

## Guided breast biopsies in Contrast-Enhanced Spectral Mammography

Over the past few years there has been a significant surge of interest in the use of contrast-enhanced spectral mammography (CESM). The reasons for the recent interest in CESM are mainly the high sensitivity of this breast imaging modality and the absence of any effect of breast density on the sensitivity. However, despite the many benefits of CESM, up until now the technique had the inconvenience that taking a biopsy of any suspicious lesion detected by CESM meant that the biopsy guidance had to be carried out using another imaging modality. This situation has now been addressed with the introduction of the Serena Bright CESM biopsy solution from GE Healthcare.



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We wanted to find out more about CESM in general and the new CESM-guided biopsy system in particular, so we spoke to Dr. Rodrigo Alcantara, head of Breast Imaging at the Hospital del Mar in Barcelona, Spain. Dr. Alcantara has a long experience of CESM and is actively involved in the evaluation of the new CESM biopsy system.

**Q** Before we get on to CESM, please tell us a bit about your clinic and the patients you see.

Hospital del Mar is part of an extensive public health complex in Barcelona (Parc de Salut Mar) and is the fourth biggest hospital in the city. We operate a large and well established breast screening program in which we carry out 17.000 mammograms per year. Screening represents almost 70% of all our breast examinations. In Spain the breast cancer screening program covers asymptomatic women aged from 50 to 70 years, who are invited every two years for a suggested mammogram appointment. Covering two of the five administrative areas in Barcelona, our hospital del Mar operates the biggest screening program in town.

The average participation rate of the women who are invited to participate in our screening program is 55-60%.

In addition to all this screening activity, on average we carry out a further 7000 mammograms per year for diagnostic/symptomatic patients, for follow-up and for examining high-risk patients. These symptomatic patients are mostly referred to us from primary care centers in our area and also from the surgical and gynecological departments associated with our breast unit.

Regarding screening, it is of course important for us to always keep in mind that women in the screening setting are

not only asymptomatic but also usually have no increased risk of breast cancer. We, as radiologists, must therefore always strive to find the optimal balance between diagnostic performance and recall rate in order to minimize unnecessary interventions while keeping the level of false positives as low as possible. In contrast, when we are dealing with a symptomatic or a high-risk patient, we can, and should favor diagnostic accuracy in order to be able to reliably answer the key clinical question as to whether we can rule out or confirm any suspected malignancy.

**Q** What breast imaging equipment do you have and from which manufacturers?

We have now 3 mammography systems, one Senographe Pristina from GE Healthcare and two Amulet Innovality from Fujifilm, all of them fully equipped with tomosynthesis and biopsy add-ons, stereo and tomo-guided unit. We previously had a Senographe Essential system (GE Healthcare), equipped with contrast enhanced mammography (Senobright) which provided us with our first contact with the remarkable technique of CESM. Nowadays, we perform our CESM examinations with the new Senographe Pristina system (Senobright HD). We have also two dedicated ultrasound systems (GE Logiq S8) and access to a 1.5 T Signa Explorer MRI (GE Healthcare).

**Q** *What is the typical work-up of a woman with a suspicious lesion on mammotomo?*

The typical work-up procedure in our department is compliant with the appropriate international recommendations and guidelines. For BI-RADS 5 non-calcified lesions in non-dense breasts, we can proceed with an ultrasound core-needle biopsy. Initial evaluation of the extent of disease is usually carried out with FFDM or DBT plus ultrasound. However, for some cases of asymmetries and distortions, we prefer to carry out CESM, given the established value of the technique as a problem-solving tool. Thus, by adding CESM to the work-up we gain further functional information which can help to avoid unnecessary biopsies. This is especially important for patients recalled from the breast cancer screening program. For example for patients with a BI-RADS 4-5 mass in a dense breast, performing CESM increases the overall diagnostic accuracy and improves the detection of additional unexpected lesions. In addition, this approach minimizes the need for second-look ultrasound in case of further MRI. Cases with calcifications are considered for stereotactic or DBT-guided vacuum-assisted biopsy. In these cases and, depending on the breast composition, we may consider further evaluation with CESM or MRI.

**Q** *And what about symptomatic women with a suspicious lesion detected on clinical examination?*

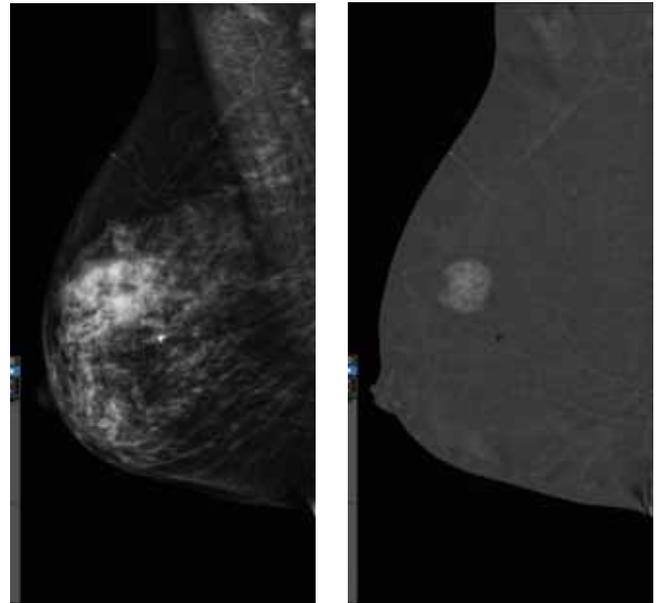
Such cases are usually referred to us from primary care centers. We have introduced CESM as an initial diagnostic technique in our institute for patients with clinically suspicious breast abnormalities. Thus, CESM is our first-line imaging modality in symptomatic women over 40 years of age and as a second-line modality in patients under 40 years with suspicious findings on ultrasound. The good correlation between the tumor size as determined by CESM with that determined by MRI and also with the final size shown on pathology increases the radiologist's confidence in establishing the local staging.

**Q** *And high breast density ?*

Dense breasts have been shown to be an independent risk factor for breast cancer and the most important cause of false negatives on mammography. In contrast to mammography, the sensitivity of CESM is not compromised by breast density. Indeed, some reports describe a statistically significant increase in CESM sensitivity in patients with dense breasts. Several different imaging approaches for the work-up of women with dense breasts are currently being evaluated by various groups of investigators.

The procedures we use in our hospital are as follows. First of all in our department we currently determine breast density by visual assessment, although we have a collaboration with a Spanish IT group which is likely to result in the installation of a dedicated breast density software in our unit in the near future.

For the evaluation of women with dense or highly dense breasts in the clinical/symptomatic setting, we usually use tomosynthesis plus ultrasound. On the other hand, for women with



The high sensitivity of contrast-enhanced spectral mammography is not affected by the density of the breasts, in contrast to other imaging modalities like Full-Field Digital Mammography. Left Panel: Low energy CESM image (MLO view) Right Panel: Recombined image (MLO view) clearly showing enhancing mass.

dense breasts in the population-based screening program, the method is FFDM only, despite the associated density issues.

Our unit is currently involved as a collaborator center in a multicentric trial evaluating different approaches to personalized breast screening. In this context, I am personally very interested in the possibilities of a rigorous evaluation of CESM vs. other imaging modalities. In fact this is the objective of a large and innovative trial that is currently being organized in the USA, namely the Contrast Enhanced Mammography Imaging Screening Trial (CMIST). The trial is designed to compare the performance of CESM in the screening of women with dense breasts with that of the combination of digital breast tomosynthesis (DBT) and whole breast ultrasound (WBUS). Managed by the American College of Radiology (ACR) with support from the Breast Cancer Research Foundation and GE Healthcare, the CMIST study is planned to start in the second quarter of 2020.

As for women with high genetic risk such as those with BRCA mutations, we generally direct them to MRI, where we use a full, standard 1.5 T MRI protocol for the initial examination and then abbreviated MRI protocols for subsequent acquisitions. As in most hospitals, our MRI system is not solely dedicated to breast examinations so in practice there is a waiting list of several weeks for our cases. The waiting list for MRI-guided biopsy is even longer. For cases where MRI is contra-indicated, e.g. because of claustrophobia, we offer CESM as an alternative.

**Q** *All in all, how many CESM examinations have you carried out?*

So far we have performed more than 1300 CESM examinations, the first 200 using the first generation of the Senobright system from GE but nowadays our contrast mammograms are carried

out with GE's latest Pristina system. The performance of the system based on the initial 329 cases showed a sensitivity of 94.0%, specificity 75%, PPV 70% and NPV 95.6%. There was an average of 16% false positive results, but this was in the beginning of our experience with the technique and we expect that those results have considerably improved by now. Indeed, the image quality has increased significantly with the updates available in the latest generation equipment and software.

The impressive performance of CESM can be explained by its underlying principle which relies on the detection of tumor vascularization. CESM detects angiogenesis by tracking the uptake of iodine-based contrast media in breast cancer, similar to the principle of breast MRI with gadolinium-based contrast. Both imaging techniques are thus based on increases in enhancement after contrast agent administration due to angiogenesis in neoplastic lesions.

Several studies have shown that CESM has similar diagnostic performance to that of MRI for detecting breast cancer and evaluation of the extent of the disease. In a systematic review and meta-analysis Tagliafico *et al* [doi 10.1016/j.breast.2016.04.008], reported sensitivity to be 98% with a post recalculation specificity estimated as 78%.

CESM has several advantages compared to MRI, for example shorter procedure times, lower cost, suitability for claustrophobic patients and no need to schedule according to menstrual cycle.

As has been described in several papers in the literature, the use of CESM instead of a normal mammogram can increase the sensitivity and the negative predictive value of the first imaging approach in symptomatic patients. The technique improves the detection for additional disease and has the potential to reduce the need of additional work up such as second look ultrasound in the case of MRI. CESM is an outstanding problem-solving tool, so we nowadays use it often when we have doubts about previous mammogram or DBT findings, as well as for some recalls from the screening program.

The CESM technique is very well accepted by the patients and in our experience is better tolerated by them than MRI, mainly due to ambiance and positioning factors. The enhancing (and non-enhancing) lesions are easily recognizable, even by the patients, so they can sometimes participate and fully understand the diagnostic process.

In practice, a CESM study consists of a set of 2 images per view, so the radiation dose is higher than FFDM, with literature reports of an increase of 20 to 54% of the Average Glandular Dose compared to mammography. Despite this, the overall CESM radiation dose is still within internationally accepted radiation dose limits. In addition, replacing a conventional FFDM by CESM study for an initial examination, e.g. in the case of symptomatic patients makes it possible to eliminate 60% of the increase in radiation dose.

### Q *Now what about biopsies?*

In our department we carry out an average of 630 core needle biopsies and 200 Vacuum - Assisted Biopsies (VAB) annually. All our core needle cases are ultrasound guided. For mammographic-guided (stereotactic, DBT and CESM) and MRI-guided biopsies



In addition to the benefit of using the same modality to guide the biopsy as was used to detect the lesion in the first place, the new Serena Bright system for CESM-guided breast biopsy system has several practical benefits such as being easy to perform and fast.

we always use a vacuum assisted needle in order to optimize sampling, avoid false negatives and minimize underestimation.

Both CESM and MRI can detect breast lesions that were initially occult by other techniques. The majority of the published data on these cases involves MRI, with the level of additional enhancing lesions being reported as between 16% and 29% of the women undergoing breast MR imaging.

Prior to the arrival of the Serena Bright biopsy system, whenever CESM showed a mammographically occult lesion, we proceeded with a targeted ultrasound, carried out on the same day. Similar

to second-look ultrasounds after a MRI, we are able to localize on average of 50-60% of the findings that had initially gone unnoticed. This biopsy is usually performed under sonographic guidance. There are also a few cases that are associated with a tomosynthesis finding, for example a distortion, which we work up with a DBT-guided procedure. When there is no sonographic or mammographic correlation, until now a biopsy had to be performed under MRI guidance.

### Q *When did you install the Serena Bright system?*

We have had this technology available in our department since last October 2019, using it under board approval and in a context of clinical validation. Our radiologists have extensive experience in the routine carrying out of mammography-guided breast biopsies, so the learning curve and implementation for CESM-guided biopsy was easy, particularly since the software interface is very intuitive. Technically, the CESM-guided biopsy is a procedure similar to a standard stereotactic biopsy (one scout and a pair of stereo images). The main difference is the additional step of contrast agent injection two minutes before starting to image. As in routine CESM examinations, each acquisition is composed of a low-energy and high-energy exposure, with the lesion being able

to be targeted on either the low energy or recombined view. Our procedures last for around 12 to 16 minutes, from the first compression to the clip placement, which our patients still find acceptable.

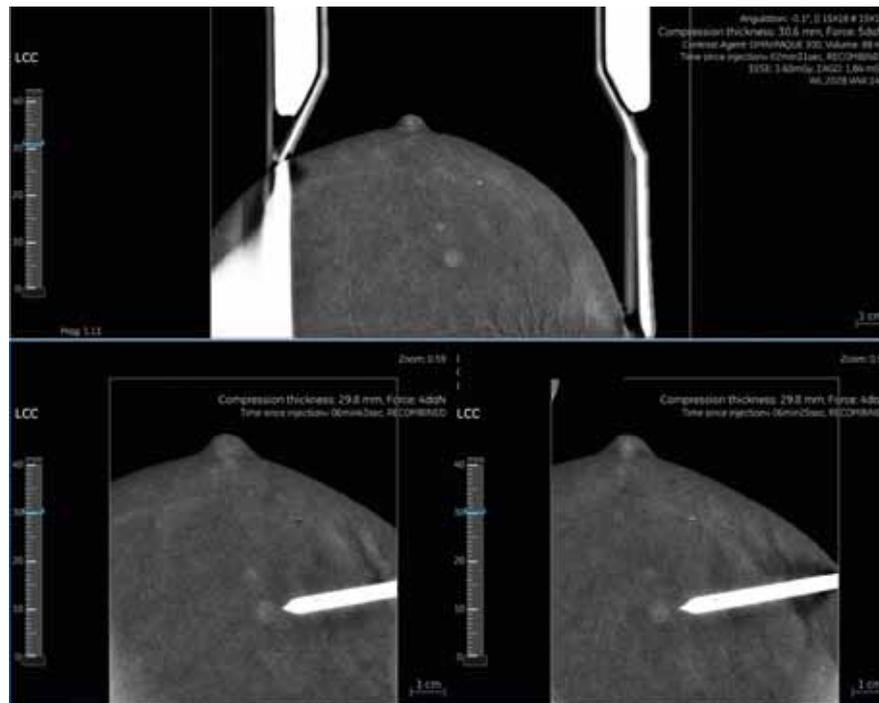
As far as the advantages of using this approach are concerned, in the first place there is the benefit of using the same modality to guide the biopsy as was used to detect the lesion in the first place.

The waiting list for a MRI-guided biopsy can be as long as several weeks, whereas the CESM-guided biopsies can be scheduled sooner, for example in our center in less than one week after the initial CESM.

The CESM-guided biopsy procedure itself is fast and easy to perform, and typically doesn't last more than 12-15 minutes, which compares favorably with the 40-60 minutes of a MRI biopsy. Overall, CESM biopsy costs less than a MRI-guided intervention. Last, but not least, for most doctors and radiographers, preparing for and carrying out MRI-guided biopsy procedures can be quite stressful. The technique is not used routinely and sometimes the lesion can be difficult to approach, making the whole procedure last longer than desirable.

So far, we have carried out 15 CESM-biopsies, all of them using a 10g VAB needle. Considering that we are still operating in a clinical validation context, our initial findings with CESM-guided biopsies have been very promising as concerns the reliable targeting of enhancing lesions. We have observed an average of 45 % of malignancies in the cases selected, i.e. more than the malignancies rates reported for MRI guidance (22-33%). This is probably related to the higher specificity of CESM compared to MRI. Also, MRI detects more non-malignant enhancing foci and seems to be more affected by background parenchymal enhancement (BPE).

The software interface of the Serena Bright, is particularly appreciated since it is very intuitive and user friendly. During the targeting, it is easy to go from the low energy image to the recombined image, so favoring image correlation. In addition, the possibility of easily switching between different biopsy modalities, e.g. from CESM to conventional stereo or DBT during the procedure, is very useful. For example, this can be done to carry out extra imaging,



CESM-guided biopsy using the Serena Bright system. Top panel shows the recombined CESM scout image acquired 2 min 31 sec. after administration of contrast. A round enhancing lesion and a satellite focus can be seen on the scout and both angulated pre-fire images. The needle tip points exactly to the enhancing suspicious lesion, confirming the targeting.

such as a DBT scout after clip placement. Given that enhancing information is not available after 10 minutes, performing a final DBT scout may avoid additional unnecessary radiation.

So far overall patient feedback to the CESM biopsy procedure has been very good — the patients usually state that the procedure was much less onerous than they expected. Of course, having a scheduled breast biopsy intervention always involves some stress for the patient, so being able to

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carry it out in a fast, efficient and easy way is of help.

In contrast, MRI-biopsy positioning can be a major issue for the patients and can be painful and uncomfortable. Since it is a complicated and limited technique, we always reserve MRI biopsy only for cases where there are really no alternatives.

Unlike MRI-biopsy, CESM-guided biopsy is a relatively simple technique and the procedure is fast. We foresee increasing use of the technique in the future.

For dubious ultrasound or mammogram cases, CESM-guided biopsy clearly has the potential to increase the success rate and avoid equivocal biopsies.

**Q** *And the future of breast imaging in general?*

The role of the breast radiologist has evolved from simply cancer screening and detection to a more complete diagnosis and management role with the widespread adoption of image-guided percutaneous procedures. One of the challenges in the near future is to find the balance between lesion detection and overdiagnosis/overtreatment, something that depends on a multidisciplinary commitment. In this context, the implementation of AI-based software could help us to improve the overall diagnostic performance, decrease false negatives and positives, while freeing us up to deal with more complex human-facing tasks.

All this means that we may be at the beginning of a whole new era where the profile of breast radiologists will be even more integrated in the clinical setting, participative and interventional.