

# Critical imaging analysis of suspicious non-palpable breast lesions

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<http://dx.doi.org/10.1590/1806-9282.66.12.1610>

Breast cancer remains the most common malignancy in the female population worldwide, with an incidence estimated at 2,088,849 new cases for 2018. It is also the most common cause of cancer death in women, with a mortality estimated at 626,679 cases for 2018<sup>1,2</sup>. In Brasil, a developing country, breast cancer is still frequently diagnosed in advanced stages, most prevalent in postmenopausal women and associated with high mortality<sup>3-5</sup>. In contrast, around one-third of cases are diagnosed as non-palpable lesions. Early clinically nonpalpable breast cancer has a unique natural history and biology, in comparison to symptomatic breast cancer, with implications in the treatment and prognosis of these patients, and increased detection is related to the introduction of screening programs and the use of diagnostic imaging methods<sup>6</sup>. Mammography (MMG), ultrasonography (US), and magnetic resonance imaging (MRI) are the most widely used and available imaging methods in our setting, despite the application of other methods and new technologies in the last few years<sup>7</sup>.

Screening programs using MMG seem to result in a general decline in breast cancer mortality and recommendations that women over the age of 40 should undergo annual screening mammography have led to an increasing number of diagnoses of non-palpable breast lesions<sup>8</sup>. The first sign of non-palpable breast

cancer may be calcifications, and MMG is currently the best modality to detect microcalcifications. Furthermore, breast cancer cases that are manifested as focal asymmetric densities, also evaluated by this method, tend to be non-palpable lesions. On the other hand, excessive diagnosis of architectural distortions (distortions of the breast parenchyma without a defined mass) leads to lower mammographic specificity<sup>9,10</sup>. It is important to consolidate and disseminate screening programs, still deficient in underdeveloped and developing countries, technical improvements, and adequate training of radiologists to recognize the imaging characteristics and behavior of these lesions so that MMG can be used in the diagnosis<sup>7</sup>.

US is another safe and available diagnostic modality, with potential precision.

It may be used in interventional procedures and is well-tolerated by patients<sup>8,11</sup>. Some authors have shown that there is not a high level of evidence to suggest the benefit of US as a supplemental screening modality, and further studies are needed. However, it is well-established that US is considered a complementary diagnostic method to MMG for the detection of non-palpable breast lesions, improving the specificity and increasing cancer detection rates, particularly in cases of asymptomatic women with dense breast tissue<sup>8</sup>. Although ultrasound screening

DATE OF SUBMISSION: 24-Aug-2020  
DATE OF ACCEPTANCE: 27-Aug-2020  
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may also increase false-positive diagnosis, added to a screening program it may improve cancer detection rates in patients with non-palpable lesions and dense breast tissue. In addition to its use in the identification of non-palpable lesions, US is also fundamental for locating suspicious preoperative lesions, allowing the localization and removal of these lesions with a higher safety margin and lower number of complications<sup>11,12</sup>.

MRI is another diagnostic modality for the detection of invasive breast cancers that are mammographically and clinically occult. It has a high sensitivity (94-100%) and low specificity (37-97%) rate for cancer detection. MRI is recommended only in high-risk populations, as a supplemental screening test<sup>13</sup>. Studies have shown that MRI identified the disease at an earlier stage than MMG and MRI combined with MMG is associated with higher survival rates, including non-palpable lesions. However, it is worth mentioning that the literature on breast-cancer screening with MRI is focused on high-risk women, in whom there is a higher prevalence of cancer and lower sensitivity to mammography<sup>13,14</sup>. Risk factors include genetic mutations, family history, and personal risk history. The Tyrer-Cuzick model (International Breast Cancer Intervention Study, or IBIS) is considered the most widely and frequently used model to determine whether an MRI of the breast should be done. The limiting factor in the use of MRI to trace non-palpable lesions is its high cost, low availability in several locations, and the need for contrast medium, along with insufficient data to recommend its use for screening patients with dense breast tissues, without other factors. Therefore, according to the ACR (Appropriateness Criteria) and the American Cancer Society (ACS), it is currently determined that MRI as adjuvant screening should be used only in women at high risk for breast cancer<sup>14,15</sup>.

Regarding new imaging modalities, digital breast tomosynthesis has been popularized as an “improved mammography” and is a valuable resource in

screening for breast cancer. Its capacity to reduce the juxtaposition of breast tissue has reduced recall rates and increased the number of cancers detected, particularly in patients younger than 50 years. Nevertheless, some cancers are not detected by tomosynthesis, since it remains a modality of anatomical study, that does not add physiological information which can be furnished by contrast-enhanced imaging modalities, such as MRI<sup>16</sup>. Nuclear medicine methods use gamma cameras to obtain images of the physiologic uptake of a radio drug in the breast, typically Tc <sup>99m</sup> sestamibi, and showed a capacity to detect occult tumors, as small as 2 mm, by MMG in screening programs, particularly in women with dense breasts. However, there is a discussion on the clinical relevance of this additional detection in reducing mortality and concern over the use of ionizing radiation<sup>17</sup>. Intravenous iodinated contrast-enhanced digital MMG demonstrated a significant increase in sensitivity for breast cancer detection in comparison to standard digital MMG in studies by Sorin et al.<sup>18</sup>. Furthermore, the use of automated breast US (ABUS) was approved in the United States in 2018. A retrospective study showed that breast cancer detection and agreement between readers were significantly increased in dense breasts when US was combined with MMG in comparison to the use of MMG alone<sup>19</sup>.

In conclusion, we highlight the importance of imaging modalities in screening programs for the diagnosis of non-palpable breast lesions. MMG, due to its features described, is the main method. Despite not being the only method, MMG requires complementary tests in some situations, particularly in patients with dense breasts. US, due to its broad availability and low cost, is a good option as a complementary method. Screening programs with patients stratified into groups with similar characteristics such as breast density, age, and risk factors for breast cancer could facilitate access to methods such as MRI and tomosynthesis in developing countries.

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