Analysis of contrast enhancement kinetics in breast cancer subtypes with a dedicated contrast-enhanced cone-beam breast CT

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Aims and objectives

Cone-beam breast-CT (CBBCT) is a novel breast imaging technique that provides isotropic 3D images with high contrast resolution. The diagnostic superiority of non-contrast CBBCT (NC-CBBCT) over MG has been shown in several studies (1-3). Administration of intravenous contrast media (CM) amplifies these diagnostic features: contrast enhanced CBBCT (CE-CBBCT) diagnostic accuracy surpasses that of NC-CBBCT(1-4), potentially by visualization of tumor angiogenesis (5-7). However, CBBCT acquisition protocols shown larger inconsistencies across studies: specifically, timing from CM injection to CE-CBBCT acquisition ranged between 52 s to 4 min (4, 8).

Therefore, the aim of our study was to evaluate contrast enhancement of breast lesions on CBBCT over time to identify the optimal acquisition time for CE-CBBCT scan for best discrimination of malignant and benign breast lesions. Further, we aimed to assess whether histopathological subtypes can be discriminated based on CBBCT lesion intensity.
Methods and materials

This prospective study was conducted between 2015-2017 in a tertiary referral center in central Germany. Patients age > 40 with suspicious BI-RADS 4/5 lesions identified on mammography and/or ultrasound in ACR density type c/d breasts were included. Exclusion criteria were enrollment in the German breast cancer screening program, pregnancy, known allergy to iodinated contrast media or renal insufficiency.

After initial NC-CBBCT, contrast media was administered as a single-shot intravenous injection of 90 mL (range 80-95 mL) non-ionic CM (Iopromide, Ultravist® 300, Bayer-Schering, Berlin, GER) at a flow rate of 3 mL/ s using followed by a 30 mL saline solution chaser. Two separate CE-CBBCT scans were performed at 2 min and 3 min post-CM injection.
Results

Patient characteristics

A total of 31 patients (31 breasts) were included, of which none withdrew consent or was lost to follow-up. NC-CBBCT, 2 min and 3 min post-CM CE-CBBCT scans were performed in all patients. One mild contrast related adverse event (nausea) was reported. The mean patient age was 56.5 years (±9.7 years). Menopausal status for twelve patients (38.7%) was pre-menopausal, and 19 patients (61.3%) were post-menopausal. Five patients (16.1%) presented with clinically palpable breast mass.

Breast lesions

In the included patient cohort, 57 were identified via NC-CBBCT or CE-CBBCT. Average number of breast lesions per patient was 1.84 (range 1-6).

A total of 41 breast lesions (71.9%) were assessed via biopsy or surgery, identifying 25 malignant lesions, 5 semi-malignant lesions (papillomas) and 11 benign lesions. Another 16 breast lesions (28.1%) rated as benign were followed up over at least 1 year via imaging.

Contrast media dynamics

On NC-CBBCT, mean lesion intensity for malignant lesions was lower than for benign lesions, although differences did not reach statistical significance (42.62 vs. 54.3 HU, p=0.3609). On 2 min and 3 min CE-CBBCT scans, malignant lesions showed nominally higher mean enhancement than benign lesions (2 min: 93.84 vs. 61.93 HU, p=0.0650; 3 min: 97.94 vs. 71.75 HU, p=0.1410).

Comparing 2 min and 3 min CE-CBBCT scans, malignant lesions did not show a significant additional HU increase (mean 93.84 vs. 97.94 HU, p=0.271), whereas intensity significantly increased for benign lesions (mean 61.93 vs. 71.75 HU, p=0.0017).

No relevant intensity changes were seen for the surrounding breast tissue (mean 21.23 vs. 19.82 vs. 26.82 HU for NC-CBBCT, 2 min and 3 min CE-CBBCT).

Further analyses were performed standardizing lesion enhancement to surrounding breast tissue. At both 2 min and 3 min CE-CBBCT scans, malignant lesions showed significantly higher mean enhancement than benign lesions (2 min: 48.17 HU vs. 0.3 HU, p<0.001; 3 min: 57.38 HU vs. 15.43 HU, p<0.001).

Kinetic analysis in malignant histological subtypes
Separate analyses of CM kinetics were conducted for malignant subtypes of IDC, DCIS and invasive carcinoma of no special type (NST) with associated DCIS.

All lesion subtypes showed increasing lesion intensity at the 2 min CE-CBBCT scan. NST with associated DCIS as well as IDC lesions demonstrated an intensity plateau to the 3 min scan, whereas intensity for DCIS lesions peaked at the 3 min CE-CBBCT scan. No significant difference in lesion intensity was found at both 2 min and 3 min CE-CBBCT between the histopathological subtypes (2 min: p=0.3755; 3 min: p=0.1993).

Evaluating lesion enhancement, DCIS showed the highest and most rapid enhancement (3 min: 100.93 HU) compared to NST with DCIS-component (3 min: 55.82 HU) and IDC (3 min: 52.31 HU). There was a significant difference of enhancement between the malignant histopathological subtypes at the 3 min CE-CBBCT scan (p=0.0314).
Fig. 1: Mean intensity of malignant/benign breast lesions and surrounding breast tissue on CBBCT. No significant difference was evident between malignant and benign lesions.

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Fig. 2: Mean contrast enhancement versus baseline for malignant/benign lesions and surrounding breast tissue. Malignant lesions showed significantly higher contrast enhancement versus benign lesions both at the 2min and 3min scan.

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**Fig. 3:** Right sided breast lesions showing enhancement at 2 min CE-CBBCT of 111.1 HU and at 3 min of 120.3 HU. Pathology confirmed DCIS.

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Fig. 4: Right sided breast lesions with contrast enhancement at 2 min CE-CBBCT of 10.4 HU and at 3 min of 15.9 HU. Pathology revealed diagnosis of fibroadenoma.

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Conclusion

Malignant breast lesions show significantly higher contrast enhancement than benign lesions on CBBCT. Contrast enhancement on CBBCT can further aid in discrimination between histopathological subtypes of malignant lesions, among which highest enhancement was evident for DCIS lesions. We recommend the acquisition of CE-CBBCT scan 2min after CM injection for best discrimination of malignant and benign lesions. Our results further show that for CBBCT malignancy assessment, both NC-CBBCT and CE-CBBCT acquired to evaluate contrast enhancement rather than absolute intensity. Simultaneous acquisition of NC- and CE-CBBCT via dual energy techniques might reduce scan-time and radiation dose.
References


