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### ACCEPTED MANUSCRIPT

#### Inflammatory breast cancer- importance of breast imaging

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Inflammatory breast cancer (IBC) is a rare form of primary cancer and accounts for only 1-5 % of all breast cancer types.[1–3] It is classified as T4d stage by TNM classification,[4] the most aggressive form of breast cancer with a 20%–30% incidence of distant metastasis at the time of diagnosis[5] and poorer prognosis than the non-IBC locally advanced breast cancers. [6–8]

IBC diagnosis is traditionally based on clinical criteria, including rapid onset of breast erythema, oedema involving at least one third of the breast and "peau d'orange" appearances of the skin, with or without a palpable breast lump, combined with a histopathological confirmation of an invasive breast carcinoma.[9,10] Although there are no established data to support specific radiological findings with IBC, imaging plays a core role in diagnosis, staging and management of the disease. Full field digital mammography (FFDM), highresolution ultrasonography (US) and magnetic resonance imaging (MRI) are key modalities for an optimal initial investigation, identifying the extent of the breast cancer and facilitating an imaging- guided core biopsy to establish histopathology diagnosis. Imaging is also to helpful to differentiate other breast pathologies which may mimic IBC, such as inflammatory breast conditions or other locally advanced tumours. Initial imaging is also important in order to define the locoregional staging, the nodal status of the disease and the presence of contralateral breast pathology. Positron emission tomography (PET/CT), Computed Tomography (CT) and whole-body scintigraphy can also help in oncological, surgical and radiotherapy planning by identifying distant metastatic disease and detecting regional and distant nodal involvement. Furthermore, imaging has an important role in monitoring and evaluation of response to primary systemic chemotherapy, which is currently the first line of treatment [7]in IBC and in surveillance/ follow up patients following modified mastectomy and radiotherapy. [11]

#### Initial diagnosis – local staging:

**Mammography:** Mammography remains the first modality of choice to assess the breast parenchyma in suspected IBC. Bilateral mammography is always recommended, not only because of the easier detection of subtle changes when comparing with the contralateral breast but also to assess the non- affected breast for a possible pathology. The advances in imaging with the use of full field digital mammography has enabled us to identify imaging features which are highly suggestive of IBC more easily than with conventional film screen mammography.[12]

Skin thickening, predominantly seen in the inferior areolar region on initial stages,[13] stromal coarsening or trabecular thickening and diffuse increase of parenchymal density/ diffuse asymmetry comprise the main mammographic findings of IBC[13,14]. Intramammary mass, architectural distortion, focal asymmetric density and micro calcification are less commonly seen in the mammography, with a percentage varying among studies, ranging between 10 - 80 %.[13,15] The presence of diffuse dense background parenchyma due to oedema can obscure an intramammary lesion and result in an underestimation of the extent of disease, making the FFDM the least sensitive modality of choice for locoregional staging.[15] A linear relationship has also been reported between increased background breast parenchyma density (BIRADS 3-4) and IBC, which also contributes in difficulties detecting a focal breast lesion. [15]

Another important finding that mammography can provide is the presence or not of contralateral breast pathology. Published data have shown that there is an increased risk of developing contralateral breast cancer in cases with IBC, with incidence ranging between 0.9 - 5 %, [12,16,17]hence initial local staging for multifocality and multicentricity is crucial. This is best achieved with a contrast enhanced MRI scan which is considered to be the most sensitive modality of choice for locoregional staging.

Almost half of the cases will have mammographic evidence of nipple inversion, which is in keeping with the frequency of this finding on clinical presentation[12,13] and examination. Axillary lymphadenopathy may also

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