Case report

Positive molecular breast imaging: challenges and problem solving with contrast-enhanced spectral mammography

Jeremy SL Ong ^{1,2}, Felicity Whitewood,³ Donna B Taylor ⁴,
Deepthi Dissanayake^{1,4}

¹Medical Imaging, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

²Department of Nuclear Medicine, Sir Charles Gairdner Hospital, Perth, Western Australia, Australia

³Breast Unit, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

⁴Department of Diagnostic and Interventional Radiology, Royal Perth Hospital, Perth, Western Australia, Australia

Correspondence to

Dr Jeremy SL Ong,
Jeremy.ong@health.wa.gov.au

Accepted 4 September 2019

SUMMARY

Molecular breast imaging (MBI) is a relatively new technique with high sensitivity for breast cancer detection. However, because it only provides limited anatomical information, cross-correlation of MBI findings with conventional breast imaging modalities such as full field digital mammography can be challenging. We report a case of a positive MBI study in a supplemental screening setting, where cross-correlation of MBI, ultrasound, mammogram and biopsy findings was difficult. Contrast-enhanced spectral mammography (CESM) demonstrated a hypervascular lesion at the biopsy clip, helping to prove imaging/histopathological concordance. This case highlights the challenges of incorporating MBI into conventional imaging workup, as well as the use of CESM in problem solving.

BACKGROUND

Breast density is becoming increasingly recognised as an independent risk factor for breast cancer. There is therefore increasing interest in supplemental screening techniques such as molecular breast imaging (MBI). While MBI offers detection of increased metabolic or vascularised lesions, it provides little anatomical detail. On the other hand, conventional ultrasound and mammography offers anatomical detail but relatively little functional or metabolic information. This disparity makes cross-modality concordance

difficult, as this case demonstrates. Contrast-enhanced mammography may have a role as a problem solver by offering information about vascularity and anatomical detail and can be an appealing alternative to MRI in this setting.

CASE PRESENTATION

A 54-year-old Australian woman with no additional risk factors for breast cancer was referred to the breast clinic for assessment of an incidental abnormality found on an MBI study. MBI had been performed for supplemental screening after the patient and her general practitioner (GP) received a letter from the state breast screening programme, stating that while no evidence of breast cancer had been found, the sensitivity of mammography was reduced by the presence of dense breast tissue.

MBI demonstrated a 5 mm focus of tracer uptake in the lower outer quadrant of the right breast ([figure 1](#)). Ultrasound revealed a 9 mm lesion in the 8 o'clock position of the right breast, thought to represent benign breast change ([figure 2](#)). 14G core biopsies were performed under ultrasound guidance and a clip placed. The biopsy showed benign breast tissue with fibrosis; however, there was apparent discrepancy between the depth of the clip on post-biopsy mammogram ([figures 3A,B](#)) compared with the lesion location on MBI ([figure 1](#)). Further imaging with contrast-enhanced spectral mammography (CESM) demonstrated a 7 mm area of enhancement

Figure 1 Molecular breast images demonstrating a small focus of tracer uptake in the lower outer quadrant of the right breast, in the deeper third of the breast (black arrows).

Figure 2 Ultrasound image showing the 9 mm lesion at the 8 o'clock position of the right breast, 5 cm from the nipple.

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Ong JSL, Whitewood F, Taylor DB, et al. *BMJ Case Rep* 2019;**12**:e230043. doi:10.1136/bcr-2019-230043

Figure 3A Postbiopsy craniocaudal mammogram of the right breast demonstrating the metallic ribbon biopsy clip positioned in the lower outer quadrant of the right breast, in the middle third of the breast.

Figure 3B Postbiopsy lateral–medial mammogram of the right breast demonstrating the metallic ribbon biopsy clip positioned in the lower outer quadrant of the right breast, in the middle third of the right breast.

Figure 4A Recombined craniocaudal iodine-enhanced image of the right breast from contrast-enhanced spectral mammography demonstrating a 7 mm contrast-enhancing lesion at the biopsy marker clip (white arrow).

Figure 4B Recombined medial-lateral oblique iodine-enhanced image of the right breast from contrast-enhanced spectral mammography demonstrating a 7 mm contrast-enhancing lesion at the biopsy marker clip (white arrow).

Patient's perspective

Having had a mammogram in August 2017 with a report of 'dense breasts', I was dissatisfied with the findings.

Prior to this, I had been aware of a discomfort in my right breast, like a burr, which was heightened when I rolled onto my right side in bed.

I knew of the use of molecular breast imaging in Asia, and even though this is new to Australia, I was keen to investigate this for piece of mind.

I then visited the GP with the results and was sent for an ultrasound which backed the findings of the MBI.

However, the lesion was too small, so it was decided to follow-up in 3 months. By that time, the lesion had grown and I was referred to the breast assessment clinic. While there it was decided, to my relief, to proceed with a biopsy. I was pleased with this as the findings would be definitive; it was 11 months from my original mammogram.

The matching of the findings of the different modalities, although time consuming, came as a relief and a resolution to the issue.

Learning points

- ▶ Molecular breast imaging is a sensitive investigation for detection of breast cancer; however, further investigation of positive results can be challenging due to difficulties in cross-modality concordance with conventional imaging.
- ▶ Contrast-enhanced spectral mammography offers assessment of morphology and function, and may have a role in problem solving positive molecular breast imaging cases.
- ▶ Imaging histopathological concordance is an extremely important principle in breast imaging.

immediately adjacent to the clip (figures 4A,B), thought to correlate with the finding on MBI.

OUTCOME AND FOLLOW-UP

On discussion with the MBI physician, the biopsy result was considered concordant with the combined imaging findings, and the patient was discharged for routine screening mammography.

DISCUSSION

MBI is a nuclear medicine imaging technique using intravenous injection of Technetium-99m labelled sestamibi and gamma cameras. Breast cancer accumulates sestamibi predominantly due to increased mitochondrial activity of neoplastic cells, in addition to other pathophysiological processes.¹ This is depicted on imaging as focally increased activity compared with background—a 'hot spot' (figure 1). MBI has comparable sensitivity to MRI of up to 96% for both invasive carcinoma and ductal carcinoma in situ, specificity of up to 77% and is becoming increasingly recognised as a useful modality in a number of settings including surveillance in high-risk patients, monitoring of neoadjuvant chemotherapy and evaluating the extent of disease in those with a recent diagnosis of breast cancer.¹ However, it has several limitations, including lengthy study times of up to 50 min, lack of structural information to assess lesion morphology and whole body exposure to ionising radiation approximating an equivalent dose of 2.3 mSv for a 250 MBq dose of 99m Technetium sestamibi, compared with 0.5 mSv for

conventional mammography.² While equipment required for MBI-guided biopsy exists, access is currently very limited.³

Concordance between findings across imaging modalities and histopathology is an essential tenet of breast imaging.⁴ However, a sonographic abnormality is not identified in up to 26% of positive MBI cases, necessitating MRI and MRI biopsy.^{1,5}

CESM is a new mammographic technique, that like MRI, provides morphological and functional information. Following intravenous injection of iodinated contrast, the breast is compressed, and low-energy and high-energy X-ray exposures obtained for each mammographic projection. The low-energy image is technically and diagnostically equivalent to a standard mammogram, and the recombined image shows areas of increased vascularity.⁶ Angiogenic lesions such as breast cancer are visible on the recombined iodine-enhanced image, while the low-energy image allows assessment of lesion morphology. A breast cancer lesion appears as a focal white area on a grey background of normal tissue, as a result of increased X-ray attenuation due to higher concentrations of iodine in areas of neovascularity.

CESM may be as accurate as MRI in a number of settings including imaging of patients with mammographically dense breasts, local staging of a known malignancy, imaging symptomatic patients and problem solving when mammography and ultrasound are inconclusive.^{7,8}

Practical advantages of CESM include lower cost, shorter examination times of around 10 min, circumventing MRI waiting lists, less patient discomfort and anxiety.^{6,7}

Drawbacks of CESM include higher glandular radiation doses when compared with conventional mammography or tomosynthesis, although the measured doses of 1.6 mGy in in vitro models non-dense breast tissue remain below the Australian diagnostic reference level of 2.0 mGy.⁹ There are also risks of administering iodinated contrast.

CESM requires only a minor modification to standard mammogram equipment as well as a software upgrade. The iodinated contrast is the same used in contrast-enhanced CT procedures, and the cost per procedure is relatively low. MBI requires high-resolution small field of view gamma cameras¹⁰ and is most commonly performed on dedicated machines with solid-state detectors and light tissue compression capabilities. The Technetium-99m sestamibi radioisotope is the same as used in nuclear myocardial perfusion and parathyroid imaging. The cost per imaging procedure is moderate, and mammography is required for anatomy-morphology cross-correlation and detection of microcalcifications. Breast MRI requires breast coil equipment and generally requires the use of gadolinium-based contrast agents, which are also used for other routine MRI scans. The cost per imaging procedure is moderate; however, scan time is a more important consideration as imaging of other body parts is also performed on the same scanners.

Although CESM has been described as a useful adjunct imaging test in the setting of equivocal mammographic and ultrasound findings,^{11,12} our case is the first documenting its use in the context of problem solving MBI findings. In particular, CESM performed following core biopsy, and clip insertion was helpful in confirming that a lesion detected on MBI had been successfully sampled. Our experience highlights the challenges of integrating positive MBI with conventional imaging techniques, achieving cross-modality imaging concordance as well as the value of CESM in this setting.

Acknowledgements Dr Matthew Brookes is acknowledged for his suggestions and advice on achieving final imaging/histopathological concordance.

Contributors JSLO contributed to the planning of the manuscript, contributed to the literature review and wrote the initial manuscript draft, and sought opinions for additions and changes to the manuscript from the other coauthors. FW contributed to the planning of the manuscript, contributed to the literature review and assisted with obtaining and formatting of the images. DBT contributed to the literature review and provided expert feedback on the draft manuscript and helped to write the final version. DD contributed to the planning of the manuscript, including the appropriate learning points, contributed to the literature review, provided and formatted some of the images and provided expert feedback on the draft manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs

Jeremy SL Ong <http://orcid.org/0000-0001-5101-6107>

Donna B Taylor <http://orcid.org/0000-0002-1481-1141>

REFERENCES

- Huppe AI, Mehta AK, Brem RF. Molecular breast imaging: a comprehensive review. *Semin Ultrasound CT MR* 2018;39:60–9.
- Mattsson S, Johansson L, Leide Svegborn S, *et al.* Radiation dose to patients from radiopharmaceuticals: a compendium of current information related to frequently used substances. *Ann ICRP* 2015;44:7–321.
- Collarino A, Valdés Olmos RA, van der Hoeven AF, *et al.* Methodological aspects of ^{99m}Tc-sestamibi guided biopsy in breast cancer. *Clin Transl Imaging* 2016;4:367–76.
- Park VY, Kim EK, Moon HJ, *et al.* Evaluating imaging-pathology concordance and discordance after ultrasound-guided breast biopsy. *Ultrasonography* 2018;37:107–20.
- Shermis RB, Redfern RE, Burns J, *et al.* Molecular breast imaging in breast cancer screening and problem solving. *Radiographics* 2017;37:1309–606.
- Hobbs MM, Taylor DB, Buzynski S, *et al.* Contrast-enhanced spectral mammography (CESM) and contrast enhanced MRI (CEMRI): Patient preferences and tolerance. *J Med Imaging Radiat Oncol* 2015;59:300–5.
- Lewin J. Comparison of contrast-enhanced mammography and contrast-enhanced breast MR imaging. *Magn Reson Imaging Clin N Am* 2018;26:259–63.
- James JJ, Tennant SL. Contrast-enhanced spectral mammography (CESM). *Clin Radiol* 2018;73:715–23.
- James JR, Pavlicek W, Hanson JA, *et al.* Breast radiation dose with CESM compared with 2D FFDM and 3D tomosynthesis mammography. *AJR Am J Roentgenol* 2017;208:362–72.
- Goldsmith SJ, Parsons W, Guiberteau MJ, *et al.* SNM practice guideline for breast scintigraphy with breast-specific gamma-cameras 1.0. *J Nucl Med Technol* 2010;38:219–24.
- Patel BK, Lobbes MBI, Lewin J. Contrast enhanced spectral mammography: a review. *Semin Ultrasound CT MR* 2018;39:70–9.
- Lobbes MB, Lalji U, Houwers J, *et al.* Contrast-enhanced spectral mammography in patients referred from the breast cancer screening programme. *Eur Radiol* 2014;24:1668–76.

Copyright 2019 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow