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SHORT COMMUNICATION

Contrast-enhanced spectral mammography (CESM)-guided breast biopsy as an alternative to MRI-guided biopsy

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Objective: Contrast-enhanced spectral mammography (CESM) breast biopsy has been recently introduced into clinical practice. This short communication describes the technique and potential as an alternative to MRI-guided biopsy.

Methods and materials: An additional abnormality was detected on a breast MRI examination in a patient with lobular carcinoma. The lesion was occult on conventional mammography, tomosynthesis and ultrasound and required histological diagnosis. Traditionally, this would have necessitated an MRI-guided breast biopsy, but was performed under CESM guidance.

Results: A diagnostic CESM study was performed to ensure the lesion visibility with CESM and then targeted

under CESM guidance. A limited diagnostic study, CESM scout and paired images for stereotactic targeting were obtained within a 10 min window following a single injection of iodinated contrast agent. The time from positioning in the biopsy device to releasing compression after biopsy and marker clip placement was 15 min. The biopsy confirmed the presence of multifocal breast cancer.

Conclusion: CESM-guided breast biopsy is a new technique that can be successfully used as an alternative to MRI-guided breast biopsy.

Advances in knowledge: CESM-guided biopsy can be used to sample breast lesions which remain occult on standard mammography and ultrasound.

INTRODUCTION

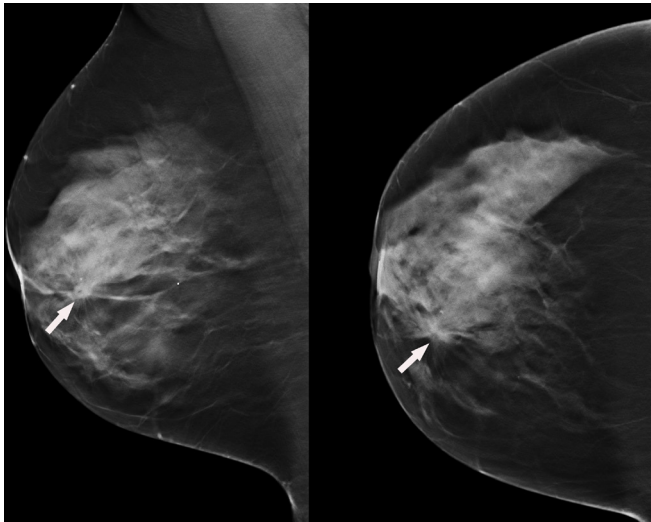
Mammography remains the examination of choice for breast cancer screening and the investigation of symptomatic females over the age of 40 years. The technique is widely available, cheap and well accepted but lacks sensitivity for breast cancer detection particularly in younger females and those with denser breast parenchymal patterns. Contrast-enhanced spectral mammography (CESM) combines standard mammography with iodinated contrast agent to improve lesion conspicuity, producing two sets of images; a low-energy image that looks like a conventional mammogram and a recombined image showing areas of contrast medium uptake.¹ The technique images the abnormal blood vasculature associated with tumours in a similar fashion to contrast-enhanced breast MRI. Studies comparing the performance of the two techniques show that CESM is a viable alternative to breast MRI exhibiting similar performance metrics.²

When used as a staging tool for primary breast cancer, CESM and breast MRI will identify additional lesions away

from the index tumour. In the case of MRI, around two-thirds of these lesions will be malignant and have the potential to affect surgical planning and patient management.^{3,4} It is very important that any additional lesions are biopsy proven to be malignant before management changes are made to avoid unnecessary mastectomies or inappropriate breast conserving surgery. The first step in the investigation of these additional lesions identified with CESM and MRI is a review of conventional mammography or the low energy component of the CESM study and a second look ultrasound targeting the area in the breast highlighted as the area of concern on the contrast study. In the majority of these cases, ultrasound will identify an abnormality for biopsy. For indeterminate MRI lesions, second look ultrasound will facilitate an ultrasound-guided biopsy in 57.5% of lesions.⁵ Inevitably, there are suspicious lesions that remain occult after additional ultrasound examinations that still require biopsy.

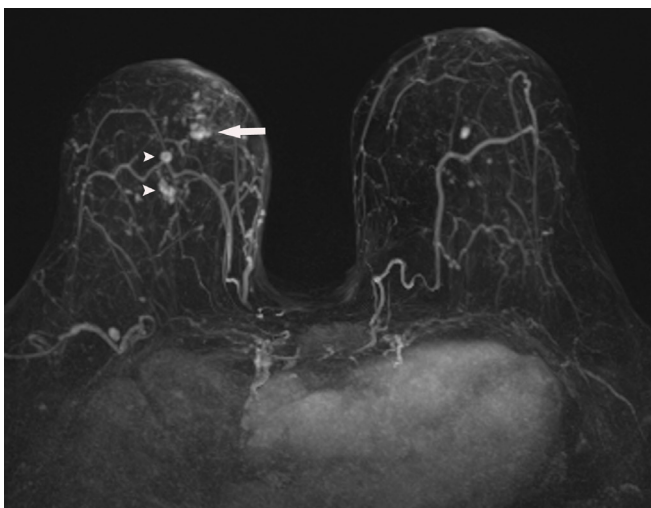
One of the challenges was that until recently, CESM-guided biopsy was unavailable and so, suspicious lesions found only

Figure 1. Single DBT slices from MLO and CC projections demonstrating a suspicious spiculate mass (arrow) lying medially within the right breast. CC, craniocaudal; DBT, digital breast tomosynthesis; MLO, mediolateral oblique.



on the recombined image would need to have a biopsy with an alternative modality, typically MRI-guided breast biopsy. MRI-guided biopsies are more challenging than other breast biopsies due to equipment availability, patient acceptance, expense, lesion visibility and location.⁶ This technical report describes the performance of CEM-guided breast biopsy and demonstrates a novel potential use of the technique as an alternative to MRI-guided biopsy.

Figure 2. A MIP MRI image of both breasts demonstrating the biopsy proven lobular carcinoma (arrow) and additional subcentimetre, suspicious enhancing nodules (arrowheads) distant from the index tumour. MIP, maximum intensity projection.



METHODS AND MATERIALS

The patient

A female attending for breast cancer screening with standard 2D full field digital mammography (FFDM) was recalled for further assessment of a possible area of distortion lying in the retroareolar area of the right breast. Two view digital breast tomosynthesis (DBT) demonstrated a suspicious 12 mm spiculate mass (Figure 1). On clinical examination, there was no palpable mass. An ultrasound of the right breast demonstrated an 8-mm malignant looking mass in the retroareolar area that corresponded with the mammographic abnormality. A 14G ultrasound-guided core biopsy was undertaken and a metallic marker clip placed at the biopsy site. Ultrasound of the right axilla showed no lymphadenopathy. Histopathology demonstrated a histological Grade 2 lobular carcinoma. The decision of the multidisciplinary meeting was to perform breast MRI for local staging in view of the tumour type and breast density.

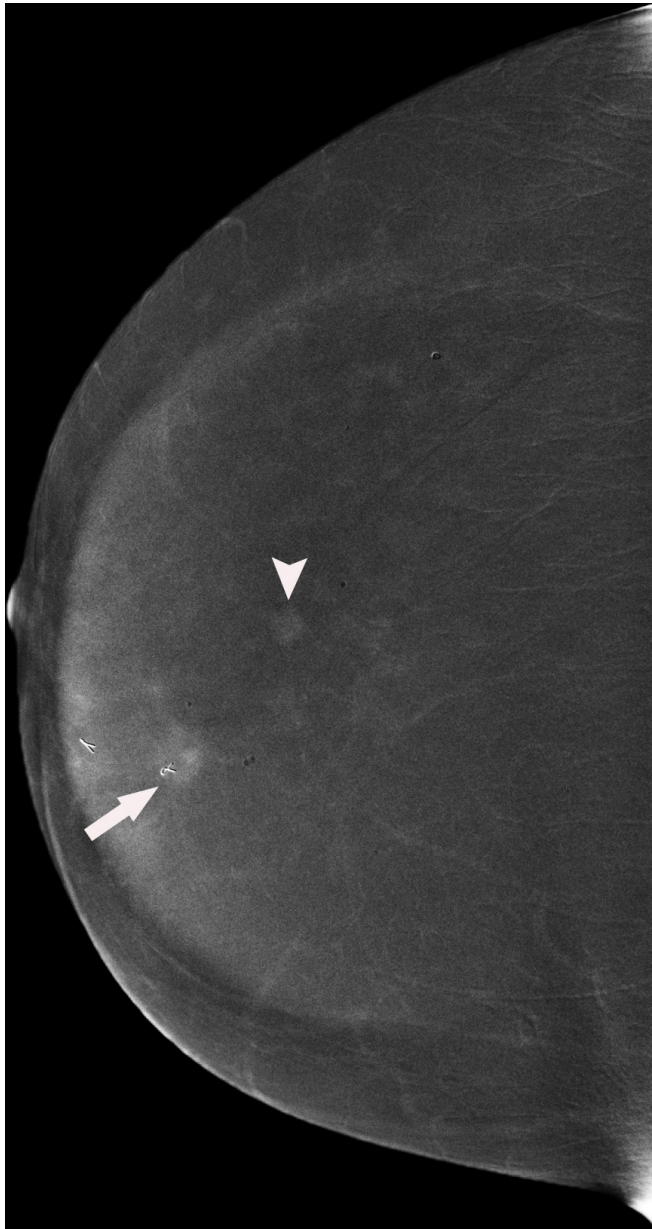
On MRI, the biopsy-proven carcinoma in the retroareolar area was seen as a 10-mm irregular mass with malignant enhancement characteristics (Figure 2). In addition, there were two subcentimetre, irregular nodules demonstrated in the 12 o'clock position in the right breast with similar enhancement characteristics to the index tumour (Figure 2). No areas of concern were identified in the left breast. The additional lesions were characterised as suspicious of malignancy and the decision was made to recall the patient for further assessment with a further ultrasound initially scheduled with a plan to obtain a histological diagnosis.

This 'second-look' ultrasound demonstrated no additional abnormalities, but given the level of suspicion biopsy was required. There were two options, the first was to attempt CEM-guided biopsy on the same visit as the second-look ultrasound or to schedule an MRI-guided breast biopsy at a later date. Following discussion with the patient, the decision was made to proceed with CEM-guided biopsy at the same clinic attendance.

The technique

The patient had not had a previous CEM study, and so it was important to determine whether the index lesion and additional abnormality detected on MRI were visible with CEM and to provide a 'road-map' to facilitate patient positioning for CEM-guided biopsy. Reviewing the MRI suggested that any additional lesions were likely to be best demonstrated on a craniocaudal (CC) projection. MRI also indicated that the area of concern lay in the upper half of the breast suggesting that CEM-guided biopsy would also be best performed in a CC position, with the patient sitting upright. A single right CC CEM mammogram was performed on a mammography machine with CEM capability (Senographe Pristina[™], GE Healthcare, Buckinghamshire, UK) using the standard detector (*i.e.* without the biopsy attachment *in situ*). A second mammography room with CEM biopsy capability (Serena Bright[™], GE Healthcare, Buckinghamshire, UK) was set up with the add-on biopsy device *in situ*, ready for patient positioning for the biopsy. There is typically a 10 min window from contrast agent injection to enhancing lesions remaining visible with CEM.² The two room approach removed some of the time pressure in performing all the imaging within

Figure 3. The recombined image from the CESM study performed 3 min after the injection of iodinated contrast agent demonstrating an additional enhancing lesion (arrowhead), distant to the biopsy proven lobular carcinoma which contains a post-biopsy marker clip (arrow). A second marker clip is seen more anteriorly which had been incorrectly positioned in an area of haematoma adjacent to the biopsy site. CESM, contrast-enhanced spectral mammography.



the 10 min window by removing the need to attach the biopsy device following completion of the limited diagnostic study.

100 ml of 300 mg ml⁻¹ iodinated contrast agent (Omnipaque™, GE Healthcare, Buckinghamshire, UK) was administered via a pump injector at a rate of 3 ml/s, through a 20G cannula. The injection was undertaken with the patient in the mammography room but without any compression. The patient was positioned and a right CC view was obtained 2 min after the injection. This

showed the biopsy proven index tumour and marker clip, but no additional abnormality. A second CESM image, taken 3 min post-injection, demonstrated an additional lesion lying posteriorly and lateral to the main mass which corresponded with the MRI abnormality (Figure 3). The patient was transferred to the second mammography room and positioned sitting upright with the breast compressed in the biopsy device in the CC position. Measurements of lesion position relative to the nipple had been taken from the CESM image to aid positioning. A single scout view was then obtained with the lesion visible in the biopsy window (Figure 4). As with a standard CESM image, the scout view consists of two images, a low-energy image and a recombined image. It is possible to toggle between the two images. Having identified the lesion for biopsy, CESM-guided biopsy is performed under stereotactic guidance and so a pair of images were obtained +15° and -15° each side of the vertical. Again, each image of the stereotactic pair consists of a low energy and recombined image and the operator is able to toggle between the two and place a biopsy target on either the low energy or recombined image. Following targeting, the needle holder was moved into the correct position, 3 ml of 1% lignocaine was injected for local anaesthesia and a 14G core biopsy needle placed into the breast. A single image was used to verify need tip placement before the samples were obtained (Figure 5). It is possible to use either a 14G core needle or a vacuum-assisted biopsy (VAB) device for a CESM-guided biopsy. As well as the ability to obtain larger tissue volumes, VAB has the additional advantage that it can be performed either vertically or using a lateral arm approach. In this case, 14G core biopsy was used, as this needle was readily available and the lesion for biopsy appeared as a focal mass located in the upper half of the breast.

RESULT AND OUTCOME

Five 14G core biopsies were obtained and a metallic biopsy marker clip placed. Check images were taken post-biopsy to verify satisfactory clip placement. The time from patient positioning in the biopsy device to releasing the compression after biopsy and post-biopsy marker clip placement was around 15 min. The time from contrast agent injection until completion of the imaging component of the procedure was 9.5 min, which consisted of two CC CESM views, a single scout view, check pair for biopsy targeting and a single post-needle insertion view to confirm needle tip location pre-biopsy.

Histopathological assessment of the 14G core samples demonstrated an invasive ductal carcinoma of no specific type (NST), histological Grade 1, which was morphologically different to the index tumour which was a Grade 2 lobular carcinoma. Following multidisciplinary team discussion, the patient underwent a mastectomy which confirmed the index tumour as an 18 mm lobular carcinoma with a solitary 6 mm tumour lying 15 mm from the index lesion.

DISCUSSION

The recent introduction of CESM-guided breast biopsy has enabled lesions which are demonstrated on the recombined CESM image but occult on conventional mammography and ultrasound to be biopsied under CESM guidance. Currently, there

Figure 4. The recombined scout image demonstrating the lesion for biopsy (arrowhead) positioned in the middle of the biopsy window and the biopsy proven index tumour anteriorly (arrow).

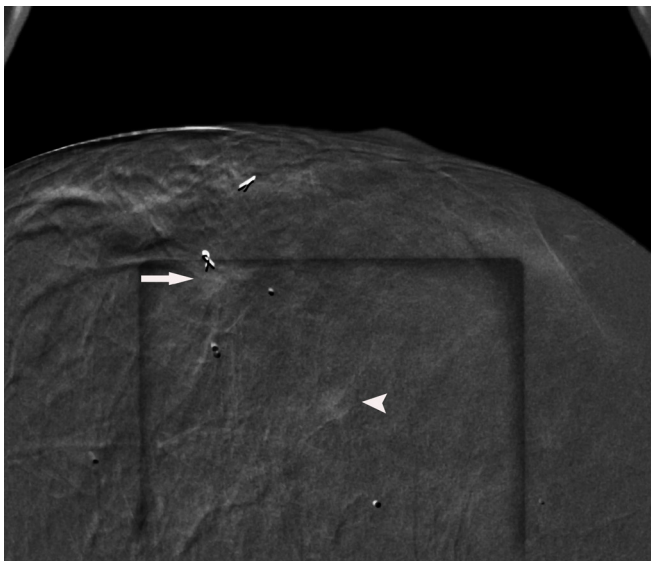
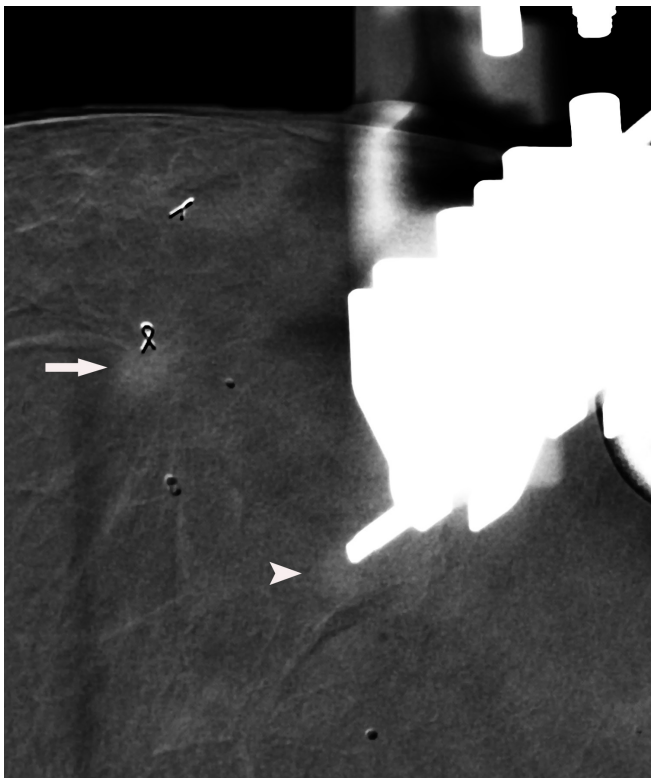


Figure 5. A single recombined image (acquired +15° from the vertical) to verify needle placement prior to obtaining the biopsy samples. The tip of the 14G core needle is seen adjacent to the lesion for biopsy (arrowhead) confirming accurate needle placement. The biopsy-proven lobular carcinoma is seen lying more anteriorly (arrow).



is little information in the literature on the technique and clinical indications.⁷ The case presented shows that it is also feasible to perform CESM biopsy on suspicious lesions identified with breast MRI that are occult on other breast imaging modalities. Although MRI-guided biopsy is a well-established technique, biopsies are more challenging, expensive and still not available at every breast imaging centre. Even when MRI-guided biopsy is available, scheduling magnet time for the procedure may lead to further delays in the diagnostic pathway. The ability to bring the biopsy of these occult lesions back into the breast clinic, using familiar stereotactic guidance principles on mammography equipment has advantages. The biopsy can be performed at the same time the patient attends for other breast imaging procedures, such as the 'second-look' ultrasound procedure as happened in this case, potentially reducing waiting times in the diagnostic pathway.

Studies have demonstrated that females find the experience of undergoing a CESM examination preferable to an MRI, with shorter procedure times, lower noise levels and improved comfort.^{8,9} The same is likely to be true for biopsy procedures. Reported biopsy time for CESM-guided biopsy from first compression to post-biopsy clip placement is up to 16 min which is likely to be more acceptable for patients with procedure times of up to 60 min for MRI.⁷ MRI-guided biopsy requires the patient to be prone which may be problematic for patients with disabilities. In addition, posteriorly located lesions may be difficult to access with the MRI biopsy coil. The ability to perform CESM-guided biopsy with an upright stereotactic device is likely to be easier in these challenging situations.⁶ Additional work is needed to clarify which lesions may be more easily sampled under CESM or MRI guidance. Reduced costs associated with CESM are likely to be advantageous with the cost of CESM examinations approximately four times less than a full MRI protocol.¹⁰

There are concerns around the use of iodinated contrast agents for CESM. The risk of contrast agent reaction with modern non-ionic, low osmolality agents is very low with reported reactions under 1% and the vast majority of these mild and self-limiting.^{10,11} Typically, 100 ml is used for a CESM study (dose of 1.5 ml/kg). CESM images are acquired between 2 and 8 min post-injection, but contrast agent is usually visible for at least 10 min following the injection allowing the acquisition of additional views after the standard four view mammographic series has been acquired.² When the biopsy is being performed for a CESM lesion that is occult on other modalities then a diagnostic CESM study would be available as a reference tool to aid patient positioning. Here, a limited diagnostic study was required, consisting of two CC views, to ensure the MRI-detected lesion was actually CESM visible as well as providing patient positioning information. The limited diagnostic study and biopsy were performed in separate rooms to keep the time from injection to biopsy targeting as short as possible by removing the need to attach the biopsy device following completion of the diagnostic study. Using this approach, it is possible to perform a very limited diagnostic study to ensure the lesion to be biopsied is visible with CESM and then still perform scout and check pair biopsy images within the 10 min window without the need for any additional

contrast agent injection. Increasing experience with this new technique will clarify the length of time lesions remain visible for biopsy, and confirm the practicalities of performing a diagnostic study and biopsy in a single clinic visit.

The diagnostic MRI study suggested the possibility of two additional tumour foci (Figure 2), but only one was demonstrated with CESM and targeted for biopsy. Final pathology from the mastectomy specimen confirmed only one additional malignant lesion. CESM compares favourably with MRI for the pre-operative staging of breast cancer with the sensitivity of CESM for detecting multifocal disease approaching MRI but with CESM demonstrating superior specificity with fewer false positives.² The improved positive-predictive value observed with CESM for

the detection of additional lesions is potentially advantageous for CESM-guided biopsy.

In conclusion, CESM is increasingly used in the evaluation of symptomatic patients, the assessment of local disease extent, monitoring response to neoadjuvant chemotherapy and as a screening tool. There are occasions when CESM demonstrates suspicious lesions that remain occult with other breast imaging modalities, and so the ability to perform CESM-guided biopsies is crucial to enable the adoption of the technique into widespread clinic practice. CESM-guided breast biopsy is feasible and practical and can be used as an alternative to MRI-guided breast biopsy. Further work is required to develop protocols and establish the efficacy of this new technique.

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