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ORIGINAL ARTICLE

Contrast-Enhanced Spectral Mammography Versus Magnetic Resonance Imaging: Intra- and Inter-Observer Agreements in Tumour Size Assessment

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ABSTRACT

Introduction: *In patients with locally advanced breast carcinomas undergoing neoadjuvant chemotherapy (NAC), imaging monitoring is important for guiding clinical management. Contrast-enhanced spectral mammography (CESM) is a recently introduced modality that may serve this purpose as an alternative to magnetic resonance imaging (MRI). We aimed to investigate intra- and inter-observer agreements in CESM and MRI in assessment of tumour size.*

Methods: *Imaging studies performed between December 2019 and March 2022 for breast cancer patients undergoing NAC were retrospectively reviewed. Two radiologists measured the largest lesion sizes, intra- and inter-observer agreements were measured using the intraclass correlation coefficient. To assess the agreement between CESM and MRI findings, Lin's concordance correlation coefficient (CCC) and Bland–Altman plots were used. Scanning time and reading time were recorded and compared.*

Results: *12 cases of patients who had undergone a total of 20 CESM studies and 18 MRI studies were assessed. The intra-observer agreement for the two radiologists on CESM was 0.983 and 0.996. The inter-observer agreement on CESM was 0.995. For MRI, the intra-observer agreement was 0.975 and 0.984, while the inter-observer agreement was 0.982. The agreement between the 10 baseline CESM and MRI studies was high (CCC = 0.972). Both the scanning time and reading time were significantly shorter for CESM than MRI (both $p < 0.001$).*

Conclusion: *Our results provide further evidence of CESM measurement reproducibility before, during, and after NAC. CESM can be considered an alternative assessment modality for monitoring NAC response.*

Key Words: *Breast neoplasms; Magnetic resonance imaging; Mammography; Neoadjuvant therapy*

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中文摘要

對比增強波譜乳房造影與磁力共振：腫瘤大小評估中觀察者內和觀察者間的一致性

高子恩、黎爾德、梁肇庭、羅嘉麒、黃可澄、錢凱、黃慧中

引言：對於接受術前輔助化療的局部晚期乳腺癌患者，影像監測在指導臨床治療方面非常重要。對比增強波譜乳房造影（CESM）是最近推出的一種模式，可用於此目的並作為磁力共振的替代方案。本文研究CESM和磁力共振中觀察者內和觀察者間評估腫瘤大小的一致性。

方法：我們對2019年12月至2022年3月期間接受術前輔助化療的乳腺癌患者的影像學檢查進行回顧性分析。最大的病灶尺寸由兩位放射科醫生測量，並使用組內相關系數評估觀察者內和觀察者間的一致性。我們使用Lin氏一致性相關系數和Bland-Altman圖評估CESM和磁力共振結果之間的一致性，以及記錄並比較掃描時間和閱片時間。

結果：12例患者接受了共20次CESM檢查和18次磁力共振檢查。兩位放射科醫生的CESM 觀察者內一致性為0.983和0.996，觀察者間一致性為0.995。磁力共振觀察者內一致性為0.975和0.984，觀察者間一致性為0.982。十次基線CESM和磁力共振檢查間的一致性很高（一致性相關系數 = 0.972）。CESM的掃描時間和閱片時間均顯著短於磁力共振（兩者p值均為 < 0.001）。

結論：我們的結果進一步證明了術前輔助化療之前、期間和之後CESM測量的可重複性。CESM可視為術前輔助化療療效監測的替代方式。

INTRODUCTION

Neoadjuvant chemotherapy (NAC) is currently the treatment of choice for patients presenting with unresectable disease, locally advanced disease, or inflammatory breast cancer, all of which NAC may render resectable.[1,2] After NAC, an improved tumour-breast ratio may allow breast-conserving surgery, which leads to a better cosmetic outcome. In patients with human epidermal growth factor receptor 2–positive and triple-negative breast cancer (TNBC) subtypes, findings of residual disease after NAC provide prognostic information and can guide further adjuvant therapy.[3,4] Accurate assessment of NAC response is therefore important to guide subsequent management. Initially, response to NAC was assessed by a combination of clinical examination, mammography, and ultrasound. Subsequently, contrast-enhanced magnetic resonance imaging (MRI) was proven to be a superior imaging modality, with better assessment of tumour extent, visualisation of additional tumour foci, and identification of residual disease after NAC.[5,6] One of the major advantages of MRI is the fact that it allows contrast-enhanced imaging. However, the relatively high cost, low availability, and long image acquisition time of MRI may restrict patient access. Recently, contrast-enhanced spectral mammography (CESM) has been developed as an imaging tool which utilises a dual-energy technique to combine the advantages of digital mammography with contrast-enhanced imaging. When evaluating tumour extent, CESM had better correlation with the size measured in histopathology specimens when compared with standard mammography and ultrasound.[7] In the setting of NAC response monitoring, early data have shown CESM to be promising when compared to MRI.[8-10] One study concluded that CESM has better agreement with histological assessment of surgical specimen in demonstrating complete pathological response as compared to MRI.[8] Initial results[8-10] have suggested CESM to be a viable alternative to MRI in the setting of NAC response monitoring.

The aim of this study was to assess the intra-observer and inter-observer agreements in CESM and MRI to further study the validity of CESM as an alternative option for tumour size evaluation before and after NAC.

METHODS

Patients

From December 2019 to March 2022, a total of 12 patients were referred to Pamela Youde Nethersole

Eastern Hospital for imaging monitoring of NAC response. All patients had confirmed locally invasive breast carcinoma through tissue sampling and underwent CESM and/or MRI prior to the commencement of NAC as a baseline study, with 10 patients undergoing both CESM and MRI within 3 days of each other. Follow-up CESM and/or MRI was performed at mid-cycle and/or end of treatment.

Contrast-Enhanced Spectral Mammography

CESM was performed using the Selenia Dimensions Mammography system (Hologic, Marlborough [MA], US). Iohexol (Omnipaque; GE Healthcare, Milwaukee [WI], US) was used as the CESM contrast agent. The amount administered was calculated at 1.5 mL/kg,[11] and administered at a rate of 3 mL/s through a power injector. CESM images were then acquired 2 minutes after contrast injection and completed within 10 minutes, allowing an 8-minute window for image acquisition (Figure 1).[11] CESM high-energy (45-49 kV) and low-energy (28-33 kV) images were obtained in the craniocaudal and mediolateral oblique projections for each breast. CESM high-energy images were used to produce subtracted images; the low-energy and subtracted images were displayed for review by radiologists. The CESM images were then immediately reviewed by the session radiologist, and additional views, e.g., magnified and compression views, were obtained if deemed necessary (Figure 1). The time required for each CESM study was recorded, starting at contrast injection and concluding at the last image acquired.

Magnetic Resonance Imaging

MRI was performed utilising the Siemens-Avanto 1.5T MRI scanner (Erlangen, Germany), with patients in the prone position. Gadoterate meglumine (Dotarem; Guerbet, Villepinte, France) was used as contrast agent. Sequences acquired included fat-suppressed axial T2-weighted sequence, coronal T2-weighted sequence, axial T1-weighted sequence with dynamic contrast (first sequence before contrast administration and seven acquisitions after contrast agent administration each spaced 1 minute apart), and axial diffusion-weighted sequences. The time required for each MRI study was recorded.

Imaging Interpretation

CESM and MRI images were interpreted by two radiologists: a specialist radiologist with > 7 years' experience in breast imaging, and a trainee radiologist with 1 year of experience in breast imaging. During image interpretation, the radiologists were blinded to the measurements of the other imaging modality as well as the measurements of the other radiologist. The images from different patients were interpreted in a randomised sequence and were interpreted twice by each radiologist with a 2-month interval. In CESM, both low-energy and subtracted images were reviewed (Figure 2). The largest lesion in each breast was measured, disregarding peritumoral calcifications. In MRI, the single largest lesion was assessed in different sequences and planes, where the largest dimension was recorded (Figures 3 and 4). The presence of any satellite lesions was also

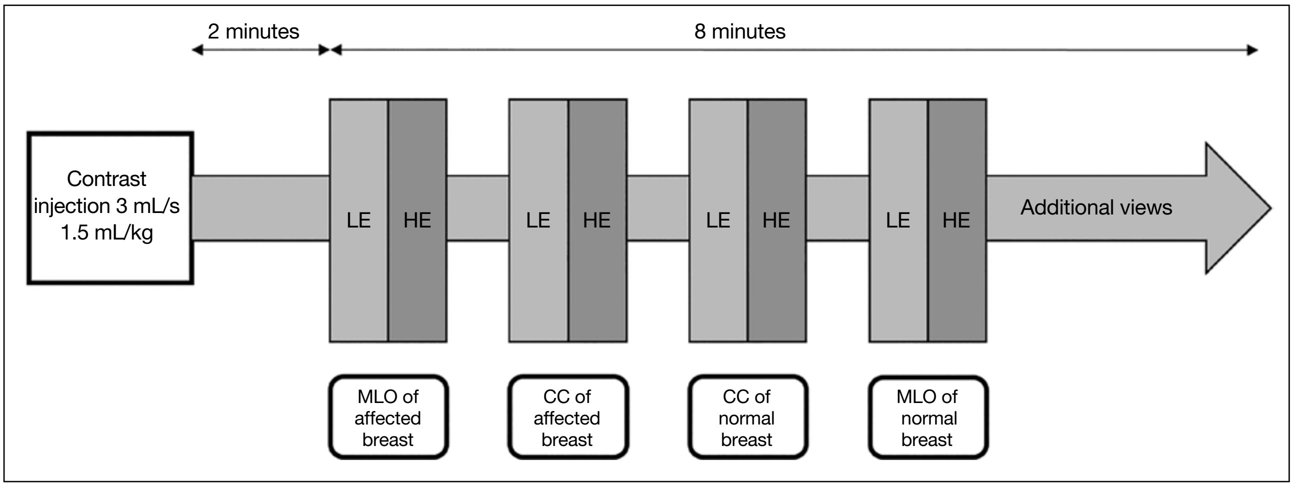

Figure 1. Workflow of contrast-enhanced spectral mammography. Contrast was injected by a power injector. After injection, the patient was disconnected from the injector and led to the mammography machine where the breasts were positioned and compressed and images were acquired. After review by a radiologist, additional views were acquired if deemed necessary.
Abbreviations: CC = craniocaudal view; HE = high-energy; LE = low-energy; MLO = mediolateral oblique view.

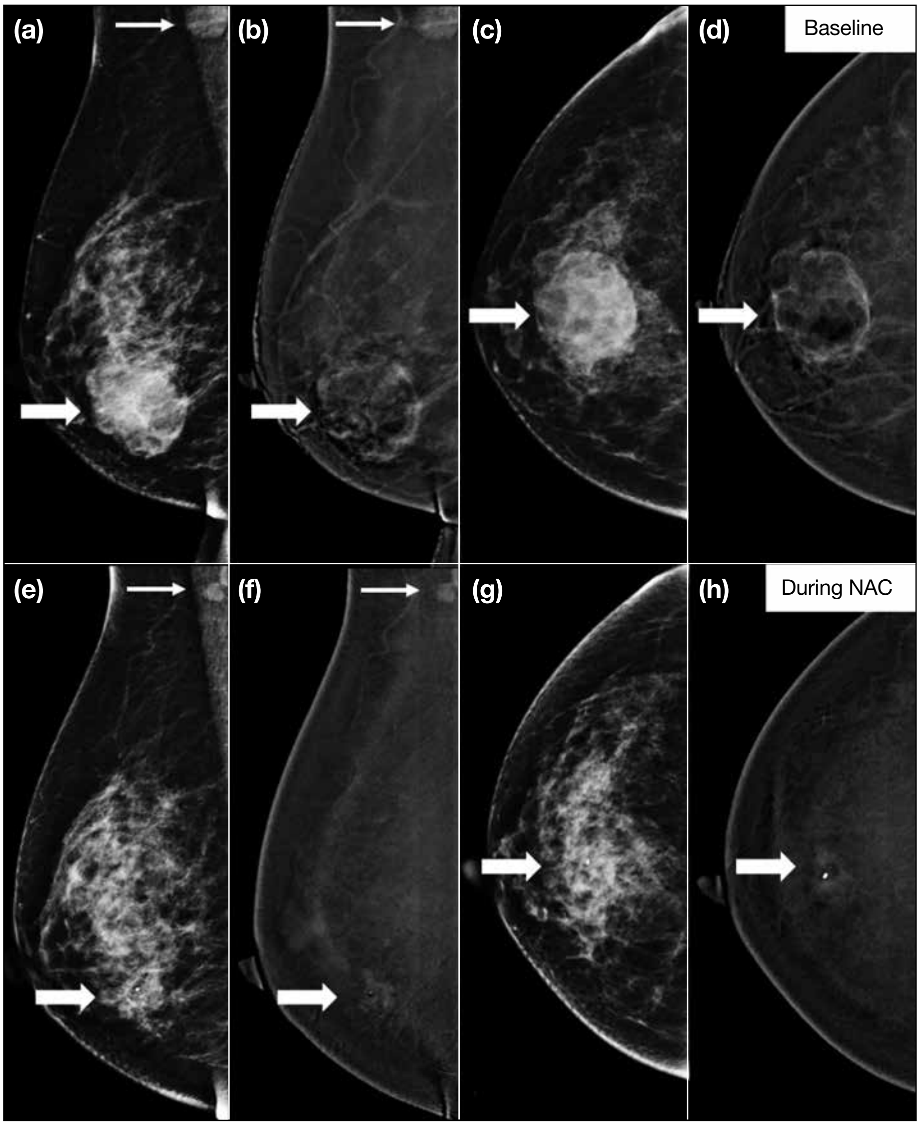

Figure 2. Contrast-enhanced spectral mammography showing partial response (comparing upper and lower rows) in a 52-year-old woman with invasive ductal carcinoma (luminal A subtype). The primary tumour (thick arrows) show size reduction from 44 mm to 18 mm. A right axillary lymph node metastasis (thin arrows in [a], [b], [e], and [f]) also shows reduction in size. A marker was placed within the tumour under ultrasound guidance before the commencement of neoadjuvant chemotherapy (NAC). (a) Low-energy right mediolateral oblique (MLO) view at baseline. (b) Subtracted right MLO view at baseline. (c) Low-energy right craniocaudal (CC) view at baseline. (d) Subtracted right CC view at baseline. (e) Low-energy right MLO view at mid-cycle. (f) Subtracted right MLO view at mid-cycle. (g) Low-energy right CC view at mid-cycle. (h) Subtracted right CC view at mid-cycle.

recorded on both CESM and MRI, and, if the entire lesion was included, the largest dimension of the satellite lesion was measured (Figure 5). Reading time for each imaging study was also recorded, defined as the time between opening and closing the images on the viewing programme after recording the dimension of the largest lesion.

Statistical Analysis

The intraclass correlation coefficient (ICC) was used to evaluate the intra- and inter-observer agreements of both CESM and MRI results, using a two-way mixed model testing for absolute agreement with a 95% confidence interval (CI). Intra-observer agreement was analysed for both radiologists, while inter-observer agreement was analysed using the first measurements by both radiologists. Subgroup analysis was performed by dividing the CESM studies into baseline studies and non-baseline studies, i.e., mid-cycle and end-of-cycle studies. Intra- and inter-observer agreements of these subgroups was calculated by ICC. Lin's concordance correlation coefficient (CCC) and Bland–Altman plots were used to evaluate for agreement between the CESM and MRI studies in the cases of 10 patients who had undergone both baseline imaging studies within 3 days. The Mann–Whitney *U* test was used to compare the scanning and reading times of CESM and MRI. Statistical analysis was performed using SPSS (Windows version 20.0; IBM Corp, Armonk [NY], US).

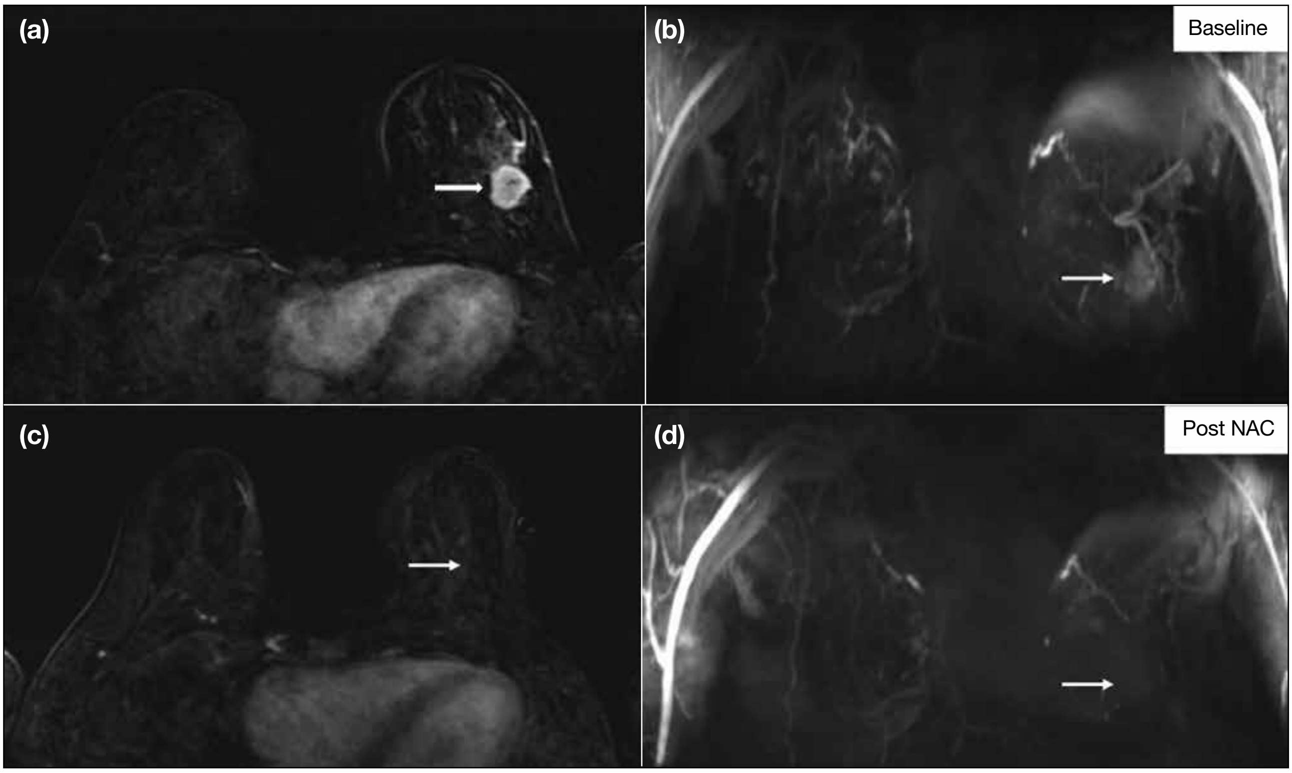

Figure 3. Magnetic resonance imaging (MRI) showing complete response (comparing upper and lower rows) in a 45-year-old woman with invasive ductal carcinoma (luminal A subtype). At baseline, the largest lesion measured 21 mm (arrows in [a] and [b]). No residual lesion was noted on post–neoadjuvant chemotherapy (NAC) MRI. Postoperative pathology confirmed no residual tumour (arrows in [c] and [d]). (a) Axial post-contrast baseline T1-weighted subtracted image at peak enhancement. (b) Coronal post-contrast baseline T1-weighted maximum intensity projection (MIP) image. (c) Axial post-contrast T1-weighted subtracted image after NAC. (d) Coronal post-contrast T1-weighted MIP image after NAC.

RESULTS

All 12 cases were female, with a mean age of 50.7 years (range, 32-66). Eleven cases were of invasive ductal carcinoma and there was one case of invasive lobular carcinoma. There were six cases of luminal A subtype, three of luminal B subtype, and three of human epidermal growth factor receptor 2–positive subtype. There were no cases of TNBC. Out of the 12 cases, one patient presented with urticaria after iodinated contrast administration during CESM. None of the patients presented with contrast reactions after gadolinium contrast administration.

In total, 20 CESM studies and 18 MRI studies were interpreted by the two radiologists. Individual measurements for the largest lesion detected for each study are summarised in Tables 1 and 2. Overall, the ICCs for both CESM and MRI were high, as summarised in Table 3. The results for the subgroup analysis comparing baseline and non-baseline CESM studies are summarised in Table 4.

Table 5 summarises the results of the baseline CESM and MRI studies. The CCC for comparing between the two sets of baseline CESM and MRI studies was 0.972 (95% CI = 0.893-0.993; n = 10). The Bland–Altman plot showed a bias of -1.1 mm and limits of agreement of -9.7 to 7.5 mm between modalities (Figure 6).

A satellite lesion was only identified in one CESM study. Both radiologists identified the lesion, with measurements of 12 mm and 14 mm, respectively. MRI was not performed on this patient; therefore, comparison cannot be made. On the end-of-cycle CESM study performed on this patient, both radiologists concurred that the satellite lesion had resolved (Figure 5).

The median scanning time for CESM was 4.9 minutes (interquartile range [IQR] = 1.3), while that for MRI was 43.9 minutes (IQR = 10.8). The median reading time for measuring the dimension of the largest lesion on CESM was 54.5 seconds (IQR = 17.5), while that for MRI was 96 seconds (IQR = 55). The results of the

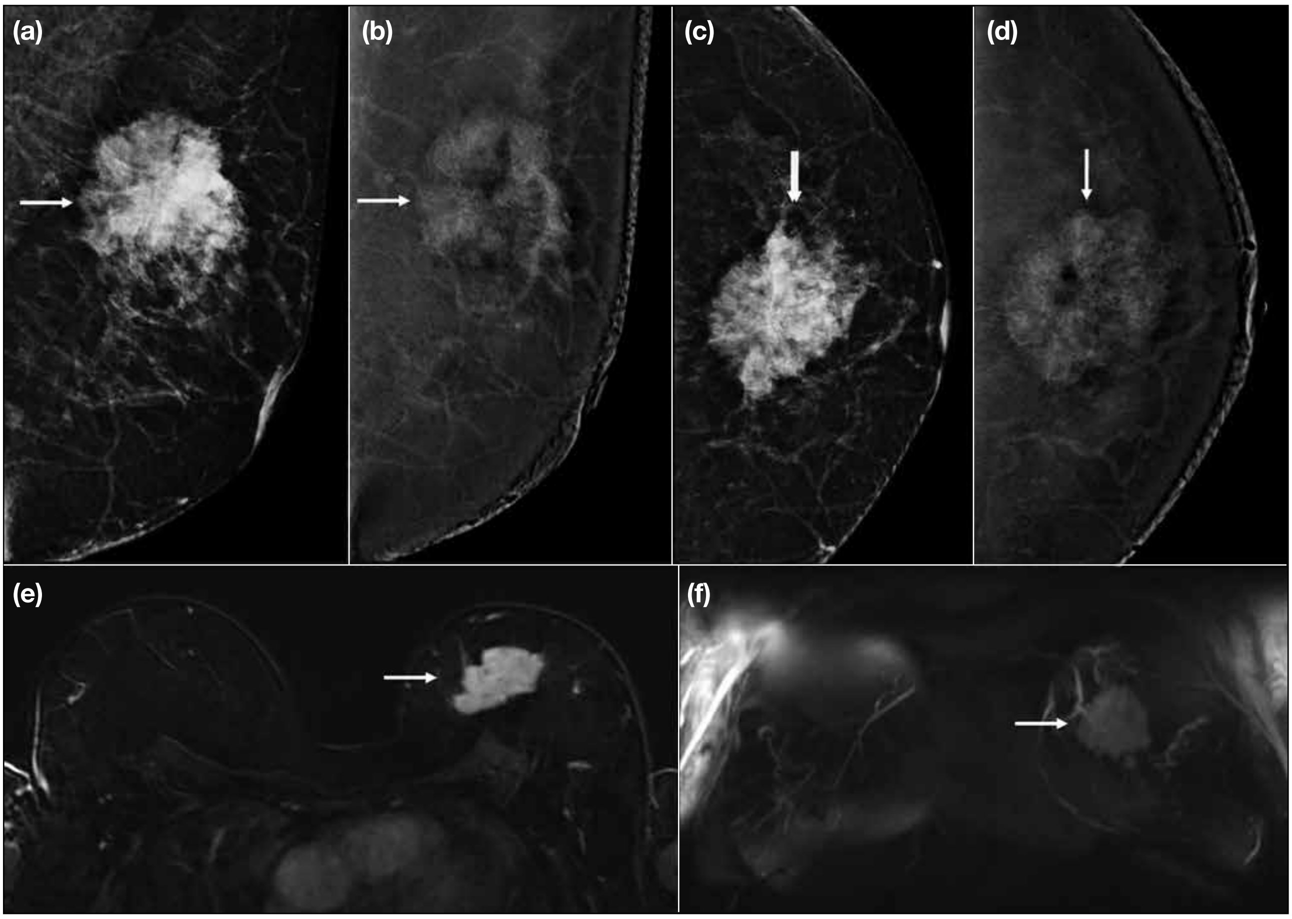

Figure 4. Contrast-enhanced spectral mammography and magnetic resonance imaging performed at baseline for a 57-year-old woman with invasive ductal carcinoma (luminal B subtype). Both modalities measured the largest dimension at 48 mm (arrows). (a) Low-energy left mediolateral oblique (MLO) view. (b) Subtracted left MLO view. (c) Low-energy left craniocaudal (CC) view. (d) Subtracted left CC view. (e) Axial post-contrast T1-weighted subtracted image at peak enhancement. (f) Coronal post-contrast T1-weighted maximum intensity projection image.

Mann–Whitney *U* test showed that both the scanning and reading times for CESM were significantly shorter ($p < 0.001$).

DISCUSSION

Contrast-enhanced imaging has substantial advantages in assessing NAC response. Contrast enhancement is based on abnormal angiogenesis in malignant tumours, which results in the leakage of contrast medium from the immature tumour vessels into the interstitial spaces. MRI, which benefits from contrast-enhanced imaging, has been proven to be a superior imaging modality to traditional mammography and ultrasound.[5,6] CESM is another emerging modality which also benefits from contrast-enhanced imaging. Intravenous iodinated contrast is administered to the patient, and after 2 minutes contrast material reaches the breast tissues,[11] allowing image acquisition to begin. It utilises a dual-energy technique, obtaining two spectral images using different energy levels in quick succession while the breast remains compressed. In the low-energy setting, the energy is below the k-edge of iodine and contrast material is not imaged, and the image can be interpreted as a standard mammogram. In the high-energy setting, which is above the k-edge of iodine, a non-interpretable image is produced. Using subtraction, an image depicting only areas of contrast enhancement results. The low-energy image and the subtracted image are then interpreted together by a radiologist. Owing to the subtraction method and contrast-enhanced imaging, CESM has been shown to be superior to standard mammography in cancer diagnosis even in dense breasts.[12]

Along with the advancements in CESM, several studies have compared the performance of CESM to MRI in monitoring NAC response. One study showed

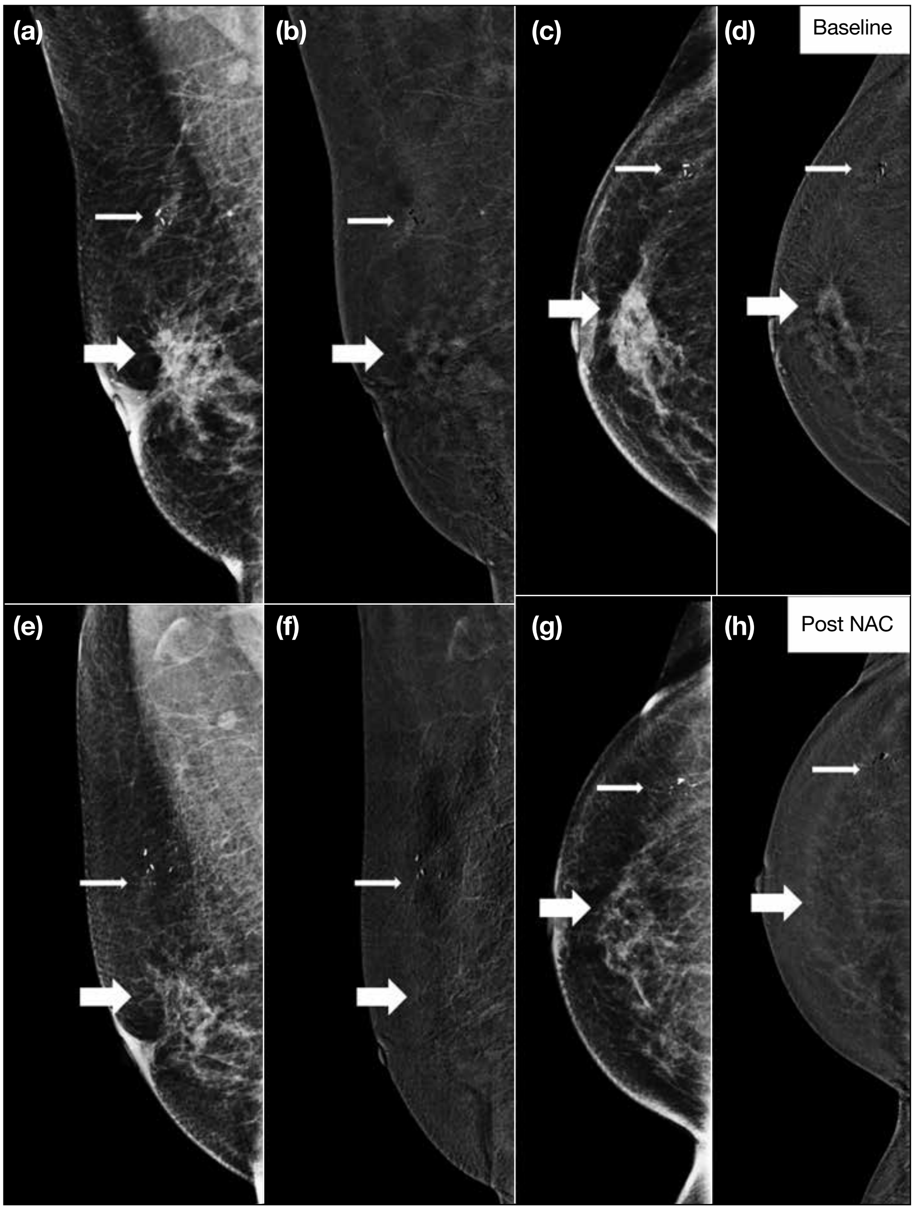

Figure 5. Contrast-enhanced spectral mammography showing complete response in a 61-year-old woman with invasive ductal carcinoma (human epidermal growth factor receptor 2–positive subtype). At baseline (upper row), a primary tumour (thick arrows) is noted in the centre of the right breast. An additional satellite lesion is noted in the upper outer quadrant (thin arrows), with associated calcifications. Both the primary tumour and satellite lesion showed resolution of enhancement after neoadjuvant chemotherapy (NAC) [lower row], while calcifications associated with the satellite lesion are more dispersed. Postoperative pathology confirmed no residual tumour. (a) Low-energy right mediolateral oblique (MLO) baseline view. (b) Subtracted right MLO baseline view. (c) Low-energy right craniocaudal (CC) baseline view. (d) Subtracted right CC baseline view. (e) Low-energy post-NAC right MLO view. (f) Subtracted post-NAC right MLO view. (g) Low-energy post-NAC right CC view. (h) Subtracted right post-NAC CC view.

that even though the use of CESM and MRI both led to underestimation of the extent of residual tumour compared to histology findings, CESM demonstrated pathologic complete responses to NAC better than MRI.[8] Other studies showed that CESM had good correlation and agreement with histopathology comparable to MRI, also showing high positive predictive values.[9,10] Despite the positive results, these studies did not thoroughly compare intra- and inter-observer agreements in CESM and MRI when assessing NAC. As shown by our results, the intra- and inter-observer agreements for CESM were excellent, all showing ICCs > 0.98. These results are comparable with the intra- and inter-observer agreements in MRI, which showed ICCs > 0.97. Despite the fact that one of the radiologists in the current study was a trainee radiologist with only 1 year of experience in breast imaging, the inter-observer agreement remained high. This concurred with findings in previous studies,[12,13] suggesting that CESM techniques could be easily learned by breast radiologists, which may be attributed to its findings being akin to basic mammography observations. Subgroup analysis was performed comparing the intra- and inter-observer agreements in studies performed at baseline prior to the commencement of NAC, and in studies during or after NAC. It was thought that after NAC, responding tumours may show shrinkage in both

Table 1. Measurements of the largest lesion detected in each contrast-enhanced spectral mammography study.

Patient	Age, y	Treatment status	CESM (largest lesion dimension, mm)			
			Rater 1		Rater 2	
			First read	Second read	First read	Second read
A	56	Baseline	55	51	56	57
		Mid-cycle	12	11	13	15
B	52	Baseline	44	45	43	43
		Mid-cycle	19	18	20	20
C	56	Baseline	50	50	51	51
D	53	Baseline	19	19	18	19
E	48	Baseline	91	109	91	93
		Mid-cycle	22	24	24	25
F	52	Baseline	39	38	37	33
		Mid-cycle	15	16	11	13
G	54	Baseline	41	41	42	41
		End-of-cycle	12	15	13	13
H	45	Baseline	22	20	23	22
		Mid-cycle	0	0	0	0
I	33	Baseline	47	51	52	50
		Mid-cycle	0	0	0	0
J	32	Baseline	35	39	32	37
K	66	Baseline	20	19	25	29
L	61	Baseline	13	15	14	13
		End-of-cycle	0	0	0	0

Abbreviation: CESM = contrast-enhanced spectral mammography.

Table 2. Measurements of the largest lesion detected in each magnetic resonance imaging study.

Patient	Age, y	Treatment status	MRI (largest dimension, mm)			
			Rater 1		Rater 2	
			First read	Second read	First read	Second read
A	56	Baseline	65	54	52	66
		End-of-cycle	0	0	0	0
B	52	Baseline	50	48	50	54
		End-of-cycle	19	18	17	20
C	56	Baseline	50	49	48	49
D	53	Baseline	24	24	31	28
		End-of-cycle	15	18	17	15
E	48	Baseline	59	109	90	85
		End-of-cycle	33	33	26	25
F	52	Baseline	41	38	34	37
G	54	Baseline	38	38	37	38
		End-of-cycle	15	15	13	15
H	45	Baseline	22	22	21	22
		End-of-cycle	0	0	0	0
I	33	Baseline	44	44	47	52
		End-of-cycle	0	0	0	0
J	32	Baseline	31	33	32	33
		Mid-cycle	22	22	22	21

Abbreviation: MRI = magnetic resonance imaging.

size and enhancement, possibly affecting the agreement in size measurement as lesions may be less conspicuous.[8] Results showed that even though there was in fact a slight drop in ICC, inter-observer agreement remained excellent in the non-baseline group with an ICC of 0.983 (95% CI = 0.917-0.997), meaning that measurement reproducibility remained high during or after NAC. Ten of the patients in the current study underwent both CESM and MRI prior to the commencement of NAC. Agreement between the measurements of the two modalities was high: CCC was 0.972 and mean difference was only 1.1 mm. This provides further support for CESM as a viable alternative.

One of the advantages of CESM over MRI is the fact that the scanning time is much shorter. This was proven in the current study; scanning time in CESM was significantly shorter than MRI ($p < 0.001$). In fact, when considering the median scanning time required, more than eight CESM studies can be performed during the time required for one MRI study. Reading time was also significantly shorter in CESM than MRI ($p < 0.001$). This could be attributed to the fact that there are more sequences and images in an MRI study compared with CESM. However, it is important to keep in mind that the reading time measured in the current study is only regarding the measurement of the dimension of the largest lesion, disregarding background and incidental findings. Regardless, in the common scenario where there are large numbers of patients, the potential time saved through both scanning time and reading time is a major advantage of CESM over MRI.

Despite the excellent results shown in the current study, there are limitations to CESM. One of the patients presented with iodinated contrast allergy in the form of urticaria. Additionally, the rate of adverse reactions in iodinated contrast, such as nausea and headache, were found to be significantly higher than those of gadolinium contrast.[14] Thorough history taking and explanation must be performed with patients before proceeding to CESM. Radiation exposure is also an additional factor to consider.

The ability to evaluate microcalcifications is an advantage of CESM over MRI. Since this study only measured the dimension of the largest lesion, the effect of microcalcifications was not examined. Some studies concluded that residual microcalcifications after NAC correlated poorly with tumour size on final pathology.[15,16] Others showed that by including both contrast enhancement and residual calcifications in post-NAC CESM, sensitivity in residual disease

Table 3. Intraclass correlation coefficient scores for intra- and inter-observer agreements in contrast-enhanced spectral mammography and magnetic resonance imaging studies.*

	Intra-observer agreement		Inter-observer agreement
	Rater 1	Rater 2	
CESM (n = 20)	0.983 (0.957-0.993)	0.996 (0.991-0.998)	0.995 (0.989-0.998)
MRI (n = 18)	0.975 (0.934-0.990)	0.984 (0.958-0.994)	0.982 (0.953-0.993)

Abbreviations: CESM = contrast-enhanced spectral mammography; MRI = magnetic resonance imaging.
* Scores in parentheses are the 95% confidence intervals.

Table 4. Intraclass correlation coefficient scores for intra- and inter-observer agreements in contrast-enhanced spectral mammography studies performed at baseline and non-baseline.*

	Intra-observer agreement		Inter-observer agreement
	Rater 1	Rater 2	
Baseline	0.971 (0.905-0.991)	0.994 (0.978-0.998)	0.993 (0.978-0.998)
Non-baseline	0.988 (0.947-0.998)	0.994 (0.963-0.999)	0.983 (0.917-0.997)

* Scores in parentheses are the 95% confidence intervals.

Table 5. Comparison of results for both contrast-enhanced spectral mammography and magnetic resonance imaging studies performed on the same patients at baseline.

Patient	Age, y	CESM (largest lesion dimension, mm)				MRI (largest dimension, mm)			
		Rater 1		Rater 2		Rater 1		Rater 2	
		First read	Second read	First read	Second read	First read	Second read	First read	Second read
A	56	55	51	56	57	65	54	52	66
B	52	44	45	43	43	50	48	50	54
C	56	50	50	51	51	50	49	48	49
D	53	19	19	18	19	24	24	31	28
E	48	91	109	91	93	59	109	90	85
F	52	39	38	37	33	41	38	34	37
G	54	41	41	42	41	38	38	37	38
H	45	22	20	23	22	22	22	21	22
I	33	47	51	52	50	44	44	47	52
J	32	35	39	32	37	31	33	32	33

Abbreviations: CESM = contrast-enhanced spectral mammography; MRI = magnetic resonance imaging.

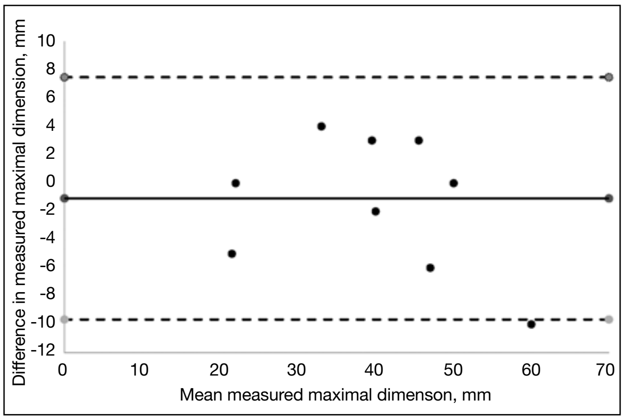

Figure 6. Bland–Altman plot of agreement between contrast-enhanced spectral mammography and magnetic resonance imaging studies performed on the same patients during baseline studies. Solid line represents the mean of differences. Dashed lines represent the 95% limit of agreement (± 1.96 times the standard deviation).

detection increased but the false positive rate also increased.[17] Therefore, the effect and reporting of residual microcalcifications on post-NAC CESM requires further research.

A satellite lesion was only detected in one case in the current study. Correct identification of satellite lesions is important for monitoring NAC response since it may impact subsequent surgical planning. Multifocal or multicentric disease are also known to be associated with higher risk of locoregional recurrence after breast-conserving surgery.[18] The performance of CESM on detecting satellite lesions may require further research.

Limitations

There were several limitations of the current study. It was a single-institution study with a small patient population. The lack of TNBC within the molecular subgroups may limit the applicability of our results to the general population, given the fact that TNBC is one of the indications for NAC. Due to the retrospective design and constraint in resources (as shown in Tables 1 and 2), patients could not be arranged to undergo both CESM and MRI at each point of the NAC cycle, therefore agreement in results of the two modalities could not always be compared to the non-baseline studies. Due to the same reason, comparison with postoperative histopathology could not be performed since most patients did not undergo both CESM and MRI as end-of-cycle imaging evaluations. Further research with histopathological correlation would be beneficial. Lastly, when evaluating intra-observer agreement, despite a 2-month interval between image evaluation, recognition of cases may produce measurement bias.

CONCLUSION

The current results showed that CESM had excellent intra- and inter-observer agreements which were comparable with MRI. Excellent agreement was found when comparing baseline CESM and MRI studies. Scanning and reading times were both significantly shorter in CESM. These results provided further evidence for CESM as a viable alternative to MRI for tumour size monitoring in assessing NAC response.

REFERENCES

1. Korde LA, Somerfield MR, Carey LA, Crews JR, Denduluri N, Hwang ES, et al. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer: ASCO guideline. J Clin Oncol. 2021;39:1485-505.
2. Ditsch N, Untch M, Thill M, Müller V, Janni W, Albert US, et al. AGO recommendations for the diagnosis and treatment of patients with early breast cancer: update 2019. Breast Care (Basel). 2019;14:224-45.
3. Morigi C. Highlights of the 16th St Gallen International Breast Cancer Conference, Vienna, Austria, 20-23 March 2019: personalised treatments for patients with early breast cancer. Ecancermedicalscience. 2019;13:924.
4. Werutsky G, Untch M, Hanusch C, Fasching PA, Blohmer JU, Seiler S, et al. Locoregional recurrence risk after neoadjuvant chemotherapy: a pooled analysis of nine prospective neoadjuvant breast cancer trials. Eur J Cancer. 2020;130:92-101.
5. Martincich L, Montemurro F, De Rosa G, Marra V, Ponzone R, Cirillo S, et al. Monitoring response to primary chemotherapy in breast cancer using dynamic contrast-enhanced magnetic resonance imaging. Breast Cancer Res Treat. 2004;83:67-76.
6. Lobbes MB, Prevos R, Smidt M, Tjan-Heijnen VC, van Goethem M, Schipper R, et al. The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review. Insights Imaging. 2013;4:163-75.
7. Ali-Mucheru M, Pockaj B, Patel B, Pizzitola V, Wasif N, Stucky CC, et al. Contrast-enhanced digital mammography in the surgical management of breast cancer. Ann Surg Oncol. 2016;23(Suppl 5):649-55.
8. Iotti V, Ravaioli S, Vacondio R, Coriani C, Caffarri S, Sghedoni R, et al. Contrast-enhanced spectral mammography in neoadjuvant chemotherapy monitoring: a comparison with breast magnetic resonance imaging. Breast Cancer Res. 2017;19:106.
9. Barra FR, Sobrinho AB, Barra RR, Magalhães MT, Aguiar LR, de Albuquerque GF, et al. Contrast-enhanced mammography (CEM) for detecting residual disease after neoadjuvant chemotherapy: a comparison with breast magnetic resonance imaging (MRI). Biomed Res Int. 2018;2018:8531916.
10. Patel BK, Hilal T, Covington M, Zhang N, Kosiorek HE, Lobbes M, et al. Contrast-enhanced spectral mammography is comparable to MRI in the assessment of residual breast cancer following neoadjuvant systemic therapy. Ann Surg Oncol. 2018;25:1350-6.
11. Jochelson MS, Dershaw DD, Sung JS, Heerdt AS, Thornton C, Moskowitz CS, 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.
12. Cheung YC, Lin YC, Wan YL, Yeow KM, Huang PC, Lo YF, et al. Diagnostic performance of dual-energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. Eur Radiol. 2014;24:2394-403.
13. Lalji UC, Houben IP, Prevos R, Gommers S, van Goethem M, Vanwetswinkel S, 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;26:4371-9.
14. Hunt CH, Hartman RP, Hesley GK. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. AJR Am J Roentgenol. 2009;193:1124-7.
15. Weiss A, Lee KC, Romero Y, Ward E, Kim Y, Ojeda-Fournier H, et al. Calcifications on mammogram do not correlate with tumor size after neoadjuvant chemotherapy. Ann Surg Oncol. 2014;21:3310-6.
16. Adrada BE, Huo L, Lane DL, Arribas EM, Resetkova E, Yang W. Histopathologic correlation of residual mammographic microcalcifications after neoadjuvant chemotherapy for locally advanced breast cancer. Ann Surg Oncol. 2015;22:1111-7.
17. Iotti V, Ragazzi M, Besutti G, Marchesi V, Ravaioli S, Falco G, et al. Accuracy and reproducibility of contrast-enhanced mammography in the assessment of response to neoadjuvant chemotherapy in breast cancer patients with calcifications in the tumor bed. Diagnostics (Basel). 2021;11:435.
18. Vera-Badillo FE, Napoleone M, Ocana A, Templeton AJ, Seruga B, Al-Mubarak M, et al. Effect of multifocality and multicentricity on outcome in early-stage breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat. 2014;146:235-44.