Brief Report

Contrast-enhanced mammography-guided biopsy: technique and initial outcomes

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Abstract: Contrast-enhanced mammography-guided biopsy (CEM-Bx), a novel technique for diagnosing suspicious enhanced lesions, was commercialized for clinical application in 2021; however, there are only a few publications documenting this technique in the existing literature. The aim of this study was to evaluate the procedural performance and preliminary outcomes of CEM-Bx performed in our hospital between from September 2021 to June 2022. We reviewed data of 12 women who underwent CEM-Bx during the study period, including their demographic and procedural characteristics, biopsy success rate, histopathological diagnosis, and average glandular dose (AGD). All women (mean age ± standard deviation: 54±6 years) showed enhanced breast lesions on CEM and underwent CEM-Bx within one week. The success rate of CEM-Bx was 100%. The vertical needle approach was used in a decubitus position (N=7, 58%), while the horizontal needle approach was used in an upright sitting position (N=5, 42%). The mean procedure time for the CEM-Bx was 17±6.3 min. The mean AGD was 14.3±12.3 mGy. Histopathologic examination revealed a malignancy rate of 66.7%. In summary, CEM-Bx is a feasible technique, with a high success rate of diagnosing contract-enhanced lesions.

Keywords: Contrast-enhanced mammography (CEM); mammography; breast cancer; biopsy; diagnosis

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Introduction

Contrast-enhanced mammography-guided biopsy (CEM-Bx) was approved by the United States Food and Drug Administration (US -FDA) for clinical use in 2020 (1). Recently, a few studies have documented a higher cancer diagnostic sensitivity of CEM than conventional mammography and sonography (2), indicating that it might be possible to discover certain cancers by means of enhancement techniques only. Likewise, in a previous clinical trial, the diagnostic sensitivity of CEM and enhanced magnetic resonance imaging (e-MRI) was found to be superior to that of conventional mammography (3). These findings support the idea that enhancement techniques can reveal certain subclinical cancers that might be morphologically inapparent on traditional images. Early diagnosis of suspicious enhancement is imperative for tailoring an appropriate treatment plan.

In clinical practice, the optimal imaging modalities including stereotactic mammography, tomography or sonography can be used as a guide to achieve biopsy. However, all of them are non-enhanced imaging. For diagnosing a suspicious enhanced lesion, e-MRI-guided biopsy is regarded a well-established technique. With the

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recent clinical use of CEM, the CEM-Bx was essentially developed to diagnose an enhanced suspicious lesion.

CEM, an imaging technique capable of providing a low-energy mammogram (LEM) and a recombined enhanced image (REI) in the same examination session, was approved for clinical use by the US-FDA in 2011 (4). Based on the theory of cancer angiogenesis, the REI is believed to enhance breast cancer secondary to interstitial pooling of the contrast medium. In addition, the diagnostic sensitivity of CEM has been reported to be comparable to e-MRI (5,6). A recent meta-analysis on diagnostic performance of CEM documented a pooled sensitivity of 89% and specificity of 84% (7). Furthermore, in women with dense breast tissues, the diagnostic sensitivity and accuracy improved from 71.5% to 92.7% and 65.9% to 85.8%, respectively (8).

However, the presence of enhancement is not exclusive to cancers. Therefore, a biopsy is essential to correctly diagnose a suspicious enhanced lesion on CEM. Herein, we report a new technique of performing CEM-Bx directly on the enhanced targets. Further, this article documents the procedural performance and preliminary outcomes of CEM-Bx performed in our hospital between September 2021 to June 2022. To the best of our knowledge, there are only a few publications on this topic in the existing literature (9-11). In this technical note, the biopsy with vertical or horizontal needle approach and procedural average glandular dose (AGD) were firstly assessed.

Methods

Participants

This study was supported by the Institutional Review Board of Chang Gung Memorial Hospital (No. 202100839B0C502) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was taken from all individual participants.

CEM-Bx was performed on 12 women who had shown enhanced lesions on a prior CEM. All lesions showed a subclinical presentation with no palpable masses. On contrast-enhanced MRI, three patients demonstrated enhanced breast masses, while nine patients had multifocal malignant-like microcalcifications. However, the inclusion criterion was the presence of suspicious enhanced lesion on CEM, but not obviously identified on convention mammography and ultrasound. The exclusion criteria were the renal function impairment and presence of allergic reaction to contrast medium. After confirming normal renal function and the absence of an allergic history to iodinated contrast medium, all patients were invited to participate in this study and asked to sign an informed consent after explaining the reason for undertaking CEM-Bx.

CEM-Bx procedure

CEM-Bx was performed by attaching a biopsy system to the mammography machine (Pristina; GE Healthcare, Buc, France), after intravenous injection of contrast medium (Omnipause 350 mg I/mL; GE Healthcare, Dublin, Ireland) at a rate of 3 mL/s (total dose of 1.5 mL/kg body weight). Based on the findings of previous CEM, the locations of the target lesions were assessed to decide whether to take a medial or lateral approach into the breast. Thereafter, breast thickness following compression was used to determine whether the biopsy needle should be approached vertically (compressed thickness over 3 cm) or horizontally (compressed thickness 3 cm or less). Medial or lateral puncture was performed after establishing the shortest distance from the skin to the target. Needle approach (vertical or horizontal), which is critical to the safety of needle firing, was determined such that the distance between the fully-open notch and the needle tip (vacuum-assisted biopsy needle, Encor, BARD, USA) was 2.7 cm. Thereafter, the locations of the enhanced targets were marked on the breast skin using a red pen.

Two minutes after initiation of the contrast medium injection, the marked target was localized and compressed within the biopsy window. Thereafter, the CEM exposure mode was used to obtain a pair of LEM and REI at angles of 0, +15, and −15 degrees. Similar to the conventional stereotactic guided biopsy, we selected the enhanced target and the machine guided the needle to the selected target using a computerized coordination system. After confirming the correct positioning of biopsy needle in front of the target by REI, the needle was fired through the target and multidirectional suction samplings were performed in a complete clockwise rotation to obtain four to six pieces of core specimen. The CEM-Bx procedure used in this study is illustrated in *Figure 1*.

Data collection

We reviewed each patient's age, breast density, the size of enhanced lesion, needle approach, procedural position, procedure time, biopsy success rate, histopathological

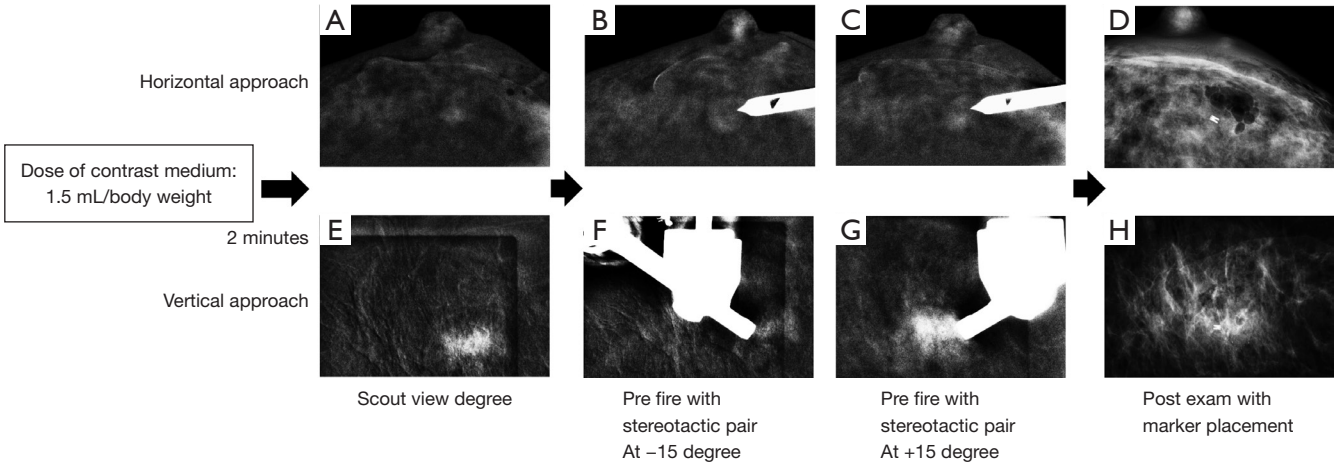

Figure 1 Performance of CEM-Bx by horizontal (above) and vertical (below) needle approaches. (A,E) Scout view imaging at 0 degree; (B,F) pre-fire imaging with stereotactic pair at –15 degree; (C,G): pre-fire imaging with stereotactic pair at 15 degree; (D,H) post-biopsy with marker placement. CEM-Bx, contrast-enhanced mammography-guided biopsy.

diagnosis, AGD. Breast density was classified according to the American College of Radiology Breast Imaging Reporting and Data System (12). Breasts in categories A and B were considered non-dense, whereas those in categories C and D were considered dense. The size of enhanced lesions was measured on the REI of CEM examination. Procedure time was defined as the interval between the first CEM exposure after the start of contrast medium injection to the last post-biopsy mammogram. A case was considered successful upon completion of the CEM-Bx procedure with the pre-fired biopsy needle being visible in front of the enhanced target on the REI at +15, and -15 degrees and concordant location of post-biopsy marker to the target (10). The AGD of the procedure was calculated as the sum of the recorded AGD in the picture archiving and communication system during individual procedures.

Results

This study enrolled 12 women (mean age ± standard deviation: 54±6 years) who underwent CEM-Bx between September 2021 to June 2022. The breast density was categorized as dense in 75% of the cases and non-dense in 16.7% of the cases. All suspicious lesions were observed to be associated with enhancement on CEM prior to the biopsy. The average size of enhanced suspicious lesions was 1.66±2.3 cm. CEM-Bx was performed smoothly with a vertical needle approach in the decubitus position (N=7, 58%) and a horizontal needle approach in the upright sitting position (N=5, 42%). All the patients tolerance to the biopsy and the success rate was 100%. The mean procedure time for CEM-Bx was 17±6.3 min (range, 6–27 min) and the mean AGD was 14.3±12.3 mGy. Histologically, eight biopsies were diagnosed as cancers (four invasive carcinomas and four ductal carcinomas in situ) and four as benign lesions (sclerosing adenosis, flat epithelial atypia, ductal hyperplasia, and foreign body reaction). This resulted in a cancer detection rate of 66.7%. Of the eight biopsy-proven cancers, six were further confirmed by subsequent operations, while two patients declined surgery in our hospital due to personal reasons. The four patients with benign diagnoses were followed-up on a regular basis. There were no major complications encountered during the procedure including allergic reactions, vasovagal reactions, or infections. The procedural and outcome data are summarized in *Table 1*.

Discussion

CEM-Bx is a new and developing technique, and only a few papers describing its application have been published to date. Alcantara *et al.* were the first to report the outcomes of a preclinical trial on CEM-Bx, concluding that it was a feasible technique for diagnosing enhanced lesions seen on CEM and could be used as an alternative to e-MRI-guided biopsy (10). They preferred the horizontal approach of biopsy needle with patients sitting upright due to better visualization of targets (10). Despite the fact that this is

Table 1 Summarized procedural and outcome data of CEM-Bx

Variables	Value (total n=12)
Age (mean ± SD), years	54±6
Breast density, n	
Non-dense (BI-RADS A, B)	2
Dense (BI-RADS C, D)	10
Image findings, n	
Mass	3
Multifocal microcalcification	9
Enhanced target size (mean ± SD), cm	1.66±2.3
Procedural time (mean ± SD), min	17±6.3
Needle approach, n (%)	
Vertical in decubitus	7 (58.3)
Horizontal in sitting	5 (41.7)
AGD (mean ± SD)	14.3±12.3
Success rate, %	100
Biopsy outcomes	
Benign, n (%)	4 (33.3)
Sclerosing adenosis, n	1
Flat epithelial atypia, n	1
Ductal hyperplasia, n	1
Foreign body reaction, n	1
Cancers, n (%)	8 (66.7)
Ductal carcinoma in situ, n	4
Invasive ductal carcinoma, n	4

CEM-Bx, contrast-enhanced mammography-guided biopsy; SD, standard deviation; BI-RADS, Breast Imaging Reporting and Data System; AGD, average glandular dose.

an agreeable approach, the vertical needle approach with patients lying in the decubitus position has the benefits of being more comfortable for the patient and causing less anxiety by avoiding direct facing of the needle towards the patient. However, the horizontal approach is clearly preferable when the breast thickness is assumed to be <3 cm after compression. Therefore, in the present study pre-procedural assessment of breast thickness, target location, and patient tolerance was performed to determine the optimal biopsy needle approach in each case.

For a lesion that showed enhancement on both CEM and e-MRI, we experienced that CEM-Bx was preferable to e-MRI-guided biopsy because of its lower cost and shorter procedure time. The mean time of CEM-Bx was 17±6.3 min in this series. The procedural time of e-MRI was experienced longer than CEM-Bx due to the longer time of image acquisition and repeat scanning for target assessment. Since the procedure of CEM-Bx is nearly identical to that of stereotactic mammographic-guided biopsy, the operators who perform the latter on a daily basis are already familiar with it. The mean procedure time of CEM-Bx and stereotactic mammographic-guided biopsy was approximate to the previous report (17±6.3 *vs.* 24.7±14.3 min) (13). The cancellation rate of e-MRI-guided biopsy has been reported to range from 8% to 13% and the cancer detection rate from 18% to 61% (14-17). Compared to the previous report, the success rate of CEM-Bx was approximate (100% *vs.* 95.4%) and the cancer detection rate was higher (67% *vs.* 39.7%) (10).

Radiation exposure is a critical issue of CEM-Bx. Based on the principle of "as low as reasonably achievable (ALARA)", radiation exposure should be maintained at an acceptable minimum level throughout CEM-Bx (18). Therefore, we used the recombine enhanced image to assess the location of targets (including upper/lower and inner/outer quarter; the distance of target from the skin) and then marked the target location on the skin before the biopsy. In our series, all the targets could be correctly localized within the 6 cm × 5 cm biopsy window in the scout image with a single dual-energy exposure. However, it is noteworthy that the dual-energy exposure of CEM has been testified to be 20% to 30% higher than a single exposure of conventional mammography (19). In the present study, one patient who had previously received a liquid silicone injection for breast augmentation demonstrated a higher mean AGD (14.3±12.3 mGy). When we excluded this patient, the mean AGD of the remaining 11 patients was only 10.7±2.5 mGy, which was comparable to digital breast tomosynthesis (DBT) guidance (10.18±3.73 mGy) and lower than stereotactic biopsy (22.06±14.92 mGy) (20). Moreover, the AGD per exposure during CEM-Bx remained under the 3 mGy dose limit set by the Mammography Quality Standards Act regulations (21).

The main limitation of this study was the small number of cases, that was unable to assess the accuracy of biopsy. In fact, this technical note aimed to introduce the new technique of CEM-Bx. The accuracy of diagnosis awaits more cases in the future. Nevertheless. the CEM-Bx can support the clinical application of CEM.

In conclusion, the protocol and outcomes of CEM-

Bx outlined in the current study demonstrate that this technique can be used for performing biopsy smoothly and efficiently. Thus, it can be inferred that CEM-Bx might prove to be beneficial in diagnosing lesions suspected of malignancy on CEM.

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-137/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (No. 202100839B0C502) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was taken from all individual participants.

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