E11. Advances in breast cancer imaging

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The goal of cancer imaging is to detect the smallest possible number of tumour cells and could be reduced to the signal-to-background ratio principle – the signal generated by the cancer must be higher than the background caused by a non specific signal or nearby normal cells (contrast resolution) – and to the spatial resolution of the imaging modality used. Breast cancer detection using mammography and ultrasound is based on natural endogenous tissue contrasts. With mammography, cancer detection is easy in fatty breasts and when the cancers exhibit distortion or associated calcifications. These clinical situations are frequent in the general population concerned (50–74 years) and explain the success of screening programmes.[1] When the breast density progressively increases, the sensitivity of mammography rapidly decreases (<50%); this limitation is particularly critical in the surveillance of high-risk young women (gene-mutation carriers and women with a significant familial history of breast/ovarian cancers).[2] Ultrasound (US) may improve this detection because the normal dense fibro-glandular tissue appears "white' whereas cancers are "black'.[3–4] However, when the normal tissue is heterogeneous or the cancer atypical (hyperechoic feature), false negative results may occur. Another problem with US is its operator dependency with a poor positive predictive value of biopsies (high percentage of false positive results). The introduction of full-field digital mammography (FFDM) since 2000 has offered the advantages of digital technologies (storage, transfer and teleradiology) and produced new technological advances that improve detection and characterisation: computed-aided detection or diagnosis systems (important to consider in the European context associating a decrease in the number of radiologists and an increase in the number of women concerned by screening in the next decade), tomosynthesis (3D approach) that generates thin contiguous slices of breast parenchyma limiting superimposition problems and increasing background-lesion contrast in heterogeneous breasts.[5–7] This 3D anatomical approach is also available now with US using a large field of view and automatic scanning coupled to mammography data. Beyond these morphological approaches, functional imaging is another tool to improve detection and characterisation. The most relevant and historical example is the detection of neoangiogenesis that appears at early stages of the disease. This detection can be obtained without contrast agents (US doppler modes, optical imaging) or after injection of nontargeted exogenous contrast agents (iodine agents for FFDM and CT, microbubbles for US, gadolinium chelates for MRI, 15O and 11C-labelled radiotracers for PET).[8] Most routine analyses are still qualitative (present or not) and semi-quantitative (e.g. with MRI: slopes of initial and late enhancement, time-to-peak of enhancement, time-intensity curves). Among all the imaging modalities available for this approach, MRI has several advantages: no use of X-Rays, 3D acquisition, analysis of both breasts, no influence of breast density and possible second opinions. Therefore, breast MRI has emerged as the most sensitive modality for detecting breast cancer and has been integrated in the surveillance protocols of high-risk women.[9–10] However, because of the use of low-molecular contrast agents, enhancement is not specific and quantitative evaluation is still confidential with MRI (no consensus about acquisition protocols and analysis tools); research on macromolecular agents has been ongoing for many years but without routine implementation at this time. Recently, dedicated breast computed tomography (CT) with low doses has been tested with interesting preliminary results and will probably re-emphasize perfusion CT, a robust method to quantify precisely tumour flow parameters (response evaluation under treatment).[8,11] Because cancers are usually stiffer than benign lesions, elastography has been studied since the 1980s and is now available in real-time with standard US (semi-quantitative and quantitative approaches) and MRI and demonstrated a significant gain in specificity.[12–13] Other functional imaging possibilities rely on the analysis of tumour cell replication and metabolism (Sestamibi with SPECT, choline components with MR-spectroscopy, diffusion MRI, glucose metabolism with FDG PET).[13–15] If there is a significant gain in specificity compared to angiogenesis imaging, the limited spatial resolution of all these technologies does not allow detection or characterisation of small lesions (under 8 mm) but are very useful, in cancers not candidates for breast-conserving surgery, to evaluate response to systemic treatments early after their initiation (one cycle of neo-adjuvant chemotherapy) and before detection of morphological changes. Technical improvements are ongoing for MRI with the introduction of higher magnetic

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fields (3 Tesla, 7 Tesla) and in nuclear medicine with dedicated breast imaging units (SPECT and PEM for positron emission mammography) providing a higher signal-to-noise ratio and spatial resolution compatible with screening objectives. Molecular imaging of breast cancer will be the next great advance for imaging mainly based on targeted contrast agents using hybrid imaging technology for detection (functional data) and localisation (anatomical data). [16–17] For example, for imaging tumour angiogenesis, specific contrast agents under evaluation target the VEGF receptor 2, the αvβ3 integrin, or the matrix metalloproteinases. [8] Other potential targets concern tumour variables such as proliferation, hypoxia, gene, and enzymatic or protein expression. These future advancements in molecular imaging capabilities should improve our ability to detect, diagnose, stage, select appropriate treatments, monitor the effectiveness of a targeted treatment and determine prognosis. It is interesting to emphasize the little difference between the molecular imaging and the molecular therapy of human cancer: if a contrast agent or radiotracer can be targeted to living cancer cells, then a cytotoxic agent can be targeted as well. This synergy between imaging and treatment is fundamental; molecular imaging could potentially shorten the time line for drug approval and lessen costs because of its availability to measure drug effects in the body.

Conflict of interest statement

None declared.

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