





# Factors that may contribute to non-radical resections in patients undergoing breast-conserving treatment for breast cancer

Andrzej J. Lorek<sup>1</sup> , Katarzyna Steinhof-Radwańska<sup>2</sup> , Wojciech Zarębski<sup>1</sup> ,  
Joanna Lorek<sup>3</sup>, Zoran Stojcev<sup>4</sup> 

<sup>1</sup>Department of Oncological Surgery, Prof. Kornel Gibinski Independent Public Central Clinical Hospital, Medical University of Silesia, Katowice, Poland

<sup>2</sup>Department of Radiology and Nuclear Medicine, Prof. Kornel Gibinski Independent Public Central Clinical Hospital, Medical University of Silesia, Katowice, Poland

<sup>3</sup>Department of Anesthesiology and Intensive Care, University Hospital in Krakow, Krakow, Poland

<sup>4</sup>Department of Oncological Surgery Faculty of Medicine Lazarski University, Warsaw, Poland

**Introduction.** Breast-conserving treatment in breast cancer consists of radical removal of the cancerous tumor combined with a satisfactory aesthetic result. This study aimed to retrospectively analyze factors that may contribute to non-radical resections in patients undergoing breast-conserving treatment for infiltrating breast cancer and carcinoma *in situ*.

**Material and methods.** This retrospective study analyzed the medical records of 1,312 patients with stage I and II breast cancer and patients with ductal carcinoma *in situ* (DCIS) who underwent breast-conserving treatment from January 2013 to December 2022.

**Results.** The number of non-radical resections (R1) was 6.4% (80 cases out of 1,237). Fifty-five (4.4%) of R1 patients were re-operated with larger margins and 25 (2%) had a mastectomy. Analysis of factors contributing to a non-radical resection showed a significant correlation with age, histological type, multifocality, preoperative treatment and clinically detectable lesions.

**Conclusions.** The use of contrast-enhanced spectral mammography as a standard method in surgical planning of breast cancer treatment, taking into account R1 resection risk factors, will allow better selection of patients eligible for breast-conserving treatment.

**Key words:** breast cancer, breast-conserving treatment, resection margin, contrast-enhanced spectral mammography

## Introduction

Breast cancer is the most common malignancy and accounts for as many as 22.9% of cancer cases in women. The peak incidence is between the ages of 50 and 69 [1, 2].

The choice of local or systemic therapy for each stage of breast cancer depends on the clinical and pathomorpho-

logical assessment, taking into account the histological type, the degree of malignancy of the cancer, the receptor status, the size of the primary tumor and the status of the regional lymph nodes, the presence and extent of metastases in distant organs. It also depends on the patient's age, menopausal status, fitness, past and coexisting diseases, as well as preferences.

### Jak cytować / How to cite:

Lorek AJ, Steinhof-Radwańska K, Zarębski W, Lorek J, Stojcev Z. *Factors that may contribute to non-radical resections in patients undergoing breast-conserving treatment for breast cancer.* NOWOTWORY J Oncol 2024; 74: 94–98.

Any decision taken on the extent of surgical treatment between breast-conserving treatment and a mastectomy primarily depends on the size of the tumor and the exclusion of the multicentricity of tumor lesions [3–5]. According to Breast Cancer Unit (BCU) recommendations in breast cancer centers, approximately 60% of patients should be treated using breast-conserving techniques [6]. Careful planning as regards the type of surgical procedure is important for treatment outcomes, and translates directly into a reduction in the incidence of local recurrence [7, 8]. In most centers, breast-conserving treatment is planned based on digital mammography, whose sensitivity in assessing tumor size and the presence of additional foci is not high, which may result in a non-radical resection [9, 10]. In the authors' own practice, the imaging method on the basis of which breast-conserving treatment was planned was contrast-enhanced spectral mammography (CESM). Contrast-enhanced spectral mammography is based on a dual-energy technique that utilizes the difference in X-ray attenuation of breast tissue and iodine. It provides not only morphological information analogous to conventional mammography, but also additionally allows the imaging of breast areas that show increased contrast uptake usually associated with neoangiogenesis, similarly to breast magnetic resonance imaging (MRI) [11].

Breast-conserving treatment aims to radically remove the cancerous tumor while achieving a good aesthetic result [12]. According to current recommendations, a negative margin in infiltrating breast cancer is defined as the absence of cancerous tissue in the line of excision confirmed by postoperative histopathological examination [13]. For ductal carcinoma *in situ* (DCIS), the minimum margin should not be smaller than 2 mm [14].

## Material and methods

This study aimed to retrospectively analyze factors that may contribute to non-radical resections in patients undergoing breast-conserving surgery for infiltrating breast cancer and carcinoma *in situ* (DCIS).

This retrospective study analyzed the medical records of 1,312 patients with stage I and II breast cancer and patients with DCIS who underwent breast-conserving treatment. Patients who had preoperative diagnostics performed outside our center were excluded from the study. A total of 1,237 patients with primary operable cancer as well as those undergoing preoperative systemic treatment were included in the study. The procedures were carried out at the Department of Oncological Surgery of Prof. K. Gibinski University Clinical Centre of the Medical University of Silesia in Katowice from January 2013 to December 2022. All patients included in the study had preoperative diagnostic tests performed at the Hospital Oncology Surgery Outpatient Clinic, which included: history-taking, physical examination, imaging studies including contrast-enhanced spectral mammography (CESM) and core needle biopsy (CNB).

The procedures were performed by the same team of four surgeons with many years of experience in breast surgery. All surgically removed lesions were marked with threads to identify the resection margins, and the bed of the removed tumor was marked with metal clips. For lesions not clinically detectable, an anchor was placed on the day of surgery in the radiology department under ultrasound or mammography guidance. All removed clinically undetectable lesions were evaluated intraoperatively with the use of mammography to assess the presence of a tracer in the tumor and the size of the margins. Tumor removal procedures were combined with a sentinel node procedure or with the removal of the axillary lymphatic system, depending on the cN category. The postoperative histopathological examination was performed at the Department of Histopathology of the Medical University of Silesia. The preparations were assessed by 2 experienced pathologists. The study included infiltrating carcinomas and carcinomas *in situ*. R0 resection in infiltrating carcinomas meant that there was no ink in the tumor margins in DCIS margins of no less than 2 mm. The number of non-radical procedures, the number of re-operations with breast conservation and the number of amputations were assessed. It was investigated whether non-radical margins were dependent on age, histopathological type of cancer, grading, biological subtype, preoperative treatment, multifocality, clinically palpable lesion or nonpalpable lesion requiring anchorage.

## Statistical analysis

Because the variables describing the characteristics under study were not measured on quotient scales and did not meet the assumption of normality of distributions, non-parametric statistical tests were used in the calculations. A non-parametric test of independence was used to assess whether the counts in the study groups differed significantly from each other. P-values <0.05 were considered statistically significant.

## Results

The age distribution of the participants was not a normal distribution, with a median of 63.23 ( $\pm 11.5$ ) years (the minimum age in the sample was 29 years, the maximum 91 years). There were 80 (6.4%) cases of R1 resection confirmed by the postoperative histopathology report. 55 (4.4%) of the 80 R1 patients were re-operated with larger margins and 25 (2%) had a mastectomy. The investigated variables that may affect the radicality of resection are shown in table I.

## Discussion

In this study, the rate of re-operation due to non-radical margins was 6.4%, far from the data available in the literature that indicate a resection rate of 20% in invasive carcinoma of no special type (NST) and often higher in infiltrating lobular carcinoma and DCIS [14, 16, 17]. Such a low percentage should be explained by the considerable experience of the surgeons, who perform more than 80 breast cancer procedures per year,

**Table I.** The analysis of variables that may contribute to non-radical resection

Characteristics	Total number n = 1,237	Resection R1 n = 80	Resection R0 n = 1,157	Statistical significance
age – yy, M (± SD)	63.23 (±11.5)	62.98 (±11.5)	66.80 (±11.2)	p < 0.11
histopathological size – mm, M (± SD)	21.0 (±14.3)	18.7 (±14.3)	21.2 (±14.4)	NS
histopathological type of cancer:				p < 0.0001
NST	65.8%	3.6%	62.2%	–
lobular	13.3%	0.4%	12.9%	–
ductolobular	7.1%	0.7%	6.4%	–
special subtype	6.3%	1.0%	5.3%	–
DCIS	3.0%	0.8%	2.2%	–
HG	0.3%	0.0%	0.3%	–
LG	4.2%	0.0%	4.2%	–
grading:				NS
G1	7.5%	0.6%	6.9%	–
G2	74.3%	3.9%	70.4%	–
G3	18.2%	0.6%	17.6%	–
biological subtype:				NS
luminal A	40.2%	3.4%	36.8%	–
luminal B (HER-negative)	34.3%	1.3%	33.0%	–
triple-negative	11.4%	0.6%	10.8%	–
luminal B (HER-positive)	12.1%	0.6%	11.5%	–
non-luminal (HER-positive)	2.0%	0.1%	1.9%	–
multifocal	84.9%	6.3%	76.0%	p < 0.029
monofocal	18.3%	0.6%	17.1%	–
clinically palpable	98.7%	10.4%	88.3%	p < 0.0001
clinically impalpable (anchor)	1.3%	1.3%	0.0%	–
treated preoperatively	26.5%	1.9%	24.6%	p < 0.037
not treated preoperatively	73.5%	9.8%	63.6%	–

yy – years; M – mean; mm – millimetres; SD – standard deviation; R0 – radical resections; R1 – non-radical resections; NST – no special type; DCIS – ductal carcinoma *in situ*; HG – high grade; LG – low grade

and treatment planning on the basis of CESM, whose sensitivity in determining the size of the tumor lesion and additional tumor foci is far superior to classical digital mammography [8, 18].

The authors' analysis of the causes of R1 resection indicates a higher risk of non-radical resection in patients under 62 years of age. The glandular-adipose structure of the breast, more common at this age, may be the reason for the difficulty in identifying the extent of the cancerous lesion. Cancers at younger ages are also characterized by greater aggressiveness than those at later ages [19]. In the conducted analysis, the size of the tumor lesion was not a significant factor in increasing the risk of non-radical resection. Histopathological type was a significant factor confirming a higher risk of non-radical resection in invasive lobular carcinoma and DCIS. This should be associated with the clinical picture and radiological features of these lesions as confirmed by numerous studies [20–22]. The grade of malignancy (G) in our analysis was not a significant factor for the increased risk of R1 resection; a higher risk in more aggressive G2–3 carcinomas was to be expected. This is probably to be explained by the relatively small study group.

Data available in the literature indicate that luminal carcinoma is diagnosed more frequently than other biological types, is associated with a lower clinical and pathological stage of the disease, and thus allows more frequent use of breast-

-conserving treatment [22–23]. In this study, the biological subtype was not a significant factor in increasing the risk of non-radical resection. Perhaps this should also be attributed to the small size of the study group.

Multifocality in the presented analysis was associated with a higher incidence of R1 resection. Identification of additional microscopic foci of cancer is sometimes possible on the basis of postoperative histopathology alone. The authors believed that with a CESM result in each patient, with a very high sensitivity in detecting additional cancer foci, comparable to that of MRI as shown in this study, non-radical procedures in these cases could be reduced completely. However, as can be seen, this is not always possible [24].

When analyzing patients who were operated on with clinically palpable lesions compared to nonpalpable lesions requiring anchor placement, a significantly higher number of R1 resections were observed for the former. Apparently, macroscopic assessment is less accurate compared to intraoperative mammographic assessment. Furthermore, for lesions with anchor placement, when the radiologist signals during intraoperative mammography that any of the margins appear too narrow or that there is no marker in the tumor, there is always the possibility of expanding the margin during the same procedure [25].

In the group of patients undergoing systemic treatment prior to surgery, non-radical resections were observed significantly less frequently compared to patients undergoing primary surgery. This is most likely related to the fact that the majority of postoperative procedures were performed with anchor placement, where intraoperative radiographic verification minimized the possibility of non-radical margins [26].

A limitation of the study was the relatively small group of patients; moreover, the volume of the mammary glands and the technique of the procedure – oncoplastic surgery *versus* tumorectomy – were not taken into account. Despite the incomplete elimination of non-radical procedures in the analyzed group, the re-operation rate of 6.4% is not high. The use of CESM as a standard method to assess the extent of the disease seems to minimize the number of non-radical resections and significantly alter the extent of planned surgery as shown in the authors' previous studies [27, 28].

## Conclusions

The use of contrast-enhanced spectral mammography as a standard method in surgical planning of breast cancer treatment taking into account R1 resection risk factors will allow better selection of patients eligible for breast-conserving treatment.

## Article information and declarations

### Ethics statement

The authors declare that the study, due to its retrospective nature, did not require the approval of the Ethics Committee. All research procedures were carried out in accordance with the ethical standards set out in the 1964 Declaration of Helsinki and its subsequent amendments.

### Author contributions

Andrzej J. Lorek – conceptualization, data curation, writing – original draft preparation.

Katarzyna Steinhof-Radwańska – conceptualization, data curation.

Wojciech Zarębski – data curation, formal analysis.

Joanna Lorek – writing – original draft preparation.

Zoran Stojcev – writing – review and editing.

### Acknowledgments

Thanks to Anna Biłska for her help in collecting data.

### Conflict of interest

None declared

### Andrzej J. Lorek

Medical University of Silesia

Prof. Kornel Gibiński Independent Public Central Clinical Hospital

Department of Oncological Surgery

ul. Medyków 14

40-742 Katowice, Poland

e-mail: ajlorek@o2.pl

Received: 29 Oct. 2023

Accepted: 30 Jan. 2024

## References

1. Wojciechowska UJ. Cancer incidence and mortality in Poland. Polish National Cancer Registry, Oncology Center – Maria Skłodowska-Curie Institute [Online]. <http://onkologia.org.pl>.
2. Miklewska MJ, Barańska K, Wojciechowska U, et al. Morbidity and mortality trends of the most common cancers in 1990-2019. Poland's position compared to other European countries. *Nowotwory. Journal of Oncology*. 2023; 73(1): 46–55, doi: 10.5603/NJO.a2022.0065.
3. Curigliano G, Burstein HJ, Winer EP, et al. St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2017. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. *Ann Oncol*. 2017; 28(8): 1700–1712, doi: 10.1093/annonc/mdx308, indexed in Pubmed: 28838210.
4. Fisher B, Anderson S, Bryant J, 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; 347(16): 1233–1241, doi: 10.1056/NEJMoa022152, indexed in Pubmed: 12393820.
5. 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(16): 1227–1232, doi: 10.1056/NEJMoa020989, indexed in Pubmed: 12393819.
6. Biganzoli L, Cardoso F, Beishon M, et al. The requirements of a specialist breast centre. *Breast*. 2020; 51: 65–84, doi: 10.1016/j.breast.2020.02.003, indexed in Pubmed: 32217457.
7. Houben IPI, Vanwetswinkel S, Kalia V, et al. Contrast-enhanced spectral mammography in the evaluation of breast suspicious calcifications: diagnostic accuracy and impact on surgical management. *Acta Radiol*. 2019; 60(9): 1110–1117, doi: 10.1177/0284185118822639, indexed in Pubmed: 30678480.
8. Lorek A, Steinhof-Radwańska K, Barczyk-Gutkowska A, et al. The Usefulness of Spectral Mammography in Surgical Planning of Breast Cancer Treatment-Analysis of 999 Patients with Primary Operable Breast Cancer. *Curr Oncol*. 2021; 28(4): 2548–2559, doi: 10.3390/curroncol28040232, indexed in Pubmed: 34287253.
9. Cuesta AC, Ríos MM, Meseguer MN, et al. Accuracy of Tumor Size Measurements Performed by Magnetic Resonance, Ultrasound and Mammography, and Their Correlation With Pathological Size in Primary Breast Cancer. *Cirugía Española (English Edition)*. 2019; 97(7): 391–396, doi: 10.1016/j.cireng.2019.08.001.
10. Iacconi C, Galman L, Zheng J, et al. Multicentric Cancer Detected at Breast MR Imaging and Not at Mammography: Important or Not? *Radiology*. 2016; 279(2): 378–384, doi: 10.1148/radiol.2015150796, indexed in Pubmed: 26605912.
11. Łuczyńska E, Heinze-Paluchowska S, Hendrick E, et al. Comparison between Breast MRI and Contrast-Enhanced Spectral Mammography. *Med Sci Monit*. 2015; 21: 1358–1367, doi: 10.12659/msm.893018.
12. Povoski SP, Jimenez RE, Wang WP, et al. Standardized and reproducible methodology for the comprehensive and systematic assessment of surgical resection margins during breast-conserving surgery for invasive breast cancer. *BMC Cancer*. 2009; 9: 254, doi: 10.1186/1471-2407-9-254, indexed in Pubmed: 19635166.
13. Moran MS, Schnitt SJ, Giuliano AE, 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. *Ann Surg Oncol*. 2014; 21(3): 704–716, doi: 10.1245/s10434-014-3481-4, indexed in Pubmed: 24515565.
14. Sachański T, Radecka B. A review of methods of intraoperative margin assessment in breast conserving surgery. *Nowotwory. Journal of Oncology*. 2021; 71(4): 225–231, doi: 10.5603/njo.a2021.0040.
15. Morrow M, Van Zee KJ, Solin LJ, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma In Situ. *Ann Surg Oncol*. 2016; 23(12): 3801–3810, doi: 10.1245/s10434-016-5449-z, indexed in Pubmed: 27527714.
16. Cody HS, Van Zee KJ. Reexcision--The Other Breast Cancer Epidemic. *N Engl J Med*. 2015; 373(6): 568–569, doi: 10.1056/NEJMe1507190, indexed in Pubmed: 26244311.
17. Landercasper J, Attai D, Atisha D, et al. Toolbox to Reduce Lumpectomy Reoperations and Improve Cosmetic Outcome in Breast Cancer Patients:

- The American Society of Breast Surgeons Consensus Conference. *Ann Surg Oncol.* 2015; 22(10): 3174–3183, doi: 10.1245/s10434-015-4759-x, indexed in Pubmed: 26215198.
18. Kaczmarek K, Wang P, Gilmore R, et al. Surgeon Re-Excision Rates after Breast-Conserving Surgery: A Measure of Low-Value Care. *J Am Coll Surg.* 2019; 228(4): 504–512.e2, doi: 10.1016/j.jamcollsurg.2018.12.043, indexed in Pubmed: 30703538.
  19. Arvold ND, Taghian AG, Niemierko A, et al. Age, breast cancer subtype approximation, and local recurrence after breast-conserving therapy. *J Clin Oncol.* 2011; 29(29): 3885–3891, doi: 10.1200/JCO.2011.36.1105, indexed in Pubmed: 21900114.
  20. Park S, Park HS, Kim SJ, et al. The impact of a focally positive resection margin on the local control in patients treated with breast-conserving therapy. *Jpn J Clin Oncol.* 2011; 41(5): 600–608, doi: 10.1093/jjco/hyr018, indexed in Pubmed: 21355001.
  21. Melstrom LG, Melstrom KA, Wang EC, et al. Ductal carcinoma in situ: size and resection volume predict margin status. *Am J Clin Oncol.* 2010; 33(5): 438–442, doi: 10.1097/COC.0b013e3181b9cf31, indexed in Pubmed: 20023569.
  22. Seo M, Cho N, Bae MS, et al. Features of Undiagnosed Breast Cancers at Screening Breast MR Imaging and Potential Utility of Computer-Aided Evaluation. *Korean J Radiol.* 2016; 17(1): 59–68, doi: 10.3348/kjr.2016.17.1.59, indexed in Pubmed: 26798217.
  23. Nowikiewicz T, Chmielowska E, Andrusiewicz H, et al. Prevalence of biological types of breast cancer and their influence on disease staging and therapeutic management – a single-center study. *Pol J Pathol.* 2017; 68(1): 16–25, doi: 10.5114/pjp.2017.67611, indexed in Pubmed: 28547976.
  24. Steinhof-Radwańska K, Lorek A, Holecki M, et al. Comparison of the efficiency of mammography and contrast-enhanced spectral mammography in female patients with multifocal and multicentric breast cancer. *Pol Arch Intern Med.* 2021; 131(7-8): 759–761, doi: 10.20452/pamw.16011, indexed in Pubmed: 34057323.
  25. Theunissen CI, Rust EAZ, Edens MA, et al. Radioactive seed localization is the preferred technique in nonpalpable breast cancer compared with wire-guided localization and radioguided occult lesion localization. *Nucl Med Commun.* 2017; 38(5): 396–401, doi: 10.1097/MNM.0000000000000659, indexed in Pubmed: 28362718.
  26. Davey MG, O'Donnell JPM, Boland MR, et al. Optimal localization strategies for non-palpable breast cancers - A network meta-analysis of randomized controlled trials. *Breast.* 2022; 62: 103–113, doi: 10.1016/j.breast.2022.02.004, indexed in Pubmed: 35151049.
  27. Steinhof-Radwańska K, Grażyńska A, Barczyk-Gutkowska A, et al. The new method, the old problem - role of contrast-enhanced spectral mammography in the diagnosis of breast cancer among Polish women. *Pol J Radiol.* 2020; 85: e381–e386, doi: 10.5114/pjr.2020.97941, indexed in Pubmed: 32817772.
  28. Steinhof-Radwańska K, Grażyńska A, Lorek A, et al. Contrast-Enhanced Spectral Mammography Assessment of Patients Treated with Neoadjuvant Chemotherapy for Breast Cancer. *Curr Oncol.* 2021; 28(5): 3448–3462, doi: 10.3390/curroncol28050298, indexed in Pubmed: 34590596.