# Re-operation Rates in Breast cancer after **Breast Conserving Surgery in Malta**

# Alexia Farrugia, Gordon Caruana Dingli

#### **Abstract**

The Agatha Breast Unit at Mater Dei Hospital, Malta performed 340 wide local excisions for cancer in 2013-4. Further surgery for close or involved surgical margins was performed in 45 cases (13%), of these 26 (58%) underwent cavity excision and 19 (42%) underwent mastectomy. Residual tumour was found in 9 (35%) in the cavity excision group and 13 (68%) of the mastectomy group. The authors discuss how their unit follows the recommendations of the "Toolbox to reduce lumpectomy reoperations and improve cosmetic outcome in breast cancer patients of the American Society of Breast Surgeons Consensus Conference" and what can be done to reduce re-operation rates further.

#### **Keywords**

**Breast** neoplasms, Margins of Excision, Reoperation

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#### **Introduction and Aim**

Breast cancer is the most prevalent cancer in European women and the incidence is increasing but mortality rates are decreasing. In our unit 70% of patients undergo breast conservation therapy (BCT) aiming to control local disease and achieve cure with the best possible cosmetic result and allowing the patient to have a good quality of life.1 An inadequate surgical margin may lead to local recurrence but re-excision to achieve an optimum margin leads to a worse cosmetic outcome and other problems.

The aim of this study is to assess re-operation rates in breast cancer patients after wide local excision in our unit. This was done by reviewing the histology results of the original surgery and those of the subsequent cavity excision or mastectomy, studying residual tumour rates in the two types of re-operation.

#### **Methods**

#### Data Collection and Sampling.

Data was collected from theatre lists of the two local breast surgeons for all wide local excision operations performed for cancer during 2013 and 2014 at the Agatha Breast Unit at Mater Dei hospital, Malta. Histology reports were accessed from the hospital database and patient records were reviewed as necessary.

#### **Results**

A total of 340 wide local excisions were performed in 2013 and 2014. Further surgery was performed in 45 (13%) to achieve clear margins. Of these, cavity excision was performed in 26 patients (58%) and mastectomy in 19 patients (42%). Residual tumour was found at the second operation in 9 patients (35%) in the cavity excision group and in 13 (68%) in the mastectomy group (49%) overall). This is outlined in table 1.

The collected data was analysed statistically using IBM SPSS to check if there is a statistically significant difference in the size of original tumour

between patients undergoing cavity excision or mastectomy at subsequent surgery.

**Table 1**: Wide local excisions and re-operations for breast cancer in 2013 and 2014

2013		2014	
Wide Local Excision		Wide Local Excision	
172		168	
Cavity Excisions	Mastectomies 12	Cavity Excisions 19	Mastectomies 7
Residual	Residual	Residual	Residual
tumour	tumour	tumour	tumour
2	8	7	5
29%	67%	37%	71%

Out of the patients who underwent cavity excisions, 23(88.5%) had invasive carcinoma at original histology while 3(11.5%) had both invasive carcinoma and DCIS. The patients who subsequently had a mastectomy had 12 (63.2%) who had invasive tumour originally and 7 (36.8%) who had both invasive carcinoma and DCIS. When comparing the two groups, more patients who eventually had mastectomy had both invasive tumour and DCIS in the original histology

(P=0.009), while more patient who had a cavity excision had only invasive tumour initially (p=0.02).

The average size of the initial tumour was 23mm (range 8-48) in those who subsequently underwent cavity excision and 33mm (range 6-75) in those who underwent mastectomy. The difference in size was statistically significant, p=0.03 using a T-test.

Out of 26 cavity excisions, 9 (35%) had residual tumour on histological assessment and out of 19 mastectomies 13 (68%) had residual disease. The mastectomy group had a statistically significant higher rate of residual cancer when compared to the cavity excision group (p=0.025, using a Pearson Chi-Square test).

In the mastectomy group 5 patients (26%) had an initial tumour which was larger than 40mm on histology of the original operation, 7 patients (37%) had multifocal disease, 2 (11%) had chemotherapy between the initial and delayed surgery, 4 (21%) had extensive DCIS and one (5%) had previously undergone risk reduction bilateral subcutaneous mastectomy and immediate reconstruction for highgrade DCIS.

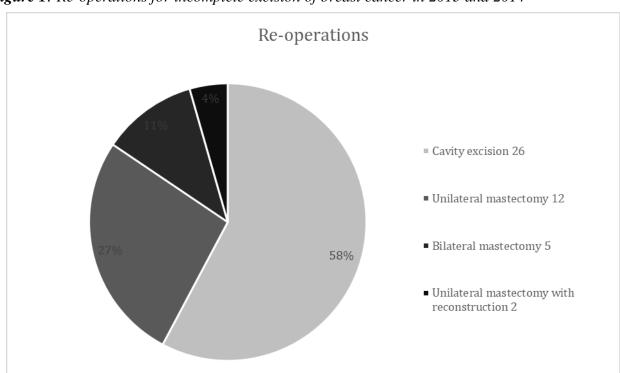


Figure 1: Re-operations for incomplete excision of breast cancer in 2013 and 2014

The average length of time in between surgeries was 58.61 days for the mastectomy group (range 27-209 days) and 62.22 days for the cavity excision group, excluding those patients who had chemotherapy in between the surgeries (range 22-205 days). The total average time between surgeries was 60.41 days. This implies that patients undergoing re-operation undergo substantial delays to start adjuvant treatment.

#### **Discussion**

Surgery is the mainstay treatment of breast cancer with breast conserving therapy now being the preferred option. Breast conserving therapy (BCT) includes breast conserving surgery (BCS) followed by moderate dose radiation therapy to eradicate residual microscopic disease. overview of completed trials and 9 prospective randomised clinical trials comparing BCT with mastectomy showed equivalent survival rates between the two approaches.2-11 The main aim of BCT is to provide a more cosmetically acceptable breast associated with a low rate of recurrence in the treated breast. 12 However in breast conserving surgery an adequate negative margin around the tumour is required to achieve full clearance. A positive margin may lead to further surgery which may either involve further local treatment (cavity excision) or mastectomy at a later stage.13 Reoperation may have consequences such as delaying adjuvant treatments, and increased rates of and distal recurrence.14-16 consequences may include poorer cosmetic outcome and emotional distress which may delay recovery, with the resulting socioeconomic impact due to inability or delay in resuming work and also additional financial burden on the healthcare system.17

The latest NCCN guidelines state that for DCIS a margin status of less than 1 mm is considered inadequate, 10mm is considered a good margin but may affect cosmetic outcome. If the margin is between 1-10mm, the wider the margin the lower the local recurrence rate. For margins of less than 1 mm between the fibroglandular boundary (i.e. chest wall or skin) re-excision is not mandatory. However, this may require higher radiotherapy doses postoperatively.18 In infiltrating carcinoma, a negative margin is considered as 'no ink on tumour' as described by the 2014 Society of Surgical Oncology — American Society for

Radiation Oncology Consensus Guidelines on Margins.19 Positive margin requires re excision in the form of further breast conserving therapy if appropriate or mastectomy, because there is increased risk of ipsilateral breast tumour local recurrence. There is still controversy regarding the appropriate margin however most surgeons take this to be 2mm. 20

It has been shown that 25% of local recurrences are associated with survival reduction at 20 years.2 Loco-regional recurrence is a product of sufficient tumour volume reduction (a clear margin is a surrogate marker), tumour biology, radiotherapy and systemic treatment. There are no prospective randomized trials that directly address the influence of margin width on local recurrence or define an optimal marginal width. What constitutes an acceptable margin must be individualized within the context of the tumour size, biology, stage and planned treatments.1

Reoperation rates after breast conserving surgery can be high, with rates of 17% to 68% quoted in various studies.21-28 Women having an in situ component were more likely to have at least one reoperation.29 The results from our unit compare well with these figures.

Our unit strives to decrease re-operation rates by following the recommendations of the Consensus Conference Toolbox to reduce lumpectomy reoperations and improve cosmetic outcome in Breast Cancer Patients of the American Society of Breast Surgeons. 30

Pre-operative imaging is done with full-field digital mammography and ultrasound as needed. MRI is used for patients with lobular carcinoma. All patients undergo breast biopsy before surgery and they are discussed at a multi-disciplinary team meeting that includes surgeons, radiologists, pathologists and oncologists. Non-palpable breast lesions are localized, and multiple wires or seeds are used for large lesions, multifocal tumours and extensive DCIS. Oncoplastic surgical techniques allow resection of larger amounts of breast tissue include contralateral this may symmetrization surgery. All operative specimens are oriented by placement of sutures at surgery, a short suture is used to label the superior margin, a medium suture for the medial margin and a long suture for the lateral margin. All specimens are weighed to facilitate reconstruction when necessary. When the lesion is not palpable the specimen is

labelled with metal clips (Ligaclips<sup>TM</sup>) and radiographed. This will document that the lesion has been removed and assessment of the margin. A cavity shave is performed if the margin is "close". We do not perform routine cavity shaves of side walls or intraoperative pathology assessment of lumpectomy margins.

Not all patients who have positive or close margins in the first operation are found to have residual tumour at the second operations. Rates of 18.8% to 33% have been quoted, while we report residual tumour in 49% of re-operated patients.20,22 Residual disease has been associated with multifocality but no other associated factors have been identified.22

Patients treated with repeat BCS had similar outcomes to those who underwent mastectomy. This was shown by a retrospective review and a prospective study which both showed no significant difference in survival rate following both management options i.e. mastectomy versus repeat BCS.31, 32

Our study compared two groups of women who underwent further excision after their initial breast-conserving surgery, for close or involved margins with tumour or in-situ disease. Some underwent a cavity excision while others had a mastectomy as their second surgery. **Patients** undergoing cavity excision were found to have residual tumour in 35% of cases compared to 68% of patients with residual tumour in the mastectomy group (p=0.025). This implies that mastectomy is more likely to result in a positive result and therefore more likely to result in complete histological excision than breast conserving cavity excision. It may also imply that in repeat cavity excision the surgeon might not manage to excise residual disease as this may be difficult to localize. There was also a significant difference in the initial tumour size, as those patients who underwent a mastectomy as a second procedure had larger average initial tumour size (p=0.03). This implies that a larger initial tumour size may influence the decision to perform a mastectomy as a second surgery if this is required.

Limitations of this study include a small sample size of re-operated patients and the retrospective nature of the study.

Lateral margin cavity shave during the initial breast conserving surgery has been shown to decrease the re-operation rates for margin clearance but the excised volume is increased and this may unnecessarily compromise cosmetic outcome.21,29,33-35 Intra-operative margin assessment using frozen section reduces re-excision rates but this is not widely available.36 A commercially available RF spectroscopy probe (MarginProbe) has been shown to decrease re-operation rates.37 Our unit proposes to study these three techniques in an effort to further improve our re-operation rate.

#### References

- 1. MacNeill F, Karakatsanis A. Over surgery in breast cancer. *The Breast* 2017 Feb; 31; 84-289 doi: 10.1016/j.breast.2016.10.023
- 2. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005 Dec; 366(9503):2087-106 DOI:10.1016/S0140-6736(05)67887-7
- 3. 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 lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1995 Nov; 333(22):1456-61
- 4. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002 Oct; 347(16):1233-41.
- Veronesi U, Salvadori B, Luini A, Greco M, Saccozzi R, Del Vecchio M et al. Breast conservation is a safe method in patients with small cancer of the breast.
  Long-term results of three randomised trials on 1,973 patients. Eur J Cancer 1995 Sep; 31A(10):1574-9
- 6. Veronesi U, Cascinelli N, Mariani L,Greco M, Saccozzi R, Luini A 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 Oct; 347)16):1227-32. DOI:10.1056/NEJMoa020989
- 7. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst* 2000 Jul; 92(14):1143-50.
- 8. Jacobson JA, Danforth DN, Cowan KH, d'Angelo T, Steinberg SM, Pierce L et al. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med* 1995 Apr; 332(14):907-11 DOI:10.1056/NEJM199504063321402

- Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewhehr DJ et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. *Cancer* 2003 Aug; 98(4):697-702 DOI:10.1002/cncr.11580
- Institut Gustave-Roussy Breast Cancer Group. Arriagada R, Lê MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data... J Clin Oncol 1996 May; 14(5):1558-64 DOI:10.1200/JCO.1996.14.5.1558
- Danish Breast Cancer Cooperative Group. Blichert-Toft M, Rose C, Andersen JA, Overgarrd M, Axelsson CK, Andersen KW, Mouridsen HT. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. *J Natl* Cancer Inst Monogr 1992;(11):19-25.
- Sabel M, Pierce L. Breast Conserving Surgery. www.uptodate.com. Accessed on 17/12/2016
- Aziz D, Rawlinson E, Narod SA, Sun P, Lickley HL, McDready DR, et al. The role of reexcision for positive margins in optimizing local disease control after breastconserving surgery for cancer. *Breast J* 2006;12(4):331-7 DOI:10.1111/j.1075-122X.2006.00271.x
- 14. Pleijhuis RG, Graafland M, de Vries J, Bart J, de Jong JS, van Dam GM. Obtaining adequate surgical margins in breast-conserving therapy for patients with early-stage breast cancer: current modalities and future directions. *Ann Surg Oncol* 2009;16(10):2717-30 doi: 10.1245/s10434-009-0609-z.
- Menes TS, Tartter PI, Bleiweiss I, Godbold JH, Estabrook A, Smith SR. The consequence of multiple re-excisions to obtain clear lumpectomy margins in breast cancer patients. *Ann Surg Oncol* 2005;12(11):881-5 DOI:10.1245/ASO.2005.03.021
- Kouzminova NB, Aggarwal S, Aggarwal A, Allo MD, Lin AY. Impact of initial surgical margins and residual cancer upon re-excision on outcome of patients with localized breast cancer. *Am J Surg* 2009;198(6):771-80 doi: 10.1016/j.amjsurg.2009.05.027.
- 17. Munshi A, Kakkar S, Bhutani R, Jalali R, Budrukkar A, Dinshaw KA. Factors influencing cosmetic outcome in breast conservation. *Clin Oncol* 2009 May ;21 (4):285-93 oi: 10.1016/j.clon.2009.02.00
- 18. Invasive Breast Cancer Version 1.2016, NCCN Clinical Practice Guidelines in Oncology *J Natl Compr Canc Netw* Mar 1, 2016:324-54
- 19. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. Int J Radiat Oncol Biol Phys Mar 1;88(3):553-64. doi: 10.1016/j.ijrobp.2013.11.012.
- Unzeitig A, Kobbermann A, Xie XJ, Yan J, Euhus D, Peng Y et al. Influence of Surgical technique on Mastectomy and Reexcision rates in Breast Conserving therapy for cancer. *Int. J. Surg. Oncol.* 2012; 725121 doi: 10.1155/2012/725121

- 21. Sabel MS, Rogers K, Griffith K, Jagsi R, Kleer CG, Diehl KA et al Residual disease after re-excision lumpectomy for close margins. *J Surg Oncol*, 2009; 99(2):99–103
- Wiley EL, Diaz LK, Badve S, Morrow M. Effect of time interval on residual disease in breast cancer. *Am J Surg Pathol* 2003; 27(2):194–198
- 23. Gray RJ, Salud C, Nguyen K, Dauway E, Friedland J, Berman C et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol* 2001; 8(9):711–715
- 24. Jacobson AF, Asad J, Boolbol S, Osborne MP, Boachie-Adjei K, Feldman SM. Do additional shaved margins at the time of lumpectomy eliminate the need for re-excision? Am J Surg 2008;196(4):556-8.
- 25. Freedman G, Fowble B, Hanlon A, Nicolaou N, Fein D, Hoffman J, et al. 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(5):1005-15
- Cellini C, Hollenbeck ST, Christos P, Martins D, Carson J, Kemper S, et al. Factors associated with residual breast cancer after re-excision for close or positive margins. Ann Surg Oncol 2004;11(10):915-20 DOI:10.1245/ASO.2004.12.037
- 27. Talsma AK, Reedijk AM, Damhuis RA, Westenend PJ, Vles WJ. Re-resection rates after breast-conserving surgery as a performance indicator: introduction of a case-mix model to allow comparison between Dutch hospitals. Eur J Surg Oncol 2011;37(4):357-63. doi: 10.1016/j.ejso.2011.01.008
- 28. Jeevan R, Cromwell AD, Trivella M et al. *Reoperation* rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics BMJ 2012;345:e4505
- Marudanayagam R, Singhal R, Tanchel B O'Connor B, Balasubramanian B, Paterson I. Effect of Cavity Shaving on Repoeration rate following breast conserving surgery. *Breast Journal* 2008 14(6): 570-3 doi: 10. 1111/j.1524-4741.2008.00649.x
- 30. The American Society of Breast Surgeons Consensus Conference. Landerscaper J, Attal D, Atisha D, Beitsch P, Bosserman L, Boughey J, et al. Toolbox to reduce lumpectomy reoperations and improve cosmetic outcome in Breast Cancer patients. *Ann Surg Oncol* 2015; 22(10):3174-83 doi: 10.1245/s10434-015-4759-x
- 31. Salvadori B, Marubini E, Miceli R, Conti AR, Cusumano F, Androla S et al. Reoperation for locally recurrent breast cancer in patients previously treated with conservative surgery. *Br J Surg* 1999; 86(1):84-7 DOI:10.1046/j.1365-2168.1999.00961.x
- 32. Alpert TE, Kuerer HM, Arthur DW, Lannin DR, Haffty BG. Ipsilateral breast tumor recurrence after breast conservation therapy: outcomes of salvage mastectomy vs. salvage breast-conserving surgery and prognostic factors for salvage breast preservation. *Int J Radiat Oncol Biol Phys* 2005; 63(3):845-51 DOI:10.1016/j.ijrobp.2005.02.035

- Hewes JC, Imkampe A, Haji A, Bates T. Importance of routine cavity sampling in breast conservation surgery. Br J Surg 2009; 96(1):47–53
- 34. Rizzo M, Iyengar R, Gabram SG, Park J, Birdsong G, Chandler KL, Mosunjac MB. The effects of additional tumor cavity sampling at the time of breast-conserving surgery on final margin status, volume of resection, and pathologist workload *Ann Surg Oncol.* 2010 Jan;17(1):228-34. doi: 10.1245/s10434-009-0643-x.
- 35. Chagpar AB, Killelea BK, Tsangaris TN, Butler M, Stavris K, Li F. et al. A randomized, controlled trial of cavity shave margins in breast Cancer. *N Engl J Med* 2015 Aug 6; 373(6):503-10
- 36. Esbona Karla, Li Zhanhai, Wilke Lee. Intraoperative imprint cytology and frozen section pathology for margin assessment in breast conservation surgery: a systematic review. *Ann Surg Oncol* 2012 Oct; 19 (10): 3236-45
- 37. Schnabel F., Boolbol SK, Gittleman M, Karni T, Tafra L, Feldman S et al. A randomized prospective study of lumpectomy margin assessment with use of MarginProbe in patients with nonpalpable breast malignancies. Ann Surg Oncol, 2014; 21(5):1589-9