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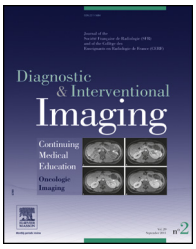

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Correlation between MR imaging — prognosis factors and molecular classification of breast cancers

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Abstract The molecular classification of breast cancers defines subgroups of cancer with different prognoses and treatments. Each molecular type representing the intrinsic signature of the cancer corresponds to a histological profile incorporating hormone receptors, HER2 status and the proliferation index. This article describes the correlations between this molecular classification obtained in routine clinical practice using histological parameters and MRI. It shows that there is a specific MRI profile for triple-negative cancers: distinct demarcation, regular edges, hyperintensity on T2 weighted signals and, particularly, a crown enhancement. It is important for the radiologist to understand this molecular classification, firstly because of the relatively suggestive appearance of triple-negative basal-like cancers in the molecular classification, secondly, and particularly, as cancers in patients with the BRCA1 mutation are often triple-negative meaning that the criteria for reading the MRI needs to be tailored to this feature of the cancers, and finally because the efficacy of MRI in assessing response to neoadjuvant chemotherapy depends on the molecular class of cancer treated.

MRI plays an essential role in the local staging assessment of breast cancer, enabling a better evaluation of tumor size, revealing multifocal or multicenter lesions or demonstrating a contralateral lesion, which is found on MRI in 3 to 4% of patients [1]. In addition to this impact on treatment, MRI is of prognostic use: it is helpful in predicting early effectiveness of neoadjuvant chemotherapy, which has been shown in a recently published multicenter trial [2] and more generally it independently predicts relapse-free

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survival in patients with breast cancer [3]. Identification of prognostic factors is an essential decision-making factor in the treatment of breast cancers. In addition to the main morphological prognostic factors such as tumor size and the presence of lymph nodes, the treatment of breast cancers in based on a number of classical histological factors, which determine different prognoses and management. These ''classical'' histological factors are histological grade, the Ki67 proliferation index, estrogen (ER) and progesterone (PR) hormone receptors and HER2 status.

In addition to these classical histological features the molecular abnormalities of breast cancers, which can be examined by genomic tests are also included. Whilst these genomic tests based on analysis of the expression of analysis of RNA and DNA have limited applications in routine clinical practice at present in France, specific correlations exist between the histological profile (incorporating hormone receptors, HER2 status and the proliferation index) and the different molecular types of breast carcinomas representing their intrinsic signature and classified as luminal A, luminal B, HER2-like, basal-like and more recently, apocrine type [4—6].

The aim of this article is to describe the correlations between MRI and histology of infiltrating carcinomas according to the different conventional histological prognostic factors and then to describe the correlations between MRI and the different molecular types of infiltrating carcinoma. Finally, in a third section we will emphasize the practical impact of the radiologist's involvement in this molecular classification through two specific situations: diagnosis in a patient with a mutation and monitoring neoadjuvant chemotherapy.

Correlations between MRI and classical histological prognostic factors

The factors studied are grade Ki67 proliferation index, hormone receptors and HER2 status.

Tumor grade

This is based on three histological, morphological features: tumor architecture with cell differentiation, the shape and size of the nucleus and the number of cells in division or exhibiting mitotic activity.

Classically, grade 1 tumors develop slowly with a large stromal reaction whereas grade 3 tumors are hypercellular with little stromal reaction and grade 2 tumors have an intermediary appearance, which is more similar to that of grade 1 tumors. All publications describe this appearance on MRI with spiculated outlines (Fig. 1) in grade 1 cancers [7]. This is not reported absolutely consistently in all series [8] for several reasons: tumor polymorphism, the fact that the small number of patients included in the different series do not always allow a statistically significant difference to be identified, and the conditions under which MRI is performed, as irregular or spiculated outlines can be more easily seen on high resolution matrix investigations (Fig. 2) on thin sections. Finally, the conditions under which the MRI is read and interpreted have a bearing as thicker sections and blurring due to subtraction may mask thin spicules seen on non-subtracted thin sections. The crown enhancement is also a classical sign of a rapidly growing tumor associated with a high histological grade (Fig. 3). This enhancement may be due to extensive angiogenesis in the periphery of

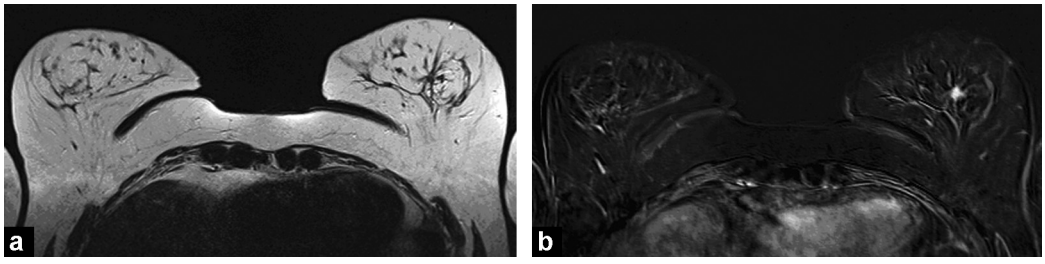

Figure 1. A 61-year-old patient with grade 1 infiltrating, ductal carcinoma of the left breast, Ki67 = 10%: a: axial section, T2 weighted image, architectural distortion in a small spiculated left infero-medial mass; b: axial section, subtraction at 3 minutes, homogeneous irregular mass enhancement with a partly spiculated irregular outlines.

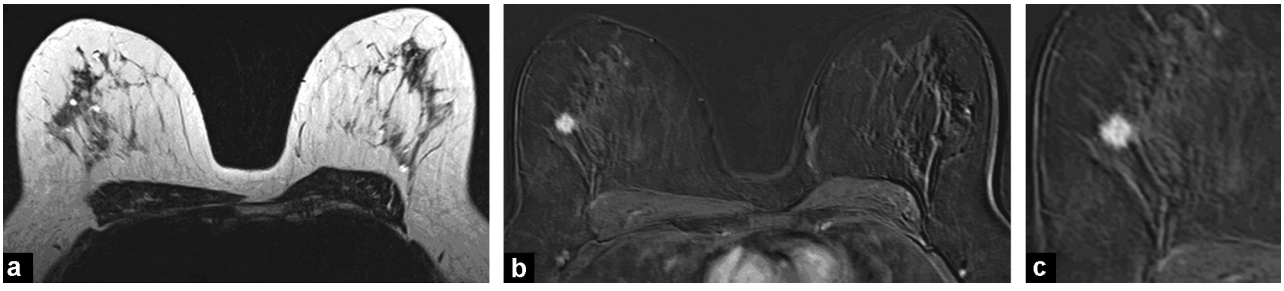

Figure 2. A 55-year-old patient with grade 3 infiltrating ductal carcinoma of the right breast, Ki67 = 50%: a: axial section, T2 weighted image, small difficult to see supero-external mass; b: axial section, subtraction at 3 minutes, small homogeneous round mass enhancement; c: enhancement at 3 minutes in thin sections providing a better view of the irregular outlines.