CEM in biopsy of extended calcifications clusters

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Contrast-Enhanced Mammography (CEM) allows a direct visualization of calcifications connected to the vascularization underneath. This unique feature could potentially increase the characterization of such a tricky finding like breast calcifications, that alone lead to about 30-40% of recalls in mammographic screening. Pathology on vacuum-assisted breast biopsy is often the only chance to dispel suspicion, due to the limited impact of ultrasound or tomosynthesis in further characterizing calcifications.

Despite the low positive predictive value (~15%) for ductal carcinoma in situ for calcifications not mass-associated, when these are spread in an extended area or in multiple clusters could even hide an invasive component. When the invasive component is missed on biopsy and diagnosed only on the surgical specimen, a close second surgical time is needed for the sentinel node biopsy.

The invasive tumour component is frequently associated with mass enhancement on CEM, while the in-situ component tends to show faint non-mass enhancement. The rationale of performing a pre-biopsy CEM is to evaluate the different features of enhancement associated with calcifications, potentially identifying the invasive component. CEM-guided stereotactic biopsy, recently introduced in the daily workflow, could therefore allow to target the biopsy on the area of most suspicious enhancement concomitant to calcifications.

In April 2021 the BoCCE trial (Biopsy of Calcifications under Contrast Enhancement guide, NCT04862429) started. This prospective randomized trial is designed to compare the accuracy of CEM-guided stereotactic biopsy (study arm) with the traditional FFMD stereotactic or DBT biopsy (control arm) in targeting the area of greatest malignancy/grade of the lesion, using the pathology of the surgical specimen as gold standard.

Secondly, it compares the waiting time between enrolment and surgery, the proportion of patients undergoing preoperative CEM in the control arm, and the proportion of upgrading on pathology comparing the biopsy and the surgical specimen.

Up to the end of August 2023, 173 women have been enrolled and data are available for 147 of them: 72 patients in the control arm, 72 in the study arm, and 3 patients considered as intention to treat because refused proceeding with the biopsy. In these preliminary observations (end of recruitment in October 2023, and 2 years of follow-up for patients that did not underwent surgery), no adverse reaction nor severe complications occurred.

In the control arm, 54% of patients underwent CEM or MRI for the post-biopsy pre-operative staging. In the study arm the initial delay of an average of 6 days between enrolment and biopsy, due to the pre-biopsy CEM, had no consequences on the surgical timing. Indeed, the waiting time between enrolment and surgery showed that patients in the study arm are associated to an average 9 days anticipation of the surgery if compared to all the control arm, and to an average 14 days anticipation of the surgery if compared to those patients who performed post-biopsy pre-operative contrast-enhanced imaging.

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In the study arm, in 45% of cases the pre-biopsy CEM revealed enhancement concomitant to the suspicious calcifications. Among these, the pathology on biopsy described B5 on 66% of them, versus only 15% (in-situ component only) on calcifications without enhancement in the study. All the invasive cancers diagnosed on biopsy in the study arm showed enhancement: 71% mass and 29% non-mass.

Upgrade of invasive component diagnosed only on surgical specimen occurred both in the control and the study arm, and in the latter both among calcification associated and not-associated with enhancement. A possible explanation is that in 85% of cases a homogeneous enhancement was observed along the entire extension of the calcifications, making it difficult to distinguish a more suspicious specific target. The final results of this trial and further investigations are necessary for a more complete analysis.

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