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Case Report

The Brilliance of Contrast Enhanced Spectral Mammography

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Abstract

Problem Statement: Breast MRI is considered the gold standard in delineating breast cancer extent. However, MRI is rarely used for breast examination due to poor availability and cost. Contrast Enhanced Spectral Mammography (CESM) has been shown to offer higher sensitivity and greater diagnostic accuracy than conventional mammography in breast cancer imaging. Breast cancers have a higher avidity to take up contrast than normal tissue. This has enabled us to demonstrate tumour extent comparable to that offered by contrast enhanced breast MRI.

Methods: Following review of initial mammogram and ultrasound images CESM was requested as it was thought this may add spatial information of clinical usefulness to the referring surgeon.

Results: CESM was able to demonstrate both invasive cancer and ductal carcinoma in-situ (DCIS), and was of particular usefulness in dense breasts. We were able to identify satellite tumour nodules that had not been appreciated on conventional imaging. On occasion CESM was able to demonstrate that cancers contained within denser breast parenchymal areas were actually quite discrete, allowing for smaller, rather than wider, tumour resections. This afforded greater confidence in planning definitive surgery.

Conclusion: CESM offers a quick, affordable and readily available alternate to MRI to obtain high resolution, anatomically precise image characterisation of breast cancers and can be readily integrated into a conventional mammographic imaging service.

Keywords: Breast cancer, Breast imaging, Mammography, Contrast mammography, CESM

Brilliance *noun*
ˈbrɪlj(ə)ns/ noun: **brilliance**; noun: **brilliancy**
1. intense brightness of light.
2. exceptional talent or intelligence.

Introduction

Contrast enhanced breast magnetic resonance imaging (CE-MRI) is regarded as the most sensitive technique for breast cancer detection [1, 2]. Some MRI pulse sequences are also considered optimal for delineating the extent of ductal carcinoma in-situ (DCIS) [3]. While this has proved useful in accurately determining tumour extent and focality, this sensitivity of MRI over conventional breast imaging, mammography (MG) and ultrasound (US), has come at the expense of specificity. Another significant disadvantage in performing breast MRI relates to the availability and cost of these studies.

In Australia, which has a hybrid health-funding model including public and private access to health resources, breast MRI is usually done as an outpatient procedure. This study is not rebatable through the universal health care model, Medicare, and patients may be expected to pay up to A$800 for this procedure.

The Strathfield Breast Centre is a private breast diagnostic and treatment clinic in Sydney managing patients both in the private domain at the Strathfield Private Hospital (SPH) or in the public domain at Concord Repatriation General Hospital (CRGH). CRGH offers high quality breast MRI read by experienced breast radiologists, however as mentioned above, the cost of such studies is not insignificant. We considered that a quicker, and more cost-effective option for workup of difficult or challenging breast cancer cases was worth pursuing.

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Contrast enhanced spectral mammography (CESM) is a relatively new development in breast imaging. Developed at the start of the new millennium [4,5] it employs a double exposure of low and high energy X-rays following administration of a dose of intravenous contrast agent (the same contrast agent as used in computerised tomography (CT) scanning.) A recombined image calculated from both the high and low-energy images shows the contrast uptake throughout the breast. Recent widespread adoption of digital mammographic equipment now makes this technique more widely practicable [6,7].

To maintain growth tumours induce local angiogenesis. These newly formed blood vessels are both more numerous and more leaky than the vasculature of surrounding tissues. This facilitates concentration of the contrast agents within the tumour.

Ideally we would have appreciated the opportunity to directly compare CE-MRI and CESM, but the 2 limitations mentioned above of MRI availability and cost meant that such a comparative review could not be conducted. The authors of this paper all have personal experience with magnetic resonance (MR) techniques [8, 9] and we considered that a familiarity with such techniques would afford us to critically evaluate the utility of CESM vis-a-vis MR.

In this paper we present a number of scenarios that show the clinical usefulness of CESM in the pre-operative workup of breast cancer cases.

Methods

Following review of the initial MG and US images CESM was requested if it was thought that this might add spatial information of clinical usefulness to the referring surgeon. All CESM examinations were performed on a GE Healthcare Senographe Essential mammogram unit with GE Senobright software modifications, which allows for dual-energy CESM acquisition.

All patients consented to the use of iodine contrast. Ultravist 370 (iopromide, Ultravist 370; Bayer Healthcare, Berlin, Germany) was administered at a dose of 1.5mL/kg body-weight through a 20G cannula in the antecubital fossa contralateral to the breast under review. The contrast medium was instilled by hand-injection and was followed by a bolus chaser of 30mL of saline.

Images were acquired following a 2-minute delay, with all images being obtained within 10 minutes following the start of the contrast injection. Standard CC and MLO projections of each breast were acquired using a dual energy image acquisition technique. Two images were taken using a distinct low energy exposure (standard mammography Kv and filtration) and a high energy exposure (Higher Kv with a strong filtration). Rhodium anode material was used for all acquisitions. Whilst obtaining the dual energy images the choice of filter was important to ensure high image quality. Low energy (LE) acquisitions used both molybdenum (Mo) and rhodium (Rh) filters with kVp ranging from 26-32 kVp whilst high energy (HE) acquisitions used both Copper (Cu) and Rhodium (Rh) filters with kVp ranging from 49-45 kVp. The Cu filter in the X-ray beam produced X-ray spectra above the K-edge of iodine (33.2 KeV), which increases the visibility of low concentrations of iodine. Subtraction images (SI) were produced by cancelling out the background breast tissue.

Results

Scenario 1 Multifocality

Case 1: Standard mammography showed a suspicious density with pleomorphic calcifications behind the left nipple. The reporting radiologist noted a linear calcification 2cm behind the primary density. The question arose as to the possible extent of DCIS beyond the primary neoplasm. CESM demonstrated a previously unrecognised satellite tumour nodule >4cm deep to the primary tumour. The involved duct (including the faint linear spicule of calcification) was demonstrated (Figure 1). Histopathology showed the 2 tumour nodules connected by a solitary duct containing DCIS.

Case 2: On regular annual review following previous treatment for a right breast cancer a patient was noted, on ultrasound, to have a small area of shadowing in the left (contralateral) breast (Figure 2A). Standard 2D and 3D imaging were reported as normal. A core biopsy of the irregular area identified a small focus of invasive lobular cancer (ILC). Recognising the diffuse nature of ILC a CESM was arranged to delineate the likely extent of tumour. 2 small enhancing areas were noted (Figure 2B). Although the second area of enhancement remained occult to both mammography and close US second review it was appreciated where anatomically this area of enhancement was situated and due care was made to include this tissue within the excision

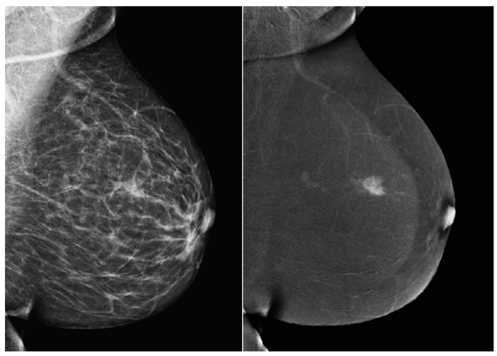

Figure 1: Multifocal (satellite) breast cancer
The MLO mammographic view shows a discrete stellate mass with pleomorphic calcifications. CESM shows a small enhancing lesion 4cm deep to the primary lesion connected by a faintly visible duct.

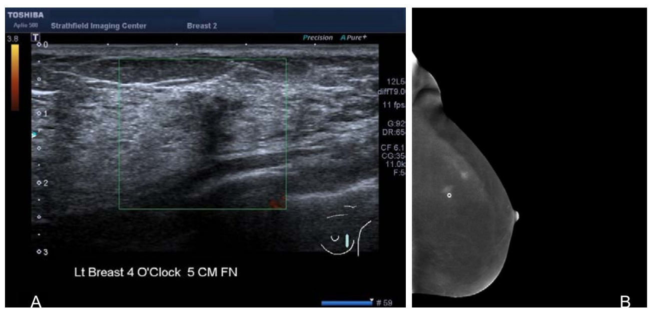

Figure 2: Multifocal discrete breast cancers
Ultrasound showed an area of hypoechoic irregularity; this was not identified on standard mammography. At the time of core biopsy, which showed a small focus of invasive lobular cancer, a circular metallic marker was placed. The CESM showed 2 separate areas of suspicious enhancement (the deeper component being that area seen on the ultrasound.)

specimen. Pathology showed 2 foci of ILC measuring 12mm and 10mm respectively. A third discrete focus, measuring only 3mm, and presumed perhaps too small for detection on CESM, was also identified within the excised tissue.

Scenario 2 Tumour extent

Case 3: A patient who had previously undergone breast reduction surgery, and who 14 years prior had been treated for a small left breast cancer, was shown now to have a new stellate density within an area of dense glandularity in her right (contralateral) breast. The US suggested a discrete lesion measuring 21 x 12 x 17mm. Could CESM be used to determine that the cancer was as small as the central stellate density implied? A minor contrast blush suggested that the tumour was relatively small (Figure 3). A focal hook-wire guided excision was performed with histopathology confirming a 16mm grade 1 invasive ductal carcinoma.

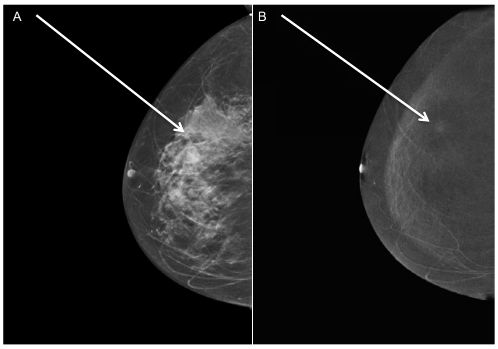

Figure 3: Small cancer within dense glandular background
The CC mammogram shows a subtle stellate density within a background of dense glandular breast tissue (A). CESM shows a small contrast blush (B).

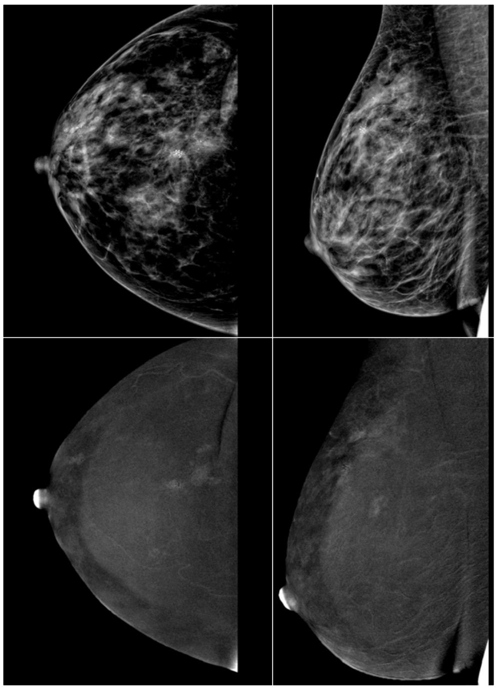

Figure 4: Extensive, widespread DCIS
2-D CC and MLO mammograms of right breast (top) with corresponding CESM views (below). Multiple enhancing areas show widespread DCIS through much of the superior part of the breast.

Scenario 3 DCIS

Case 4: The standard mammogram showed multiple areas containing clustered calcifications with varying degrees of pleomorphism. Extensive, patchy DCIS was suspected. CESM (Figure 4) highlighted all regions containing indeterminate to suspicious calcifications; all were confirmed as being DCIS on the mastectomy specimen.

Scenario 4 Bilateral Breast Cancer

Case 5: A patient presented with a palpable lump in her left breast. The surgeon noticed a small suspicious nodule medially on the right side. The 2D magnification mammogram view showed a subtle stellate density (Figure 5). CESM demonstrated enhancement in 2 areas in the right breast and one area in the left. Pathology confirmed a multifocal invasive lobular carcinoma on the right side and an invasive ductal cancer on the left.

Scenario 5 Neoadjuvant chemotherapy

Case 6: A patient presented with a locally advanced left breast cancer. The primary lesion measured 5 x 5cm and axillary lymph nodal involvement was present. Neoadjuvant chemotherapy was prescribed to downstage the tumour with one of the aims being to conserve the breast. The pre-chemotherapy CESM (Figure 6B) showed an area of enhancement comparable to the size of the tumour as estimated on ultrasound; following chemotherapy enhancement was absent, albeit a small area of negative enhancement was seen in the centre of the area of response (Figure 6D). Histology showed a 100% complete pathological response.

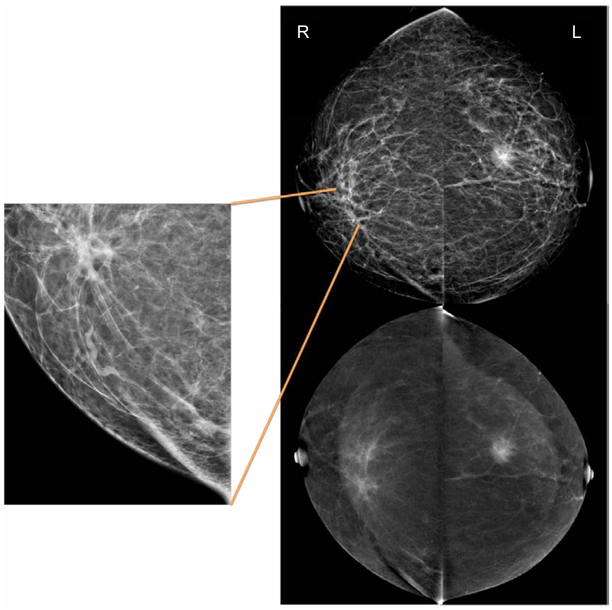

Figure 5: Bilateral breast cancers
Top: Bilateral CC mammogram showing subtle stellate density behind right nipple and a more obvious stellate density behind left nipple. Bottom: Bilateral CC CESM showing 2 cancer foci R, solitary cancer left.

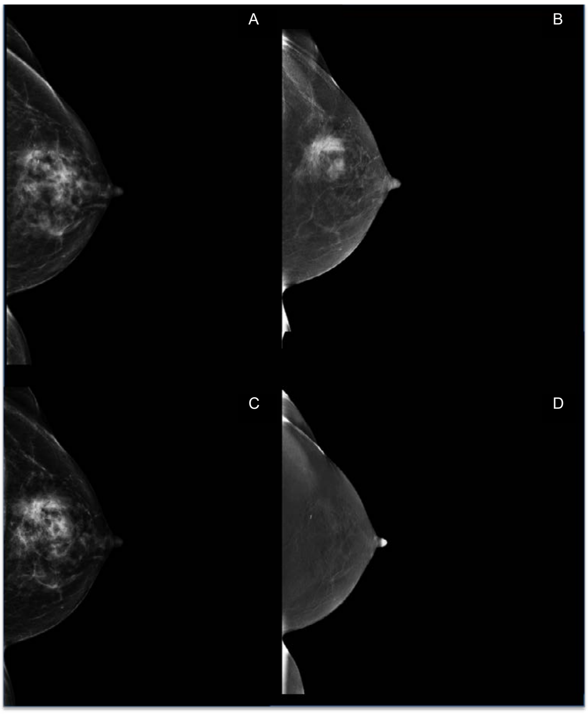

Figure 6: Pre- and post-neoadjuvant chemotherapy Craniocaudal mammogram views of left breast. Pre-neoadjuvant 2-D (A), pre-neoadjuvant CESM (B), post-neoadjuvant 2-D (C), post-neoadjuvant CESM (D).

Discussion

There have been momentous advances in the management of breast cancer over the past 100 years [10]. From a period of routine ablative and disfiguring surgery has evolved the need to balance the objectives of preserving the aesthetic appearance of the breast with the requirement to optimally remove the cancer. In few other areas of Medicine do the various members of a treating team work so closely than the multidisciplinary approach that has come to represent ideal breast cancer care. In some parts of the world the radiologist may assume primacy in initial cancer imaging and workup; in Australia a surgeon may often be called on earlier to perform this task. Irrespective of who may initially see such patients the surgeon and radiologist should collaborate as best as possible to accurately determine the extent of breast cancer at all stages of the treatment journey. Utilising the best available tools should be part of this approach. CE-MRI, which may be regarded as the most accurate imaging tool at our disposal, is unfortunately not that available or affordable.

There are now papers comparing the performance of CESM to standard mammography, CE-MRI and US [7,11-15]. In a review of the diagnostic performance of CESM Tagliafico et al [16]. Concluded that CESM has high sensitivity (96-100%) but low specificity (38-77%). Comparison with CE-MRI shows that CESM has sensitivities approaching and specificities exceeding that of CE-MRI [7,13,14].

Low specificity should not necessarily detract from a test's usefulness. Such criticisms have always been present in evaluating breast-imaging techniques and seem more to relate to the complex pathological, anatomical and physiological relationships within the breast than necessarily only that of the test being reviewed. Utilising a number of imaging modalities, and being aware of the limitations of each, is necessarily the approach adopted by clinicians; we believe that any additional information that may be derived in the preoperative workup and that may help the surgeon in the performance of his task should be critically and clinically evaluated.

Fallenberg et al. showed CE-MRI and CESM to have improved tumour size estimation over MG, with CE-MRI being slightly superior; however CESM was demonstrated to be robust, not requiring much training and having the highest inter-reader agreement [7]. This study concluded that "CESM appears to be a suitable alternate to MRI to improve the pre-operative assessment of breast cancer". Tagliafico et al. also contend that "patients prefer the experience of CESM to MRI" [16], a preference also reported by Hobbs et al [17]. Lee-Felker showed that CESM had a greater positive predictive value than CE-MRI in determine the malignant nature of a breast lesion, and was equal in its capacity to find secondary cancers within either breast [14].

CESM has been compared to CE-MRI and MG in its ability to assess tumour response to neoadjuvant chemotherapy (NAC) [14, 18, 19]. These studies have concluded that CESM is a feasible, easily performed method for evaluating residual tumour volume. In assessing the response to treatment, studies subsequent to the initial workup imaging can be confined to a single breast to minimise radiation dosages. CESM has been shown to be as good as or better than CE-MRI in predicting treatment response [19], however both of these modalities may underestimate (in up to a third of cases) the extent of residual tumour [18-20]. This observation may derive from the fact that Taxanes, one of the chemotherapeutic agents commonly used in neoadjuvant breast cancer therapy, exhibit a direct effect on angiogenesis (and thus contrast enhancement) independent of their cytotoxic effect [21]. An additional advantage of CESM over CE-MRI is that the former modality permits evaluation of both the enhancing areas as well as the extent of micro-calcifications (on the low energy image) within a single study. These calcifications may delineate the areas of DCIS, often less responsive to neoadjuvant treatment than the invasive components of the tumour, thus facilitating more accurate estimates of the volume of tissue necessitating surgical excision.

Conclusion

We have found access to breast MRI to be costly and restricted; waiting times of up to a few weeks not that unusual. As a result we have chosen to explore the utility of CESM in working up the extent of breast cancers before surgery, and after neoadjuvant chemotherapy. Although our experience is presently limited, we have not found this modality wanting. CESM has allowed us to determine more accurately than conventional MG and US alone the size of tumours, the extent of DCIS, and the response to chemotherapy. Tagliafico posits: "CESM might be an alternate cost-effective imaging method for MRI, especially when MRI availability is limited." We would contend that MRI availability is always limited; we encourage our surgical colleagues to encourage their radiologists to adopt what in our hands has become an indispensible, rapid and readily available tool in the managing of breast cancer.

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