Contrast-enhanced spectral mammography - a pictorial review

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Learning objectives

- To perform a review about Contrast Enhanced Spectral Mammography (CESM) and its technical aspects.

- Illustrate the main advantages, clinical indications and limitations of this technique with cases from our hospital.
Background

Breast cancer is an important problem in women worldwide. The imaging techniques now available and most commonly used in the screening and diagnosis of breast cancer, as mammography and ultrasound, are based on morphological changes of breast tissue. [2]

These techniques have limitations, as in the case of dense breast tissue, inconclusive studies and in the evaluation of the local extent of disease. In dense breasts the sensitivity of mammography for the detection of lesions is as low as 48%, whereas in fatty breasts it is 98%. [3-9] Inconclusive studies include those where the lesion is visualized in only one mammographic view, subtle architectural distortions, equivocal lesions or lesions not seen in ultrasound. [3] The local extent of disease is commonly not correctly evaluated with mammography and ultrasound, and in these cases magnetic resonance imaging (MRI) is usually performed.

Since digital mammography is available, the acquisition is faster and a better image quality is obtained as well as other applications become possible such as digital breast tomosynthesis and CESM. [6-8]

In CESM, functional information is present as well as morphological information. [3] The tumor cells in breast cancer induce the process of neoangiogenesis, that is necessary for the tumor growth, invasion and metastatic spread. This process leads to the formation of new vessels and capillaries from a preexisting network, which have an abnormal wall structure making them abnormally permeable and tortuous. [2,5,10]

Contrast agents in imaging studies explore the angiogenic process in breast cancer. The first techniques being used were digital subtraction angiography and contrast enhanced computed tomography. These techniques have a high radiation dose and a long procedure time for the angiography and therefore they are not widely used. [2,3,11] MRI is the most widely used technique that explores the angiogenic process, with gadolinium as the contrast agent. [12,13]

Recently, CESM is available as a new technique to explore this process. [3,6,14]
Findings and procedure details

**TECHNIQUE**

There are two approaches that have been used in contrast-enhanced digital mammography: the temporal subtraction technique and the dual-energy technique (CESM). [14]

Temporal subtraction was the first technique that was used. One high energy image is obtained before and several high energy images are obtained after the administration of an iodinated intravenous contrast agent. The precontrast image is subtracted from the postcontrast images and a kinetic curve is analyzed as occurs in MRI. [2,3,6,15] In some studies, however, there was poor correlation between the pattern of the kinetic curve and the probability of malignancy and this curve was of no clinical significance. [3,4] Limitations of the temporal subtraction technique include movement artifacts and the possibility to analyze only one breast in one view, and for these reasons this technique is less used in comparison with the dual-energy technique. [2,5,11,14]

The dual-energy technique (CESM) is the most widely used technique. The equipment is the same as in conventional digital mammography with an additional copper filter. An iodinated contrast agent is administered with an iodine concentration of 350 mg/mL, with a dose of 1-1.5 mL/kg, with a power injector at an injection speed of 3 mL/sec. [14] The patient positioning is the same as in conventional digital mammography, and the image acquisition starts 2.5 to 5 minutes after the contrast injection. A low energy image (below the keV of iodine) and a high energy image (above the keV of iodine) are obtained in the same acquisition for each view. The final image results from the combination of the low and high energy images, which suppresses the background breast tissue and highlights the areas that show contrast enhancement. [2-4,6,12,14] The contrast enhancement lasts for 10 minutes which makes possible the acquisition of several views in both breasts. [12] Comparing to the temporal subtraction technique, the dual-energy technique has less movement artifacts and permits to obtain multiple views in both breasts. [3,4,14]

The characteristics that are analyzed include the enhancement intensity, the morphology and the findings are compared with conventional mammography images and ultrasound. Spiculated margins, an irregular shape and heterogeneous enhancement are findings suggestive of malignancy. [4,14,15]
Several studies demonstrated the feasibility of contrast enhanced digital mammography with sensitivities of 78-96%. [3,4,5,11,12,13]

ADVANTAGES AND INDICATIONS

- **Dense breast tissue** - it has been demonstrated an increase in the detection rate of suspicious lesions with contrast enhanced digital mammography comparing to conventional digital mammography or mammography with ultrasound (**Fig. 1**). [3,4,11,12,14]

- **Problem solving** - CESM is also useful in the evaluation of equivocal lesions in mammography and ultrasound, indicating the most suspicious lesions and thus permitting a better selection of the lesions to be biopsied (**Fig. 2,3,4**). [3,4,11,13,14]

- **Assessment of extent of disease** - Another application of CESM is the determination of the extent of a lesion, detection of multifocality/multicentricity and possible contralateral lesions (**Fig. 5,6,7**). This could be useful in the local staging of breast cancer, especially in patients who cannot undergo MRI. [3,4,12-14]

- Other applications include evaluation of symptomatic patients, patients with axillary metastases, residual or recurrent disease, monitoring of the response to chemotherapy and possibly screening in patients with elevated breast cancer risk. [12,14,15]

Studies have demonstrated a good correlation of the tumor size in CESM and the pathologic size. [4,11,12] CESM, especially the low energy images which are equivalent to conventional mammography images, also permits the detection of microcalcifications and for this reason this may be more sensitive to ductal carcinoma in situ than MRI. [2,4,13]

Other advantages include the good acceptance by the patients, an easy implementation in breast imaging departments, the immediate availability in the mammography room and the possibility of a direct correlation with the standard mammogram images. [6]

LIMITATIONS

- Limitations of this technique include the **false positive** lesions such as fibroadenomas (**Fig. 8**), phyllloid tumors, intraductal papillomas (**Fig. 9,10**),
radial scars, cytosteatonecrosis, sclerosing adenosis (Fig. 11) fibrocystic changes (Fig. 12) and other benign lesions (Fig. 13,14). [4]

- The need for an intravenous iodinated contrast agent is also a limitation in patients with contraindications to the administration of this agent. [15]

- Other limitation is the need of ionizing radiation. The radiation dose in a CESM study is about 1.2 times of the dose in a standard mammogram or the equivalent of one additional view. [12,14]
Fig. 1: Heterogeneously dense breast tissue. 51-year-old woman with previous history of left breast cancer. Right craniocaudal (CC) and mediolateral oblique (MLO) view before and after contrast administration. A nodule in the upper quadrant transition is only depicted in CESM. Histopathology: Invasive ductal carcinoma G1 in a fibroadenoma.

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Fig. 2: Equivocal lesion. 57-year-old woman with left breast discomfort. Right and left craniocaudal view before and after contrast. There is an asymmetry in breast tissue density in the left upper outer quadrant, equivocal on ultrasound. CESM demonstrates an irregular enhancement. Histopathology: Invasive carcinoma NOS G1.

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Fig. 3: Problem solving and intramammary lymph node. 67-year-old woman with previous history of left breast cancer. Conventional mammograms showed a nodular density in the upper quadrants transition, that has slightly increased in size. CESM showed enhancement of this nodule. Histopathology revealed a medullary breast cancer. CESM also showed a well-defined nodular enhancement in the upper outer quadrant corresponding to an intramammary lymph node.

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**Fig. 4:** The same nodule as in Figure 3. The nodule is hypoechogenic on ultrasound, and has slightly increased in size. Histopathology: medullary breast cancer.

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Fig. 5: Assessment of the extent of lesion. 39-year-old patient with a poorly defined spiculated lesion in the upper outer quadrant of the right breast. CESM permits a better depiction of the real extension of the lesion, with an enhancement of $7 \times 5 \times 4$ cm which approximated to the histopathologic size. Histopathology: invasive carcinoma NOS G2.

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Fig. 6: Equivocal lesion and assessment of the extent of disease. 39-year-old woman with a palpable right breast mass. Mammography showed an asymmetry of breast tissue, with higher density in the right upper outer quadrant. CESM showed an asymmetric, diffuse contrast enhancement which is more intense in the right upper outer quadrant. Histopathology: invasive lobular carcinoma.

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Fig. 7: Assessment of the extent of lesion. 48-year-old woman with palpable breast nodules and poorly defined lesions in the upper inner quadrant and upper quadrants transition on conventional mammograms. CESM permits a better delineation of the extent of lesion, showing an enhancement of 6 x 5 cm. Histopathology: invasive carcinoma G1.

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**Fig. 8:** Fibroadenoma. 55-year-old woman, with a previous history of breast carcinoma and a heterogeneously dense breast tissue. CESM permits a better visualization of a well defined nodule that shows contrast enhancement. Core-needle biopsy revealed to be a fibroadenoma.

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**Fig. 9:** Intraductal papillomas. 53-year-old woman with painful left breast. Several nodules are seen in conventional mammograms. The nodule chosen to be biopsied was the largest and the one that showed more intense enhancement in CESM. Histopathology: intraductal papilloma and low grade papillary carcinoma.

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Fig. 10: The same nodule as in Figure 9. The nodule had an intraductal component on ultrasound. Histopathology: intraductal papilloma and low grade papillary carcinoma.

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Fig. 11: Sclerosing adenosis. 50-year-old woman with a nodular area of dense tissue in the upper inner quadrant of left breast, equivocal on mammography and not seen on ultrasound. CESM showed a nodular low intensity enhancement. Histopathology revealed sclerosing adenosis.

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**Fig. 12:** Fibrocystic changes. 38-year-old woman with dense breast tissue. CESM showed a nodular enhancement in the inferior quadrants of the right breast. Core-needle biopsy revealed fibrocystic changes.

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**Fig. 13:** Other benign changes: 65-year-old woman with bloody nipple discharge. Mammography showed an asymmetric retroareolar density on the right breast. CESM showed enhancement in this area. Histopathology: benign changes with dilated ducts surrounded by inflammatory process.

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**Fig. 14:** Ultrasound of the same area as in Figure 13. Ultrasound showed a hypoechoogenic ill-defined area in relation to dilated ducts. Histopathology: benign changes with dilated ducts surrounded by inflammatory process.

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Conclusion

CESM is a new technique that allows the detection of angiogenesis, and can be easily performed in the same day and with the same equipment and has the potential to reduce the time between the detection and diagnosis of breast cancer.

Its main indications include the evaluation of dense breasts, problem solving of equivocal situations and the assessment of extent of disease.

Other indications include the evaluation of symptomatic patients, patients with axillary metastases, residual or recurrent disease, monitoring of the response to chemotherapy and possibly screening in patients with elevated breast cancer risk.

Further research is still needed to define the role of CESM among the other techniques used in the detection and diagnosis of breast cancer, especially in comparison with MRI, and in combination with digital breast tomosynthesis.
References


