Breast cancer screening is essential in lowering breast-cancer related mortality and the prevalence of invasive and advanced breast cancer in high risk women. High risk women should receive a screening that is based on at least three imaging modalities, i.e. mammography, magnetic resonance imaging and ultrasonography, for the primary prevention of breast cancer. The use of these three modalities allows for the early detection of breast cancer or precancerous lesions.

Risk Factors for Breast Cancer

Women who received a breast biopsy before for breast cancer or lesion evaluation are at an increased risk of developing breast cancer in the contralateral breast. Additionally, recurrent breast cancer in the ipsilateral breast is more likely compared to the occurrence of breast cancer in a healthy woman with no previous history of breast cancer.

Women diagnosed with lobular carcinoma in situ on a previous biopsy study are also at an increased risk of developing breast cancer. Atypical lobular or ductal hyperplasia are also associated with an increased risk of invasive breast cancer.
Women with a family history of breast cancer have a 13% lifetime risk of developing breast cancer, whereas those with two first-degree relatives diagnosed with breast cancer have a 21% lifetime risk of developing breast cancer. **Women with positive family history of breast cancer with a specific genetic mutation might develop breast cancer during the reproductive years or when they are old.**

Certain genetic mutations are known to put the patient at a significantly higher risk of breast cancer compared to the general population. For instance, women who carry the BRCA1 or BRCA2 genes are at a significantly higher risk of breast cancer. Mutations in the PTEN gene, TP53 gene, MSH2 gene, and MLH1 gene also put the woman at an increased risk of developing breast cancer.

Therefore, **women with a documented family history of genetic abnormality associated breast or reproductive system cancers should be screened for these specific genes.** If the woman is found to be positive for one of the previously mentioned genes, she should receive breast cancer imaging screening at a considerably younger age compared to women who do not have such genetic abnormalities.

**Breast Imaging as a Screening Tool for Women at High Risk for Cancer**

Randomized clinical trials showed a clear benefit from breast cancer screening in lowering cancer-related mortality and morbidity. The most studied imaging modalities are:

- Mammography
- Breast magnetic resonance imaging
- Ultrasonography

**Mammography**

Mammography was constantly shown to allow for the early detection of breast cancer or precancerous lesions before they develop into invasive breast cancer. Nowadays, it is **recommended to start routine annual mammography screening after the age of 40 years.** The American College of Obstetricians and Gynecologists recommended annual mammography screening for breast cancer in all women aged between 40 and 49 years.

The **main question regarding mammography screening in high-risk women for breast cancer is whether the age to start screening should be lowered.** A recent study has shown that women who are considered as high risk for breast cancer who received annual mammography after 30 years of age and up to 39 years of age had a cancer detection rate of 3.4 per 1000. Surprisingly, the cancer detection rate by mammography in high-risk women aged between 40 and 49 years is around 3.3 per 1000.

Based on this, one can clearly deduce that **commencing routine annual mammography screening at the age of 30 years,** 10 years younger than your typical screened woman, is certainly beneficial to the patient.

The issue with using mammography in women younger than 40 years of age is the reduced sensitivity and specificity due to the presence of a denser breast in young women. Therefore, **many women who get a mammogram before the age of 40 years (up**
(to 8.6%) will be recalled to redo the exam.

To lower the recall rate, we recommend comparing the current mammography images with previous mammography images for the same patient. Comparing to previous examinations lowers the recall rate to 3.66%.

**Mammography is superior to magnetic resonance imaging** in the detection of early precancerous regions, such as intraductal carcinoma in situ, which is characterized by small microcalcifications on mammography.

Finally, women with BRCA mutations should receive mammography routine screening starting from the age of 25 years. If the quality of the mammograms is very low due to the very dense breast at that age, one can:

- Compare different mammograms focusing more on changes rather than the isolated interpretation of a single mammogram
- Compare the results of the mammogram with magnetic resonance imaging
- Use ultrasonography for screening purposes

**Magnetic Resonance Imaging**

In contrast to a mammography, the utility and benefits of magnetic resonance imaging studies, such as screening tools for breast cancer in high-risk women, are based on low-evidence research such as:

- Case series
- Descriptive studies
- Prospective observational studies

Randomized clinical trials were not performed to assess the efficacy of magnetic resonance imaging in screening for breast cancer in healthy or high-risk women.

Multiple observational studies compared the efficacy of magnetic resonance imaging in the detection of early breast cancer compared to mammography. **Of all the breast cancers detected on magnetic resonance imaging, only 41% were also detectable by mammography.**

This result is based on seven huge observational studies from the Netherlands, Canada, the United Kingdom, Germany, Italy, Norway and Austria. Despite the clear added benefit of magnetic resonance imaging in the detection of breast cancer, no sophisticated randomized clinical trials have been carried out so far.

**Similar to a mammography, magnetic resonance imaging of the breast is of low quality in younger women**; therefore, the current recommendation is to start magnetic resonance imaging in high-risk women with BRCA gene mutations at the age of 30.

False-positives with magnetic resonance imaging are more common. Of the identified lesions on magnetic resonance imaging, up to 8% were later found to be benign.

**Ultrasonography**

**Similar to magnetic resonance imaging, ultrasonography was only evaluated in observational studies** as a tool to screen for breast cancer. Women with an intermediate risk for breast cancer, i.e. a second degree relative with previous breast surgery for an unknown cause might benefit from early screening with ultrasonography instead of mammography or magnetic resonance imaging for two main reasons:
1. Mammography is based on x-ray and is therefore not risk free.
2. Magnetic resonance imaging is very costly for a patient with an intermediate risk of developing breast cancer.

Very young women who are at high-risk for breast cancer should receive ultrasonography in addition to mammography and magnetic resonance imaging. The goal is to combine the results of the different imaging modalities to make it possible to detect as many cancers as possible before the cancer becomes invasive. The added benefits of ultrasonography are based on cross-sectional and observational studies.

Other Imaging Modalities for Screening for Breast Cancer

Patients who document a previous history of breast cancer might benefit from a positron emission tomography scan to screen for ipsilateral recurrent disease or contralateral breast cancer microscopic depositions.

High resolution computed tomography scans of the breast are also becoming a promising technique for the detection of early breast cancer in younger women whose magnetic resonance imaging studies and mammograms were not conclusive. Contrast-enhanced magnetic resonance imaging studies, or contrast-enhanced computed tomography scans, are helpful in the differentiation between malignant and benign breast lesions.

References

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