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Breast Imaging in High Risk Populations

Recent evidence suggests that contrast-enhanced breast MRI is becoming an established technique that offers good quality in safety, performance and patient outcomes. In this article, Prof. Francesco Sardanelli, a frequently invited speaker and educator on this topic at international meetings, writes about the growing effectiveness of breast MRI, the special attention that must be paid to high-risk patient groups, and the need for radiologists to interact with other relevant medical professionals in an interdisciplinary paradigm.

Breast Cancer: The Case for High-Risk Patients

Breast cancer affects from 1:7 up to 1:11 women in western countries. Although this disease is mainly a sporadic one, about 15 percent of cases are clustered in families with highly or moderately elevated incidence. Pathogenic mutations in high-risk genes at autosomic dominant inheritance are held responsible for about 5 percent of cases, in which the disease may have early onset, with an estimated cumulative lifetime risk as high as 50 – 85 percent. About 50 percent of hereditary breast cancers can be explained by mutations in BRCA1 and BRCA2 genes.

In women at high risk of developing breast cancer, screening mammography has shown a lower sensitivity (29–50 percent) compared with that of screening of the general female population (70–80 percent), with higher percentages of interval cancers (35–50 percent versus 20-25 percent) and a higher rate of nodal involvement (20 - 56 percent versus 22 percent). In the last decade, a number of prospective, non-randomised studies have been conducted in Europe and North America to assess the value of dynamic contrast- enhanced MRI as a screening tool to be used as an adjunct to mammography, or to mammography plus ultrasonography, for the surveillance of women at high genetic- familiar risk of breast cancer. The general result of these studies is that MRI largely outperforms mammography and/or ultrasound in detecting breast cancers in asymptomatic high-risk women, as confirmed by reviews and meta-analyses.

Evidence Points to MRI as a Screening Tool in High-Risk Women

In 2007, on the basis of the early evidence available in the literature, the American Cancer Society issued a recommendation in favour of screening with MRI as an adjunct to mammography for high-risk women, a group defined as follows: women with an approximately 20 - 25 percent or greater lifetime breast cancer risk, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin's disease between eight and 30 years of age with mantle radiation therapy.

Despite the general agreement on the use of MRI as a screening tool in high-risk women, breast cancer specialists face three problems:

1. How to model the risk of breast cancer for an individual woman? Software is freely available, also from certain websites, such as that derived from the Tyrer-Cuzick model (http://www.ems-trials.org/riskevaluator). However, all the models show relevant limitations. Better performance is expected with the inclusion of breast density (from mammography, or better, from MRI) as a parameter in risk modeling.
2. Which level of risk justifies an annual MRI? A cost-effectiveness analysis agrees on MRI screening for highrisk women, but further research is needed to clarify what to do for lower risk levels.
3. Do we still need mammography and ultrasound if screening MRI is negative? Evidence in favour of screening high-risk women with MRI alone comes from two recent studies from Germany and Italy, which demonstrate no significant added value from mammography and/or ultrasound when MRI is used as a screening tool.

The choice to reduce the use of mammography in BRCA mutation carriers is corroborated by the higher risk of breast cancer induction from x-ray radiation. Moreover, a word of caution is needed for triple negative cancers, defined by lack of oestrogen and progesterone receptor expression and absence of HER2 amplification, as there is a potential for false negatives also in MRI screening, especially in BRCA1 mutation carriers.

Development of Contrast-Enhanced Breast MRI

Contrast enhancement on breast MRI offers another avenue of diagnosis in the case of breast cancer imaging. The first analysis of breast tissues was closely connected to the origins of medical use of nuclear magnetic resonance (NMR), since Damadian's experiments during the 1970's. However, the first clinical studies using standard T1-, proton density-, and T2- weighted sequences were disappointing. A dramatic change came about in 1986, when S.H. Heywang firstly obtained contrast-enhanced (CE) MR images after intravenous administration of gadopentetate dimeglumine (Gd-DTPA). The availability of faster T1- weighted gradient-echo sequences allowed for dynamic imaging, permitting the combination of morphologic and dynamic parameters, the latter studied by W.A. Kaiser and finally classified by C.K. Kuhl in 1999.

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Two methods for breast MRI followed, on either side of the Atlantic ocean: dynamic CE imaging with temporal resolution in Europe and fat-saturated high-resolution CE imaging in the US, now partially unified by protocols which permit high spatial resolution and sufficient temporal resolution with or without fat-saturation. on the other hand, clinical research studies on 1-H (proton) MR spectroscopy using single-voxel technique were performed looking for the choline peak as a marker of malignancy, while during the nineties, MR-guided breast needle biopsy became available, finally filling a fundamental gap in clinical practice. Afterwards, especially in the last decade, technical developments such as strong and rapid field gradients, multichannel dedicated coils and parallel imaging, high-field magnets (3T), new dedicated sequences, including those for diffusion-weighted imaging or 2D/3D multi-voxel proton MRS, made breast MRI technology more and more robust and attractive in terms of multiple options offered to clinicians and researchers.

Diagnostic Performance of Breast MRI

Notwithstanding the growing evidence for the increasing diagnostic performance of breast MRI, including high sensitivity not only for invasive but also in situ cancers, there propounds a long-standing false idea, frequently repeated also by breast radiologists, that has unfortunately acted against its clinical adoption: that breast MRI as a diagnostic tool has high sensitivity but low specificity, a “mantra” to be abandoned, as recently remarked by W. A Kaiser.

In 2008, the large meta-analysis by Peters et al. finally offered a reference point for this discussion, demonstrating 90 percent sensitivity and 72 percent specificity, even though the diagnostic performance of each test depends on many factors, including the clinical setting and patient selection. Last but not least, new contrast materials with a higher diagnostic performance are now entering breast MRI with promising results in terms of higher diagnostic performance.

A large debate among breast cancer specialists is open on the indications for breast MRI. Some indications are largely accepted: high-risk screening, carcinoma unknown primary, breast implant integrity evaluation, and evaluation of the effect of neoadjuvant chemotherapy. other indications, especially preoperative MRI, are under discussion. As radiologists, we should be more and more able to interact for clinical use of breast MRI with surgeons, oncologists, radiation therapy specialists, and other colleagues, in the European perspective of the breast unit. While future directions are already proposed in terms of technical developments, such as diffusion tensor imaging or MRI-PET fusion, a new change of paradigm is around the corner: breast MRI, from diagnosis to prognosis.

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