BJR

https://doi.org/10.1259/bjr.20210765

Received: 23 June 2021 | Revised: 28 January 2022 | Accepted: 14 February 2022 | Published online: 09 March 2022

Cite this article as:
Montrognon F, Clatot F, Berghian A, Douvrin F, Quieffin F, Defta D, et al. Impact of preoperative staging with contrast-enhanced mammography for localized breast cancer management. *Br J Radiol* (2022) 10.1259/bjr.20210765.

FULL PAPER

Impact of preoperative staging with contrast-enhanced mammography for localized breast cancer management

[1]FANNY MONTROGNON, MD, [2]FLORIAN CLATOT, MD, PhD, [3]ANCA BERGHIAN, MD, [4]FRANÇOISE DOUVRIN, MD, [4]FARZANEH QUIEFFIN, MD, [4]DIANA DEFTA, MD, [4]ANAÏS BUQUET, [4]MARTINE FERRET, [5]JUSTINE LEQUESNE, [2]MARIANNE LEHEURTEUR, MD, [2]MAXIME FONTANILLES, MD, [6]DRAGOS GEORGESCU, MD and [4]FRANÇOISE CALLONNEC, MD

[1]Department of Radiology, University Hospital Center, Rouen, France
[2]Department of Medical Oncology, Henri Becquerel Center, Rouen, France
[3]Department of Anatomopathology, Henri Becquerel Center, Rouen, France
[4]Department of Radiology, Henri Becquerel Center, Rouen, France
[5]Department of Clinical Research, Henri Becquerel Center, Rouen, France
[6]Department of Gynecology and Breast surgery, Henri Becquerel Center, Rouen, France

Address correspondence to: Pr Florian Clatot
E-mail: *florian.clatot@chb.unicancer.fr*

Objective: A precise evaluation of the disease extent is mandatory before surgery for early breast cancer (EBC). Contrast-enhanced mammography (CEDM) is a recent technique that may help define adequate surgery.
Methods: This retrospective study included consecutive patients referred to a cancer center between November 2016 and July 2017 for biopsy-confirmed invasive EBC management. The primary objective was to evaluate the rate of surgical changes after incorporating the results of the preoperative staging examination, including CEDM.
Results: A total of 231 patients were screened for inclusion, and 132 patients were included, corresponding to 134 lesions. The first surgical plan was modified for 33 patients (25%), which represented 34 lesions. For 8 patients (6%), the surgery was cancelled in preference for neoadjuvant chemotherapy; for 16 patients (12.1%), the primary tumor procedure was enlarged; and for 23 patients (17.4%) the lymph node management was modified. Surgery was changed only due to the CEDM results for 24 patients (18.5%) and consisted of a more invasive procedure due to a more extended, multifocal or multicentric lesion than seen on the standard imaging. Anatomopathological surgery piece findings were well correlated with contrast-enhanced mammography results. Overall, there was no increase in the delay between the planned date of surgery and the effective surgical procedure (median 0 days).
Conclusion: CEDM added to preoperative staging helped define better surgical management without increasing delay in the surgical procedure.
Advances in knowledge: CEDM is a reliable technique that should be considered as part of preoperative staging for EBC.

INTRODUCTION

Breast cancer (BC) is the most frequent cancer in females.[1] Radiology has a prominent place in the management of BC for screening, confirming diagnosis, aiding therapeutic decisions and follow-up during treatment. Preoperative staging of breast cancer is based on the association of mammography and ultrasonography (US).[2] Preoperative MRI is also frequently performed in that setting. Indications are not consensual, but MRI is usually recommended in the case of:

- High risk patient : known familial mutation, age<40
- Invasive lobular carcinoma, Paget disease with normal mammography and US findings
- Large discrepancies between conventional imaging (mammography and US) and clinical examination
- In the case of a difficult therapeutic choice: neoadjuvant treatment, partial breast irradiation and intraoperative radiotherapy, surgery with oncoplasty.

However, MRI is not available everywhere and due to its low specificity, MRI frequently requires complementary explorations to precisely determine the nature of the suspected lesions, leading to a delay in patient management.[3–8] Contrast-enhanced digital mammography (CEDM) is a recent imaging technique that associates X-ray imaging with iodine contrast injection. CEDM is regarded as a highly sensitive (from 86 to 100%) technique to detect breast lesions,[9] with a high accuracy,[10] and may improve BC

preoperative staging. Currently, there is no official recommendation regarding the applications of CEDM. A first retrospective study on 101 patients showed that the use of CEDM modified surgical tumor management in 20% of the patients.[11] Similarly, a retrospective study on 326 patients who underwent mammography, tomosynthesis and US before CEDM, showed an 18.4% surgical management change based on the contrast-enhanced results (27). In these two studies, patient selection was restricted to those treated by surgery; thus, patients who were treated by neoadjuvant chemotherapy were not included. Moreover, these studies did not evaluate the impact of preoperative staging on the lymph node procedure.

In that context, this study aimed to assess the rate of surgical management changes after performing a radiological preoperative staging process that included CEDM.

METHODS AND MATERIALS

Population

All patients planning for treatment of localized BC who underwent mammography and US with a positive biopsy performed outside of our center between November 2016 and July 2017 were retrospectively considered for inclusion. We then included patients who underwent CEDM as part of the preoperative staging for an ACR6 breast lesion. The exclusion criteria were as follows: females who underwent CEDM for another indication, such as surveillance for a recent history of breast cancer/hereditary high-risk BC; complementary explorations for ACR4/ACR5/undetermined lesions; patients with metastatic breast cancer; and/or contraindication to iodine injection. This retrospective study was performed in accordance with French laws. All of the patients signed written consent allowing the use of their clinical and imaging data. This study was approved by the Henri Becquerel institutional review board (registration number 2010B).

Treatment proposal

In daily practice, patients with positive biopsies performed outside of our center first meet a surgeon. For all the patients included, we collected the planned surgery for the treatment of the ACR6 lesion based on the surgeon's consultation and external radiological evaluations. Then, the patients underwent radiological preoperative staging performed by experienced radiologists. The final treatment decision was made by our multidisciplinary breast board (Figure 1). Of note, as a reference center, we do not perform breast screening. Thus, all the patients addressed had a primary radiological examination performed outside our center.

Preoperative staging procedure

The preoperative staging included a clinical exam, bilateral CEDM and bilateral US including axillary areas, with additional biopsies/cytologies of the breast or the axillary area based on the radiologist's decision.

CEDM was performed using the Hologic system (Selenia Dimension mammograph with an I-View™ module, Hologic®, Marlborough, Massachusetts, USA) by trained imaging technicians. While the patient was seated, a bolus of iodinated contrast medium was administered by a peripheral intravenous line using an automatic injector (Iomeron®350, Bracco, 1.5 cc/kg at 3 cc/sec). The image acquisition started 2 min after the injection: for each view, a low-energy and a high-energy (45 kV) image were taken under compression. Our preoperative protocol started with a craniocaudal view of the nonsuspicious breast and then craniocaudal and lateral oblique views of the pathologic breast, plus the lateral oblique view of the nonsuspicious breast, and it ended with the strict profile of the pathologic breast. The total time for the whole acquisition was 5 min. Only the low energy and the recombined views were transferred for interpretation. After CEDM, a clinical examination was performed by the radiologist, and US (Logiq™, General Electric Health care, Chicago, Illinois, USA) which explored both the breast and lymph nodes, was performed. Contrast-enhanced features were described using the standard lexicon of mammography for the low-energy images, and the MRI BI-RADS lexicon for the recombined images.[12] The enhancement kinetics and intensity were also described. CEDM was interpreted by two experienced radiologists. In case of discordance, CEDM was presented to a dedicated radiological breast board. A lesion was considered more extended if there was a δ of at least 10 mm between the external radiological evaluation and the preoperative staging. A lesion was considered as multifocal if there was more than one lesion in the same breast quadrant and multicentric if there were at least two lesions in different quadrants. An additional lesion was considered if it was 10 mm or greater distant from the index lesion. In case of additional enhancement or suspicion of a more

Figure 1. Patients management when referred to our center for an ACR6 lesion

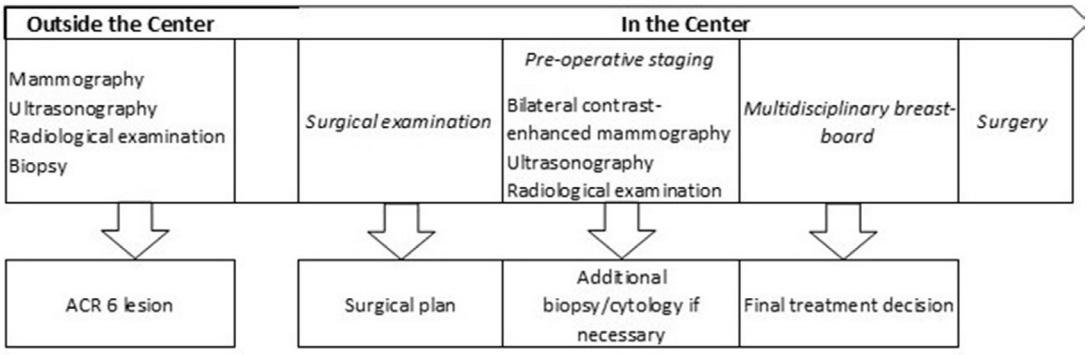
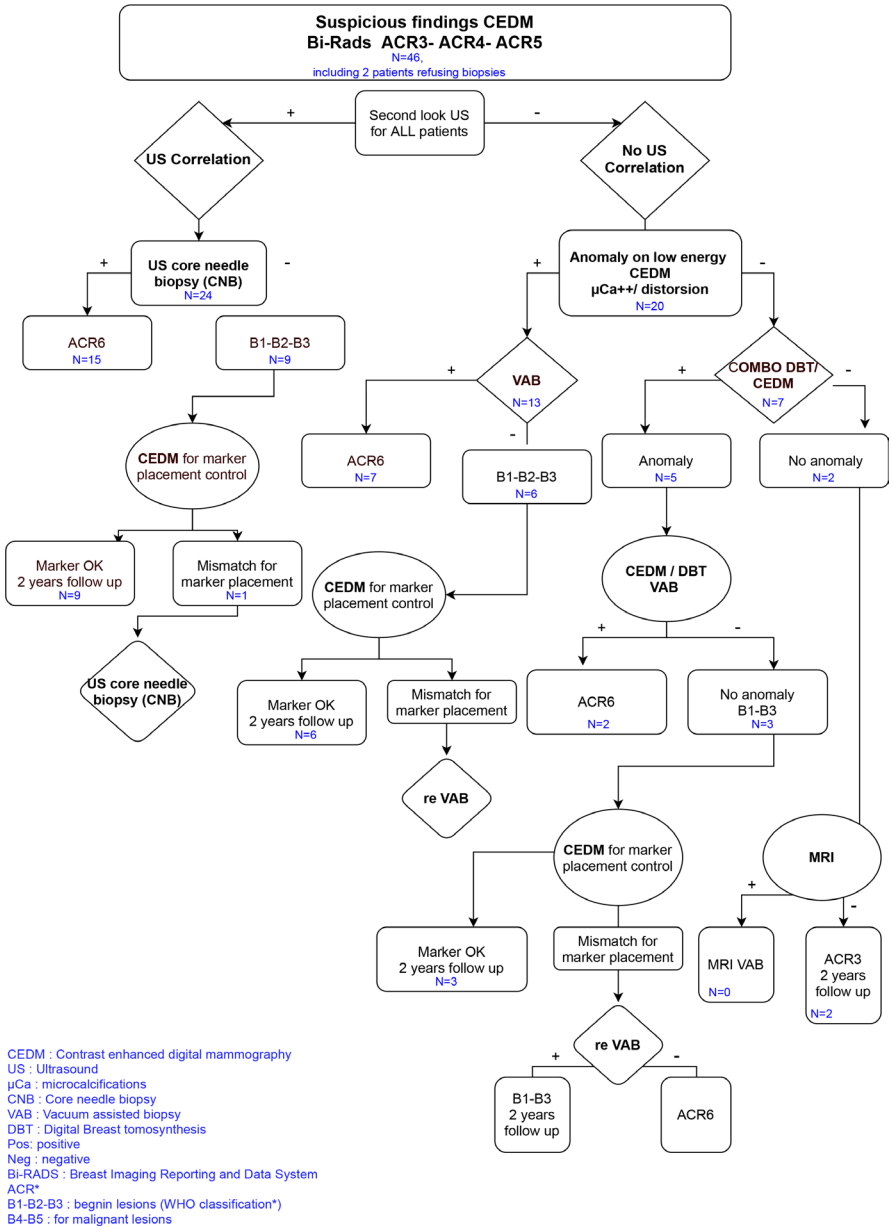


Figure 2. – *Algorithm for management of additional enhancement on CEDM*



Number of patients considered in this study are detailed in each box

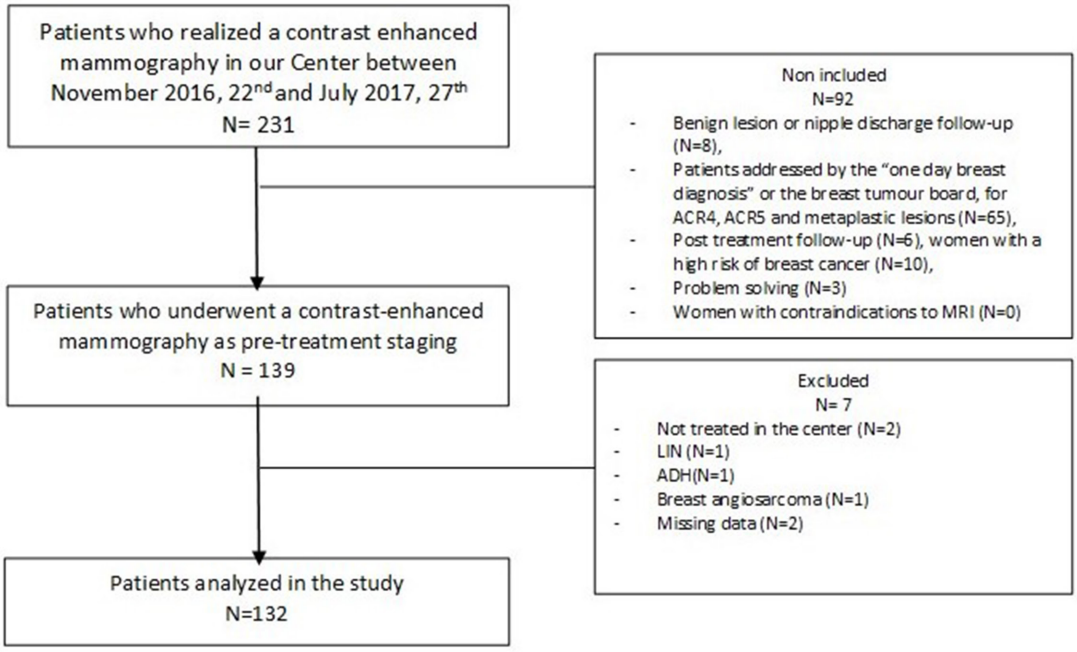
extended lesion, a specific algorithm was performed to address these suspicious findings (Figure 2). A histological assessment of any additional enhancements was mandatory before modification of the surgical procedure.

Outcomes

The primary objective of this study was to evaluate the rate of surgical changes between the initial treatment proposed by the surgeon based on external radiological evaluations and the final treatment proposal after our preoperative staging procedure.

A surgical management change could concern the surgery planned for the primary tumor: extension of a lumpectomy with an oncoplasty or a round block technique; conversion from lumpectomy to mastectomy; conversion from lumpectomy or mastectomy to neoadjuvant chemotherapy, or the addition of a contralateral procedure. A surgical management change could also concern the axillary procedure: converting from sentinel lymph node to axillary dissection or canceling any planned surgical management of the axillary area. Of note, changes in tumor management based only on the patient's choice or histological features on the external biopsy were not considered an event for this primary outcome. However, if the patient preferred radical treatment because of a more extended lesion seen on the preoperative staging, or if an additional biopsy performed during the preoperative staging revealed another histological feature that necessitated a therapeutic change, it was considered a preoperative staging consequence and considered an event for the primary outcome.

Figure 3. *Flowchart of patient enrollment*



LIN: Lobular Intra epithelial Neoplasia; ADH: Atypical Ductal Hyperplasia.

The secondary objectives were to evaluate the median delay between the first surgeon consultation and the effective surgery and to compare the estimated tumor size based on the preoperative staging (maximum axis of the enhancement on the contrast-enhanced mammography) and the pathological size (maximum axis of the lesion on the pathological examination). We considered the measures concordant if the δ between the two methods was under 10 mm. All greater than 10-mm discordant files were blindly re-evaluated by the most experienced breast radiologist at the center.

Statistics

Descriptive statistics are summarized by numbers and percentages for qualitative variables and by median and extreme values for quantitative variables. To determine the rate of surgical project change after the results of the internal preoperative staging with a 15% width of the 95% confidence interval, at least 129 patients should be analyzed.

Concordance of the lesion size between CEDM and histological examination was measured with the intraclass correlation index (ICC); additionally, a paired t-test was used to test the differences between the means. The statistical analysis was conducted with R software (V. 4.0.2).

RESULTS

Initial treatment proposal

A total of 231 patients were screened for inclusion (Figure 3), and 132 patients with 134 breast cancer lesions were included. All the included patients underwent mammography and US performed outside our center, and 30 patients (23%) also underwent MRI before coming to our center. The baseline characteristics of the patients included in the study are shown in Table 1. Following the initial examination by the surgeon and before the preoperative staging, the planned management for the 134 primary tumors was lumpectomy for 107 lesions (79.9%), mastectomy for 17 lesions (12.7%), and neoadjuvant chemotherapy for 10 lesions (7.5%) (Table 2). The planned axillary procedure was reported for 130 lesions: sentinel lymph node for 102 lesions (78.5%), axillary dissection for 15 lesions (11.5%), and no axillary procedure for seven lesions (5.4%) because of a previous history of axillary dissection (Table 3). Finally, neoadjuvant chemotherapy was planned for six lesions (4.6%) without any previous lymph node assessment.

Preoperative staging

All the patients had a clinical exam, bilateral CEDM and US performed in our center. One patient had a transient Grade 2 iodized contrast medium allergic reaction, managed using oral antihistamine. For 2 patients with marked background enhancement on CDEM, an additional MRI was then performed, which also reported marked background enhancement.[13]

Overall, 46 additional enhancements in 44 patients were revealed by CEDM. Two of these enhancements were considered ACR3 lesions after complementary MRI. Thus, an additional breast biopsy was indicated for 44 lesions. Two patients refused the additional biopsy. Details of the biopsy outcomes are detailed in Figure 2 and Table 4. Overall, 24 biopsies were positive among the 42 biopsies performed (57%). Of note, in the case of positive biopsy, no discordance between the histological characteristics of the primary tumor and the additional biopsy was observed. This result suggests that the additional biopsy was related to the same primary tumor and not due to a heterogeneous disease or a synchronous independant tumor.

Table 1. Patient and index lesion characteristics

Age (median,years, min-max) (N = 132)	**61[31-86]**
Menopausal status (*N* = 132)	
Post-menopausal	87 (65.9%)
Pre-menopausal	45 (34.1%)
Personal breast history (*N* = 130*)	
None	114 (87.7%)
Malignant	10 (7.7%)
Homolateral breast	5 (3.8%)
Contralateral breast	5 (3.8%)
Benign	6 (4.6%)
Radiotherapy history (*N* = 132)	
Yes	10 (7.6%)
For a homolateral breast cancer history	5 (3.8%)
For a contralateral breast history	4 (3.0%)
Chest radiotherapy for Hodgkin lymphoma history	1 (0.8%)
None	122 (92.4%)
Histological type on the external biopsy (*N* = 134)	
DCIS	11 (8.2%)
IDC	100 (74.6%)
ILC	18 (13.4%)
Other type	5 (3.7%)
SBR grade on the external biopsy (*N* = 124)**	
I	26 (21%)
II	79 (63.7%)
III	19 (15.3%)
Palpable tumor (*N* = 114)	
Yes	85 (63.4%)
No	49 (36.6%)
Lesion size (median,mm, min-max)	
External examination (radiological evaluation, available for 118)***	15[3-100]
Surgical examination (clinical evaluation, available for 114)	15 [0–100]

DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; SBR, Scarff-Bloom-Richardson.

(*)For 2 patients the medical history was incomplete. (**)For 10 patients there was no SBR grade reported on the external biopsy results. (***)For 16 patients, the lesion size was not reported and the external imaging report was not available

[a]

Regarding lymph node invasion, an additional biopsy/cytology was performed for 44 patients (32.8%), among which 20 were positive (45.5% of the additional samples). In cases of positive lymph node biopsy/cytology, a thoraco-abdomino-pelvic CT scan was then performed, looking for potential metastases.

Outcomes

Regarding our primary objective, the first surgical plan was modified for the primary tumor management and/or the axillary procedure after preoperative staging for 34 lesions (25.4%, 95% CI [18.3–33.6]), which represented 33 patients.

A modification of the surgery planned for the primary tumor was observed for 25 lesions and 24 patients. Among them, for eight patients, the surgery was canceled in favor of neoadjuvant chemotherapy: one for carcinomatous lymphangitis, two for a more extended lesion, four for restaging metastatic disease after preoperative staging (contralateral metastatic adenopathy or multiple metastatic adenopathy that led to an additional CT scan identifying distant metastases) and one for breast preservation. The surgical procedure was changed from lumpectomy to mastectomy for 14 lesions (10.5%), which represented 13 patients, due to a more extended lesion for four patients and the identification of multifocal disease for nine patients. The procedure was changed from lumpectomy to oncoplasty for one patient, and for two patients, a contralateral procedure was necessary (Table 2).

Based on the preoperative staging, the axillary procedure was changed for 23 patients (17.4%, 95% CI [11.4–25.0]), consisting of conversion from sentinel lymph node to axillary dissection because of an axillary positive cytology for 11 patients, as well as a high suspicion of lymph node infiltration on the preoperative staging for three patients, and based on the tumor extent or interlesional distance for seven patients. Three patients had neoadjuvant chemotherapy instead of the axillary procedure planned because of a metastatic disease found on the preoperative staging. For one patient, axillary dissection was planned but then converted to sentinel lymph node procedure because of the expected morbidity of the surgery (Table 3).

Overall, when combining tumor and axillary procedures, the surgery was changed for 24 patients (18.5%, 95% CI [12.2–26.2]) only due to the CEDM results, while for the others, the surgery was changed due to the results from both CEDM and US.

Regarding our secondary endpoints, the median delay between the external evaluation and the first surgical consultation was 22.5 days, and it was 39 days between the external evaluation and the preoperative staging. The median delay between the first surgical consultation and the surgical procedure was 34 days (min 15 days–max 99 days). Of note, the median delay between the date of surgery planned after the initial surgical consult and the effective surgical procedure was 0 days (min 14 days before - max 64 days after). A 64-day delay was reached for a patient with multifocal disease on preoperative staging, which led to a CT scan evaluation that revealed follicular lymphoma, which delayed BC management.

The tumor size was determined using the maximum axis of the enhancement on the CEDM. The mean tumor size on the preoperative staging was available for 125 lesions. For three lesions there were only microcalcifications without contrast enhancement (one patient) or with a marked background enhancement

Table 2. Breast lesion management

		After initial surgical examination			
		Lumpectomy	**Mastectomy**	**Neo-adjuvant CT**	**Total**
After pre-operative staging	**Lumpectomy**	86 (64.2%)*, **	0 (0.0%)	0 (0.0%)	**86 (64.2%)**
	Mastectomy	14 (10.5%)	16 (11.9%)	0 (0.0%)	**30 (22.4%)**
	Neo-adjuvant CT	7 (5.2%)	1 (0.75%)	10 (7.5%)	**18 (13.4%)**
	Total	**107 (79.9%)**	**17 (12.7%)**	**10 (7.5%)**	**134**

CT, chemotherapy.
(*)For one patient, an oncoplasty has been realized instead of a simple lumpectomy. (**) For two patients, the preoperative staging identified two controlateral invasive lesions

(two patients). For six lesions no maximum axis could have been measured because of carcinomatous lymphangitis or multicentric disease with safe glandular tissue between lesions. Among the 125 lesions available, the mean tumor size was 27.4 mm, with a median of 22 mm (min 7–max 96 mm). Overall, we found excellent agreement between CEDM and the histological examination (intraclass correlation index 0.82, 95% CI [0.75–0.88]) but with a significant difference between the two measures (mean difference = 4.25 mm, $p < 0.001$): on CEDM, the mean lesion size was 27 mm (min 6 - max 96), whereas for the material removed during surgery, the mean lesion size was 20.5 mm (min 4–max 105 mm). All discordant evaluations (delta≥10 mm) seemed to show a tendency to overestimate the tumor extent with CEDM. Actually, mass enhancement was well correlated with the infiltrating lesion size, while non-mass enhancement usually represented an *in situ* lesion. The sizes of these *in situ* lesions were frequently not mentioned in the pathologist report.

Of note, 22 tumors were reclassified as multifocal based on the preoperative staging. All were indeed multifocal after pathological evaluation.

As an example, we present the case of a 43-year-old patient referred to the center for invasive grade II ductal carcinoma evaluated to be 10 mm by an outside center (Figure 4). Based on external mammography and ultrasonography, the planned surgery was a lumpectomy with a sentinel lymph node technique. The low-energy images are difficult to read because of the high breast density, classed C. We note a para-areolar increased opacity in the suprainternal quadrant of the left breast. The recombined pictures show a 56 mm enhancement, corresponding to a ductal *in situ* lesion on pathological examination.

DISCUSSION

In this retrospective study based on 132 early breast cancer patients, we showed that preoperative staging including CEDM helps to choose the best therapeutic approach, particularly by adapting the surgical procedure for 25.4% of our patients. Of note, CEDM was directly involved in surgical procedure changes for 18.4% of the patients.

Several studies have compared CEDM to other modalities of breast imaging for specificity, sensitivity to detect cancer lesions, and accuracy in determining lesion size. CEDM has a better sensitivity compared to standard digital mammography.[14] CEDM performance is quite similar to contrast-enhanced MRI (CEDMRI), with a sensitivity of nearly 100 versus 93%, and an accuracy of approximately 79 versus 73% in the Luczynska et al study.[15] CEDM has a better positive predictive value, estimated at 97 versus 85% for the CEDMRI in the Jochelson et al study[16] and approximately 93 versus 60% in the Lee-Felker et al study.[7] Some studies also evaluated CEDM for breast cancer preoperative staging, concluding that its performance for evaluation of the disease extent was good[7,17,18] and that it did not require complementary MRI.[19]

Table 3. Lymph node management

		After initial surgical examination			
		Sentinel lymph node	**Axillary dissection**	**No axillary procedure**	**Total**
After pre-operative staging	**Sentinel lymph node**	83 (63.8%)	0	1	**85 (65.4%)**
	Axillary dissection	14 (10.8%)	11	0	**25 (19.2%)**
	No axillary procedure	5 (3.9%)	3	12	**20 (15.4%)**
	Total	**102 (78.5%)**	**15 (11.5%)**	**13 (10.0%)**	**130**

Of note, the planned axillary procedure after initial surgical examination was not available for four lesions
*No axillary procedure" includes neoadjuvant chemotherapy and no surgical procedure because of comorbidities or previous axillary procedure.

Table 4. Outcome of the additional contrast enhancements

Additional enhancement on CEDM	***46 additional contrast enhancements on 44 patients***	
Biospy performed	*42 biopsies on 41 patients*	
No biopsy performed	*ACR3 on MRI (2 patients)* *Refusal of additional biopsy (2 patients*)*	
Microbiopsy (US-guided)	***24 biopsies on 23 patients***	
Positive	15 biopsies on 14 patients	IDC (n = 9) ILC (n = 3) DCIS (n = 3)
Negative	nine biopsies on 9 patients	DH(n = 2) Metaplasia (n = 1) Intra cystic papilloma (n = 1) Fibroadenoma (n = 1) Adenosis (n = 1) No abnormality (n = 3)
Macrobiopsy (tomosynthesis)	***13 biopsies on 13 patients***	
Positive	seven biopsies on 7 patients	IDC (n = 2) DCIS (n = 3) Intragalactophoric carcinoma (n = 2)
Negative	six biopsies on 6 patients	DH (n = 1) Fibrocystic mastopathy (n = 1) No abnormality (n = 4)
Macrobiopsy (combo angiotomo)	***five biopsies on 5 patients***	
Positive	two biopsies on 2 patients	Carcinomatous lymphangitis (n = 1) IDC(n = 1)
Negative	three biopsies on 3 patients	DHA (n = 1) DH (n = 1) No abnormality (n = 1)

DCIS, ductal carcinoma *in situ*; DH, ductal hyperplasia; DHA, ductal hyperplasia with atypia; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

*One of these 2 patients accepted additional biopsy on the index breast but refused additional biopsy on the other one

However, to our knowledge, only two previous studies have evaluated the impact of CEDM on the surgical management of breast cancer. The first one by Ali-Mucheru et al,[11] with a surgical plan management modified to enlarged surgery in 20% of patients, included all patients who had CEDM even for a benign or suspicious lesion. More recently, Bicchierai et al[20] included 326 patients with ACR4/ACR5 lesions and compared a combination of mammography, tomosynthesis and US to CEDM, reporting a breast surgery procedure change in 18.4% due to CEDM. However, they included only patients who underwent breast cancer surgery, excluding patients treated with neoadjuvant chemotherapy. Moreover, they did not evaluate the impact of CEDM on the lymph node procedure. In our center, we use CEDM with indications comparable to those of MRI, except for high hereditary risk patients. Based on the literature data, we also use CEDM for patients with contraindications to MRI and due to its accessibility.[4–7,21] In this study, only a few patients had a previous breast surgical or radiotherapeutic history. We can only wonder if the performance of preoperative staging is similar in that population.

Our study population is homogeneous and representative of daily practice, with the females first assessed for a breast anomaly in a primary care imaging center, and then referred to our reference center for treatment of the suspicious lesion. Since our aim was to evaluate the impact of preoperative imaging staging on the surgical procedure and its delay, we restricted inclusions to patients with a confirmed BC lesion (ACR6 lesion). We did not explore here the place of CEDM in the ACR5 and ACR4 lesion support, which could also benefit from this technique as reported by Bicchierai et al..[20]

The protocol used in this study differs from the literature data.[22,23] Indeed, the breast cranio-caudal and mediolateral oblique views were taken after a first view of the nonsuspicious breast to apply the best enhancement time for that side. A mediolateral oblique view of the supposedly healthy breast was then taken, and an ultimate shot was performed with the profile of the concerned breast looking for late enhancement. This last profile view is not usual in other studies. It allows enhancement kinetics on the pathological breast, such as that used in breast MRI, and it was taken at the request of the center's surgeon to have two orthogonal views for the surgical procedure.

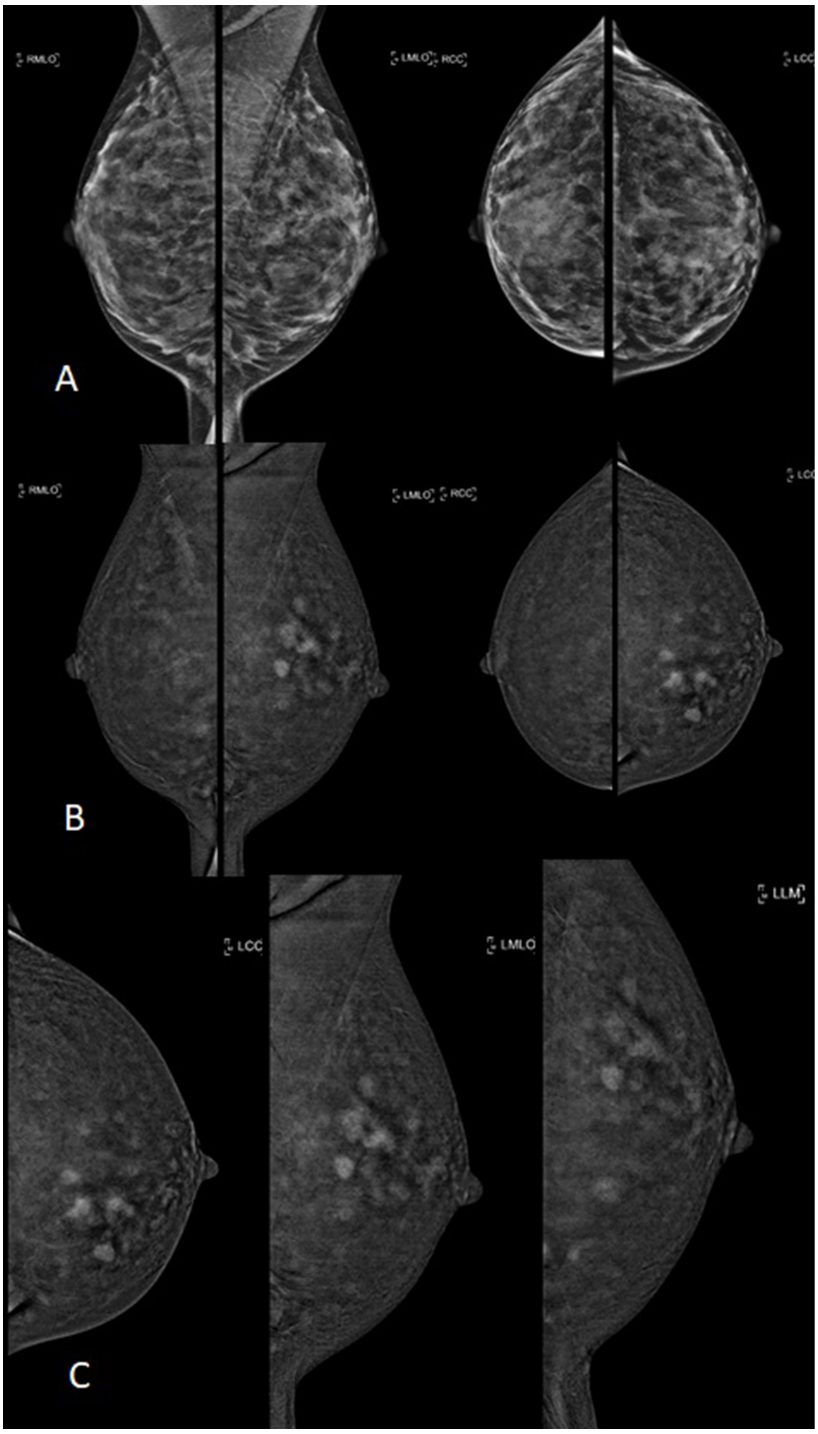
Of note, this study evaluated CEDM as part of a multimodal preoperative staging performed by trained breast cancer radiologists with more than 10 years of experience in breast imaging. Of note, we cannot distinguish the impact of CEDM on its own, but since US and CEDM are complementary, in particular US is the gold standard for axillary evaluation, both techniques should be performed together for preoperative staging. Interestingly, even if CEDM does not directly evaluate axilla, a higher tumor stage such as T3 instead of T2 or multifocality revealed by CEDM will change the axillary procedure: moving from sentinel node to axillary dissection[24] whatever the result of the US axillary evaluation.

Moreover, because of our radiologists' experience in a reference breast cancer center, some could argue that our results may not apply to a primary care center. Nevertheless, the CEDM learning curve is minimal[25–29] and accessible to most of breast radiologists.

Approximately half of the patients had an additional biopsy or cytology based on the preoperative examination. Indeed, any contrast enhancement revealed by CEDM that would modify the surgery must be confirmed by a biopsy. Moreover, any morphological abnormality of a lymph node should also be assessed by cytology. These additional explorations are one limit of highly sensitive radiological methods, such as MRI or CEDM.[30]

This study has some biases. First, since this is a retrospective study, all of the relevant clinical data may not have been recorded, such as the occurrence of a postbiopsy hematoma that could

Figure 4. *A 43-year-old patient referred to the center for an invasive ductal carcinoma, grade II, evaluated at 10 mm in primary care*. Contrast enhanced mammography performed in the center. (A) Low-energy images: C density, no microcalcifications focus, in the left breast an increased opacity in the suprainternal quadrant, para-areolar. (B)Recombined images corresponding, moderate background enhancement, nodular enhancement retro-areolar in the suprainternal quadrant of the left breast, extended over 43 mm in a transversal axis. (C) Recombined images only of the pathological left breast. The enhancement extends over a height of 56 mm, so additional biopsies were suggested. The patient refused additional biopsies and preferred a mastectomy immediately. On the anatomopathological evaluation, there was a grade II invasive ductal carcinoma on a 1.5 mm focus associated with extension of an *in situ* ductal carcinoma over 50 mm.



overestimate the lesion size when the surgeon first examined the patient. Beyond this study, the benefit of CEDM for reducing repeat operation rates or loco-regional treatment failure should be determined in dedicated prospective studies. Second, since the correlation between the radiological evaluation and the anatomopathological evaluation was not predefined, we cannot exclude that the axis of the measurements differed between the two techniques. Third, the anatomopathological measurements considered only the infiltrating tumors, without any systematic measurement for any *in situ* associated foci. This bias may have altered the correlation index and prevented us from evaluating the potential accuracy of CEDM in tumors combining infiltrating and *in situ* tumors. Fourth, patients included had a primary radiological examination performed outside of our center, with no quality control possible and no information regarding the experience of the radiologists and pathologists. However, this method of recruitment represents the daily practice of a reference center such as ours. Fifth, this study was not designed to determine the potential clinical benefit of surgical project modification due to our radiological preoperative staging. Of note, such a study could only be performed prospectively and would include thousands of patients in a randomized way.

CONCLUSION

CEDM as part of a multimodal preoperative staging is a reliable technique for breast cancer local extension evaluation. Such evaluation in our center led to a rate of surgical project modification of 25.4%, with a direct impact of CEDM for 69.9% of these. This method of preoperative staging is feasible in daily practice without delaying surgery and should be considered as part of preoperative staging for EBC.

REFERENCES

1. WHO | Breast cancer. WHO. 2020. Available from: http://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/
2. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, et al. Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up†. *Ann Oncol* 2019; **30**: S0923-7534(19)31287-6: 1194–1220: . https://doi.org/10.1093/annonc/mdz173
3. Lewin J. Comparison of contrast-enhanced mammography and contrast-enhanced breast MR imaging. *Magn Reson Imaging Clin N Am* 2018; **26**: S1064-9689(17)30163-0: 259–63: . https://doi.org/10.1016/j.mric.2017.12.005
4. Kim EY, Youn I, Lee KH, Yun J-S, Park YL, et al. Diagnostic value of contrast-enhanced digital mammography versus contrast-enhanced magnetic resonance imaging for the preoperative evaluation of breast cancer. *J Breast Cancer* 2018; **21**: 453: 453–62: . https://doi.org/10.4048/jbc.2018.21.e62
5. Li L, Roth R, Germaine P, Ren S, Lee M, et al. Contrast-enhanced spectral mammography (CESM) versus breast magnetic resonance imaging (MRI): A retrospective comparison in 66 breast lesions. *Diagn Interv Imaging* 2017; **98**: S2211-5684(16)30212-1: 113–23: . https://doi.org/10.1016/j.diii.2016.08.013
6. Wang Q, Li K, Wang L, Zhang J, Zhou Z, et al. Preclinical study of diagnostic performances of contrast-enhanced spectral mammography versus MRI for breast diseases in china. *Springerplus* 2016; **5**(1): 763. https://doi.org/10.1186/s40064-016-2385-0
7. Lee-Felker SA, Tekchandani L, Thomas M, Gupta E, Andrews-Tang D, et al. Newly diagnosed breast cancer: comparison of contrast-enhanced spectral mammography and breast MR imaging in the evaluation of extent of disease. *Radiology* 2017; **285**: 389–400. https://doi.org/10.1148/radiol.2017161592
8. Patel BK, Gray RJ, Pockaj BA. Potential cost savings of contrast-enhanced digital mammography. *AJR Am J Roentgenol* 2017; **208**: W231–37. https://doi.org/10.2214/AJR.16.17239
9. Zhu X, Huang J-M, Zhang K, Xia L-J, Feng L, et al. Diagnostic value of contrast-enhanced spectral mammography for screening breast cancer: systematic review and meta-analysis. *Clin Breast Cancer* 2018; **18**: S1526-8209(18)30008-9: e985–95: . https://doi.org/10.1016/j.clbc.2018.06.003
10. Patel BK, Garza SA, Eversman S, Lopez-Alvarez Y, Kosiorek H, et al. Assessing tumor extent on contrast-enhanced spectral mammography versus full-field digital mammography and ultrasound. *Clin Imaging* 2017; **46**: S0899-7071(17)30122-5: 78–84: . https://doi.org/10.1016/j.clinimag.2017.07.001
11. Ali-Mucheru M, Pockaj B, Patel B, Pizzitola V, Wasif N, et al. Contrast-enhanced digital mammography in the surgical management of breast cancer. *Ann Surg Oncol* 2016; **23**: 649–55. https://doi.org/10.1245/s10434-016-5567-7
12. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. *ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System*. Reston, VA: American College of Radiology; 2013.
13. Sogani J, Morris EA, Kaplan JB, D'Alessio D, Goldman D, et al. Comparison of background parenchymal enhancement at contrast-enhanced spectral mammography and breast MR imaging. *Radiology* 2017; **282**: 63–73. https://doi.org/10.1148/radiol.2016160284
14. Jochelson MS, Lobbes MBI. Contrast-enhanced mammography: state of the art. *Radiology* 2021; **299**: 36–48. https://doi.org/10.1148/radiol.2021201948
15. Łuczyńska E, Heinze-Paluchowska S, Hendrick E, Dyczek S, Ryś J, et al. Comparison between breast MRI and contrast-enhanced spectral mammography. *Med Sci Monit* 2015; **21**: 1358–67. https://doi.org/10.12659/MSM.893018
16. Jochelson MS, Dershaw DD, Sung JS, Heerdt AS, Thornton C, et al. Bilateral contrast-enhanced dual-energy digital mammography: feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. *Radiology* 2013; **266**: 743–51. https://doi.org/10.1148/radiol.12121084
17. Patel BK, Davis J, Ferraro C, Kosiorek H, Hasselbach K, et al. Value added of preoperative contrast-enhanced digital mammography in patients with invasive lobular carcinoma of the breast. *Clinical Breast Cancer* 2018; **18**: e1339–45. https://doi.org/10.1016/j.clbc.2018.07.012
18. Bozzini A, Nicosia L, Pruneri G, Maisonneuve P, Meneghetti L, et al. Clinical performance of contrast-enhanced spectral mammography in pre-surgical evaluation of breast malignant lesions in dense breasts: a single center study. *Breast Cancer Res Treat*

2020; **184**: 723–31. https://doi.org/10.1007/s10549-020-05881-2
19. Lobbes MBI, Lalji UC, Nelemans PJ, Houben I, Smidt ML, et al. The quality of tumor size assessment by contrast-enhanced spectral mammography and the benefit of additional breast MRI. *J Cancer* 2015; **6**: 144–50. https://doi.org/10.7150/jca.10705
20. Bicchierai G, Tonelli P, Piacenti A, De Benedetto D, Boeri C, et al. Evaluation of contrast-enhanced digital mammography (CEDM) in the preoperative staging of breast cancer: large-scale single-center experience. *Breast J* 2020; **26**: 1276–83. https://doi.org/10.1111/tbj.13766
21. Mann RM, Cho N, Moy L. Breast MRI: state of the art. *Radiology* 2019; **292**: 520–36. https://doi.org/10.1148/radiol.2019182947
22. Bhimani C, Matta D, Roth RG, Liao L, Tinney E, et al. Contrast-enhanced spectral mammography: technique, indications, and clinical applications. *Acad Radiol* 2017; **24**: S1076-6332(16)30220-3: 84–88: . https://doi.org/10.1016/j.acra.2016.08.019
23. Perry H, Phillips J, Dialani V, Slanetz PJ, Fein-Zachary VJ, et al. Contrast-:enhanced mammography: A systematic guide to interpretation and reporting. *American Journal of Roentgenology* 2019; **212**: 222–31. https://doi.org/10.2214/AJR.17.19265
24. Lyman GH, Somerfield MR, Bosserman LD, Perkins CL, Weaver DL, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: american society of clinical oncology clinical practice guideline update. *J Clin Oncol* 2017; **35**: 561–64. https://doi.org/10.1200/JCO.2016.71.0947
25. Lalji UC, Houben IPL, Prevos R, Gommers S, van Goethem M, et al. Contrast-enhanced spectral mammography in recalls from the dutch breast cancer screening program: validation of results in a large multireader, multicase study. *Eur Radiol* 2016; **26**: 4371–79. https://doi.org/10.1007/s00330-016-4336-0
26. Lobbes MBI, Lalji U, Houwers J, Nijssen EC, Nelemans PJ, et al. Contrast-enhanced spectral mammography in patients referred from the breast cancer screening programme. *Eur Radiol* 2014; **24**: 1668–76. https://doi.org/10.1007/s00330-014-3154-5
27. Lancaster RB, Gulla S, De Los Santos J, Umphrey HR. Contrast-enhanced spectral mammography in breast imaging. *Semin Roentgenol* 2018; **53**: S0037-198X(18)30067-1: 294–300: . https://doi.org/10.1053/j.ro.2018.08.003
28. Dromain C, Balleyguier C, Adler G, Garbay JR, Delaloge S. Contrast-enhanced digital mammography. *Eur J Radiol* 2009; **69**: 34–42. https://doi.org/10.1016/j.ejrad.2008.07.035
29. Barra FR, Ribeiro AC, Mathieu OD, Rodrigues AC. Dual-energy contrast-enhanced digital mammography: examination protocol. *Diagn Interv Imaging* 2014; **95**: S2211-5684(14)00020-5: 351–52: . https://doi.org/10.1016/j.diii.2014.01.019
30. . Xing D, Lv Y, Sun B, Xie H, Dong J, Hao C, et al. Diagnostic Value of Contrast-Enhanced Spectral Mammography in Comparison to Magnetic Resonance Imaging in Breast Lesions. J Comput Assist Tomogr. 2018 Dec 7;