Advanced Imaging for Precision Medicine in Breast Cancer: From Morphology to Function

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Breast cancer is the most common cancer in women, the 2nd leading cause of female cancer deaths and thus remains a major medical and socio-economic burden. Medical imaging has always been an integral part in breast cancer care ranging from diagnosis and staging to therapy monitoring and post-therapeutic follow-up [1–5]. Screening mammography has significantly contributed to the detection of breast cancer especially at an early, prognostically favorable stage and mammography has been demonstrated to reduce breast cancer mortality [6–9]. Mammography is relatively inexpensive and widely available. However, its sensitivity is limited, ranging from 70 to 85% [10–12] overall but is significantly reduced to 30–50% in women with dense breasts, which can be attributed to the ‘masking effect’ of dense breast tissue. This effect is due to overlap with normal breast tissue thus obscuring breast lesions and is most pronounced in extremely dense breast parenchyma [13, 14]. Supplemental imaging examinations to overcome the limitation in sensitivity traditionally includes screening ultrasound, and combined mammography and ultrasound can improve sensitivities for breast cancer detection to 91% [10, 15].

Recently, digital breast tomosynthesis (DBT) has been introduced. DBT is an imaging technique that in contrast to mammography allows the 3-dimensional (3D) evaluation through the volumetric reconstruction of the whole breast from a finite number of low-dose 2D projections obtained by different X-ray tube angles. Thereby DBT minimizes the effect of overlapping breast tissue and significantly improves lesion detection. Several studies have consistently shown that DBT detects up to 50% more cancers and it can be expected that DBT will eventually replace mammography in breast imaging and screening [16–27].

Although DBT and ultrasound can increase cancer detection, there are still limitations in breast cancer detection, prognosis, and prediction. Medical research has entered the genomic era, aiming to devise precise cancer therapies targeting the underlying oncogenic mechanisms. Genetic profiling has revolutionized breast cancer classifications, with molecular tumor subtypes being unevenly

distributed among women with breast cancer [28–30]. Molecular subtypes are not only associated with different tumor phenotypes but also with distinct variations in response to therapy and patient survival. Accordingly, subtype-based recommendations for systemic therapies have now been implemented in clinical practice [28–31]. To match advanced therapeutic strategies in the era of precision medicine, diagnostic tests must be equally multilayered and complex to identify the underlying functional processes of cancer development and progression.

However, with conventional imaging methods such as mammography, DBT, and sonography, which are qualitative tests that detect morphologic, non-specific tissue changes, the assessment and comprehension of breast cancer in all its diversity is not possible. To overcome these limitations, functional imaging techniques to improve breast cancer diagnosis have been explored. In this context, magnetic resonance imaging (MRI) has emerged as an exceptionally powerful, versatile, and precise imaging technique. MRI is an essential non-invasive technique in breast imaging with multiple established indications, such as pre-operative staging of breast cancer, evaluation of therapy response in patients receiving neoadjuvant treatment, differentiation between scar tissue and tumor recurrence, examination of patients with breast implants, and screening of high-risk patients [1, 5]. Dynamic contrast-enhanced MRI of the breast provides both high-resolution morphologic and functional quantitative information on neovascularity as a tumor-specific feature [32–35]. MRI is the most sensitive exam for the detection of breast cancer in women at any given risk [32–36] and often detects cancers that are occult in mammography, DBT and sonography [37, 38]. Due to these excellent results specific screening programs for high-risk women that include both annual mammography and MRI have been developed [32, 39] and there is discussion about screening of women at average of risk cancer with abbreviated MRI protocols [40–42]. In addition to breast cancer detection there is evidence that quantitative dynamic contrast enhanced (DCE)-MRI models are useful in the assessment and prediction of

response to neo-adjuvant chemotherapy (NAC) [43, 44]. However, despite these excellent results for breast cancer detection and prediction of treatment response, MRI may not be an option for every woman, due to either lacking availability or contra-indications to MRI, such as metallic implants, allergic reactions to MRI contrast agents, or severe claustrophobia.

Contrast enhanced digital mammography (CEDM) is a novel mammography technology which, similar to MRI, is based on the principle of imaging neovascularity. CEDM uses intravenous iodinated contrast medium to detect breast cancer on a digital mammography platform. Compared to MRI, CEDM is relatively inexpensive and potentially more accessible to women. Several studies in the diagnostic setting have demonstrated that CEDM is significantly more sensitive and specific than mammography alone in women with abnormal screening mammograms, ultrasound, clinical symptoms, and known cancer. Early studies have even demonstrated that the performance of CEDM is superior to that of mammography alone in the diagnostic setting, especially in women with dense breast tissue [45] and comparable to the performance of MRI in women with known cancers [46–50].

The current issue of *BREAST CARE* with focus on ‘Imaging in Breast Cancer’ will provide a comprehensive summary of the re-

cent advances and current possibilities in clinical breast imaging. The added value of DBT to mammography in BI-RADS assessment and follow-up management is investigated by Galati et al. [51]. Knogler et al. [52] present results on CEDM for breast lesion detection, characterization and comparison to DCE-MRI. The potential of DCE-MRI including quantitative pharmacokinetic modeling for the assessment and prediction of response to neo-adjuvant chemotherapy in breast cancer overall (Dietzel et al. [53]) and with a special focus on inflammatory breast cancer (van Uden et al. [54]) is discussed. In addition, Clauser et al. [55] provide data on the usefulness of short-term imaging follow-up in patients with BIRADS 3 and 4a lesions and the benign histopathologic diagnosis of a fibroadenoma at image-guided biopsy.

The field of breast imaging has moved beyond morphology towards function and is a still evolving. More significant advances are expected, which will further aid the development of novel approaches for precision medicine in breast cancer.

Disclosure Statement

The author has nothing to disclose.

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