The Effect of Intraoperative Margin Assessment During Breast Conserving Surgery for Breast Cancer in a Dutch Cohort

Wooldrik, Sophie; van de Voort, Elles M.F.; Struik, Gerson M.; Birnie, Erwin; van Dalen, Thijs; Verhoef, C.; Klem, Taco M.A.L.

Published in:
Clinical Breast Cancer

DOI:
10.1016/j.clbc.2023.10.002

Check for updates

The Effect of Intraoperative Margin Assessment During Breast Conserving Surgery for Breast Cancer in a Dutch Cohort

Sophie Wooldrik,[1,2,#] Elles M.F. van de Voort,[1,2,#] Gerson M. Struik,[1,2,3] Erwin Birnie,[4,5] Thijs van Dalen,[2] C. Verhoef,[2] Taco M.A.L. Klem[1]

Abstract

In this monocenter retrospective cohort study (n = 1007), we investigated the impact of implementing Intraoperative digital margin specimen mammography (IDSM) on duration of surgery, positive margins and re-excision rates. IDSM use was associated with 8 minutes shorter surgery time. Significantly more cavity shaves were more often performed when IDSM was used, while the proportion of radical first surgeries was comparable.

Introduction: Intraoperative specimen radiography is a routinely used procedure to ensure adequate resection of non-palpable breast tumors. Intraoperative digital specimen mammography (IDSM) is an alternative to conventional specimen radiography (CSR) which provides immediate specimen evaluation and can potentially decrease operation time. IDSM may also result in lower positive margin and re-excision rates. IDSM was implemented in our hospital in 2018. The objective of this study was to evaluate the effect of using IDSM versus CSR on operation time, margin status and re-excision rates in breast conserving surgery. **Methods:** The present study is a single-center retrospective cohort study with 2 patient cohorts: one which underwent CSR (n = 532) and one which underwent IDSM (n = 475). The primary outcome was the operation time. Secondary outcomes were the margin status of the primary surgery, the cavity shaving rate, and the re-excision rate. Differences between cohorts were compared using univariate statistics and multiple regression analyses to adjust for variables that were significantly different between the groups. **Results:** IDSM use was associated with an 8-minute reduction in surgery time (B = -8.034, 95% CI [-11.6, -4.5]; $P < .001$). Treatment variables independently associated with the operation time included use of IDSM, type of surgery, and performance of cavity shaving. Cavity shaves were more often performed when IDSM was used (24% for IDSM vs. 14% for CSR, $P < .001$), while the proportion of negative margin rates (93% for IDSM vs. 96% for CSR, $P = .070$) was comparable. **Conclusion:** IDSM was associated with a modest reduction in operation time. Surgeons performed more cavity shaves since the introduction of IDSM, but this increase was not reflected by difference in negative margin rates.

Clinical Breast Cancer, Vol. 24, No. 1, e31–e39

Keywords: Intraoperative digital specimen mammography, Operation time, Margin status, Re-excisions, Peripoerative cavity shaving

Introduction

Due to the implementation of national breast screening programs, the detection of small breast cancers has increased.[1-5]

[1]Department of Surgery, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands
[2]Department of Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands
[3]Department of Surgery, Reinier de Graaf Gasthuis, Delft, The Netherlands
[4]Department of Statistics and Education, Franciscus Gasthuis & Vlietland, Rotterdam, The Netherlands
[5]Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Submitted: Sep 11, 2023; Revised: Oct 7, 2023; Accepted: Oct 9, 2023; Epub: 12 October 2023

Address for correspondence: Sophie Wooldrik, Department of Surgery, Franciscus Gasthuis & Vlietland, Kleiweg 500, 3045 PM, Rotterdam, The Netherlands
E-mail contact: s.wooldrik@franciscus.nl

[#] S. Wooldrik and E.M.F. van de Voort contributed equally to this work.

1526-8209/$ - see front matter
https://doi.org/10.1016/j.clbc.2023.10.002

In the Netherlands, all women between the ages of 50 and 75 are invited for breast screening, and approximately half of newly diagnosed breast cancers are screening detected. Surgical treatment of small, non-palpable tumors requires pre-operative tumor localization to guide surgical excision.[6] Several techniques are available for this procedure, such as preoperative guidewire, radioactive seed, or magnetic marker placement.

Image-guided operations routinely include intraoperative breast specimen imaging to plan appropriate tumor removal. Conventional specimen radiography (CSR) is commonly used to confirm tumor removal and assess margin status. A major limitation of this strategy, however, is that it is time-consuming. Transporting the specimen to the radiology department and assessing the image extends the operation time of the surgical procedure. Alternatively, with intraoperative digital specimen mammography (IDSM) a 2-view mammography of the specimen without compression is made in the operation room (OR), thereby providing immediate information on complete removal of the tumor. As such, it can decrease operative time.[7,8] Additionally, intraoperative breast specimen imaging could potentially reduce the likelihood of positive margins and re-excision rates, as it may guide additional cavity shaving.[9,10] However, previous studies on these outcomes investigating the effects of IDSM have shown inconsistent results.[11-13]

In this large-cohort retrospective study, we investigated the effect of IDSM implementation on operation time of breast conserving surgery for patients with clinical invasive cancer or ductal carcinoma in situ (DCIS). Additionally, the percentage of cavity shaving on positive margin and re-excision rates is explored.

Methods

Design and Patients

The present study was a single-center retrospective cohort study performed in a large teaching hospital in the Netherlands. This hospital has a breast clinic treating approximately 350 new patients with primary breast cancer and/or DCIS per year.

IDSM was introduced in our hospital in October 2018. From this point forward, all operative cases employed IDSM. Data on operation time were collected for patients who underwent breast conserving surgery (BCS) for nonpalpable primary invasive breast cancer or DCIS between 2016 and 2021 using either CSR or IDSM. The following procedures were excluded from the analysis on operation time: procedures in which more than 1 tumor was excised and procedures including a plastic surgeon performing a reconstruction. These procedures were included when analyzing secondary outcomes.

Clinicopathological information about patients was obtained from patients' electronic charts and supplemented with information from the Nabon Breast Cancer Audit (NBCA), a national database. Patient, tumor, and procedural characteristics were entered into a digital case report form (Castor EDC).

Ethical Approval

The study protocol was reviewed by the institutional reviewing board of the study hospital (advisory committee on science), and an ethical waiver was granted. The study was conducted in accordance with the Declaration of Helsinki.

Procedure

Breast conserving surgery was performed under general anesthesia. During the study period, preoperative guidewire tumor localization was gradually replaced by radioactive iodine seed localization. The sequencing of breast and axillary surgery (ie, sentinel lymph node removal) varied among surgeons. Before the implementation of IDSM, axillary surgery was typically performed (using clean instrumentation) while waiting for the result of the specimen radiography. After implementation of IDSM, however, axillary surgery was performed first. A KubTec Xpert 40 device was used to perform IDSM®. The generated images were assessed intraoperatively by the surgeon and subsequently reviewed by the radiologist. Intraoperative re-excision of additional cavity margins were not routinely used, but was allowed at the surgeon's discretion if macroscopic evaluation, the localization signal, and/or CSR or IDSM images suggested that the resection was incomplete.

Outcomes

The primary outcome measure was the operation time, measured from the time of incision to either 1) the end of the operation in the case of a standalone excision surgery or 2) until a plastic surgeon continued the operation in the case of reconstructive surgery. Time utilized to perform additional cavity shaves was included in the operation time.

Secondary outcomes were the performance of perioperative cavity shavings during the primary surgery, the pathological assessment of resection margins and the need for a secondary procedure to re-excise the primary tumor bed (ie, re-excision rate).

The pathological assessment of resection margins of the primary surgery was categorized as no tumor extension into inked margins (R0); focally involved resection margins when tumor, invasive carcinoma and/or DCIS extended into a limited area (≤4 mm) within an inked plane (R1); or more than focally involved margins (R2). The distinction between R1 and R2 is clinically relevant, as the Dutch national guidelines recommends repeated surgery in BCS only when margins are more than focally involved, whereas an extra radiotherapy boost to the tumor bed is commonly advised in the case of an R1 resection. [14]

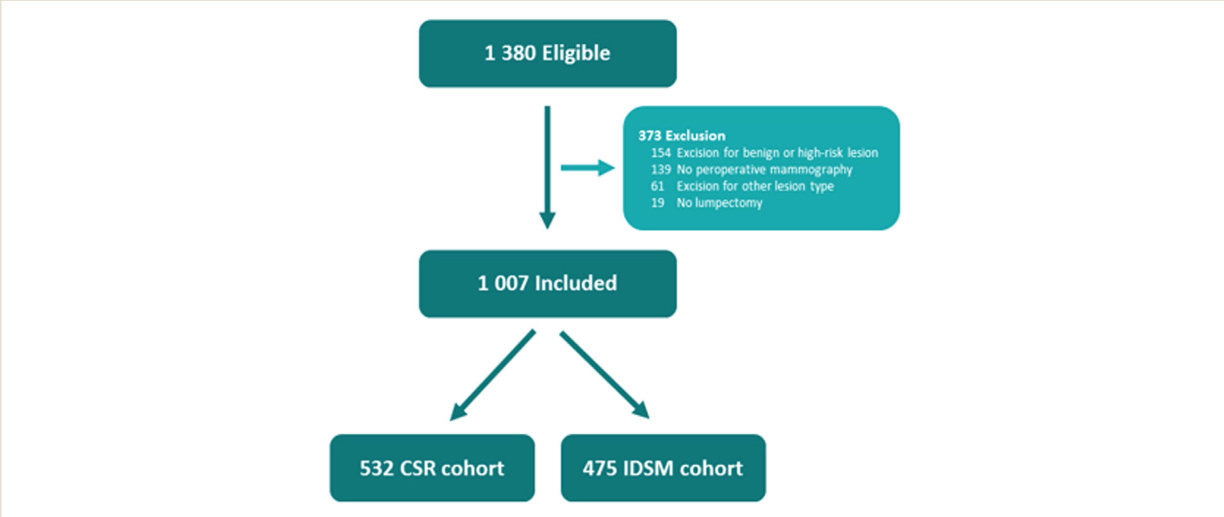
Sample Size Calculation

A difference in mean operation time of 10 minutes was considered clinically relevant, since such a reduction in operation time could increase the number of patients that can be treated daily. A standard deviation of approximately 25 minutes was expected based on previous literature.[12,13] To achieve a power ($1 - \beta$) of 90%, and using a 2-sided significance level (α) of 5%, at least 132 patients per arm were required for the analysis. Note that a sample size calculation based on the noninferiority of re-excision rates between the IDSM and CSR cohorts would require considerably larger numbers. That is, assuming a relatively low re-excision rate of 15% in the IDSM cohort and a somewhat higher re-excision rate of 18% in the CSR cohort, at least 369 patients per arm would be necessary to claim that IDSM is non-inferior to CSR with a power ($1 - \beta$) of 90% and a 1-sided significance level (α) of 2.5% and a non-inferiority limit (d) of 5%. To adjust the sample size for missing data, an additional 10% of patients was extracted, meaning that data from at least 812 patients with a breast conserving surgery must be retrieved. Data from January 2016 through December 2020 were extracted to include this number of patients.

Statistical Analyses

Baseline characteristics were summarized using mean standard deviation (SD) for continuous variables and numbers (expressed as percentages) for categorical variables. Differences between CSR and IDSM cohorts were univariately compared using a Student's t test for numerical data, and a Chi-square or Fisher's exact test was used for categorical data depending on the numbers per cell. A multiple regression analysis was performed to adjust for covariables for the operation time as well as for re-excision rate. Variables that differed

Figure 1 Overview of in-and excluded patients in the 2 cohorts.



at baseline were tested for their impact on operation time and re-excision rate using bivariate logistic regression analysis, linear regression analysis, and Pearson correlation tests. Adjustment covariables were included in the multiple regression analysis when the univariate had a *P* value below .20 (2-sided).

Based on the hypothesis that the sequencing of breast and axilla treatment would have a confounding effect on the potential time gain of the IDSM technique, we performed a subgroup analysis for patients who underwent breast surgery without axillary surgery. In this patient subgroup, operation time was compared univariately. A learning curve effect of the introduction of I-125 seed localization was addressed by separately categorizing the first 10 I-125 procedures performed by each surgeon. All analyses were performed using IBM SPSS 28 (IBM Corp. Armonk, NY), and a *P* value below .05 (2-sided) was considered statistically significant.

Results

After exclusion, 1007 breast conserving surgical procedures for a new nonpalpable breast cancer were included for analysis (Figure 1). The primary reasons for exclusion were involvement of benign or high-risk lesions or lack of intraoperative imaging.

Baseline Characteristics

The median age of the patients in the IDSM cohort was 2 years higher in comparison with the CSR cohort. Tumor characteristics such as tumor type, Bloom and Richardson grading, hormone and Her2neu status, and TNM-stage were comparable between cohorts. The mean maximum diameter of the initial resected specimen (without cavity shave) was significantly smaller in the IDSM cohort, but the weight of the initial specimen was comparable between cohorts (44 ± 55 g vs. 47 ± 40 g, 95% CI [-2.6, 10.1], $P = .246$; Table 2). Significant baseline differences were observed between the CSR and IDSM cohorts. In the IDSM cohort, more patients had been treated with neoadjuvant chemotherapy, I-125 seeds were the prevailing localization approach, more procedures were combined with reconstructive procedures by the plastic surgeon, and more patients with relatively smaller cup sizes were treated with breast conserving surgery compared to the CSR cohort (Table 1).

Operation Time

Operation time was registered in 99.8% (1005/1007) of the surgical procedures. After excluding procedures in which more than 1 tumor was excised (n = 55 in the CSR cohort, n = 59 in the IDSM cohort) and in which the operation times of the plastic and oncologic surgeries were not separately registered (n = 22), 869 procedures (467 for CSR, 402 for IDSM) were analyzed.

The mean operation time was 62.8 ± 28.4 minutes for the CSR cohort and 61.8 ± 26.0 minutes for the IDSM cohort (95 % CI of mean difference: [-2.9, 4.6]; univariate $P = .603$). Variables that impacted the operation time were the type of (axillary) surgery, the performance of additional cavity shaving, localization technique, surgeon's level of experience with the localization technique, quadrant of the tumor, whether neoadjuvant chemotherapy was given, and the age of the patient (Table A.1). In the subgroup of patients in whom only lumpectomy was performed, no difference in operation time was observed between the CSR (44.29 ± 24.14 min) and the IDSM (44.62 ± 13.64 min) cohorts (95% CI of the mean difference: [0.2, 0.1]; univariate $P = .234$).

In the subgroup of patients who underwent iodine seed localization, the mean operation time differed significantly in favor of the IDSM cohort (75.54 ± 28.36 min for CSR vs. 61.59 ± 26.34 min for IDSM; mean difference of 13.96 min; 95% CI [9.3, 18.6], $P < .001$).

According to the multivariable analysis, after log transformation, the operation time was significantly shorter in the IDSM cohort

Table 1 Baseline Characteristics of the CSR Versus the IDSM Cohort[a]

	CSR Cohort		IDSM Cohort		*P*-Value
	n = 532	SD/%	n = 475	SD/%	
Age (years), mean ± sd	60.74	10.89	62.72	12.29	.007
Cup size					<.001
A/B	105	20	144	30	
C	143	27	136	29	
D	126	24	120	25	
> E	82	15	64	14	
Unknown	76	14	11	2	
Quadrant					.022
Lateral upper	276	52	243	51	
Medial upper	103	19	75	16	
Lateral lower	62	12	64	14	
Medial lower	68	13	49	10	
Retromammillar	15	3	27	6	
Unknown	8	2	17	4	
Neoadjuvant chemotherapy					<.001[d]
Yes	63	12	108	23	
No	469	88	367	77	
Tumor localization type					<.001
Iodine seed	236	44	429	90	
Wire	276	52	32	7	
Other[b]	20	4	14	3	
Operator					.122[d]
Surgeon	444	84	378	80	
Surgeon in training	88	17	97	20	
Tumor size maximum diameter (mm), mean ± sd	14.22	8.90	14.24	12.40	.974
Tumor type					.037
NST	451	85	378	80	
Lobular	47	9	42	9	
NST and lobular	2	0	3	1	
No residual tumor in specimen	32	6	52	11	
Surgery type					<.001
Lumpectomy without SN	80	15	80	17	
Lumpectomy with SN	380	71	264	56	
Lumpectomy with ALND	37	7	45	10	
Lumpectomy with plastic surgeon	29	6	65	14	
Other[c]	6	1	21	4	
Number of excised tumors					.320[d]
1	477	90	416	88	
> 1	55	10	59	12	

Abbreviations: ALND = axillary lymph node dissection; NST = no special type; SN = sentinel node.
[a] Data are expressed as Number. (%) of participants unless otherwise indicated.
[b] Other includes: MaMaLoc (magnetic marker), no localization, or both a wire and iodine seed.
[c] Other includes: Surgical procedure at both sides with SN or ALND or a lumpectomy with SN and MARI (Marking Axillary lymph nodes with Radioactive Iodine seeds) procedure.
[d] Fisher's exact.

than in the CSR cohort (B = -0.107, 95% CI [-0.2, -0.05]; P < .001). This relative difference corresponded to an approximately 8-minute reduction in operation time in the IDSM cohort when the operation time was not log transformed (B = -8.034, 95% CI: [-11.6, -4.5]; P < .001).

Re-Excision Rate and Negative Margin Rate

More additional cavity shaves were performed after the introduction of IDSM (24% vs. 14%, P < .001; Table 2). However, the proportion reported as having "no ink on tumor" (96% for CSR vs. 93% for IDSM, P = .070) and the proportion of secondary

Table 2 Results of Surgery in the CSR Versus the IDSM Cohort [a]

	CSR Cohort		IDSM Cohort		*P*-Value
	n = 532	SD/%	*n* = 475	SD/%	
Specimen weight (grams), mean ± sd[b]	47.36	40.23	43.62	55.14	.246
Missing	81	15	28	6	
Specimen maximum diameter(mm), mean ± sd	62.19	19.47	59.44	21.57	.038
Cavity shave					<.001
Yes	76	14%	115	24%	
No	456	86%	360	76%	
Margins					.274
Free	450	85%	389	82%	
Focally irradical	60	11%	56	12%	
More than focally irradical	22	4%	30	6%	
Margins					.070
Free/focally irradical	510	96%	443	93%	
More than focally irradical	22	4%	32	7%	
Re-excision					.128[c]
Yes	42	8%	51	11%	
No	490	92%	424	89%	

[a] Data are expressed as number (%) of participants unless otherwise indicated.
[b] Missing: n = 81 (15%) in the CSR cohort, and n = 28 (6%) in the IDSM cohort.
[c] Fisher's exact. Based on the sample size calculation, noninferiority could not be demonstrated.

surgeries of the breast were comparable in the CSR and IDSM cohort (8% for CSR vs. 11%,% for IDSM, P = .128; Table 2). Of all variables that differed at baseline, only the age of the patient and whether neoadjuvant chemotherapy was administered impacted secondary surgery rate (Table A.2). In the multivariable analysis, the secondary surgery rate was significantly higher in the IDSM cohort than in the CSR cohort (B = 1.699, 95% CI [1.094, 2.636;]; P = .018).

Discussion

In this single-center cohort study, the use of IDSM resulted in a modest reduction in operation time. Before the implementation of IDSM, the time for transportation to radiology and return to the OR was approximately 30 minutes. After adjustment for covariables, the estimated time for BCS was approximately 8 minutes shorter in the ISDM group and did not reach the prespecified threshold of 10 minutes. In addition, more cavity shaves were performed in the ISDM cohort than the CSR cohort (23% vs. 14%, $P < .001$). This might explain the smaller gain in operation time than expected.

Previous studies showed a reduced or similar operation time when IDSM was introduced. Kaufman et al. and Muttalib et al. reported a decrease of 19 minutes and 7 minutes, respectively,[7,9] while Kim et al. did not find a reduction in operation time. Key explanatory factors reported included the proximity of the radiology department to the OR, type of surgery, specimen volume, surgeon expertise, and number of cavity margins re-excised.[12] The modest gain in operation time in the present study may be explained in part by the prevailing strategy at the beginning of the study period to first excise the breast tumor and subsequently perform the sentinel node procedure while waiting for radiography results.

In line with Kim et al. and Carraro et al., more cavity shaves were conducted after the implementation of IDSM.[12, 13] Even though the number of cavity shaves increased, implementation of IDSM was not associated with a reduction of positive margins. In contrast, Kim et al. observed a substantial reduction in positive margins from 26.6% to 12.7%. The fact that the numbers of positive margins were already low before implementation of IDSM (4%) may have contributed to this result (Table 2). Hence, the proportion of re-excisions was also low in both groups in the present study. Of note is the definition of negative margins in the Dutch guideline. In the case of focally involved margins, defined as extension of the tumor into a limited area of the surgical margin (<4 mm), further breast surgery is usually not recommended, and a radiotherapy boost to the tumor bed is commonly advised as part of irradiation of the breast. In the study by Kim et al., higher re-excision rates were reported (17.1% for CSR, 14.6% for IDSM).[12] The stricter definition for focally involved margins in their study (<1 mm tumor in the surgical margin) may explain this difference. It is important to note the difference between the Dutch guidelines and the NCCN guidelines. In the NCCN guidelines, a positive margin is defined as "ink on tumor" (any invasive cancer or DCIS cells on ink). In patients, with these positive margins, either re-excision to achieve a negative margin or a mastectomy is recommended.[15] Following NCCN guidelines, the implementation of IDSM would not have resulted in fewer re-excisions in the present study, as the number of free margins (defined as "no ink on tumor)") did not differ between the IDSM and CSR groups.

Many surgeons consider routine cavity shaving to be the standard of care. Chapgar et al. compared standard cavity shaving with no standard cavity shaving. A significant difference in positive margins was observed in favor of the standard cavity shave group (19% vs.

34%, $P = .01$).[16] In this study, positive margins were defined as tumors touching the edge of the specimen that were removed in the case of invasive cancer and tumors within 1 mm of the edge of the specimen that were removed in the case of DCIS. Considering that the number of positive margins in our study was already lower prior to the implementation of IDSM, coupled with the less stringent criteria for re-excision, the benefit of performing standard cavity shaving is likely to remain limited.

Furthermore, the impression of a 3D image, due to the absence of compression, is perceived as an advantage by the surgeons in our hospital: surgeons obtain an image of the specimen in its original orientation, which is considered helpful when determining the need for a cavity shave.

Patients in the IDSM cohort received neoadjuvant chemotherapy significantly more often compared to patients in the CSR cohort (108 vs. 63, $P < .001$). This fact contributed to an increased proportion of patients who exhibited no residual disease, potentially leading to a reduction in the incidence of positive margins and re-excisions within the IDSM cohort. Consequently, this effect somewhat mitigated the disparity in occurrences of positive margins and re-excisions. Landercasper et al. described a significant reduction in re-excisions among patients who underwent neoadjuvant chemotherapy.[17] This effect was also shown in the multivariable regression analysis, in which we adjusted for this difference in neoadjuvant chemotherapy administration between both cohorts. After accounting for these baseline variations, a significant difference in the number of re-excisions was observed.

Lastly, IDSM use did not result in a reduction in specimen weight. Previous studies have demonstrated a positive effect of IDSM on specimen weight. However, the mean weight of specimens in the before cohorts of these studies was considerably higher (110 g and 74 g) than in our center (47 g).[18,19]

Key limitations of this study include its retrospective nature and our use of historical controls, which increase the susceptibility to confounding and misinterpretation of data. In recent years, a number of changes have been implemented in breast cancer care that have meaningfully impacted operation time and re-excision rates. I-125 guidance, introduced during the study period, was associated with longer operation times on average. Similarly, there was a shift in the sequencing of breast and axillary surgery. The strengths of this study include the large sample size and the multivariable analysis with adjustments for covariables.

Conclusion

In this study the use of IDSM recent in breast-conserving surgery resulted in a modest reduction of operation time compared to CSR. Surgeons have begun to perform more cavity shaves since the introduction of IDSM, but this practice did not affect the number of positive margins or re-excision rates. Analysis of both primary and secondary outcomes was complicated by the shift in breast conserving surgery towards more neo-adjuvant chemotherapy, seed localization techniques and concomitant plastic surgery reconstructions. The immediate ability to independently appraise a 3D image of the specimen is considered fast and convenient by surgeons in our hospital. Prospective research could answer the potential benefit on operation time, oncological outcomes and cost-effectiveness of this promising technique.

Clinical Practice Points

- In this current study, the use of IDSM was associated with a statistically significant 8-minute reduction in surgical duration.
- Factors independently influencing the duration of surgery included the utilization of IDSM, the type of surgery performed, and the implementation of cavity shaving.
- Surgeons increased their use of cavity shaving procedures following the adoption of IDSM; however, this did not result in a lower proportion of patients with positive margins.
- The absence of specimen compression in IDSM allows our surgical team to promptly and directly assess a three-dimensional (3D) image of the specimen—an advantage highly regarded.
- The ability to independently evaluate the specimen immediately is perceived as efficient and convenient, underscoring the user-friendliness of IDSM as a significant asset.

Author Contributions

All co-authors have contributed to the development of the manuscript, approved its content and submission to the journal, and have authorized the corresponding author to represent all coauthors in prepublication discussions with the journal. The authors guarantee that neither this manuscript nor 1 with substantially similar content has been previously published or is being considered for publication elsewhere. The manuscript contains original, unpublished work.

Ethical Approval

This article does not contain any studies involving animals or human participants.

Disclosure

The authors have stated that they have no conflicts of interest.

Acknowledgements

We would like to thank Willem van Veghel MSc, business intelligence analyst, Department of Finance and Control, Franciscus Gasthuis & Vlietland Hospital, for data support. No funding or sources of support were received.

Appendix

Table A.1 Variables Tested for Their Impact on Duration of the Procedure. All Variables are Tested Using Linear Regression

			Multivariate Regression	
Variable	**B**	***P-value***	**B**	***P-value***
Cup size				
Unknown	Ref			
A/B	-0.194	.957		
C	-0.380	.915		
D	2.457	.498		
>E	0.094	.981		
Neoadjuvant chemotherapy				
No	Ref			
Yes	5.886	**.015**	3.151	0.210
Intraoperative shave performed				
No	Ref			
Yes	6.261	**.009**	8.873	**< 0.001**
Type of surgery				
Lumpectomy without SN[a]	Ref			
Lumpectomy with SN	0.341	**<.001**	18.551	**< 0.001**
Lumpectomy with ALND[b]	0.896	**<.001**	60.621	**< 0.001**
Lumpectomy in combination with plastic surgeon	0.288	**<.001**	16.276	**< 0.001**
Other	0.516	**<.001**	38.074	**< 0.001**
Localization technique with level of experience				
Surgeon > 10 iodine seed procedures	Ref			
Operator ≤ 10 iodine seed procedures (incl residents)	10.180	**<.001**	12.510	**< 0.001**
Wire	-9.087	**<.001**	-10.384	**< 0.001**
Other localization	-6.289	.204		
Quadrant				
Retromammillar	Ref			
UOQ[c]	0.118	**.126**	3.251	**0.030**
UIQ[d]	0.097	.241		
LOQ[e]	0.098	.251		
LIQ[f]	-0.046	.587		
Age	-0.002	**.149**	-0.220	**0.002**

[a] Sentinel node.
[b] Axillary lymphnode dissection.
[c] Upper-outer quadrant.
[d] Upper-inner quadrant.
[e] Lower-upper quadrant.
[f] Lower-inner quadrant.

Table A.2 Variables Tested for Their Impact on Secondary Surgery Rate. All Variables are Tested Using Logistic Regression

			Multiple Logistic Regression	
	B	*P-value*	B	*P-value*
Cup size				
Unknown	Ref			
A/B	-0.002	.997		
C	0.282	.522		
D	0.343	.440		
	-0.174	.734		
Neoadjuvant chemotherapy				
No	Ref			
Yes	-0.698	**.053**	-1.237	**0.001**
Intraoperative shave performed				
No	Ref			
Yes	0.028	.921		
Type of surgery				
Lumpectomy without SN[a]	Ref			
Lumpectomy with SN	-0.290	.301		
Lumpectomy with ALND[b]	-0.535	.275		
Lumpectomy in combination with plastic surgeon	-0.516	.265		
Other	-0.521	.501		
Localization technique with level of experience				
Surgeon > 10 iodine seed procedures	Ref			
Operator ≤ 10 iodine seed procedures (incl residents)	0.275	.321		
Wire	0.001	.997		
Other localization	-1.112	.285		
Quadrant				
Retromammillar	Ref			
UOQ[c]	-0.305	.542		
UIQ[d]	-0.247	.648		
LOQ[e]	-0.250	.658		
LIQ[f]	-0.483	.412		
Age				
	-0.034	**<.001**	-0.047	**<0.001**
Tumor type				
NST	Ref			
Lobular	0.251	.464		
NST and lobular	-18.994	.999		
No residual tumor in specimen	-18.994	.997		

[a] Sentinel node.
[b] Axillary lymfnode dissection.
[c] Upper-outer quadrant.
[d] Upper-inner quadrant.
[e] Lower-upper quadrant.
[f] Lower-inner quadrant.

References

1. Eijkelboom A, Luyendijk M, Linda de Munck MVM, Schreuder K, Siesling S, Verloop J. *Borstkanker in Nederland: trends 1989-2020*. Integraal Kankercentrum Nederland; 2021.
2. Fracheboud J, Otto SJ, van Dijck JA, Broeders MJ, Verbeek AL, de Koning HJ. Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. *Br J Cancer*. 2004;91:861–867.
3. Saadatmand S, Bretveld R, Siesling S, Tilanus-Linthorst MM. Influence of tumour stage at breast cancer detection on survival in modern times: population based study in 173,797 patients. *BMJ*. 2015;351:h4901.
4. van der Meer DJ, Kramer I, van Maaren MC, et al. Comprehensive trends in incidence, treatment, survival and mortality of first primary invasive breast cancer stratified by age, stage and receptor subtype in the Netherlands between 1989 and 2017. *Int J Cancer*. 2021;148:2289–2303.
5. Clarke M, Collins R, Darby S, 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;366:2087–2106.
6. Department of Public Health EM, Erasmus University Medical Center Rotterdam, Department of Epidemiology, Biostatistics, and Health Technology Assessment, Radboud University Medical Center Nijmegen. National Evaluation of Population-Based Breast Cancer Screening in the Netherlands 1990–2007.
7. Kaufman CS, Jacobson L, Bachman BA, et al. Intraoperative digital specimen mammography: rapid, accurate results expedite surgery. *Ann Surg Oncol*. 2007;14:1478–1485.

8. Camp MS, Valero MG, Opara N, et al. Intraoperative digital specimen mammography: a significant improvement in operative efficiency. *Am J Surg*. 2013;206:526–529.
9. Muttalib M, Tisdall M, Scawn R, Shousha S, Cummins RS, Sinnett HD. Intra-operative specimen analysis using faxitron microradiography for excision of mammographically suspicious, non-palpable breast lesions. *Breast*. 2004;13:307–315.
10. Chagpar A, Yen T, Sahin A, et al. Intraoperative margin assessment reduces reexcision rates in patients with ductal carcinoma in situ treated with breast-conserving surgery. *Am J Surg*. 2003;186:371–377.
11. McCormick JT, Keleher AJ, Tikhomirov VB, Budway RJ, Caushaj PF. Analysis of the use of specimen mammography in breast conservation therapy. *Am J Surg*. 2004;188:433–436.
12. Kim SH, Cornacchi SD, Heller B, Farrokhyar F, Babra M, Lovrics PJ. An evaluation of intraoperative digital specimen mammography versus conventional specimen radiography for the excision of nonpalpable breast lesions. *Am J Surg*. 2013;205:703–710.
13. Carraro do Nascimento V, Bourke AG. Comparison of the time taken for localised breast surgery pre- and post-introduction of intra-operative digital specimen mammography. *J Med Imaging Radiat Oncol*. 2018;62(1):39–42.
14. Specialisten, FM. Richtlijn Borstkanker: Borstsparende therapie (MST). Available at: https://richtlijnendatabase.nl/richtlijn/borstkanker/invasief_carcinoom/lokale_behandeling_stadium_i_ii/borstsparende_therapie_mst.html#:~:text=Re%2Dexcisie%20is%20ge%C3%AFndiceerd%20bij,clips%20en%20gesloten%20te%20worden.
15. Network NCC. *NCCN Guidelines: Breast Cancer*; 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
16. Chagpar AB, Killelea BK, Tsangaris TN, et al. A Randomized, controlled trial of cavity shave margins in breast cancer. *N Engl J Med*. 2015;373:503–510.
17. Landercasper J, Bennie B, Parsons BM, et al. Fewer reoperations after lumpectomy for breast cancer with neoadjuvant rather than adjuvant chemotherapy: a report from the national cancer database. *Ann Surg Oncol*. 2017;24:1507–1515.
18. Carmichael AR, Ninkovic G, Boparai R. The impact of intra-operative specimen radiographs on specimen weights for wide local excision of breast cancer. *Breast*. 2004;13(4):325–328.
19. Layfield DM, May DJ, Cutress RI, et al. The effect of introducing an in-theatre intra-operative specimen radiography (IOSR) system on the management of palpable breast cancer within a single unit. *Breast*. 2012;21:459–463.