Recommendations of Colégio Brasileiro de Radiologia e Diagnóstico por Imagem, Sociedade Brasileira de Mastologia, and Federação Brasileira dasAssociações de Ginecologia e Obstetrícia for imaging screening for breast cancer*

Recommendações do Colégio Brasileiro de Radiologia e Diagnóstico por Imagem, da Sociedade Brasileira de Mastologia e da Federação Brasileira das Associações de Ginecologia e Obstetrícia para rastreamento do câncer de mama por métodos de imagem


INTRODUCTION

The need for consensus in Brazil

Breast cancer is the most frequent type of cancer and main cause of cancer deaths among women in Brazil and worldwide. On the other hand, this is the tumor whose screening has demonstrated the greatest impact on mortality reduction. Just in United States of America, there was a 30% decrease in breast cancer mortality rates since 1990 when programs of mammographic screening started being implemented[1]. In Europe, some countries such as Sweden recorded 36% decrease in mortality as compared with the pre-screening period, while other countries, such as Norway, demonstrated 10% decrease in mortality connected with only the screening[2,3].

In Brazil, there is no population screening policy; only opportunistic screening is undertaken. Thus, it is essential to encourage actions towards standardization of breast cancer screening, bringing information to the population about its relevance.

With a view on this subject, Colégio Brasileiro de Radiologia e Diagnóstico por Imagem (CBR) (Brazilian College of Radiology and Imaging Diagnosis), Sociedade Brasileira de Mastologia (SBM) (Brazilian Society of Mastology), and Federação Brasileira das Associações de Ginecologia e Obstetrícia (FEBRASGO) (Brazilian Federation of Gynecology and Obstetrics Associations), through the National Commission on Mammography, present their recommendations for breast cancer imaging screening in Brazil.

Current status of breast cancer in Brazil and worldwide

The global breast cancer incidence is progressively increasing both in developed and developing countries at a yearly rate of 3.1%[4]. From 641,000 cases in 1980 its incidence has grown to 1,643,000 cases in 2010, and was responsible for 27% of new cases of cancer diagnosed in women[4]. Out of this total, about 2/3 of cases have occurred in women aged above 50, particularly in developed countries. On the other hand, in women aged under 50 (between 15 and 49 years), breast cancer incidence was two-fold higher in developing countries than in developed countries[4].

In Brazil, 52,680 new cases of breast cancer are expected to occur in 2012, with an estimated risk of 52 cases per 100,000 women. Such a risk presents a great variation according to the region in the country, as follows: in the Southeastern region, it corresponds to 69/100,000; in the Southern region, 65/100,000; in the Center-Western region, 48/100,000; in the Northeastern region, 32/100,000; and in the Northern region, 19/100,000 women[5]. Differences in relation to age range are also observed, with a specific rate of four cases per 100,000 women between 40 and 49 years, and five cases per 100,000 women aged above 50[5]. In a study developed in the city of Goiânia, 15% of the tumors were observed in women aged under 40, 27% between 41 and 50 years, and 57% above 50[6]. That is to say, more than 40% of cases of breast cancer occurred in patients aged under 50.
On the other hand, the breast cancer mortality rate is quite different among developed and developing countries worldwide. In developed countries, there was a significant mortality reduction over the last years, while stability or even a continuous increase has been observed in developing countries. Such a disparity might be attributed to differences in early-detection policies, as well as to the difficulty to access appropriate treatment in poorer countries\(^{(4,5,7)}\).

Working method and revision preview

Available scientific studies were reviewed and data were compiled in order to present the recommendations according to age range. In the absence of evidentiary data, the recommendations reflected the consensus of the Commission comprised by specialists representing the three entities. The recommendations were classified into four categories according to the degree of scientific evidence and consensus between specialists, as follows:

**Category 1** – Recommendation based on strong scientific evidences, with a uniform consensus between CBR, SBM and FEBRASGO on a vigorous support to such recommendation.

**Category 2a** – Recommendation based on reasonable scientific evidences, with a uniform consensus between CBR, SBM and FEBRASGO, with a vigorous support to such recommendation.

**Category 2b** – Recommendation based on few scientific evidences, but with a consensus between CBR, SBM and FEBRASGO on a vigorous support to such recommendation.

**Category 3** – Recommendation consensually supported by CBR, SBM and FEBRASGO specialists.

The present recommendations should be revised every three years.

**RECOMMENDATIONS FOR BREAST CANCER SCREENING**

**Women aged under 40**

**MAMMOGRAPHY** – Generally, at this age range mammography is not recommended, except on an individual basis for women at high risk for breast cancer, as shown on Table 1.

**ULTRASONOGRAPHY** – At this age range, sonographic screening is not recommended, except on an individual basis for women at high risk for breast cancer in whom screening by magnetic resonance imaging might be appropriate but, for any reason, cannot be performed.

**MAGNETIC RESONANCE IMAGING** – At this age range, breast MRI screening is not recommended, except on an individual basis for women at high risk for breast cancer, as shown on Table 2.

**Women aged between 40 and 69**

**MAMMOGRAPHY** – At this age range, mammography is recommended for all women with annual periodicity.

**ULTRASONOGRAPHY** – Generally, at this age range, sonographic screening is not recommended, except on an individual basis for women in the situations described on Table 3.

**MAGNETIC RESONANCE IMAGING** – Generally, at this age range, MRI

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**Table 1** Recommendations for mammographic screening for high-risk women aged under 40.

<table>
<thead>
<tr>
<th>Category</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1</td>
<td>Women with genetic mutation (BRCA1 or BRCA2) or with first-degree relatives with proved mutation: Starting at 30 years of age (but not before the age of 25)</td>
</tr>
<tr>
<td>Category 1</td>
<td>Women at lifetime risk of ≥ 20%, according to one of the mathematical models based on the patient’s family history: Starting at the age of 30, or 10 years before the age of diagnosis of the youngest relative affected by the disease (but not before the age of 25)</td>
</tr>
<tr>
<td>Category 2a</td>
<td>Women with previous history of chest irradiation between 10 and 30 years of age: Starting 8 years after the radiotherapy treatment (but not before the age of 25)</td>
</tr>
<tr>
<td>Category 2b</td>
<td>Women with Li-Fraumeni or Cowden syndrome, or family history (1st degree relatives) of such syndromes: Starting at the time of the diagnosis (but not before the age of 25)</td>
</tr>
<tr>
<td>Category 3</td>
<td>Women with personal history of lobular neoplasia (ALH and ISLC), ADH, ISDC, invasive breast cancer or invasive ovarian cancer: Starting at the time of the diagnosis (but not before the age of 25)</td>
</tr>
</tbody>
</table>

ALH, atypical lobular hyperplasia; ISLC, in situ lobular carcinoma; ADH, atypical ductal hyperplasia; ISDC, in situ ductal carcinoma.

**Table 2** Recommendations for screening with magnetic resonance imaging for high-risk women aged under 40.

<table>
<thead>
<tr>
<th>Category</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1</td>
<td>Women with genetic mutation (BRCA1 or BRCA2) or with first-degree relatives with proved mutation: Annually, starting upon confirmation of the genetic mutation (but not before the age of 30)</td>
</tr>
<tr>
<td>Category 1</td>
<td>Women at lifetime risk of ≥ 20%, according to one of the mathematical models based on the patient’s family history: Annually upon risk calculation or 10 years before the age of diagnosis of the youngest relative (but not before the age of 30)</td>
</tr>
<tr>
<td>Category 2b</td>
<td>Women with previous history of chest irradiation between 10 and 30 years of age: Annually, starting 8 years after the radiotherapy treatment (but not before the age of 30)</td>
</tr>
<tr>
<td>Category 3</td>
<td>Women with Li-Fraumeni or Cowden syndrome, or family history (1st degree relatives) of such syndromes: Annually, starting at the time of the diagnosis (but not before the age of 30)</td>
</tr>
<tr>
<td>Category 2a</td>
<td>Women with personal history of lobular neoplasia (ALH and ISLC), ADH, ISDC, invasive breast cancer or invasive ovarian cancer: Annually, starting at the time of the diagnosis (but not before the age of 30)</td>
</tr>
<tr>
<td>Category 2a</td>
<td>It may be considered in women with recent diagnosis of breast cancer and with a normal breast at conventional imaging methods and physical examination: Single evaluation of the contralateral breast at the moment of the diagnosis</td>
</tr>
</tbody>
</table>

ALH, atypical lobular hyperplasia; ISLC, in situ lobular carcinoma; ADH, atypical ductal hyperplasia; ISDC, in situ ductal carcinoma.
screening is not recommended, except on an individual basis for women at high risk for breast cancer, as shown on Table 4.

Women aged above 70

MAMMOGRAPHY – At this age range, mammographic screening is recommended on an individual basis, as shown on Table 5.

JUSTIFICATION

Breast cancer screening is aimed at early detection of small, asymptomatic tumors with the primary objective of reducing the mortality by the disease. Secondary objectives of breast cancer screening include increase in patients’ survival and reduction of surgical treatment extent, allowing less mutilating surgeries and reducing the need for chemotherapy(8,9). Mammography is the only screening method that demonstrated to be capable to promote an absolute decrease in mortality rates(10-18). Ultrasonography and magnetic resonance imaging have demonstrated similar capacity to detect early-stage breast cancer, but there is a lack of randomized, prospective studies testing their impact on the mortality reduction(19-21).

The first prospective, controlled and randomized population-based study investigating the mammographic screening impact on breast cancer mortality was developed in the 1960’s in the United States of America and was named Health Insurance Plan (HIP)(22). Such study demonstrated a 25% decrease in breast cancer mortality in a group of women submitted to mammographic screening and stimulated the development of similar studies in Canada, United Kingdom and Sweden. Independent meta-analyses of such population-based studies demonstrated a reduction of 7% to 23% in breast cancer mortality in women submitted to mammographic screening, stimulating the medical societies to recommend the method(23,24). Population-based mammographic screening programs were implemented in some countries and confirmed the findings reported by population-based studies, showing reduction of 16% to 36% in mortality rates(25). Such studies were developed with patients aged between 40 and 70, and the magnitude of the mortality reduction varied according to the patients’ age range.

For the group of patients aged between 50 and 69, all the medical societies in the world recommend the mammographic screening(1,26-28). Meta-analyses of the population-based studies have shown reduction of 20% to 35% in mortality among women at this age range(23,24). Additionally, the adverse effects of mammographic screening are less intense in such women and lower number of them must be screened to avoid breast cancer death. The U.S. Preventive Services Task Force (USPSTF) has estimated that 1,339 women aged between 50 and 59 plus 377 women aged between 60 and 69 must be screened to avoid one breast cancer death(29). Other more recent publication estimated a lower number of screened women to avoid one death: 351 women aged between 50 and 59 plus 233 aged between 60 and 69(30). Thus, CBR, SBM and FEBRASGO recommend mammographic screening for such groups of women, in agreement with the other medical societies.

For women aged under 40 who are not under high risk for breast cancer, no medical organization recommends mammographic screening. In such group the tumor frequency is low (less than one case/1,000 women), mammography is less sensitive, and the breast parenchyma is more radiosensitive(23,31). For patients at high risk for breast cancer, it is recommended the screening strategy be individualized for each patient in consultation with her specialist. The expected benefit should always be weighed against the involved risks, considering that the youth breast is most sensitive to the carcinogenic effects from ra-

| Table 3 | Recommendations for screening with ultrasonography for women aged between 40 and 69. |
|-----------------------------------|---------------------------------|-----------------|---------------|
| It may be considered in high-risk women, particularly those where MRI screening might be appropriate but, for any reason cannot be performed | Individualized | Category 2a |
| It may be considered for women with dense breast tissue, as an adjuvant to mammography | Individualized | Category 2a |

| Table 4 | Recommendations for screening with magnetic resonance imaging for high-risk women aged between 40 and 69. |
|-----------------------------------|---------------------------------|-----------------|---------------|
| Women with genetic mutation (BRCA1 or BRCA2) or with first-degree relatives with proved mutation | Annually, starting upon confirmation of genetic mutation | Category 1 |
| Women at life time risk of ≥ 20%, according to one of the mathematical models based on the patient’s family history | Annually, upon risk calculation | Category 1 |
| Women with previous history of chest irradiation between 10 and 30 years of age | Annually, starting after 8 years of treatment | Category 2b |
| It might be considered for women with personal history of lobular neoplasia (ALH and ISLC), ADH, ISDC, invasive breast cancer or invasive ovarian cancer | Annually starting at the time of the diagnosis | Category 2b |
| It might be considered in women with recent diagnosis of breast cancer and with a normal breast at conventional imaging methods and physical examination | Single evaluation of the contralateral breast at the moment of the diagnosis | Category 2b |

ALH, atypical lobular hyperplasia; ISLC, in situ lobular carcinoma; ADH, atypical ductal hyperplasia; ISDC, in situ ductal carcinoma.

| Table 5 | Recommendations for mammographic screening of women aged above 70. |
|-----------------------------------|-----------------|---------------|
| Women with life expectancy > 7 years, with basis on comorbidities | Annually | Category 2b |
| Women who can be submitted to invasive diagnostic investigation and treatment after abnormal result of screening | Annually | Category 2b |
Major debate occurs in relation to mammographic screening in women aged between 40 and 49. In this group, the breast cancer incidence is smaller and the frequency of dense breasts and fast-growing tumors is higher. Thus, according to the USPSTF estimates, the number of screened tumors is higher. Thus, according to the frequency of dense breasts and fast-growing cancer incidence is smaller and the frequency of tumors is higher at such age range. Feigl et al. have estimated that nearly 20% of breast cancer deaths and 34% of life expectancy years lost because of breast cancer occurred in women aged under 50. In a meta-analysis published about the mammographic screening benefits between 40 and 49 years reported by randomized trials initiated in the period from 1963 to 1982, Smart et al. found a 23% decrease in mortality rates. Such authors have suggested that the modern mammography benefits must be greater, also because the screening intervals were excessively longer in those studies (18 to 28 months), utilizing only one mammographic view and without utilization of the novel technologies. Such authors have also emphasized that the more delayed demonstrations of the mortality reduction could be attributed to several reasons, among them the lower number of women at this age range included in their study (less than 1/3 of the total of women included in the mentioned eight trials). In other recent publication focused on this age range, Hellquist et al. have demonstrated 26% to 29% reduction in mortality as compared with the patients who did not undergo screening in Sweden. In Brazil, there is Law signed in 2010 guaranteeing Access to mammography for all women aged above 40. Additionally, a Brazilian study developed in Goiânia has shown that about 42% of breast cancer cases recorded in the city occurred in patients aged under 49. Thus, CBR, SBM and FEBRASGO, in agreement with the main medical societies, recommend mammography for women at this age range. Studies estimating the potential benefit of screening suggest that, if all the women aged 40 and over were submitted to mammographic screening, the breast cancer mortality rate could drop by about 50%. For women aged 70 and over, particularly above 75, the available data still remain scarce. Breast cancer is one of the main causes of death among women aged above 75, but some facts suggest that the mammographic screening benefit might be smaller at this age range, namely, lower life expectancy, higher frequency of tumors with good prognosis and higher risk for death caused by other diseases. Thus, it is suggested that the decision about the screening continuity should be individually made, taking the patient’s general health conditions and estimated life expectancy into consideration. As far as the general health conditions of the patient enable her to be submitted to a treatment for breast cancer, the mammographic screening should be continued.

Other screening techniques were also considered. Ultrasonography is not appropriate as initial screening method for the general population, particularly because of the method limitations to evaluate microcalcifications. However, some studies have demonstrated the usefulness of ultrasonography as a screening method for asymptomatic patients with negative mammographic results, but with dense breasts. One of the first studies was published by Kolb et al., involving 11,130 asymptomatic patients, has demonstrated that ultrasonography performed in addition to mammography increased the detection of breast cancer in 42% in patients with dense breasts. Other study evaluating the role of ultrasonography in the assessment of women with dense breasts has demonstrated that the prevalence of cancers sonographically detected corresponded to 0.41% and that the proportion of sonographically detected cancers in relation to the total was 22%, most of them invasive. The results of the multicenter study for screening of high-risk patients with dense breasts (American College of Radiology Imaging Network – ACRIN) demonstrated that the addition of a single sonographic screening to mammography leads to an additional detection of 1.1 to 7.2 cancers per 1,000 women at high risk, although the number of false positive results is elevated. So, CBR, SBM and FEBRASGO recommend that the sonographic screening might be considered for high-risk women who do not tolerate magnetic resonance imaging, as well as for those at intermediate risk and for women with dense breasts.

As compared with mammography and ultrasonography, magnetic resonance imaging presents higher sensitivity for detecting breast cancer. Such data have stimulated the development of cohort studies focused on high-risk patients of countries in different continents: Holland, Canada, United Kingdom, Germany, Italy, United States of America and Norway. One of the first studies was published by Krieger et al. in 2004, where the accuracy of mammography, ultrasonography and magnetic resonance imaging was compared in 1,909 women with a remarkable family story of breast cancer or with genetic alteration (BRCA1 and/or BRCA2), demonstrating sensitivity of 33%, 60% and 100%, respectively. Recently, Kuhl et al. demonstrated sensitivity for breast cancer detection in high-risk patients of 33%, 37% and 92%, respectively for mammography, ultrasonography and magnetic resonance imaging, with 98% specificity for all the three methods. In such study, no case of interval carcinoma was observed, while other tumors were < 1 cm. A review of these studies has confirmed that, by adding magnetic resonance imaging in the screening of high-risk patients, there was a 44% increase in sensitivity as compared with mammography and ultrasonography. The key issue is the absence of studies demonstrating reduction of mortality. However, the small dimensions of the tumors diagnosed by magnetic resonance imaging, as well as the low rate of lymph node involvement suggest that magnetic resonance imaging can bring benefits. Thus the Commission that prepared the present document, in agreement with the other medical societies, rec-
ommends magnetic resonance imaging together with mammography in the screening of high-risk women, provided the technical quality of the MRI scan is assured: the scan must be performed in a center of recognized quality, relying on specifically experienced physicians, apparatus with at least 1.5 tesla and dedicated breast coil. The center should also offer MRI-guided biopsy or being capable of indicating other service in the region that is able to do it. In the absence of access to a qualified magnetic resonance imaging service, the present Commission recommends additional screening with ultrasonography.

NOTES ABOUT SCREENING WITH OTHER TECHNOLOGIES

The mentioned studies demonstrate that the diagnostic performance of digital mammography in the detection of breast cancer was comparable or superior to the performance of conventional mammography for the majority of women in spite of discussions about the most benefited age range. In 2005, the results of the Digital Mammographic Imaging Screening Trial (DIMIST) were presented. In such study developed over a two-year period, 33 centers in the United States of America and Canada selected 49,528 women who were randomly submitted to digital and conventional mammography. The results demonstrated that, in terms of accuracy, digital and conventional mammography were similar for the general population, but digital mammography was superior in women aged under 50, in those with heterogeneously or extremely dense breasts (types 3 and 4) and in women in the pre- and perimenopausal period.

In 2007, Skaane et al. presented the final results of the Oslo II study. Such randomized clinical trial evaluated the local population aged between 45 and 69, submitted to screening with conventional mammography (n = 16,985) and digital mammography (n = 6,944). A significant difference was observed in the rate of early stage cancer detection between digital (0.59%) and conventional (0.38%) mammography, demonstrating the better performance of digital mammography in women aged up to 69. In 2009, Vinnicombe et al., in a meta-analysis involving eight large randomized studies, observed that the rate of detection by digital mammography was higher than by conventional mammography, particularly in women aged up to 60. Thus, CBR, SBM and FEBRASGO consider that digital mammography can be utilized for breast cancer screening for women aged between 40 and 69, provided it is available and accessible.

Tomsynthesis is a relatively new technology which, for reducing the effects from breast tissue overlapping, may provide a better characterization of mammographic findings, reducing the necessity of additional views, potentially detecting tumors previously occult at conventional mammography. However, data for the utilization of this method for screening the general population are not available yet. The preliminary results of the Malmö Breast Tomsynthesis Screening Trial (MBTST) were presented in the current year at the satellite symposium of the European Congress of Radiology. Such study, whose final results should be presented in 2015, is intended to evaluate 15,000 women aged between 40 and 79, by means of digital mammography and tomosynthesis (with a mediolateral oblique view). Its preliminary results show an increase of approximately 15% in sensitivity, and that tomosynthesis is at least as good as digital mammography in the identification of microcalcifications, although it also presents false positive and false negative results. Thus, CBR, SBM and FEBRASGO consider that it is still early to recommend tomosynthesis as a population screening method, but emphasize that such data shall be revised every three years.

REFERENCES

3. Kalager M, Zelen M, Langmark F, et al. Effect of screening mammography, demonstrating the better performance of digital mammography in women aged up to 69. In 2009, Vinnicombe et al., in a meta-analysis involving eight large randomized studies, observed that the rate of detection by digital mammography was higher than by conventional mammography, particularly in women aged up to 60. Thus, CBR, SBM and FEBRASGO consider that digital mammography can be utilized for breast cancer screening for women aged between 40 and 69, provided it is available and accessible.

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