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Rate of residual tumor after repeat surgery for positive margins in ductal carcinoma in Situ, and predictive factors

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A B S T R A C T

Aims: To evaluate the rate of residual tumor in re-excision specimen of patients with positive margins in ductal carcinoma in situ (DCIS) following breast-conservative surgery, and to identify predictive factors of residual tumor.

Material and methods: We conducted a monocentric, retrospective study, from January 2010 to December 2020. All 103 patients who underwent re-excision for positive margins in DCIS following breast-conservative surgery for in situ or invasive breast carcinoma were included. Positive margins were defined as inferior to 2 mm from the DCIS component. Two groups were defined, depending on the presence of residual tumor or not, and were compared on their clinical and histopathological characteristics to identify predictive factors of residual tumor.

Results: Residual tumor was found in re-excision specimen of 46 patients (44.7 %). The risk of residual tumor was increased in patients with more than 2 tumor foci (aOR: 12.4; 95 % CI: 1.2-124.1; $p = 0.032$) and in those with extensive margin involvement (aOR: 3.2; 95 % CI: 1.3-8.2; $p = 0.013$). Finally, surgery performed after 2013 was associated with a lower risk of residual tumor (aOR: 0.23; 95 % CI: 0.09-0.058; $p = 0.002$).

Conclusion: The rate of residual tumor in re-excision specimen of patients with positive margins in DCIS is high. Both the number of tumor foci and the extension of positive margins were identified as risk factors. Finally, the surgical learning curve for this procedure seems to be significantly correlated with the risk of residual tumor and needs to be considered.

Introduction

Ductal carcinoma in situ (DCIS) accounts for 85 to 90 % of all breast carcinoma in situ [1]. It is defined as a proliferation of ductal neoplastic cells confined to the involved canal, without stromal invasion [1-4]. Treatment is primarily based on complete surgical excision, defined by the achievement of at least two millimeters of healthy stroma around the tumor [1]. When conservative, surgery is to be complemented by radiotherapy. One of the challenges when managing DCIS is to not neglect the possibility of associated invasive carcinoma, especially when the DCIS lesion is extensive. In such cases, adapted adjuvant therapies are to be offered to the patient.

Although efforts should be made to minimize the morbidity associated with the surgical procedure, the primary objective is to achieve

negative margins, thus minimizing the risk of residual disease. This step is crucial as residual tumor rate has been estimated to be around 40 % following positive margins [5,6]. However, due to its intraductal nature, DCIS is difficult to visualize macroscopically, possibly resulting in inadequate intra-operative assessment of the exact area to be excised [7]. Consequently, it has been estimated that 20 to 25 % of patients undergoing conservative surgical treatment for DCIS will require repeat surgery to achieve complete excision [8-10]. This situation has led some teams to consider the possibility for systematic re-excision at the end of the procedure [11].

The notion of margin status itself is complex. It has been estimated that approximately 3000 sections are required to accurately analyze the margins of a spherical lumpectomy [2,12]. Additionally, margins are likely to be distorted by the widespread use of monopolar energy during

surgery, rendering analysis even more difficult [13,14]. For all these reasons, the commonly accepted minimal threshold of 2 mm to define negative margins for DCIS remains debated. This point is well illustrated in the literature, with a wide range of practices reported regarding the threshold itself but also the management of positive margins [15,16]. Although the French national guidelines recommend that repeat excision surgery depending on minimal margins distance should not be systematic and could be avoided in selected cases, the identification of such cases remains a genuine challenge [17]. This concern arises in the current context of personalized medicine, where the possibility of precise adaptation of treatments to patients' features and molecular characteristics emerges. Better understanding of such characteristics would allow for better management of DCIS heterogeneity. Furthermore, the panel of adjuvant therapies available brings additional arguments for the surgical de-escalation in the management of DCIS [2,18]. Lastly, it should be noted that a repeat surgery is a risk factor for delayed initiation of adjuvant therapy [19].

Although the rate of residual tumor resulting from positive margins is well documented, the identification of risk factors for residual tumor remains difficult. Finally, the literature on that topic is poor, with studies limited by a small number of included cases and/or methodological flaws. Thus, in previous observational studies, various breast carcinologic affections were grouped together to compensate for the small number of inclusions, leading to very heterogeneous groups and to the impossibility to extract significant, relevant, and transposable results [5, 6].

The aim of this study is to determine the proportion of patients with a residual tumor following repeat excision surgery for positive margins in DCIS following breast-conservative surgery. The secondary aim is to identify predictive factors for residual tumor in these patients.

Methods

Study design

We conducted a retrospective observational study in the two gynecologic surgery departments of our institution.

Population of interest

All patients diagnosed with positive margins in DCIS following primary breast-conservative surgery who underwent repeat surgery between January 2010 and December 2020 were included for analysis. According to current guidelines, margins were considered as positive when inferior to two millimeters [1]. Only patients who underwent both procedures in our institution were included.

Clinical data

For each patient, the following clinical characteristics were collected from medical records: age, BMI, breast size, menopausal status, use of menopausal hormone replacement therapy, smoking status and parity. Precise carcinologic data were also collected: size and precise location of the lesion on initial breast imaging and complete histology of the tumor. Finally, data on surgical procedure were gathered: presence of preoperative localization clip or wire, performance of an intraoperative imaging, and lastly performance of a re-excision during the initial procedure. Although surgical techniques were left to the discretion of the surgeon and adapted to the tumor location and morphology of the patient, all excisions had the pectoral muscle as the profound limit.

Histological data

Data on excision specimens were collected directly from the histological reports: largest dimension, volume, and precise status of the resection margins. The margins were either characterized as involved if

there was no healthy tissue between the tumor and the margin, or millimetric if there was. Margins characteristics were collected, specifically the number of involved edges, the location of the positive margin on the resection specimen, and whether the positive margin was focal or extended. Margins were considered "extensively" positive when not "focally" positive. Grades of DCIS were systematically recorded (low, intermediate, or high). When more than one grade was present, only the highest was used. For second procedures, any tumor presence was considered as residual tumor, regardless of the size or of the histological type.

Ethics

The study design was approved by the Comité d'Éthique pour la Recherche en Obstétrique et Gynécologie (CEROG numéro #2022-GYN-1106) (20). It was declared to the Portail d'Accès aux Données de Santé de l'Assistance Publique des Hôpitaux de Marseille under the number PADS 21-43. All our data were collected in compliance with the European personal data protection act.

Statistical analysis

Clinical, radiological, surgical, and pathological characteristics were summarized as categorical and continuous variables and expressed as numbers (%) and mean (\pm standard deviation) or median [25th - 75th percentiles] respectively. Categorical variables were compared with the χ^2 (χ^2) test, or Fisher's test when the conditions for the χ^2 test were not met. Differences between continuous variables were analyzed with Student's t-test. A multivariate analysis (binary logistic regression) was then performed to identify factors associated with the risk of residual tumor. In all two-sided analyses; a p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed with IBM SPSS Statistics 20 software.

Results

Population characteristics

Of the 1785 patients who underwent surgery for breast cancer during the study period, 103 met the inclusion criteria and were finally included. Patients' characteristics are reported in Table 1. The mean age was 59.1 years (SD \pm 10.7). The mean size of the initial radiological (mammography + ultrasound) anomaly was 19.6 mm (SD \pm 15.5). DCIS was not associated with any infiltrative contingent in 43 (41.7 %) cases. Residual tumor was found in 46 cases (44.7 %), of which 40 (87.0 %) were exclusively DCIS. For 6 (13.0 %) of these, an invasive carcinoma component was found after the second procedure. It was associated with DCIS in 4 (8.7 %) of them, and isolated in the other 2 (4.3 %).

Overall patients' characteristics were comparable. Only an earlier onset of disease was significantly more frequently associated with the presence of residual tumor. Thus, initial surgery was performed later in time for patients without residual tumor, compared to those with residual tumor ($p < 0.01$).

DCIS characteristics

DCIS characteristics and management are reported in Table 2. Re-excision during the initial surgical procedure was performed in 32 (56.1 %) cases in the no-residual-tumor group, whereas it was performed in only 18 (39.1 %) patients with residual tumor ($p = 0.08$). The type of repeat surgery did not seem to have any impact on the probability of residual tumor, including the performance of a mastectomy. There was no significant difference linked to the use of a preoperative wire to localize the tumor, nor on the practice of surgical specimen x-ray imaging during surgery. Two or more tumor sites on the initial excision specimen was significantly associated with the probability of residual

Table 1

Population characteristics (n = 103).

Characteristics	n	Total population	Residual tumor	No residual tumor	p
Age at diagnosis - mean ± SD	103	59.1 ± 10.7	59.3 ± 9.8	59.0 ± 11.4	0.87
BMI - kg/m ² - mean ± SD	79	24.9 ± 4.1	24.2 ± 3.3	25.4 ± 4.6	0.21
Parity - mean ± SD	78	2 ± 1.6	2.1 ± 1.6	2.0 ± 1.6	0.71
Active smoking	73	12 (16.4)	7 (17.9)	5 (15.6)	1.00
Menopause	93	64 (68.8)	26 (68.4)	38 (69.1)	0.95
Year of diagnosis - mean [25th - 75th percentiles]	103	2014 [2012 - 2017]	2013 [2011 - 2016]	2015 [2013-2017]	0.011
Year of onset of disease - mean [25th - 75th percentiles]	101	August 2014 [Apr 2012- Nov 2016]	August 2013 [June 2011- Aug 2015]	June 2015 [July 2013- May 2017]	< 0.01
Isolated DCIS	103	43 (41.7)	19 (41.3)	24 (42.1)	0.60
Size of radiologic anomaly - mm, mean ± SD	86	19.6 ± 15.5	22.2 ± 18.5	17.7 ± 12.7	0.18

All numbers are expressed as n(%), otherwise, expression mode is specified.

SD: standard deviation.

BMI: body mass index.

DCIS: ductal carcinoma in situ.

Table 2

Tumor and specimen histopathological characteristics.

Characteristics	Residual tumor	No residual tumor	p
DCIS grade:			
- Low	10 (22.2)	10 (17.9)	0.84
- Intermediate	16 (35.6)	22 (39.3)	
- High	19 (42.2)	24 (42.9)	
Tumor size - mm, mean ± SD	34.7 ± 18.3	29.9 ± 17.8	0.19
Specimen volume - cm ³ , mean ± SD	118.5 ± 134.9	97.1 ± 78.6	0.32
Histopathological type of invasive component:			
- Ductal	1 (2.2)	2 (3.5)	0.28
- Lobular	2 (4.3)	0 (0)	
- Papillary	2 (4.3)	0 (0)	
- Mucinous			
Vascular tumor emboli	5 (11.9)	10 (18.2)	0.40
Number of tumor foci >2	6 (13.0)	1 (1.8)	0.04
Margin size:			
- < 1 mm	40 (88.9)	47 (82.5)	0.36
- 1-2 mm	5 (11.1)	10 (17.5)	
Margins « in contact »	37 (80.4)	37 (64.9)	0.08
Number of specimen edges with positive margins:			
- 1	22 (47.8)	34 (59.6)	0.07
- 2	7 (15.2)	14 (24.6)	
- 3	6 (13.0)	5 (8.8)	
All edges with positive margins	11 (23.9)	4 (7.0)	0.02
Diffuse involvement of margin	21 (46.7)	16 (28.1)	0.05
Performance of intra-operative re-excision	18 (39.1)	32 (56.1)	0.08

All numbers are expressed as n (%), otherwise, expression mode is specified.

SD: standard deviation.

DCIS: ductal carcinoma in situ.

tumor: 1 (1.8 %) case in the no-residual-tumor group vs. 6 (13.0 %) in the residual tumor group ($p = 0.04$).

Surgical margins characteristics

Extensive margin involvement was associated with a higher risk of

residual tumor, with 16 (28.1 %) cases in the no-residual-tumor group vs. 21 (46.7 %) in the residual tumor group ($p = 0.05$) (Table 2). Similarly, involvement of all resection margins was significantly associated with the presence of residual tumor: 4 (7.0 %) vs. 11 (23.9 %), respectively ($p = 0.02$). There was also a lower proportion of the number of involved margins in the no-residual-tumor group than in the other: 37 (64.9 %) vs. 37 (80.4 %), respectively ($p = 0.08$). The precise location of the involved margin did not appear to have any significant impact on the outcome. Lastly, it is worth nothing that when repeat surgery was performed for margins between 1 and 2 mm, residual tumor was found in only 5 patients (11,1 %) ($p = 0,36$).

Multivariate analysis

Using multivariate analysis, the disease onset after 2013 was identified as a protective factor for residual tumor: ORa: 0.23 (95 % CI: 0.09-0.58); $p < 0.01$ (Table 3). Factors found to be significantly and independently predictive of residual tumor were extensive margin involvement (ORa: 3.2; 95 % CI: 1.3 - 8.2; $p = 0.01$), and the existence of more than two initial tumor sites (ORa: 12.4; 95 % CI: 1.2 - 124.1; $p = 0.03$).

Discussion

Our study evaluated the risk of residual tumor following repeat surgery for positive DCIS margins to be less than 50 %. Factors significantly and independently predictive of this risk were the presence of more than two tumor foci (ORa: 12.4; 95 % CI: 1.2 - 124.1; $p = 0.03$) and diffuse positive margin involvement (ORa: 3.2; 95 % CI: 1.3 - 8.2; $p = 0.01$). Surprisingly, an onset of disease after 2013 was found to be protective for the risk of residual tumor (ORa = 0.23; 95 % CI: 0.09 - 0.58; $p < 0.01$).

The rate of residual disease found in our study is consistent with the current literature [20,21]. The fact that we found an influence of the time of surgery on the risk of residual lesion is a point worth discussing. This finding could be explained by the improvement in surgical techniques, and therefore reflect the surgeons' learning curve [22]. It should be noted that the same finding has also been reported in a previous study [23]. Although not being statistically significant, we also find important to emphasize the possible protective role of intraoperative systematic re-excision. The performance of a systematic re-excision remains controversial. Although possibly effective, its indications must be carefully weighed as it could potentially render the surgical procedure heavier and alter the cosmetic result [11].

In today's context of therapeutic de-escalation, our study brings valuable information for optimal management of patients with positive margins for DCIS. It allows us to sharpen our clinical approach and identify a selected population for which a repeat surgery would be relevant. Thus, two or more tumor locations possibly compromises the possibility for conservative breast surgery, as an underestimation of the lesion is to be feared. Additionally, a diffuse involvement of the resection margin could indicate a surgical re-excision procedure. Finally, in accordance with current literature, the characteristics of tumor such as the grade, the presence or absence of an invasive component, or the nature of the anomaly on the initial imagery (microcalcifications or

Table 3

Multivariate analysis (binary logistic regression) of predictive factors for residual tumor.

Characteristics	Adjusted Odds Ratio (95 % CI)	p
Year of onset > 2013	0.23 (0.09 - 0.58)	0.002
Tumor foci > 2	12.4 (1.2 - 124.1)	0.032
Diffuse involvement	3.2 (1.3 - 8.2)	0.013
Intra-operative re-excision	0.53 (0.22 - 1.3)	0.161

CI: confidence interval.

nodule) was not found to have any impact on the proportion of residual tumor found and should not be considered when discussing the possibility for re-excision in patients with DCIS with positive margins [5,23].

Such personalized approach is currently supported by many authors and recommended by the International Senologic Society [24,25]. French guidelines indicate that a surgical revision for margins inferior to 2 mm should not be systematic and should rather be discussed in a multidisciplinary consultation meeting, depending on known risk factors: young age, presence of extensive necrosis and extensive in situ [17]. Additionally, the limitations and difficulties of the anatomopathological analysis should always be kept in mind when managing these patients, especially before deciding repeat excision. The two-dimensional interpretation of a three-dimensional specimen is inherently problematic [26]. Many factors are known to influence the anatomopathological rendering, such as the delay in managing specimen, specimen alteration due to monopolar energy use during surgery, and the fixation techniques used. This leads some authors to consider that margins status should, at best, be interpreted as a reflection of potential residual tumor to better guide adjuvant therapy [27].

In identifying risk factors for residual tumor in re-excision specimen of patients with DCIS with positive margins, we believe our results to help define a group of patients at low risk of residual tumor. These findings are of genuine value in decision making algorithms. Thus, in case of DCIS with positive margins defined by minimal distance margins of less than 2 mm, the presence of less than two tumor foci and a focal involvement of a sole positive margin could be taken into consideration along with the age, the absence of extensive necrosis, or of extensive DCIS on specimen for not performing systematic re-excision procedure [17]. Finally, the experience of the surgeon who has performed the initial procedure should also be taken into consideration.

To our knowledge, our study is the first French study to evaluate the proportion of residual tumor following repeat surgery for positive margins for DCIS, and to identify predictive factors associated. Although bringing relevant data for routine clinical practice, our results should be interpreted in consideration with possible limitations and bias. First, the small number of patients included must be considered. Although this study is likely to suffer from biases inherent to its retrospective nature, we believe this bias to be minimized by the use of an exhaustive and systematic data collection. Because of these possible limitations, prospective trials remain needed to confirm our findings, particularly in analyzing patients' long-term outcomes and prognosis.

Conclusion

Patients should be informed of the possibility of absence of residual lesion when performing re-excision breast surgery for positive margins in DCIS territory following conservative surgical treatment. The probability of residual lesion is highest in patients with two or more initial tumor foci and/or diffuse margin involvement. Finally, the surgeon's experience and learning curve should be taken in consideration. Although our findings help define patients who should benefit from re-excision following DCIS with positive margins, prospective trial remain needed, particularly for analyzing patients' long-term outcomes and prognosis.

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Publishable conflict of interest statement

All authors have no conflict of interest to declare.

Declaration of competing interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] Prise en charge du carcinome canalaire in situ – Questions d'actualité – Rapport intégral - Ref: RECORAPCCIS15 [Internet]. [cité 21 févr 2023]. Disponible sur: <https://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Prise-en-charge-du-carcinome-canalaire-in-situ-Questions-d-actualite-Rapport-integral>.
- [2] van Seijen M, Lips EH, Thompson AM, Nik-Zainal S, Futreal A, Hwang ES, et al. Ductal carcinoma in situ: to treat or not to treat, that is the question. *Br J Cancer* 2019;121(4):285–92. 13 août.
- [3] Bane A. Ductal carcinoma in situ: what the pathologist needs to know and why. *Int J Breast Cancer* 2013;2013:914053.
- [4] Masson E. EM-Consulte. [cité 10 nov 2022]. Épidémiologie, diagnostic et bilan d'extension. Disponible sur: <https://www.em-consulte.com/article/1551223/ale-rtePM>.
- [5] Sabel MS, Rogers K, Griffith K, Jaggi R, Kleer CG, Diehl KA, et al. Residual disease after re-excision lumpectomy for close margins. *J Surg Oncol* 2009;99(2):99–103.
- [6] Wei S, Kragel CP, Zhang K, Hameed O. Factors associated with residual disease after initial breast-conserving surgery for ductal carcinoma in situ. *Hum Pathol* 2012;43(7):986–93. 1 juill.
- [7] Philpott A, Wong J, Elder K, Gorelik A, Mann GB, Skandarajah A. Factors influencing reoperation following breast-conserving surgery. *ANZ J Surg* 2018;88(9):922–7. sept.
- [8] Dillon MF, Mc Dermott EW, O'Doherty A, Quinn CM, Hill AD, O'Higgins N. Factors affecting successful breast conservation for ductal carcinoma in situ. *Ann Surg Oncol* 2007;14(5):1618–28. 1 mai.
- [9] Krickler A, Armstrong B. Surgery and outcomes of ductal carcinoma in situ of the breast: a population-based study in Australia. *Eur J Cancer* 2004;40(16):2396–402. 1 nov.
- [10] Houvenaeghel G, Lambaudie E, Bannier M, Rua S, Barrou J, Heinemann M, et al. Positive or close margins: reoperation rate and second conservative resection or total mastectomy? *Cancer Manag Res* 2019;11:2507–16.
- [11] Delannoy L, Foulon A, Naepels P, Mancaux A, Thérêt P, Sergent F. Intérêt des recoups systématiques pour éviter les réinterventions dans la chirurgie conservatrice du cancer du sein. *Gynécologie Obstétrique Fertil Sénologie* 2022;50(5):395–401. 1 mai.
- [12] Carter D. Margins of "Lumpectomy" for breast cancer. *Hum Pathol* 1986;17(4):330–2.
- [13] Cocca CJ, Selmic LE, Samuelson J, Huang PC, Wang J, Boppert SA. Comparison between optical coherence tomographic and histopathologic appearances of artifacts caused by common surgical conditions and instrumentation. *Vet Surg VS* 2019;48(8):1361–71. nov.
- [14] Türkan A, Akkurt G, Yalaza M, Değirmencioglu G, Kafadar MT, Yenidünya S, et al. Effect of LigaSure™, monopolar cautery, and bipolar cautery on surgical margins in breast-conserving surgery. *Breast Care Basel Switz* 2019;14(4):194–9. août.
- [15] Azu M, Abrahamse P, Katz SJ, Jaggi R, Morrow M. What is an adequate margin for breast-conserving surgery? Surgeon attitudes and correlates. *Ann Surg Oncol* 2017;2010. p. 558–63. févr.
- [16] Pilewski M, Morrow M. Margins in breast cancer: how much is enough? *Cancer* 2018;124(7):1335–41. 1 avr.
- [17] Cancer-Sein-infiltrant-non-metastiques-Thesaurus-1.pdf [Internet]. [cité 10 mars 2023]. Disponible sur: <https://ressources-aura.fr/wp-content/uploads/2022/11/Cancer-Sein-infiltrant-non-metastiques-Thesaurus-1.pdf>.
- [18] Coles CE, Chatterjee S, Jaggi R, Kirby AM. Breast radiotherapy for ductal carcinoma in situ: could less be more? *Lancet* 2022;400(10350):408–10. 6 août.
- [19] Meyer C, Bailleux C, Chamorey E, Schiappa R, Delpech Y, Dejode M, et al. Factors involved in delaying initiation of adjuvant chemotherapy after breast cancer surgery. *Clin Breast Cancer* 2022;22(2):121–6. févr.
- [20] Sarre-Lazcano C, Clemente-Gutiérrez U, Pastor-Sifuentes FU, Medina-Franco H. Risk factors associated to residual tumor in re-excision for positive margins in breast conservative surgery. *Am Surg* 2022;88(9):2368–73. sept.
- [21] Biglia N, Ponzzone R, Bounous VE, Mariani LL, Maggiorotto F, Benevelli C, et al. Role of re-excision for positive and close resection margins in patients treated with breast-conserving surgery. *Breast Edinb Scotl* 2014;23(6):870–5. déc.
- [22] Plichta JK, Perez CB, He E, Bloom A, Abood GJ, Godellas C. Does practice make perfect? Resident experience with breast surgery influences excision adequacy. *Am J Surg* 2015;209(3):547–51. 1 mars.
- [23] Lamb LR, Mercaldo S, Oseni TO, Bahl M. Predictors of reexcision following breast-conserving surgery for ductal carcinoma in situ. *Ann Surg Oncol* 2021;28(3):1390–7. 1 mars.
- [24] Azaïs H, Maingon P, Da Maia E, Nikpayam M, Gonthier C, Belghiti J, et al. Pour quelles patientes peut-on envisager une désescalade dans la prise en charge des carcinomes canauxaires in situ ? *Gynécologie Obstétrique Fertil Sénologie* 2019;47(12):872–9. 1 déc.

- [25] Mathelin C, Lodi M, Alghamdi K, Arboleda-Osorio B, Avisar E, Anyanwu S, et al. The Senologic international society survey on ductal carcinoma in situ: present and future. *Eur J Breast Health* 2022;18(3):205–21. 1 juill.
- [26] Graham RA, Homer MJ, Katz J, Rothschild J, Safaii H, Supran S. The pancake phenomenon contributes to the inaccuracy of margin assessment in patients with breast cancer. *Am J Surg* 2002;184(2):89–93. août.
- [27] Holland R, Veling SH, Mravunac M, Hendriks JH. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical trials of breast-conserving surgery. *Cancer* 1985;56(5):979–90. 1 sept.