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REVIEW ARTICLE **CME**

Recent Advances and Application of Breast Imaging in Clinical Practice

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ABSTRACT

Breast imaging is an essential cornerstone in the management of breast cancer. It serves not only as breast cancer screening, but also in diagnosis, treatment, and follow-up of patients with breast disease. Attempts to enhance the current imaging modalities and development of new technology are underway. We provide a short overview of the existing imaging modalities including mammography, tomosynthesis, ultrasound and magnetic resonance imaging, and recent technological advances including positron emission mammography, contrast digital mammography, elastography, three-dimensional / contrast-enhanced ultrasound and automated whole-breast ultrasound screening. Magnetic resonance spectroscopy, new state-of-the-art applications in optical imaging, cone-beam computed tomography, magnetic resonance–ultrasound navigation, and molecular imaging techniques are also briefly discussed.

Key Words: *Magnetic resonance imaging; Mammography; Molecular imaging; Ultrasonography, mammary*

中文摘要

乳腺影像的最新發展以及在臨床實踐中的應用

余黃莉、薛靜雯、馮倩如、鄧珮儀

乳腺影像是診治乳腺癌的重要基礎；它不僅用作乳腺癌病人篩查，而且用於診斷、治療和隨訪。醫學界正不斷嘗試加強當前的影像方式以及開發新技術。本文為乳腺影像技術作一簡短綜述，包括現存技術如乳腺鉬靶、X線層析合成攝影、超聲和磁共振成像，以及新興技術如正電子發射乳腺攝影、對比數字化乳腺攝影、彈性成像、三維／對比—增強超聲造影和自動化全乳腺房超聲篩查。本文同時簡略討論磁共振波譜、光學成像的新型最先進用途、錐束電腦斷層掃描、磁共振—超聲導航和分子成像技術。

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INTRODUCTION

Breast cancer is the leading cause of cancer in Hong Kong females, with a recent increasing trend in the incidence and number of new cases. The number of new breast cancers in female was 3508 in 2012, compared with 2059 in 2002, which corresponds to a 70% rise in the incidence, according to the statistics of the Hong Kong Cancer Registry.[1] With technological advances, breast imagers now have a wide range of tools to enable more accurate assessment and detection of breast pathologies, in particular cancer. The aim of this review was to give a brief overview of the recent advances and their application in breast imaging.

MAMMOGRAPHY

Mammography has been the primary imaging modality for breast cancer screening and diagnosis for more than five decades. Meta-analysis of 11 randomised controlled trials of mammographic screening with 13 years of follow-up estimated a 20% reduction in breast cancer mortality in women invited for screening.[2] Currently, digital mammography (DM) is increasingly used for diagnosis and screening of breast cancer. Compared with film screen mammography, it has the advantages of speed, lower radiation dose, and easy image transfer and storage. The results from the Digital Mammographic Imaging Screening Trial showed that the overall diagnostic accuracy of digital and film mammography was similar although DM was significantly better than film mammography in the subgroups of women younger than 50 years, pre- and peri-menopausal women, and women with heterogeneously dense or extremely dense breasts.[3,4] The meta-analysis of Souza et al[5] on screening trials also showed no significant diagnostic difference between digital screening and film-screen mammography although DM was more accurate in women younger than 50 years.[3,4,6] With further advances in technology, there is potential to improve the sensitivity and specificity of DM.

DIGITAL BREAST TOMOSYNTHESIS

Digital breast tomosynthesis (DBT) is a three-dimensional (3D) imaging technique that produces images of a stationary compressed breast at multiple angles during a short scan. The X-ray tube is moved through a limited arc angle and a series of exposures are obtained. These images are reconstructed into a series of thin high-resolution in-focus slices that can be displayed individually or in a dynamic cine mode.[7]

Large screening trials have shown that DBT has a higher sensitivity than DM and when used in combination with DM, an improved detection rate and diagnosis of cancer by 40% to 53% results.[8,9] The improvement in cancer detection rate is likely due to reduced obscuration by overlapping tissue, leading to better detection and lesion characterisation. Studies have also shown a significant reduction in recall rates, especially for non-cancer lesions (ranging from 6-67%).[8,10] Decrease in recall rate results in reduced patient anxiety, cost, and possible radiation dose due to additional images.

There are concerns about the detection and characterisation of calcifications on DBT. A cluster of microcalcifications may not be easily perceived on a sliced image or correctly interpreted on DBT. Conflicting data have been published on detection of microcalcifications by DBT.[11,12] DBT has also been assigned lower Breast Imaging Reporting and Data System (BI-RADS) classes and may have missed some malignant and premalignant lesions. Other challenges include extra cost and interpretation time. It may, however, have the advantage of avoiding unnecessary biopsies in patients with benign conditions.[13] The advantages and disadvantages of DBT must be carefully balanced.

There is also concern about the radiation dose of DBT. The dose of a single tomosynthesis acquisition is reported as 1.5- to 4 mGy, approximately equivalent to the dose of a 1- or 2-view full-field DM.[7] Nonetheless the total patient radiation dose depends on the number of views of tomosynthesis and its combination with a 1- or 2-view traditional planar DM. Currently the US Food and Drug Administration (FDA) has approved the use of reconstructed 2D images obtained from DBT. Studies have shown that the diagnostic accuracy of synthesised mammography is similar to that of standard DM, and has the potential to lower the overall radiation dose.[14]

With technological advances, further developments in DBT and its possible synergistic combination with other modalities such as ultrasonography (USG) or optical imaging of the breasts will continue to evolve.[15-17]

NEW ADVANCES IN MAMMOGRAPHIC EXAMINATIONS

Positron Emission Mammography

Positron emission mammography (PEM) is a new imaging modality that uses a pair of dedicated gamma radiation detectors placed above and below the mildly compressed breast to detect gamma rays following

administration of fluorine-18 fluorodeoxyglucose, the positron emitting radionuclide used in whole-body positron emission tomography (PET) studies. It has been approved by the FDA as a diagnostic adjunct to mammography and USG. Relative to whole-body PET, PEM has the advantage of being able to detect smaller hypermetabolic lesions. In addition, the sensitivity is comparable with magnetic resonance imaging (MRI) and significantly higher than that of PET, particularly for small tumours.[18] A meta-analysis of eight studies has reported the sensitivity and specificity of PEM to be 85% and 79%, respectively with some benign lesions accumulating the radionuclide such as fibroadenoma, fibrocystic change, and fat necrosis.[19] Nonetheless despite its high sensitivity, a disadvantage of PEM is the radiation exposure: it is associated with a 15-fold higher risk of cancer induction than a single screen film or digital mammogram. In PEM, all body organs are irradiated with radionuclide, so cancer induction is possible in any radiosensitive organ.[18] The indications for PEM include initial staging, evaluation for multifocal or multicentric disease, distinguishing recurrence from scar tissue, and response monitoring for neoadjuvant chemotherapy.[20] The clinical utility of PEM requires further investigation in order to justify its radiation risk.

Contrast-enhanced Digital Mammography

Contrast-enhanced digital mammography is a mammogram in conjunction with intravenous injection of iodinated contrast agent. It utilises the same concept as gadolinium-enhanced MRI of the breast to identify and analyse enhanced lesions that are otherwise occult or inconclusive on routine mammography. Due to the low absolute contrast concentration in breast tissue, subtraction mammographic images are usually obtained for analysis. There are currently two techniques under development, namely the temporal technique and the dual energy technique.

The temporal technique involves taking a baseline pre-contrast image and multiple post-contrast images that are obtained over a period of 5 to 7 minutes. The dual energy technique requires two exposures, one below and one above the K-edge of iodine.[21] The temporal technique provides the kinetic curves of the enhancement pattern of lesions but the principal concern is motion artefacts, and only one single view of one breast can be examined. Recent study by Diekmann et al[22] using contrast-enhanced temporal mammography showed increased sensitivity from 0.43 of conventional mammography to an average of 0.62, particularly pronounced in the case of dense breasts. The added value of kinetic analysis of contrast enhancement, however, could not be established, probably related to the augmented blood flow in a compressed breast.

Although the dual-energy technique does not provide detailed enhancement kinetics, it allows acquisition of multiple views of the same breast or bilateral examination. It is also less sensitive to motion artefacts, with shorter acquisition time and has better patient acceptance due to a shorter breast compression time. Dromain et al[23] studied 142 breast lesions using contrast-enhanced spectral (or dual-energy) mammography (CESM) and demonstrated an increased sensitivity to 93% compared with conventional mammography of 78%, with no loss of specificity. All multifocal breast cancers were correctly diagnosed.

Jochelson et al[24] compared the sensitivity of CESM and breast MRI. The overall lesion detection rate was 64/77 (83%) for CESM and 72/77 (94%) for MRI. The true-positive detection rate was significantly higher than that of MRI: 64/66 (97%) for CESM versus 72/85 (85%) for MRI. A recent study by Lobbes et al[25] also showed comparable good agreement in tumour size measurement between histopathology and CESM (0.905) versus breast MRI (0.915).

These initial studies have shown promising results for contrast-enhanced digital mammography. With increased availability of contrast-enhanced digital mammography, large-scale studies can be conducted to assess its sensitivity and specificity in cancer detection, and establish its role in breast imaging.

BREAST ULTRASONOGRAPHY

Clinical Application of Breast Ultrasonography

USG has a pivotal and indispensible role in breast imaging. Currently established applications of breast ultrasound can be broadly divided into three areas: diagnostic, screening, and interventional guidance, as stated in the American College of Radiology (ACR) Practice Parameter.[26] The current use of breast USG is briefly discussed here.

Diagnostic

Ultrasound has an established role in the imaging of clinically palpable breast lesions, as a first-line investigation in patients younger than 30 years

and lactating and pregnant women, and to evaluate abnormalities identified by other modalities such as mammography and MRI.[27] Studies have demonstrated a high accuracy in identification of malignant breast lesions using BI-RADS ultrasound lexicon.[27,28] Ultrasound also has a high sensitivity and negative predictive value in evaluation of focal breast symptoms or signs in women younger than 30 years.[29] In lactating and pregnant women, ultrasound has a high negative predictive value of malignancy.[30] With regard to the utility of ultrasound to check MRI-detected lesions, a recent meta-analysis showed heterogeneous results from available studies with a higher likelihood for detection of malignant and mass lesions.[31] Nonetheless, it is helpful for clinical decision-making and management.[31,32]

Screening

The Society of Breast Imaging and ACR recommend screening ultrasound be used to supplement mammography in women at high risk of developing breast cancer and who cannot undergo MRI examination. It is also recommended as a possible screening tool for women at intermediate risk and with dense breast tissue.[33] Many studies have investigated the use of hand-held bilateral whole-breast screening ultrasound in women with dense breast tissue (BI-RADS density 3-4 in 2003 version,[34] corresponding to category c and d in the 2013 version[35]), with detection of additional cancer ranging from 2.02 to 4.2 per 1000 women screened.[36-40] Mammographically occult breast cancers detected by screening ultrasound were usually small, invasive, and node-negative cancers.[37] There is not yet firm evidence of the survival benefits of screening ultrasound, and the high false-positive rate and recall rate remain a concern.[41,42]

Guidance for Intervention

Ultrasound is the major primary modality used for image-guided interventions in breast imaging. It offers the advantages of real-time evaluation, easy access, freedom from ionising radiation, and better patient comfort.[43] Fine-needle aspiration, core-needle biopsy, and vacuum-assisted biopsy are common diagnostic procedures to evaluate palpable breast lesions and lesions detected by other modalities. The choice depends on the degree of clinical suspicion of the lesions according to the BI-RADS classifications. Ultrasound-guided percutaneous removal of small benign breast lesions (approximately 1 cm) using a vacuum-assisted device is gaining in popularity, and studies show promising results with complete removal and a low rate of recurrence.[44-46] The feasibility of ultrasound-guided percutaneous ablation of small breast cancers using radiofrequency ablation, cryoablation, and irreversible electroporation has also been evaluated although it remains controversial.[47] Ultrasound has also been used to localise non-palpable breast lesions including hookwire insertion, radioguided occult lesion localisation, and sentinel node and occult lesion localisation.[48-50]

Advances in Breast Ultrasound

Advances in ultrasound technology have allowed the novel application of techniques such as elastography, 3D ultrasound, and contrast ultrasound in breast imaging. These are exciting developments for both clinical practice and research.[51]

Elastography

Elastography evaluates and quantifies tissue elasticity. It applies the principle of clinical palpation, where it is assumed that pathological conditions and malignancy increase tissue stiffness.

Two types of sonoelastography techniques are available: strain elastography (SE) and shear-wave elastography (SWE). SE measures tissue displacement along the axis of applied force, usually with mild compression, and compares it with adjacent normal tissue.[52] In SWE, an acoustic radiation force is generated by application of the ultrasound probe to the tissue. The propagation velocity of shear waves (m/sec), which is proportional to the square root of stiffness (Young's modulus) of the tissue travelled, is measured and thus allows quantification of tissue elasticity in kilopascals (kPa).[53]

The application of elastography has been widely investigated. For SE, a grey-white or colour map displaying the relative strain of the selected lesion and background tissue on mild compression is generated. Qualitative assessment of the colour spectrum of the lesion such as relative strain level and its surrounding, lesion shape, size, diameter relative to B-mode imaging, and strain level homogeneity are used to differentiate malignant from benign lesions.[54,55] Malignant lesions tend to have an irregular shape and heterogeneous strain level within and in the surrounding tissue, and are larger than their B-mode image. A semi-quantitative method using strain ratio (ratio of pathological tissue to surrounding normal tissue strain or tissue-fat strain

ratio) or size-ratio relative to B-mode imaging has also been studied.[56] Automated measurements and ratios are not currently approved by the FDA for use in the United States.

SWE is less operator-dependent and provides quantitative measurement of lesion stiffness. Similar to SE, it enables qualitative assessment from the colour spectrum map displaying lesion and adjacent tissue stiffness value, lesion size, shape, diameter relative to B-mode imaging, stiffness homogeneity of the lesion and its adjacent tissue, and rim stiffness. Quantitative assessment of the lesion concerned — including the mean elasticity, maximum elasticity, and elasticity ratio — can also be analysed.[57-60] Various cutoff values for these parameters have been proposed by different studies.[57-59] A cutoff value of maximum elasticity value of 80 kPa by Chang et al[60] had a sensitivity of 95.8% and specificity of 84.8%. Lee et al[61] advocated a cutoff value of 30 kPa with a sensitivity of 100% and specificity of 57.2% while a cutoff value of 65 kPa had a specificity of 81.1%. Berg et al[59] studied 939 masses and showed that maximum visual colour stiffness, irregular shape, or maximum stiffness of 160 kPa were useful features to upgrade BI-RADS 3 lesions to biopsy. Features of soft colour, oval shape, or maximum stiffness of 80 kPa or less could be used to downgrade BI-RADS 4a lesions to follow-up. The addition of SWE increases the specificity of B-mode ultrasound in assessing breast lesions with no statistically significant increase in sensitivity.[59]

Both SE and SWE improve diagnostic performance when used as an adjunct to breast ultrasound. They help improve lesion characterisation and specificity, and avoid unnecessary biopsies.[60,62] Based on the available evidence, the European Federation of Societies for Ultrasound in Medicine and Biology has recommended the use of elastography as an adjunct to conventional ultrasound in breast imaging, with a principal aim to improve classification of BI-RADS 3 and 4a lesions.[63]

Both SE and SWE suffer from depth limitation and pre-compression variation. The complexity of breast lesions may also affect elastography performance: some cancers are soft and of low stiffness whereas some benign lesions, such as hyalinised fibroadenoma, appear quite stiff. A combination of correlation B-mode ultrasound, careful scanning technique, and awareness of potential artefact and pitfalls will make elastography a useful aid in breast sonography.

Three-dimensional Ultrasound

The 3D ultrasound technique has been widely applied in obstetrics and gynaecology but its application in breast imaging has been relatively limited. 3D ultrasound has been shown to have similar diagnostic performance to 2D ultrasound.[64-66] A characteristic retraction pattern on the coronal plane was found to be of high specificity (94.6%) but low sensitivity (54.7%) for malignancy.[64] Additional roles of 3D ultrasound include assessment of tumour volume, evaluation of colour and power Doppler vascular imaging, and guidance for biopsy, in which needle localisation is better.[67] It has also been shown to have potential prognostic value in breast cancer evaluation.[68]

Automated Whole-breast Ultrasound Screening

Automated breast ultrasound removes the need for manual ultrasound and can be performed with the patient prone or supine. There are three systems: (1) patient in a prone position with breast in a water or gel bath, with transducer scanning in a rotational manner and acquisition of 3D data; (2) mechanical rotation of the arm with a standard ultrasound probe, and continuous acquisition of image data during scanning; and more recently (3) an automated breast ultrasound system comprising a large transducer paddle (similar in size to compression paddle in mammography), with the patient in a supine position, and data acquisition of the whole breast volume.[69,70] Subsequent 3D reconstruction can be performed at the workstation for interpretation. The latter has been recently granted approval by the FDA for use in breast cancer screening as an adjunct to mammography. Several advantages of automated whole-breast ultrasound screening (ABUS) include: standardised data acquisition resulting in consistent and reproducible results; a cost-effective method as the presence of a radiologist or ultrasound technologist is not required during the scanning; and consistent time of data acquisition that allows a fast scanning time of approximately 15 minutes. Nonetheless more time may be required by the radiologist to review the scan when compared with real-time handheld ultrasound screening.[70] A recently published large-scale trial, the SomoInsight Study, investigated the addition of ABUS to screening mammography in more than 15,000 patients with dense breast tissue.[71] It demonstrated an additional 1.9 cancers detected per 1000 women screened: these cancers were invasive node-negative cancers. There is the potential for more widespread clinical application of ABUS, in particular for screening patients with dense breast tissue.

Contrast-enhanced Ultrasonography

Contrast-enhanced ultrasonography (CEUS) allows characterisation of tumour vascularity and perfusion pattern. More promising results have emerged with the introduction of second-generation contrast agents.[72] Additional effort has been made to characterise the enhancement pattern using various parameters. CEUS was found to have good correlation with MRI findings in characterisation of breast masses.[73] It has also been shown to be accurate in assessing tumour size of invasive ductal cancer.[74] It may also have a role in the prediction of prognostic factors of breast cancers.[75] Nonetheless the clinical role of CEUS in breast imaging remains uncertain because the enhancement characteristics do not provide a definitive diagnosis that is still based on biopsy. The high cost of contrast agents also limits the clinical application of CEUS.[72]

MAGNETIC RESONANCE IMAGING IN BREAST IMAGING

Breast MRI is an imaging technique that is increasingly used in clinical practice, in both diagnosis for symptomatic patients and in screening of asymptomatic subjects.

Clinical Applications

Diagnosis in Symptomatic Patients

Excellent data from both single institution and multicentre studies have confirmed that MRI is more sensitive in the assessment of tumour size and detection of multifocal and multicentric cancers (including lesions in the same breast or contralateral breast) than conventional imaging. It has a role in staging before treatment is planned, and may influence the decision for breast conservation therapy (BCT) versus mastectomy. According to the recommendations of the EUSOMA working group in 2010,[76] indications for preoperative MRI with potential advantages include: (1) patients with newly diagnosed invasive lobular carcinoma (where MRI is proven to be of particularly high pooled sensitivity of 93% and high correlation with pathology in previous systematic review); (2) patients at high risk for breast cancers; (3) patients under 60 years of age with discrepancy in size of more than 1 cm between mammogram and USG, with expected impact on treatment decision; and (4) patients eligible for partial breast irradiation on the basis of conventional imaging and clinical evaluation.

It should be noted that although MRI is more accurate in the assessment of size of ductal carcinoma in-situ (DCIS) and extensive intraductal component than other conventional methods, which is essential when selecting BCT over mastectomy, it is also associated with over- or under-estimations. There are also other limitations: some malignant lesions remain undetectable by imaging, waiting time, and suboptimal MR specificity. Treatment planning should therefore be made by a multidisciplinary team, where MRI findings are interpreted with reference to conventional imaging findings and clinical evaluation. Any MRI findings that may impact on patient treatment should be verified by percutaneous biopsy whenever possible, and total treatment delay due to MRI staging and other associated work-up should not exceed 1 month. Patients should also be informed of the potential risks and benefits of preoperative MRI if this is being considered prior to treatment.[76]

MRI has additional roles in the following scenarios: (1) evaluation of response to neoadjuvant chemotherapy; (2) detection of breast cancers that have distant metastasis (e.g. histologically proven adenocarcinoma in axillary lymph nodes[77]) but with the primary tumour remaining occult on clinical evaluation and conventional imaging; (3) assessment of symptomatic patients with breast augmentation or reconstruction, either suspicious of implant rupture or breast parenchymal disease (e.g. breast lump, or in high-risk patients with suspicion of tumour); (4) differentiation of breast cancer recurrence from scar tissue in treated patients with inconclusive conventional imaging findings or biopsy results; (5) characterisation of equivocal findings on conventional imaging in patients where needle biopsy is not feasible; (6) work-up for abnormal nipple discharge when conventional ductography has failed for technical reasons or has been declined by the patient; (7) diagnosis of inflammatory breast cancer, when an unresolved presumed mastitis remains suspicious for malignancy after appropriate antibiotic and anti-inflammatory treatment. Careful patient selection and close correlation with conventional imaging or biopsy findings (whenever available) remain the cornerstone for prompt and appropriate use of the imaging technique.[76]

For Screening of Asymptomatic Subjects

MRI has been increasingly used to screen selected subsets of women who have an increased lifetime risk for breast cancer. The American Cancer Society (ACS) recommends annual MRI screening as an adjunct to mammography for women with the *BRCA*

gene mutation; untested first-degree relatives of *BRCA* carriers; those with a 20% to 25% or greater life-time risk of breast cancer; patients aged 10 to 30 years who have undergone chest radiation; and patients with Li-Fraumeni, Cowden and Bannayan-Riley-Ruvalcaba syndromes or with an affected first-degree relative.[78,79]

There is insufficient evidence to recommend MRI screening in women at average risk (life-time risk, 15%-20%) for breast cancers, including those with lobular carcinoma in situ, atypical lobular hyperplasia, atypical ductal hyperplasia, heterogeneously or extremely dense breast on mammography, or women with a personal history of breast cancer including DCIS. The application of MR screening in these women remains debatable. Nonetheless, with the greatly superior diagnostic power of breast MRI documented across almost all possible clinical scenarios, expert opinion (e.g. from Kuhl[79]) has stated that it is no longer justifiable to further discourage its use for screening in average-risk individuals who have made an informed choice. MRI screening in women at <15% life-time risk, however, is generally not recommended by the ACS expert consensus opinion.

Recent Advances

Diffusion-weighted Imaging

In an effort to improve the specificity of MRI for characterisation of breast lesions, diffusion-weighted imaging (DWI) has been utilised to yield physiological information about the functional environment and movement of water in normal versus abnormal breast tissue. Quantitative analysis of apparent diffusion coefficient (ADC) values has proven to be useful in distinguishing malignant from benign focal breast lesions, where malignant lesions usually have a lower value indicating restricted water diffusion and increased cellularity. More recent literature suggests that 'glandular tissue-normalised ADC mapping', compared with using absolute ADCs, further improves the diagnostic performance of DWI. In particular, the overlap of ADC values between benign and malignant lesions can be substantially improved by normalising them to those of the remote glandular tissue. This improvement even exceeds that achieved with conventional 3D T1-weighted and dynamic MRI at 3.0T.[80]

Magnetic Resonance Spectroscopy

Proton magnetic resonance spectroscopy (MRS) is a non-invasive functional imaging technique that may complement dynamic contrast-enhanced MRI by increasing its specificity. Most MRS use hydrogen-1 signals to determine the presence and concentration of various metabolites in tissue. MRS of the breast evaluates for a resonance peak at 3.2 parts per million; this peak signifies increased levels of choline metabolites referred as total choline.[81]

Total choline is a marker for increased cell membrane turnover that is detected not only primarily in malignant breast lesions but also at a lower level in benign lesions and normal fibroglandular tissue.[81] Previous meta-analysis by Baltzer and Dietzel[82] of 19 breast MRS studies showed promising results with reasonably good pooled sensitivity (73%) and specificity (88%). At 3T, metabolite peaks are more widely separated than at 1.5T, so although no significant difference in diagnostic performance has been shown to date, it is proposed that MRS at 3T may improve sensitivity over that at 1.5T, especially for smaller lesions.[82]

MRS has also been investigated in the evaluation of neoadjuvant chemotherapy response, with mixed results.[81] Larger-scale studies are needed to further evaluate its use in this respect.

Magnetic Resonance–Ultrasound Navigation

In recent years, real-time ultrasound using a fusion imaging system has been developed in which a position tracking system is coordinated with a magnetic sensor. This helps synchronise an ultrasound image and the MR image with multiplanar reconstruction of the same section in real time. The application of this new technique is versatile and can help improve both tumour staging and image-guided biopsies.

For Assessment of Tumour Margins During Tumour Staging

Studies have shown that preoperative MR assessment for breast cancers, although sensitive for detecting multiple tumours in the same or contralateral breast, fails to improve postoperative margin status or subsequent local recurrence when compared with conventional imaging modalities.[83,84] It has been suggested that MR-navigated ultrasound, with the combined benefit of high sensitivity and real-time assessment under multiplanar reconstruction, can predict tumour extent more accurately than ultrasound alone. This may be of particular use in patients with non-mass lesions on MRI or those who have undergone neoadjuvant systemic chemotherapy.[85]

For Biopsy of Incidental Lesions Depicted on Magnetic Resonance Imaging But That Remain Occult on Repeated Ultrasound

With the high sensitivity yet limited specificity of contrast-enhanced MRI, there is a tendency to identify more incidental breast lesions of indeterminate nature during routine tumour work-up. As many of these are too small and remain sonographically occult, even on repeated assessment, they are resolved by MR-guided biopsies that also have limitations, e.g. limited availability, procedure cannot be done under real-time visualisation, costly use of MR time and personnel etc.[86] Ultrasound-guided biopsies remain the preferred option whenever technically feasible. The emerging technique of MR-navigated ultrasound is cheaper and can be performed in real-time within a reasonable time.[87] It is generally preferred by operators and may offer a solution.

The Use of a Dedicated Magnetic Resonance System to Improve Diagnostic Accuracy

Hillman et al[88] has demonstrated improved diagnostic performance of a dedicated 1.5T breast MR using high-spatial-resolution and high-contrast-resolution spiral trajectory acquisitions. They demonstrated good sensitivity of 92%, specificity of 88.8%, positive predictive value of 49.7%, negative predictive value of 98.9%, and high accuracy, as well as a low number of false positives and false negatives; the results were significantly better in all case metrics when compared with those historically recorded from breast MRI using whole-body imagers. Such results have favourable implications for patient care as it allows use of MRI with a low risk of harm to the patient in both the screening and diagnostic environments.

STATE-OF-THE-ART TECHNOLOGIES IN BREAST IMAGING

Cone-beam Computed Tomography

The use of cone-beam computed tomography (CT) in breast imaging was first described by Lindfors et al in 2008.[89] A flat-panel detector for cone-beam CT application was used, with the patient in a prone position without compression of the imaged breast, and the detector and the X-ray tube rotated 360 degrees around the breast. The data acquired could be reconstructed in multiplanar format. They compared the performance of cone-beam CT with film-screen mammography, and found that masses were better visualised with CT while mammography outperformed for microcalcification detection.[89] Similar results were demonstrated by a subsequent study, which found that details of microcalcification were better delineated by mammography.[90] The group subsequently worked on contrast-enhanced cone-beam CT and demonstrated an improvement in detection of malignant microcalcifications, similar to mammography, and increased conspicuity of malignant mass lesions.[91] Another study demonstrated a high correlation between cone-beam CT and mammography in the evaluation of BI-RADs 4 and 5 lesions, with better patient comfort.[92] A pilot study investigated the potential role of cone-beam CT in monitoring tumour response.[93] In terms of radiation dose, cone-beam CT had a similar or lower glandular dose than conventional mammography.[89-92] The current available evidence is derived largely from small-scale studies: further large population studies are needed to investigate the potential application of cone-beam CT in breast imaging.

Optical Imaging

Optical imaging is a novel imaging technique that utilises near-infrared light propagation through tissues to assess their different optic properties.[94] It can be performed by utilising the intrinsic breast tissue contrast alone such as oxy- and deoxy-haemoglobin, water, and lipid. Near-infrared lasers — either radiofrequency modulated, continuous-wave or pulsed — are used to probe the tissue structure non-invasively. Oxy- and deoxy-haemoglobin, water, and lipid have their own specific absorption and scattering characteristics as a function of wavelength. Their concentration and distribution mappings within tissue can be reconstructed by measuring the optic signals at multiple wavelengths.[94,95] These mappings may potentially help in differentiating malignant from benign lesions.

Leff et al[96] reviewed 34 studies with approximately 2000 women in whom optical mammography was used to evaluate breast conditions. About 85% of breast lesions were detectable on optical mammography; most results involved retrospective comparison with X-ray mammography detection. A higher detection rate was noted for cysts with low scattering characteristics and cancer with high blood volume and strong optic absorption. Fibroadenoma and small malignant lesions were problematic with the latter due to low spatial resolution of optical imaging.

A multimodality approach such as combined imaging with mammography, ultrasound, or MRI[16,97,98] has

been employed to enhance lesion detection and discrimination. Multimodal registration can potentially increase the specificity of optical imaging and allow for the fusion of functional and anatomical information. Most studies have shown that both the maximum and mean haemoglobin concentrations were significantly higher in malignant cancers compared with benign, likely related to neovascularisation in cancer. Some showed a lower oxygen saturation value in cancer lesions.

Exogenous optic contrast probes to enhance optic signals have also been investigated.[99] Molecular contrast probes on specific tumour receptors or tumour-associated enzymes are also under development.

With the advances in technology and molecular imaging, optical imaging holds great promise as a non-radiation imaging technique in breast screening, lesion detection, and diagnosis.

Breast-specific Gamma Imaging

In contrast to conventional mammography that uses an anatomical approach to display physical features of breast cancer within normal surrounding breast tissue (which is often limited by breast density), breast-specific gamma imaging (BSGI), also known as molecular breast imaging, has now been proposed as an adjunct modality that uses a physiological approach to identify breast lesions.[100] Promising results from studies have shown that it has high sensitivity in detecting cancers, comparable with that of MRI, and an even higher specificity. Furthermore, the performance is equally good in non-dense and dense breasts (i.e. its use is not limited by breast density).[101]

A dedicated breast-specific gamma camera is designed to allow an acquisition technique similar to traditional mammography: patient's breasts are compressed in the conventional craniocaudal and mediolateral oblique positions with a high-resolution gamma camera directly in contact with the surface of the breast. The BSGI images can be directly correlated with mammograms, and used to guide needle biopsy when necessary. Gamma camera–guided stereotactic localisation has also been developed recently for biopsy of lesions depicted only on BSGI.[100]

Compared with MRI, BSGI has the advantage of being more comfortable for the patient, more cost-effective and less time-consuming for radiologists and clinicians to interpret.[101] There remain concerns about the high whole-body radiation dose from the radioactive tracer currently used for these examinations.[77] To date, BSGI has not been validated as an effective screening tool in large prospective studies.[100]

CONCLUSION

Over the past few decades, extensive and advocate-driven research has led to extraordinary progress in technological advances in breast imaging. More options for screening and diagnosis have improved our ability to detect and diagnose breast cancer early. Breast imaging remains an exciting field of study with a bright future.

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