgery (BCS) with and without frozen section- 49 and 54 patients respectively - for assessment of margins intraoperatively were studied at General Surgery Department, kasr Alainy University hospital, Faculty of Medicine, Cairo University in a period of 21 months duration starting from January 1st, 2015 till October 31st, 2016. **Results:** Thirty eight patients out of total 54 (70.4%), who were randomized not to undergo frozen section for margins evaluation, were deemed to have clear margins on gross assessment and did not undergo re-excision for residual tumor which is confirmed on subsequent microscopic examination (paraffin section).While 16 females of the same group (29.6%) were found to have compromised margin(s) necessitating a second operation based on microscopic examination (paraffin section).On the other hand, ten patients out of 49 (20.4%), who were randomized to undergo frozen section for margins evaluation, underwent re-excision in order to have adequate safe margins in cases subjected to frozen section assessment of margins intraoperatively. **Conclusion:** Intraoperative gross assessment of margins depending on the type of margins excision is an effective technique to obtain safe margins in BCS with rates of re-excision near to cases subjected to frozen section for margins assessment intraoperatively. This is particularly useful in situations where frozen section technique is not available or represents added cost.*

***Key words:** breast conserving surgery, safe margins, gross assessment, frozen section*

INTRODUCTION

Most early-stage breast cancers (stage I and stage II) are now managed with breast-conserving surgery (BCS) followed by radiation therapy. The aim of BCS is to completely remove the identified cancer while preserving adequate breast tissue for an acceptable cosmetic result. The presence of a microscopically clear margin is an important indicator to ensure completeness of surgical excision [1,2].

A number of factors affect the outcome of BCS, including patient age, tumor stage, multicentricity and multifocality, and surgical margins [3-7]. Of these, surgical margins have proven to be the strongest predictor of local recurrence [8-11]. Therefore, the primary goal of surgeons and radiotherapists is to obtain adequate negative margins. The definition of a positive margin can vary greatly, being either gross assessment at surgery or microscopically determined by the presence of tumor cells at a fixed distance from the cut edge of the surgical specimen [1].

Safety Margins in breast conserving surgery (BCS) have been a long debatable subject. This arises from the absence of a consensus on definite definition of adequate margins, resulting in re-excision rates of 25 to 40% for close or positive margins and its consequent impact upon cosmoses, costs, patient dissatisfaction. local recurrences (LR) in BCS in the last decade is decreasing by better surgical techniques as regards assessing negative margins, use of targeted therapy and in general with the multidisciplinary treatment in the management of

breast cancer patients. In recent practice, surgeons are considering margins management in the context of all factors including not only patient and tumor characteristics but also the regional and systemic treatment the patient is receiving [12].

PATIENTS AND METHODS

A prospective, randomized study (card picking by the patient under supervision of the ward nurse) of 103 female patients that were planned to undergo breast-conserving surgery (BCS) with frozen section for microscopic assessment of margins intraoperatively (49 patients) and without frozen section (54 patients) were studied. They were histologically proven primary breast carcinoma (both, invasive and duct carcinoma insitu) and categorized as being early stage breast cancer (stage 0, I and II) at General Surgery Department, kasr Alainy University hospital, Faculty of Medicine, Cairo University within the period of 21 months starting from January 1st, 2015 till October 31st, 2016.

Ethically, all patients were given an explanation of the research and about the investigative and operative procedure with their merits and demerits, expected results, and possible re-entry to operating theatre for re-excision and its possible consequent unpleasant cosmetic result (which is the main aim of BCS). If she agreed then the case had been selected for our study. The study did not involve any additional investigation or any significant risk (on the short run of follow up as we explained this to the patients). We followed the inclusion and exclusion criteria strictly. It did not cause economic burden to the patients or our institution

Primary Outcome was to evaluate the feasibility of performing wide local excision (BCS) without intraoperative pathological assessment, depending on the gross evaluation of the specimen margins. This was achieved through the results of the final microscopic pathological assessment (paraffin section) in our histopathology department. The rate of re-excision for residual foci in the assessed margins in both groups of intraoperative frozen section and gross assessment were compared in relation to the number of cases of BCS totally.

We allocated the included females as postmenopausal according to the following:

- Prior bilateral oophorectomy.
- Age ≥60 y.
- Age <60 y and amenorrheic for 12 or more months.

Selection of patients was based on certain inclusion criteria as all female patients diagnosed with early breast cancer (stage 0, I and II), within the mentioned duration, fulfilling the criteria of feasibility of BCS and agreed upon the procedure were included. Otherwise, the case is excluded from our study.

In our study, staging of the cases according to American Joint Committee on Cancer (AJCC) TNM Staging System for Breast Cancer was followed:

Tis Carcinoma in situ (DCIS)

T1 Tumor ≤20 mm or less in greatest dimension

T2 Tumor >20 mm but ≤ 50 mm in greatest dimension

Interpreted into anatomic stage **(table 1)**:

Table 1: anatomic stages of early breast cancer

STAGE 0	Tis	N0	M0
STAGE IA	T1	N0	M0
STAGE IB	T0 T1	N1 N1	M0
STAGE IIA	T0 T1 T2	N1 N1 N0	M0
STAGE IIB	T2	N1	M0

The exclusion criteria of cases not to perform BCS in our study were:

- Pregnancy.
- Diffuse suspicious or malignant-appearing microcalcifications.
- Widespread disease that cannot be incorporated by local excision through a single incision that achieves negative margins.
- Prior radiation therapy to the chest wall or breast.
- Active connective tissue disease involving the skin.
- Tumors >5 cm.

N.B. strong positive family history suggesting genetic predisposition and cardiological status were considered and the patient was counselled about the pros and cons of BCS followed by radiation therapy.

In our study, we settled the following as safe/accepted margins after discussing each case in the multidisciplinary team(MDT) meeting:

A-DCIS:

- Margins greater than 10 mm are widely accepted as negative.
- Margins of 1 mm are considered inadequate but accepted.
- Close surgical margins (<1 mm) at the fibroglandular boundary of the breast (chest wall or skin), no surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site.

B-INFILTRATING CARCINOMA:

- Positive margin cases (either infiltrated by tumor cells or less than 1 mm) underwent re-excision (entire original cavity excised) and if the re-excised margins are still positive then mastectomy is done. If cosmesis is compromised, then mastectomy is done directly without re-excision.

The biodata of the patients in the form of name, age, sex, address, comorbidities, parity, contraception and menopausal status were noted. Importantly, family history was obtained in details. Furthermore the date of admission, date of operation and date of morbidity were recorded.

Patients were diagnosed using sono-mammogram and image guided (ultrasound) 14 gauge needle core biopsy. The biopsies were evaluated for the presence of invasive carcinoma or DCIS including histological subtype. MRI was done in cases with dense glandular element to be sure of the exact disease extension. Axillary dissection or sentinel lymph node biopsy was performed in all patients with invasive/DCIS cancer**. (Fig.1, 2)**

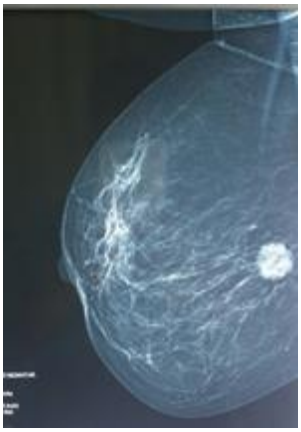

Fig.1: mammogram (MLO) showing malignant lesion

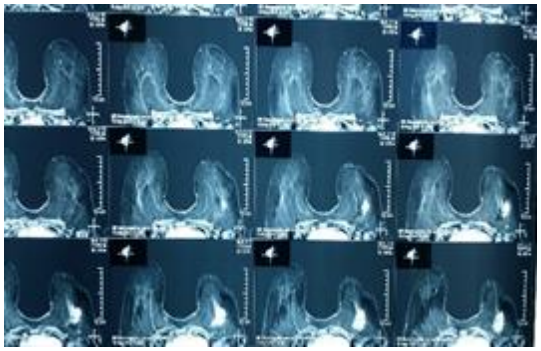

Fig. 2: MRI of the breast showing malignant lesion

Marking of the site of incision preoperatively was done. All cases were aimed at having at least 1 cm gross clearance of the surrounding margins (**fig.3).**

Fig. 3: preoperative incision site marking (kite incision)

Impalpable tumours were localized for surgical excision by ultrasound guided wire placement (**Fig.4).**

Fig.4: wire-localization for non-palpable mass

The superficial and deep margins of excision extended up to the skin and pectoralis fascia, respectively. According to intraoperative judgement, the surgical margins were obtained (marginal or cavitary). At the time of surgery, the excised tumour specimen was orientated

according to an established protocol (long thread lateral, short thread superior and double thread deep surface) and the specimen was placed over cartoon paper or disposable drape with the side of the breast and axilla drawn and the specimen was placed in its proper orientation then captured **(Fig. 5,6,7)**. Afterwards, it is transferred to the pathology department for microscopic assessment of paraffin sections (this is done for cases intended not to perform intraoperative frozen section for them depending on gross assessment). Cases planned for intraoperative frozen section examination have been processed almost the same way except that the excised specimen is sent to the pathologist directly intraoperatively and the results of the margins examination is conveyed to the surgeon inside the operating theatre. The compromised margin was then re-excised if surgically indicated. The main tumour specimen and the re-excised specimen(s)(if any) were then further sent to the histopathology department for definite paraffin section examination and the final pathology report regarding tumour size, tumour grade, DCIS, lymphovascular invasion and margins status.

Fig.5: WLE and ASNB technique

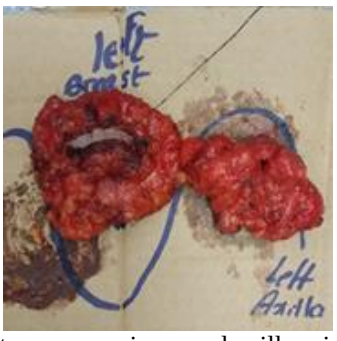

Fig. 6: tumour specimen and axilla orientation

Fig. 7: tumour specimen and axilla orientation

Statistical analysis

Results are expressed as mean ± standard deviation or number (%). Association between variables (categorical data) was performed using Chi square test or Fisher's exact test whenever it was appropriate. Statistical Package for Social Sciences (SPSS) computer program (version 19 windows) was used for data analysis. P value ≤ 0.05 was considered significant.

RESULTS

This prospective, randomized study was conducted to find out if we can depend on alternatives for assessment of safe margins in cases treated with BCS and how safe not to depend entirely on frozen section intraoperatively. This was achieved through reporting self-practice pattern of gross assessment of excised margins and its comparison with the utilization of frozen section assessment. Consequently, observing the rate of wider margins after both ways. One hundred and three patients were included in the study and their clinical and pathological details are outlined in **table 2**.

Table (2): clinical and pathological features of the studied patients

	Number
Age (yrs.)	
Minimum-maximum	30-72
Mean ± SD	52.25 ± 11.20
Premenopausal	43 (41.7%)
Postmenopausal	60 (58.3%)
T-stage	
T1(Tumor ≤20 mm)	49 (47.6%)
T2(Tumor >2cm but ≤ 5cm)	54 (52.4%)
N-stage	
N0	61 (59.2%)
N1	42 (40.8%)
Tru-Cut Needle Biopsy (histopathology)	
Cribriform carcinoma	1 (1.0%)
Duct carcinoma insitu	15 (14.6%)
DCIS+invasive carcinoma	2 (1.9%)
Invasive duct carcinoma	72 (69.9%)
IDC+DCIS	2 (1.9%)
Invasive lobular carcinoma	6 (5.8%)
Invasive mammary carcinoma	5 (4.9%)
Wire Localization	23 (22.3%)
Frozen section for margins	49 (47.6%)
Axillary clearance	42 (40.8%)
Sentinal node biopsy	61 (59.2%)
Wider margins	26 (25.2%)
Post re-excision mastectomy	3 (2.9%)

Data are expressed as mean ± SD or number (%).

Thirty eight patients out of 54 (70.4%), who were randomized not to undergo frozen section for margins evaluation, were deemed to have clear margins on gross assessment and did not undergo re-excision to achieve safe margins which is based on subsequent microscopic examination. while 16 patients (29.6%) of the same group were found to have a compromised margin(s) necessitating a second operation on microscopic examination.

While ten patients out of 49 (20.4%), who were randomized to undergo frozen section for margins evaluation, underwent re-excision in order to have adequate safe margins. By observing the outcome of data, there were three cases that underwent mastectomy out of 26 patients who were subjected to re-excision (p value 0.002). It was because of either compromised BCS or still positive margin, duct carcinoma insitu (DCIS), invasive lobular carcinoma (ILC) on re-excision. Twelve cases out of 26 patients that had re-excision of margins were T1 stage (24.5%), on the other hand 14 patients out of the re-excision cases were T2 (25.9%) **(Table 3)**

Table (3): Association between different variables and rate of re-excision of margins in the studied patients.

		Re-excision of margins		*P value*
		No (n=77)	**Yes (n= 26)**	
Frozen for margins	No(gross)	38 (70.4%)	16 (29.6%)	0.282
	Yes	39 (79.6%)	10 (20.4%)	
MRM	No	77 (77.0%)	23 (23.0%)	0.002*
	Yes	0 (0.0%)	3 (100.0%)	
T-stage	T1	37 (75.5%)	12 (24.5%)	0.867
	T2	40 (74.1%)	14 (25.9%)	
Wire localization	No	57 (71.2%)	23 (28.7%)	0.126
	Yes	20 (87.0%)	3 (13.0%)	
Histopathology	CFC	1 (100.0%)	0 (0.0%)	0.656
	DCIS	10 (66.7%)	5 (33.3%)	
	DCIS+IC	1 (50.0%)	1 (50.0%)	
	IDC	55 (76.4%)	17 (23.6%)	
	IDC+DCIS	1 (50.0%)	1 (50.0%)	
	ILC	4 (66.7%)	2 (33.3%)	
	IMC	5 (100.0%)	0 (0.0%)	

Data are expressed as number (%) - MRM: modified radical mastectomy
p> 0.05= not significant.
*p< 0.05= significant.

The need for a second procedure (re-excision), either same setting in cases with frozen section or second one in patients with gross assessment of margins, was in seventeen cases of IDC. While it occurred in 33.3% in both DCIS and ILC (total number of cases with ILC were 6 patients).

DISCUSSION

The precise link between compromised surgical margins and subsequent local recurrence (LR) is still debatable, partly due to the fact that much of the data is retrospective, the study groups are not homogenous, and there is no uniform definition of a compromised or clear margin, frequently resulting in conflicting findings [13, 14].

A surgical margin may be considered positive if cancer cells are present at the inked resection margins[15-19]. However, there is no consensus as to what constitutes a negative or close surgical margin. A negative margin has been considered to be 'not positive' by many authors, whilst others have used varying definitions of greater than 1 mm,[20] greater than one high power field,[15] greater than 2 mm,[21–23] greater than 3 mm[18], or greater than 5 mm [14].

Adjuvant radiotherapy decreases the rate of local recurrence after BCT **24-26**. In patients with negative margins the risk of ipsilateral breast tumour recurrence decreases with adjuvant chemotherapy and endocrine therapy [27-29].

Our study has examined the efficacy of gross intraoperative margin assessment in a homogenous patient population group aged 30-72 years with early stage primary breast cancer. Intraoperative gross margin assessment was successful in 70.4% of patients. This goes alongside with Fleming et al. which showed a rate of success approaching 63%. Particularly with invasive ductal carcinoma (no need for re-excision) in 55 patients representing a ratio of 76.4% of total cases with IDC alone [30] .Given that this histological tumour subtype had been correctly identified in 69.9% of the total number of patients in our study on pre-operative core biopsy, these patients could be identified pre-operatively and selected for intraoperative margin assessment.

Keskek et al. had a rate of 24.1% positive margins for tumour in the CMs in patients underwent BCS. They found that tumour type and tumour size were the only significant factors predicting CM positivity by both univariate and multivariate analysis [31]. They also demonstrated that re-excision surgery is a realistic choice as a second procedure to achieve clear margins in those with close or involved margins. Most patients in whom secondary re-excision was

unsuccessful in achieving clear margins progressed to mastectomy. Re-re-excision also appears to be a valid option to mastectomy following a failed secondary re-excision. Poor cosmetic outcome from severe volume loss is, of course, an important factor to bear in mind when offering re-re-excision and oncoplastic techniques to fill volume loss need to be considered [31].

Intraoperative margin assessment was less successful in patients with invasive lobular carcinoma and DCIS as shown in **table 3**.

Almost Thirty three percent (33%) of patients with invasive lobular carcinoma underwent re-excision achieving clear margins. This goes almost close to the results of Fleming et al. stating that (28%) of patients with invasive lobular carcinoma required re-operation to achieve clear margins in his study [30].

And is similar to the results of other series of invasive lobular carcinoma treated conservatively [32,33]. The significant difference between the median gross (20 mm) and the median microscopic (25 mm) tumour size in patients with invasive lobular carcinoma, is in keeping with the insidious growth pattern of this histological tumour subtype and reflects the difficulty in accurately assessing tumour-margin distance macroscopically.

CM positivity was twice more likely in patients with lobular carcinoma and DCIS compared to women with invasive ductal carcinoma. A similar finding was reported by Jenkinson et al. who found tumour bed positivity in 22% of invasive ductal carcinoma and 57% of invasive lobular carcinoma [34]. Beck et al., also found that lobular carcinomas were associated with increased margin positivity rates when evaluated by both tumour bed biopsy and entire cavity wall margin excision [35].

Analysis of the subgroup that required re-operation for compromised margins in our study found large tumour size and invasive lobular carcinoma to be associated with higher risk of re-operation. This finding confirmed the results of Moore et al. with the impact of histological subtype of ILC on the rate of positive margins and need for reoperation to get safe margins [32].

Similar findings have been observed in previous studies that have reported a significant association between young age, large tumour size, axillary node positivity, lymphovascular invasion, extensive intraduct component, and positive margins [36,37].

This compares favourably with the experience of Niemann et al. which examined the results of frozen section analysis (FSA) in a series of breast biopsies with no mammographic abnormality. The sensitivity in the group which included tumours less than 10 mm in diameter was only 0.84 with a false negative rate of 3.3%, while the 10 mm group had a sensitivity of 0.96 with a false negative rate of only 1.0% [38].

Tumour bed excision has been used in several centres and has been associated with a low rate of local tumour recurrence in patients where negative margins have been achieved [39].

REFERENCES

1. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg* 2002;184: 383-93.
2. Klimberg VS, Harms S, Korourian S. Assessing margin status. *Surg Oncol* 1999;8:77-84.
3. Fowble B, Schultz D, Overmoyer B, et al. The influence of young age on outcome in early stage breast cancer. *Int J Radiat Oncol Biol Phys*. 1994;30:23– 69.
4. Fowble B, Schultz DJ, Overmoyer B, et al. The influence of young age on outcome for life, relapse, and second primary tumors. *Int J Radiat Oncol Biol Phys*. 1992;23:969 –975.
5. Fisher B, Jeong JH, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med*. 2002;347:567–575.
6. Recht A, Connolly JL, Schnitt, et al. The effect of young age on tumor recurrence in the treated breast after conservative surgery and radiotherapy. *Int J Radiat Oncol Biol Phys*. 1988;14:3–10.
7. Kurtz J, Jacquiemier J, Amalric R, et al. Breast-conserving therapy for macroscopically multiple cancers. *Ann Surg*. 1990;212:38–44.
8. Bedwinek JM, Perez CA, Kramer S, et al. Irradiation as the primary management of

stage I and II adenocarcinoma of the breast. *Cancer Clin Trials*. 1980;3:11–18.
9. Chu A, Cope O, Russo R, et al. Patterns of locoregional recurrence and results in stages I and II breast cancer treated by irradiation following limited surgery. *Am J Clin Oncol*. 1984;7:221–229.
10. Harris JR, Botnick L, Bloomer WD, et al. Primary radiation therapy for early breast cancer: the experience at the Joint Center for Radiation Therapy. *Int J Radiat Oncol Biol Phys*. 1981;7:1549 –1552.
11. Smitt M, Nowels K, Carlson R, et al. Predictors of reexcision findings and recurrence after breast conservation. Int J Radiat Oncol Biol Phys. 2003;57:979 –985.
12. Rubio IT, Ahmed M, Kovacs T, Marco V. Margins in breast conserving surgery: A practice-changing process. Eur J Surg Oncol [Internet]. 2016;42(5):631–40.Available from: http://dx.doi.org/10.1016/j.ejso.2016.01.019
13. Freedman G, Fowble B, Hanlon A. Patients with early stage invasive cancer with close or positive margins treated with conservative surgery and radiation have an increased risk of breast recurrence that is delayed by adjuvant systemic therapy. Int J Radiat Oncol Biol Phys 1999;44:1005—1015.
14. Touboul E, Buffar L, Belkacemi Y. Local recurrences and distant metastasis after breast-conserving surgery and radiation therapy for early breast cancer. Int J Radiat Oncol Biol Phys 1999;43:25—38.
15. Ryoo MC, Kagan AR, Wollin M, et al. Prognostic factors for recurrence and cosmesis in 393 patients after radiation therapy for early mammary carcinoma. Radiology 1989;172: 555–9.
16. Borger J, Kemperman H, Hart A, Peterse H, van Dongen J, Bartelink H. Risk factors in breast-conservation therapy. J Clin Oncol 1994;12:653–60.
17. Kurtz JM, Jacquemier J, Amalric R, et al. Risk factors for breast recurrence in premenopausal and postmenopausal patients with ductal cancers treated by conservation therapy. Cancer 1990;65:1867–78.
18. Anscher MS, Jones P, Prosnitz LR, Blackstock W, Hebert M, Reddick M. Local failure and margin status in early-stage breast carcinoma treated with conservation surgery and radiation therapy. Ann Surg 1993;218:22–8.
19. Pittinger TP, Maronian NC, Poulter CA, Peacock JL. Importance of margins status in outcome of breast-conserving surgery for carcinoma. Surgery 1994;116:605–9.
20. Park C, Mitsumori M, Recht A, et al. The relationship between pathologic margin status and outcome after breast conserving therapy. Int J Radiat Oncol Biol Phys 1998;42: 125.
21. Dewar JA, Arriagada R, Benhamou S, et al. Local relapse and contralateral tumor rates in patients with breast cancer treated with conservative surgery and radiotherapy (Institut Gustave Roussy 1970–1982). IGR Breast Cancer Group. Cancer 1995;76:2260–5.
22. Rose MA, Henderson IC, Gelman R, et al. Premenopausal breast cancer patients treated with conservative surgery, radiotherapy and adjuvant chemotherapy have a low risk of local failure. Int J Radiat Oncol Biol Phys 1989;17:711–7.
23. Kini VR, White JR, Horwitz EM, Druchowski CF, Martinez AA, Vicini FA. Long term results with breast-conserving therapy for patients with early stage breast carcinoma in a community hospital setting. Cancer 1998;82:127–33.
24. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227–32.
25. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233–41.
26. Fisher B, Wickerham DL, Deutsch M, Anderson S, Redmond C, Fisher ER. Breast tumour recurrence following lumpectomy with and without breast irradiation: an overview of recent NSABP findings. Semin Surg Oncol 1992;8(3):153–60.
27. Veronesi U, Salvadori B, Luini A, et al. Breast conservation is a safe method in patients with small cancer of the breast. Long-term results of three randomized trials on 1973 patients. Eur J Cancer 1995;31:1574–9.

28. Fisher B, Anderson S, Redmond CK, Wolmark N, Wickerham DL, Cronin WM. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lympectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1995;333:1456–61.
29. Gage I, Schnitt SJ, Nixon AJ, et al. Pathologic margin involvement and the risk of recurrence in patients treated with breast-conserving therapy. Cancer 1996;78:1921–8.
30. Fleming FJ, Hill ADK, Mc Dermott EW, O'Doherty A, O'Higgins NJ, Quinn CM. Intraoperative margin assessment and re-excision rate in breast conserving surgery. Eur J Surg Oncol. 2004;30(3):233–7.
31. Keskek M, Kothari M, Ardehali B, Betambeau N, Nasiri N, Gui GPH. Factors predisposing to cavity margin positivity following conservation surgery for breast cancer. Eur J Surg Oncol. 2004;30(10):1058–64.
32. Moore MM, Borossa G, Imbrie JZ et al. Association of infiltrating lobular carcinoma with positive surgical margins after breast-conservation therapy. Ann Surg 2000;231(6): 877—882.
33. Mai KT, Yazdi HM, Isotalo PA. Resection margin status in lumpectomy specimens of infiltrating lobular carcinoma. Breast Cancer Res Treat 2000;60:29—33.
34. Jenkinson AD, Al-Mufti RAM, Mohsen Y, Berry MJ, Wells C, Carpenter R. Does intraductal breast cancer spread in a segmental distribution? An analysis of residual tumour burden following segmental mastectomy using tumour bed biopsies Eur J Surg Oncol 2001;27:21–5.
35. Beck NE, Bradburn MJ, Vincenti AC, Rainsbury RM. Detection of residual disease following breast-conserving surgery. Br J Surg 1998;85:1273–6.
36. Peterson ME, Schultz DJ, Reynolds C. Outcomes in breast cancer patients relative to margin status after treatment with breast conserving surgery and radiation therapy: the University of Pennsylvania experience. Int J Radiat Oncol Biol 1999;43:1029—1035.
37. Obedien E, Haffty BG. Negative margin status improves local control in conservatively managed breast cancer patients. Cancer J Sci Am 1999;6:28—33.
38. Niemann TH, Lucas JG, Marsh WL. To freeze or not to freeze: a comparison of methods for the handling of breast biopsies with no palpable abnormality. Am J Clin Pathol 1996;106: 225—228.
39. Maliz HZ, George WD, Mallon EA, Harnett AN, Macmillan RD, Purushotham AD. Margin assessment by cavity shaving after breast-conserving surgery: analysis and follow-up of 543 patients. Eur J Surg Oncol 1999;25(5):464—469.