Use of Contrast-Enhanced Spectral Mammography for Intramammary Cancer Staging:

Preliminary Results

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Rationale and Objectives: To prospectively evaluate and compare the accuracy of contrast-enhanced spectral mammography (CESM) and ultrasound (US) in size measurement of breast cancer with histologic tumor sizes as gold standard.

Materials and Methods: Twenty women aged between 40–73 years (mean age, 57 ± 10 years) with histologically proven invasive ductal/lobular carcinomas were included in the study. Agreement between imaging tumor size (CESM and US) and histopathologic tumor size was evaluated with Bland–Altman analysis. Stereotactically guided vacuum biopsy was performed in four patients after CESM. Two independent reviewers described artifacts of CESM.

Results: Motion artifacts did not occur in the study. CESM-specific artifacts caused by scattered radiation mostly occurred in oblique view of CESM. Background enhancement of breast tissue was seen in four patients. Mean difference of tumor sizes was 0.3 mm (6.34%) between CESM and histology and −2.2 mm (−7.59%) between US and histology. Limits of agreement ranged from −18.9 to 19.48 mm for CESM and from −17.1 to 12.7 mm with US. Especially smaller tumors with a size <23 mm were measured more precisely with CESM. Enhancement of breast tissue around microcalcifications correlated with abnormalities.

Conclusions: CESM is accurate in size measurements of small breast tumors. On average CESM leads to a slight overestimation of tumor size, whereas US tends to underestimate tumor size. Assessment of the breast tissue can be limited by the scattered radiation artifact and background enhancement of breast tissue. CESM seems to be helpful in the characterization of breast tissue around microcalcifications.

Key Words: Contrast-enhanced spectral mammography; tumor staging; ultrasound; artifacts.

Contrast-enhanced spectral mammography (CESM) is an imaging technique combining digital mammography with intravenous injection of iodinated contrast media to detect hypervascularized lesions, especially in dense breast tissue (1). Although it was developed several years ago, knowledge about the performance of this technique in clinical routine, especially in breast cancer screening, is still limited. However, a recent study proposes similar indications for CESM as for magnetic resonance imaging (MRI), namely preoperative staging, detection of occult lesions, monitoring of treatment response (2). Initial results comparing this new technique with mammography, ultrasound (US) and breast MRI show a better detection of suspicious lesions with CESM compared to full-field digital mammography and the combined imaging of mammography and US (3) but a lower detection rate of hypervascularized breast lesions compared to breast MRI (4). Studies evaluating the accuracy of CESM compared to MRI in preoperative tumor staging show a similar accuracy in lesion size measurement compared to MRI (5).

Preoperative staging of cancer extent in the breast is necessary to plan the optimal treatment (6). MRI is the most commonly used approach to determine the extent of the tumor in the breast and to decide which surgery should be performed and if the breast should be radiated (7,8). Besides its high cost and limited availability, one major problem of breast MRI is background enhancement of breast tissue, which decreases the detection of breast lesions and affects breast cancer staging (9). In such patients, US is a good alternative method for breast cancer staging. Studies correlating tumor size determined with imaging and histopathology describe a tendency to underestimate tumor size with US (10–13), whereas MRI tends to overestimate tumor size

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TABLE 1. Details of Patients Included in the Study

Number of Patients	Age (Mean Age; Standard Deviation)	Disease	ACR (Artifacts) ACR2	ACR3	ACR 4
20	40–73 (57; 10)	Invasive cancer	2	4	1
		Invasive cancer with EIC	4 (1)	6	3 (2)

The majority of patients had invasive cancer with additional extensive in-situ component (EIC).

(13,14). The good performance of CESM in the detection of multifocal and multicentric cancer dissemination has been shown (4), as well as the high accuracy of tumor size measurements with CESM compared to MRI (5). The performance of CESM in preoperative tumor size measurement compared to US has not been investigated so far.

For CESM a technical artifact has been reported which is called "scattered radiation artifact" caused by differences in breast tissue thickness from the thorax to the edge of the breast and different characteristics of mammography with low and high energy (3). Motion artifacts or background enhancement of the breast parenchyma interfering with image quality of CESM has not been reported to date.

Therefore, the purpose of this study was to compare the accuracy of local tumor staging with CESM compared to US, with histopathology serving as the gold standard. In addition, CESM was assessed for artifacts potentially limiting interpretation of the CESM data set. In four patients, a proof of principle was performed to show that CESM imaging before stereotactically guided vacuum-assisted core biopsy is feasible.

MATERIAL AND METHODS

The local ethics committee approved this prospective study, which was performed in accordance with the Declaration of Helsinki. Written consent of all patients was obtained before enrollment of the study.

Patients

Women with histologically proven invasive breast cancer, older than 30 years, were enrolled in the study between February and October 2013. Carcinoma was diagnosed with mammography or US and histologically proven by biopsy, before CESM. CESM was clinically indicated for determination of tumor size. Additional MRI was performed if CESM results were not clear (n = 4). Patients with impaired renal function, pregnant or breastfeeding patients, patients with hyperthyroidism, and patients with a history of anaphylactic reaction to contrast media were excluded. CESM was not performed at the same day with other investigations in which application of contrast media was necessary (MRI and computed tomography). Neoadjuvant chemotherapy was an exclusion criterion, as well as hormone treatment or radiotherapy of the breast.

Breast density was classified with low-energy mammography of CESM by the standardized classification system of the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS).

CESM Imaging

A Senographe Essential CESM (GE Healthcare, Solingen, Germany) was used for CESM examinations. Dual-energy CESM was performed with automated parameters acquiring a low- and high-energy mammography during one breast compression. Molybdenum (Mo) or rhodium (Rh) target and Mo or Rh filter were used depending on the breast density and compression thickness. Peak kilovoltage (kVp) values ranging from 26 to 31 were used for the acquisition of low-energy mammography, whereas high-energy mammography of CESM was acquired with 45–49 kVp, with x-ray spectrum above the k-edge of iodine (33.2 keV). Solutrast 300 (Bracco Imaging Germany, Konstanz, Germany) was used as contrast media with a weight-adapted dose of 1.5 mL/kg body weight with a flow rate of 3 mL/s, followed by an injection of 20-mL sodium chloride. Mediolateral (MLO) view and craniocaudal (CC) view of the nonaffected breast were acquired 2 minutes after the initiation of contrast media application, followed by MLO- and CC-CESM of the affected breast. The Senographe Essential CESM generated iodine-enhanced images from the low- and high-energy images. Regions of contrast media uptake were displayed with recombined image-by-image processing.

Ultrasound

An Aixplorer Supersonic ultrasound system (Supersonic Imaging, Munich, Germany) or Toshiba Aplio MX (Toshiba Medical Systems, Neuss, Germany) were used for second look US before biopsy or surgery. Three gynecologists with 5–12 years of experience in US investigated and staged both breasts. Measurements were performed in all three axes. The largest tumor diameter, which was defined in consensus, was recorded to compare lesion size with histopathologic lesion size. Investigators were blinded to measurements in CESM.

Image Analysis

Contrast-Enhanced Spectral Mammography. Anonymized images were evaluated with a high-resolution workstation