SCREENING & BEYOND

MEDICAL IMAGING IN THE DETECTION, DIAGNOSIS AND MANAGEMENT OF BREAST DISEASES

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BY **EVA M. FALLENBERG** AND **MICHAEL FUCHSJÄGER**

> Each year since 2012, as a part of its celebration of the International Day of Radiology (IDoR), the European Society of Radiology (ESR) has brought together several professional medical societies to create a special book to demonstrate the dedication, hard work and special skills of a particular radiological topic.

The ESR, together with the Radiological Society of North America (RSNA) and the American College of Radiology (ACR), introduced the IDoR as a way to raise general awareness of medical imaging and to help highlight the contribution of all the teams of experienced and highly-trained radiology professionals to improving the diagnostic opportunities for patients. Every IDoR so far has also had a main theme; one of the many 'subspecialties' of radiology that focus on specific diseases or anatomical regions. Therefore, the purpose of this book you are reading is to highlight the people, methods, and technology involved in this year's main theme: breast imaging.

Breast cancer is the most common malignant tumour that affects women all over the world. Roughly one woman in every eight suffers from breast cancer during her lifetime, and over the years, the average age of women affected by breast cancer has been decreasing. Most breast cancer patients are found in industrialised nations, but the number of affected patients in lesser developed countries is increasing.

Breast cancer is not a modern disease; it has been known about for a very long time. The first attempts to search for and establish imaging examinations to visualise and diagnose the breast are more than hundred years old. Since then, the enormous improvements made in this subspecialty field of radiology have resulted in a highly complex diagnostic approach that relies upon consultants with high levels of expertise to ensure the most accurate quality of detection, diagnosis, image-guided tissue sampling, pre-operative tumour location, intraoperative specimen radiography, and post therapy follow-up.

As the professions within the field of breast imaging have grown, so have the structures surrounding them, and naturally national and international breast imaging and senology societies have been founded, like the Society of Breast Imaging (SBI) in the US in 1985, and the European Society of Breast Imaging (EUSOBI) in 1998. Most of the authors of this book are board members of such national and international breast radiology or senology societies (including the SBI or EUSOBI), which exist to support the medical field of breast imaging. These societies are dedicated to promoting research, training, and the exchange of knowledge within the field; they organise conferences, forums, symposia, workshops and congresses, and publish journals, papers, and professional guidelines, all in the name of keeping the practitioners of the profession up to date with the full potential of their medical discipline. They also represent the interests of the field of breast imaging to public authorities, nationally and internationally, and work toward increasing public awareness of breast healthcare and the role that imaging plays within it.

We, as professionals working in breast radiology, are very happy to have the unique opportunity to share our working experience with you and explain the different aspects and developments of the wide spectrum of radiological methods for the diagnosis of breast cancer, including x-ray mammography, ultrasound, magnetic resonance imaging, and minimally invasive biopsies.

In this book we have tried to give you a broad look at the wide world of breast imaging, from the different aspects and controversies regarding breast cancer screening programmes and radiation therapy, to important points for achieving high quality in imaging, diagnosis and reports. We also provide an overview of the history of breast imaging, an insight into the research behind the technology, and recommendations for women's information about the common breast imaging methods, in cooperation with Europa Donna, an independent non-profit organisation that represents the interests of European women regarding breast cancer.

As well as these articles, written by some of the most prominent experts in the field, we have also conducted interviews with top representatives of the breast imaging world from Australia, Europe, South Africa, South America and the USA about the different aspects of daily breast imaging practice in each region. Finally, the book is concluded with an interview with a radiographer, representing one of the most important professions involved in medical imaging, responsible for performing safe and accurate imaging examinations, and generating the radiological images that are used by radiologists to diagnose diseases.

We are delighted and proud to provide you with an insight into our daily work and expertise, and we hope that you will enjoy reading this book, improving your own knowledge of breast imaging, and getting to know the medical field that is dedicated to serving not only breast cancer patients, but all of the millions of women who undergo screening every year, throughout the world.

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IT'S TIME TO STOP THE MISINFORMATION ABOUT BREAST CANCER SCREENING

BY **DANIEL B. KOPANS**

> For unclear reasons, breast cancer screening has been one of the most contentious medical issues of all time.

The debate about its merits has been going on for more than fifty years. Much of the debate has been due to the publication of scientifically unsupportable concepts such as the fallacious suggestion that invasive breast cancers would disappear if left undetected by screening[1]. This has come to be considered 'conventional wisdom' by some, even though that there are virtually no credible reports of this ever happening, in the few cases that have been published, the cancers were all palpable (not detected by screening), and the phenomenon is so rare that reports represent 'miraculous' events rather than the common occurrence that has been falsely suggested.

The debate has persisted because those trying to limit access to screening have repeatedly promoted scientifically false concepts. When these are scientifically refuted, new fallacious ideas are proposed. In the 1950s and 1960s it was argued that breast cancer was systemic from the start and that early detection would have no benefit. This was proven wrong by the first of the randomised, controlled trials done in the Health Insurance Plan of New York (HIP) which showed that earlier detection saved lives[2]. It was then argued that it was not possible to screen women efficiently, but this was disproven by the Breast Cancer Detection Demonstration Project[3]. Exaggerated concerns were raised about radiation risk to the breast[4], but careful analysis showed that risk to the breast diminishes rapidly with increasing age with no measurable risk by the age of 40, and that even

the extrapolated risk is far outweighed by even a small benefit[5]. Even opponents of screening, if informed, no longer argue using the radiation risk.

In the 1990s the fact that the trials lacked the statistical power to analyse women ages 40–49, separately, was ignored[6]. Although the trials, when analysed as planned, showed a significant benefit from screening women starting at the age of 40[7], analysts made the scientifically unsupported claim that there was no benefit from screening women in their forties. By ignoring the science, these faulty analyses continue to guide other countries that find it expedient to wait until the age of 50 to encourage screening.

Efforts to reduce access to screening included the false claim that screening was leading to earlier deaths for women ages 40–49 in the Canadian National Breast Screening Study. After causing international concern, the PI withdrew the scientifically unsupportable claim[8]. In fact, the excess deaths were clearly due to an allocation imbalance due to an un-blinded allocation process[9].

As the data became more clear in support of screening women ages 40–49[10], analysts seeking to limit access claimed that the benefit was not as great for women in their forties. This was originally observed in the HIP study where deaths for women ages 50–64 appeared to drop as soon as screening began while there was a delay for women ages 40–49. What analysts ignored was the well known 'length bias' that explains that an immediate benefit is unlikely and that a delayed benefit is what would be expected from periodic screening[11], but analysts once again ignored the science and to this day continue to claim the benefit is greater among older women, when the data do not support this.

By grouping and averaging data, analysts made it appear as if there was a major change in the parameters of screening that happened at the age of 50[12] when, in fact, none of the parameters change abruptly at age 50 or any other age[13]. There are absolutely no data to support the use of the age of 50 as a threshold for screening. It is a completely arbitrary choice, while the data show that lives are saved by screening starting at the age of 40. The randomised, controlled trials have proven this and observational studies have confirmed this, and this is why the age of 40 is the appropriate threshold.

In fact, every major group in the U.S. now agrees that the most lives are saved by screening starting at the age of 40. The United States Preventive Services Task Force (USPSTF), despite being comprised of individuals with no breast cancer expertise, nevertheless, stated in their latest guidelines: "the USPSTF found adequate evidence that mammography screening reduces breast cancer mortality in women aged 40 to 74 years."[14]

The American Cancer Society, also relying on an inexpert panel, nevertheless, clearly agreed that most lives are saved by annual screening starting at the age of 40: "Women should have the opportunity to begin annual screening between the ages of 40 and 44 years (qualified recommendation)."

It was a qualified recommendation only because, as they state: "The majority of individuals in this situation would want the suggested course of action, but many would not."[15]

In other words, the panel agreed that the most lives are saved by screening starting at the age of 40. The qualification was not what the science showed, but reflected the individual biases of the panel and their guess (no science) at what women might or might not 'want'.

In fact, the scientific evidence shows that breast cancer screening is one of the major advances in women's health in the last fifty years. In the U.S. the death rate from breast cancer had been unchanged for fifty years dating back to at least 1940. Screening began in large numbers in the mid 1980s[16] and soon after, the death rate began to fall. As more and more women have participated in screening it has continued to fall, so that now there are more than 35% fewer women dying of breast cancer each year. Therapy has improved, but in numerous studies where screening has been introduced into the general population where women have access to modern therapy, the major decline in deaths is among women with access to screening[17].

There has never been a randomised, controlled trial comparing annual screening to biennial or longer, but

Tabar et al showed that the number of cancers detected between screens (interval cancers) as expected, increases with the time between screens[18]. Computer modelling can be used to determine the importance of the time between screens (screening interval). The computer models of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET) all show that the most lives are saved by annul screening starting at the age of 40[19]. Comparing women who are screened every year to those screened every two years shows, as would be expected, that the size and stage of the lesions is still important[20] and that women screened with a shorter interval have more favourable tumour characteristics[21,22].

The decline in deaths from screening was proven in the randomised controlled trials (RCT's), and has been confirmed in multiple observational studies[23–38]. As has been seen in the United States, when screening is introduced into the general population, the death rate from breast cancer declines.

Additional support for screening comes from evaluating women who have died from breast cancer. In two of Harvard's main teaching hospitals, more than 70% of the women who died from breast cancer were among the 20% who were not participating in screening (this was true for women in their forties as well[39].

As the value of mammography becomes clearer each year, the effort to reduce access has accelerated.

'OVERDIAGNOSIS' – 'OVERSTATING': AN UNSUBSTANTIATED PROBLEM

As noted earlier, there are legitimate concerns about the management of ductal carcinoma *in situ* (DCIS), but these are not new, and there have been numerous efforts to try to 'tailor' treatment, but they have resulted in undesirable recurrence rates. These should be kept separate from discussions of invasive cancers, but, in an effort to confuse the issues, some analysts have grouped DCIS with small invasive cancers. This is a ploy to dilute the results for the invasive lesions and should not be tolerated in publications.

There is not enough space here to address all of the misinformation that has been promulgated concerning the suggestion by a few that there are thousands of invasive cancers diagnosed each year as a result of mammography screening that would regress and even disappear if left undetected by screening. The prestigious *New England Journal of Medicine* published a paper that should have never passed peer review that claimed that in 2008 alone there were 70,000 breast cancers that would have regressed or disappeared had they not been found by mammography. It is astonishing that mammography was blamed, since the authors actually had no idea which cancers were found by mammography since they had no idea which women actually had mammograms. In addition, they based their claims on, as they admitted, their "best guess" as to what the rate of cancers would have been had screening not begun in the 1980s! Based on the difference between the actual numbers of cancers diagnosed in 2008, and their "best guess" (which was lower), they claimed that the numbers of cancers above their guess must not be real and would have disappeared had they not been detected by screening. In fact, actual data (and not a "best guess") show that there has been no overdiagnosis of invasive cancers[40].
A paper in the *New England Journal of Medicine* that provided no data on mammography, and was based on a "best guess" has been given great credibility, and, as a consequence it is now 'common knowledge' that mammography leads to massive overdiagnosis. This is sheer scientific nonsense. There are now two additional independent analyses of this paper that show that it is not scientifically supported[41,42], yet it is repeatedly referenced in efforts to reduce access to screening.

Others have suggested huge numbers of overdiagnosed breast cancers. All have suffered from scientific flaws[43]. The treatment of lesions classified as DCIS had raised legitimate disagreement about management, but the data show that small invasive cancers will grow to become large invasive cancers and that early detection saves lives. If there is overdiagnosis, it is a challenge for pathologists just as 'overtreatment' is a challenge for oncologists, since the possibilities are not confined to mammographically detected cancers. At most, 10% of women who are treated for breast cancer actually benefit from systemic treatment[44]. Preventing overdiagnosis and overtreatment

by denying women access to screening is like preventing car accidents by removing all the engines.

'VALUE BASED' MEDICINE

Knowing that they would lose if they argued that they did not want to spend the money to save lives, those seeking to reduce access to screening have coined a new phrase: 'value based medicine'[45]. As Harris has clearly stated: "... people need to understand that with this approach, there will be some cancer deaths if we go to a high value approach rather than a maximal detection approach, we are going to miss some cancers. You have to give in to that"[46].

The effort to reduce access to screening is clearly about the money. Welch argued for the insurance companies by suggesting that they should no longer be rated based on the participation of their insured women in screening[47]. An article in the *Annals of Internal Medicine* claimed to compare the cost/benefit of annual screening starting at the age of 40 vs. biennial starting at the age of 50. They left out the benefit part, but claimed a $7 billion saving. What they left out was that premature deaths cost society substantial amounts of money so that allowing women to die unnecessarily may not be such a money saver[48]. The premature death of a woman in her forties costs $1.4 million, and the costs of care in the final year of life for a women dying of breast cancer is an additional $250K. 'Value based screening' may not be as big a 'value' as some would like us to believe.

RISK BASED SCREENING

Risk based screening will deny most women who are diagnosed with breast cancer each year access to screening[49].

To the uninformed it makes great sense when it is suggested that we should concentrate screening on women who are going to develop breast cancer. Those seeking to reduce access to screening like the folksy quote "one size doesn't fit all". They suggest the obvious – we need to tailor care and should only screen women who are going to develop breast cancer! What a brilliant idea (as if no one ever thought of it before). Unfortunately, at this point in time it is 'pie in the sky'. There are indeed some identifiable women who are at higher risk of developing breast cancer. In particular are those who have inherited a Breast Cancer 1 (BRCA1) or Breast Cancer 2 (BRCA2) gene mutation. These women are at extremely high risk of developing breast cancer. However, they only account for less than 10% of the women diagnosed each year. Women who do not have an identifiable genetic abnormality, but have a family history of breast cancer or other high risk factors only account for another 10–15% of cancers. The fallacy of the argument for tailoring screening to patients at high risk is that this would mean that 75% of women who are diagnosed with breast cancer each year would not be screened. Furthermore, since none of the RCT's stratified participants based on risk there are actually no data to show that concentrating on screening only high risk women would save any lives. To add a folksy reply "If it sounds too good to be true, it is!"

At this point in time, the way to save the most lives is annual screening starting at the age of 40. Clearly no one is forcing women to participate in screening and each woman (regardless of age) should make her own decision as to whether or not to participate. The decision should not be made by some politically driven panel of individuals who have no expertise or even experience in caring for women with breast cancer, who superimpose their own values on their guidelines and guess what women might or might not want to do. It should be based on accurate information so that each woman can decide for herself. It is certainly time to stop the misinformation.

REFERENCES

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END THE CONFUSION ON MAMMOGRAPHY SCREENING: COMMUNICATIONS TOOLS AND STRATEGIES USED BY THE SOCIETY OF BREAST IMAGING

BY **MURRAY REBNER** AND **JOY BURWELL**

> During the last five years, breast imagers in the United States have been fighting an uphill battle

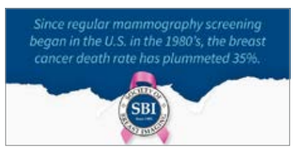
to communicate the importance of life-saving mammographic screening to women. Despite the obvious advantages of mammography as a key component of preventive healthcare for women (breast cancer mortality in the United States has decreased by 35% since widespread screening mammography began in the 1980s), considerable variance in guidelines from researchers and stakeholders on when to start screening, and how frequently women should get mammograms, is leaving many women and their providers frustrated and confused.

They are confused because they are receiving different recommedations from respectable experts and organisations. In addition, the American media do not always relay the information on mammography screening in a clear, understandable manner. Instead, they often focus on its controversies. The two biggest points of contention in this debate are when to begin screening and how often to get screened. The confusion began in 2009 when the United States Preventive Services Task Force (USPSTF) did not recommend that women aged 40 to 49 receive annual screenings and, furthermore, recommended that women aged 50 to 74 just be screened every other year. In 2015, the American Cancer Society also released new guidelines that stated that women should begin annual mammography screening at age 45 and could transition to biennial screening at age 55. The release of these guidelines has compounded the confusion created by academic journal articles, which argued that annual mammograms lead to overdiagnosis and overtreatment of breast cancer. Regardless of these studies' scientific flaws, they receive significant media attention and have had a negative impact on women's healthcare decisions.

It is dangerous and deadly to let the confusion surrounding mammography continue. Breast imaging experts in the United States recommend that women begin annual mammography screening at 40 (and earlier if they are at high risk). Recognising the importance of these recommendations and that lives are at stake, the Society of Breast Imaging has implemented several communications methods to ensure women are getting accurate information on breast cancer screening. Below we describe these tactics, which can also easily be employed for other breast cancer screening issues.

The SBI's strategies were developed and implemented to not only reach women directly but also indirectly through the media, advocates, policymakers and stakeholders. Communicating with all these groups maximises the chances of the message getting through to the intended audience. When developing a campaign, you need to target a multitude of audiences (especially ones your main audience trusts) in order to realise your goals.

One strategy the SBI executed was the creation and implementation of End the Confusion (https://www.sbi-online.org/endtheconfusion/Home.aspx), a campaign and website built to inform and engage providers, stakeholders and the public so that the confusion associated with screening mammography is



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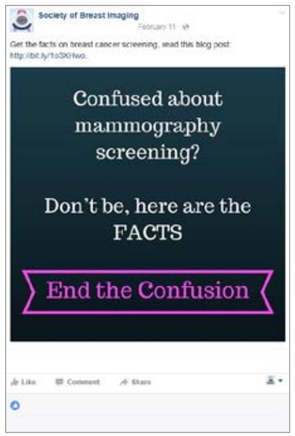
addressed directly and the benefits are better understood. It builds on other educational efforts, including the American College of Radiology's excellent website, http://www.mammographysaveslives.org/. End the Confusion empowers women with clear and accurate information on mammography screening so they are prepared to make informed decisions after they have conversed with their healthcare providers. In addition, resources are also available for providers.

The Society of Breast Imaging does not want women to delay or forego screening mammography, as science shows that these actions can lead to increased mortality. By visiting www.endtheconfusion.org, women, media, stakeholders and providers can access a host of materials, including multimedia presentations, fact sheets, lists of resources and articles. The creation of a variety of materials is important because different stakeholders opt for different formats of information.



To promote the campaign, we issued a press release, posted announcements on social media and encouraged our membership to inform their colleagues, especially those outside of radiology. Additionally, we sent promotional materials to stakeholder organisations for use within their networks. This proved to be a very successful tactic for getting the word out about End the Confusion and educating about the importance of mammographic screening. The SBI's goal is to promote the campaign widely and target those who would most benefit from the information. Since the site launched at the beginning of 2016, it has been visited 4,149 times (as per September 30, 2016).

Given the insurance coverage implications of the USPSTF's recommendations, it is critical to make sure policymakers are aware of the benefits of mammography screening. A tactic that was successful for the SBI was to co-host, with a stakeholder organisation, a Capitol Hill Briefing, which targeted legislators and their staff. Panellists included experts in the field, as well as policymakers who champion this issue. The SBI used this formula successfully, and partnering with other organisations that have a stake in breast cancer issues, helped to amplify the message.

Garnering accurate media coverage is not easy. With regard to breast cancer screening, reporters like to wade into the controversy instead of the science. However, creating a consistent level of awareness at local and national levels helps the media take notice and stay focused. To that end, it is critical to push out consistent messaging on a regular basis, using a variety of traditional media tools, including press releases, statements, op-eds and letters to the editor (LTEs). In 2015, the SBI issued joint statements with the American College of Radiology, when both the USPSTF and American Cancer Society released their recommendations. In addition, letters to the editor and op-eds written by SBI leaders and members were submitted to publications at the national and local levels. In addition, the SBI membership was encouraged to submit op-eds and LTEs to their local news outlets. To assist in these efforts, the Society provided talking points on the benefits of annual screening mammography. Several members have also been interviewed by their local media for print, TV and radio stories.

Social media is another tool that should be used when communicating about the importance of breast cancer screening. Social media reaches millions of individuals for little or no cost. In order to maximise the impact of social media, it is important to tailor the posts to the medium. For the SBI, graphics and stories with human elements do well on Facebook, whereas Twitter is a good tool for communicating research and updates in real-time. On both Facebook and Twitter, it is important to engage with followers – both individuals and organisations – who may respond and react to your social media posts.

These actions may ultimately result in an increase in total followers and enhance the reach of your messages.

Creating engaging social media posts that communicate the importance of breast cancer screening has led to a substantial increase in the SBI's followers. As of September 2016, the SBI has attracted 962 followers on Twitter and 3,983 likes on Facebook. When appropriate, the SBI responds to questions and engages in conversations started in response to a post. Multiple members and individuals have responded to social media posts, proving that the information has resonated with them.

Breast cancer has ended the lives of too many women and has devastated their families. It remains the second leading cause of cancer deaths among women in the United States, and the death rate is highest among women who are not screened regularly and present with advanced cancers.

From experience with our patients, breast imagers know that mammograms have detected cancers at an early stage when treatment is most effective. Patients are alive today because they practice the kind of preventive healthcare that is recommended by the Society of Breast Imaging, the American College of Radiology and other respected organisations. Ultimately, this is why the SBI has dedicated so much of its time and resources to communicating the importance of screening mammography. It goes back to our mission: we want to save lives through early detection.

Although our efforts have been successful, it has not been an easy road, and the work is far from over. The SBI is committed to continuing to communicate the importance of annual mammography screening using the techniques described in this article. As new techniques are developed, they will be explored, and, if appropriate, disseminated (especially on social media). If you have questions about any of these tactics, including End the Confusion, please contact the Society of Breast Imaging at info@sbi-online.org. The SBI encourages you to visit the website (www.endtheconfusion.org) and share it with your colleagues. Most importantly, continue to discuss breast cancer screening with your patients, their providers and your colleagues outside of breast imaging, and provide them with appropriate information and recommendations. The SBI also encourages the use of any or all these tactics with any breast cancer screening issue you are trying to communicate. We have seen great success and believe you will too. Be persistent, be clear and be passionate.

BREAST DENSITY AND SUPPLEMENTAL SCREENING

BY **JENNIFER A. HARVEY** AND **WENDIE A. BERG**

IMPORTANCE OF BREAST DENSITY

Dense breast tissue is common and normal.

About 40% of women over the age of 40 have dense breasts. Dense breasts are more common in younger women and the breasts tend to become more fatty after menopause. Dense breast tissue reduces the effectiveness of mammography and increases the risk for developing breast cancer.

Defining breast density

In clinical practice in the United States, Breast Imaging Reporting and Data System (BI-RADS) breast density categories are included in reports to indicate the degree of mammographic breast density (Figure 1). The 'heterogeneously dense' and 'extremely dense' categories are considered 'dense'. In their early 40s, about 13% of women have extremely dense breasts and 44% have heterogeneously dense breasts; by the early 70s, 2% have extremely dense and 24% heterogeneously dense breasts[1]. Because radiologists vary in how they use BI-RADS density categories, computer based methods have been developed to improve consistency.

Density and breast cancer risk

At least 15 studies have demonstrated a moderate to strong association between mammographic density and breast cancer risk[2]. Women in the extreme density group are about four times more likely to develop breast cancer than women with fatty breasts. Since most women are in the middle two categories of density, it is more appropriate to communicate that women with extremely dense breasts are about twice as likely to develop breast cancer as the average woman. Extreme breast density as the sole risk factor does not put women into a high lifetime or 10-year risk of breast cancer.

Density and masking

Breast cancers, which appear as white areas on the mammogram can be hidden by dense breast tissue; this is referred to as 'masking'. Women with

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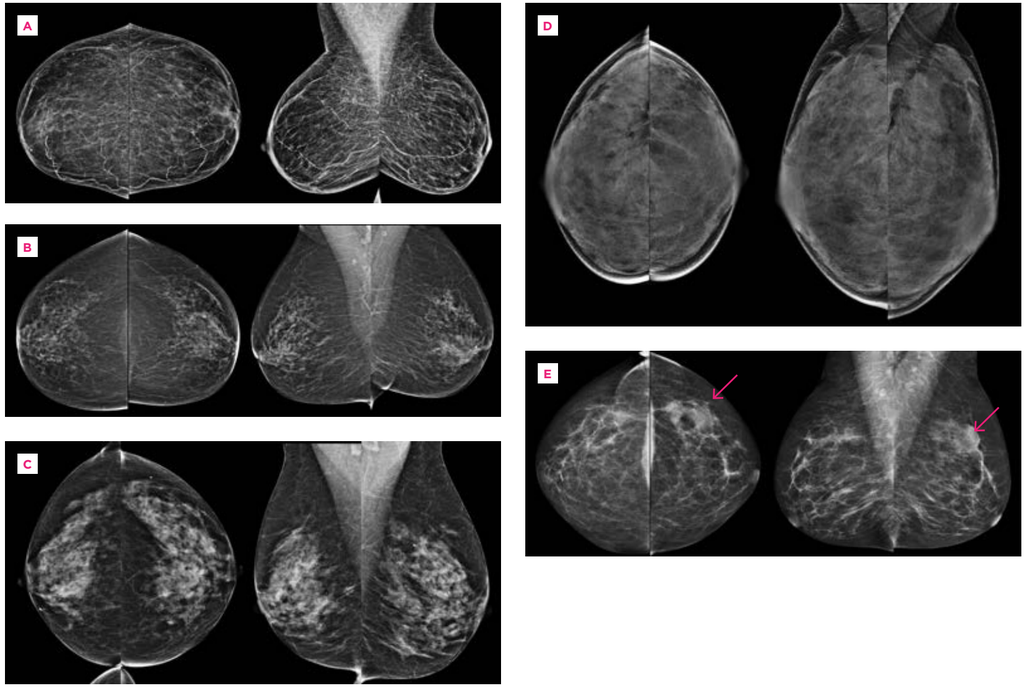


Images courtesy of Dr. Jennifer A. Harvey.

FIGURE 1

BI-RADS breast density categories: A) the breasts are almost entirely fatty; B) there are scattered areas of fibroglandular density; C) the breasts are heterogeneously dense, which may obscure small masses; and D) the breasts are extremely dense, which lowers the sensitivity of mammography. Women with extremely dense breasts are four times more likely than women with fatty breasts (A) to develop breast cancer but twice as likely as the average woman to develop breast cancer. When there is a more focal area of density in an otherwise low density mammogram (E, arrow), the density should be classified as heterogeneous rather than scattered.

dense breast tissue are at greater risk of having a cancer that is not detected by screening mammography. Because of this, women with dense tissue are at increased risk of having a cancer that presents due to symptoms, such as a lump, during the interval between recommended rounds of screening (one year in the U.S., but may be two or three years in other countries), which is considered an 'interval cancer'. These can represent up to one-third of the cancers diagnosed in women undergoing screening mammography[3,4].

Even when breast cancer is detected at screening, women with dense tissue have cancers that are larger, more likely lymph node positive (i.e. cancer has spread to the lymph nodes), and of higher stage than women without dense tissue[5,6]. A study from Sweden with 25-year follow-up showed an almost double risk of death for women with dense tissue compared with non-dense tissue[6].

In the United States, the masking of cancer by dense tissue has become a political issue beginning with Connecticut, which became the first state to enact legislation requiring that women receive notification about breast density with their mammography results. Advocacy efforts, generally spearheaded by women who were diagnosed with breast cancer after a negative screening mammogram[12], have now resulted in 27 state laws[7].

Digital mammography improves performance for women with dense tissue compared with film-screen mammography[8] though the improvement is modest. Supplemental screening in addition to mammography is increasingly utilised for women with dense tissue.

SUPPLEMENTAL SCREENING IN DENSE BREASTS

Mammography is the only type of imaging that has been studied in long-term randomised trials and has been proven to reduce breast cancer deaths. Adding supplemental screening beyond mammography may allow earlier detection, thereby producing improved outcomes.

Tomosynthesis

Digital breast tomosynthesis (DBT), often referred to as '3D' mammography, creates image 'slices' through the breast, reducing overlap of normal dense tissue and thereby allowing improved invasive cancer detection. DBT is associated with about twice the amount of radiation exposure when used in combination with a standard mammogram, which is still low in comparison to background radiation. Some facilities have software to generate a 'synthetic' 2D mammogram from the same images used for tomosynthesis and the radiation exposure is then about the same as a standard mammogram.

TABLE 1

Cancer detection rates using standard mammography and supplemental imaging in women with dense breasts[a]

	# Cancers found per 1,000 women screened	# Women without cancer recalled for additional testing
Digital mammography alone	**5 to 7**	**100**
Change with supplemental imaging:		
Tomosynthesis ('3D') mammography	**+ 1 to 2[b]**	**-18 to -30**
Ultrasound-handheld	**+ 3 to 4**	**+70 to +130**
Ultrasound-automated	**+2**	**+130**
MRI	**+10**	**+60 to +120**
Molecular breast imaging (MBI)	**+8**	**+65 to 77**

Adapted from www.DenseBreast-info.org/Technology.aspx accessed 6/6/16

[a] Results presented are from studies where the vast majority of women were not at high risk for breast cancer.

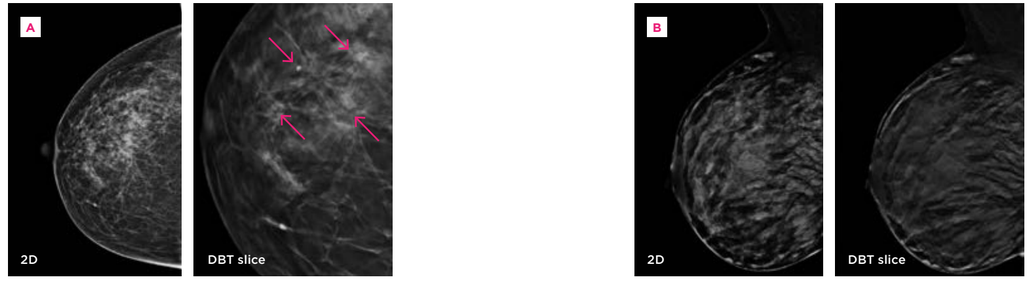
[b] Significantly improved cancer detection has been shown using 3D-mammography for women with heterogeneously dense breasts but not for women with extremely dense breasts.

Numerous studies have shown an improvement in invasive cancer detection with DBT in women with heterogeneously dense breasts, of 1 to 2 cancers per 1,000 women screened (Table 1). There is typically a lack of soft tissue contrast within slices of extremely dense breast tissue, which may still mask cancer detection even on DBT (Figure 2).

A reduction in the number of women recalled due to a detected cancer that was later found to be false (known as a 'false positive') has been observed with DBT across all breast densities[2-4].

Screening ultrasound

Supplemental screening with ultrasound after mammography has been extensively studied in women with dense breasts. This can be performed by using traditional ultrasound, where the transducer is moved by hand over the entirety of both breasts (handheld ultrasound: HHUS), or using automated devices. Most studies used HHUS performed by radiologists, and showed a significant increase in cancer detection over mammography alone of 3 to 4 cancers per 1,000 women screened[6,7] (Table 1, Figure 3) with the first, prevalent screen. This detection benefit persists with subsequent (incident) screening rounds[6]. The vast majority of cancers seen only on ultrasound are invasive and have not spread to lymph nodes. Slightly lower cancer detection rates have been observed with ultrasound performed by technologists. About 13–15% more women will be recalled from screening the first year, and 7% in subsequent years, when screening ultrasound is added to mammography[6-9]. About 4–5% of women screened with ultrasound may be recommended for biopsy of a benign



Images courtesy of Dr. Jennifer A. Harvey.

FIGURE 2

Digital 2D and 3D mammography (digital breast tomosynthesis, DBT) of women of different breast densities. A) Digital mammogram and DBT slice image of a woman with heterogeneously dense breasts. Multiple irregular masses (arrows) are apparent on the DBT study that are hidden on the digital mammogram due to overlapping structures. This was due to multicentric invasive lobular carcinoma. B) Digital mammogram and DBT slice of a woman with extremely dense breasts demonstrating little improvement in visualisation of structures with DBT due to homogeneity of the dense tissue. Detection of cancer may not be improved when the breast tissue is of this extreme density.

finding[3,6,8], which is higher than for screening mammography, where 1–2% of women screened undergo biopsy.

Adding ultrasound to mammography in women with dense breasts reduces the chance that cancer will be found as a lump after a normal screening. This has been shown in studies in multiple countries, including Italy, the United States, and Japan.

Because HHUS can be time consuming, automated ultrasound (AUS) has been developed for screening.

Studies of AUS show slightly lower cancer detection rates and fewer benign biopsies[12,13]. Similar to HHUS, it takes about 15 minutes to acquire AUS images for most breasts. Most women with a finding on AUS require further evaluation with targeted HHUS.

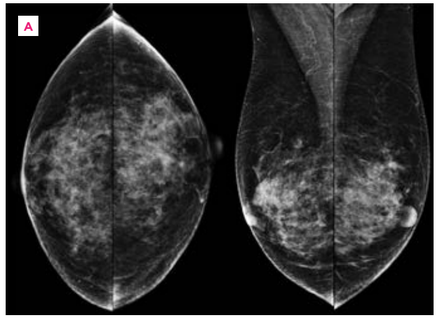
As use of 3D-mammography for screening increases, an important question is whether or not screening ultrasound is still beneficial after 3D-mammography. For facilities that have not yet implemented 3D-mammography, ultrasound appears to show greater improvements in cancer detection than 3D-mammography when added to standard mammography in women with dense breasts. A large study including five centres in Italy evaluated screening ultrasound after DBT and reported a cancer detection rate of 7.1/1,000 for HHUS compared to a cancer detection rate of 4.0/1,000 for DBT15. Only one cancer was seen on 3D-mammography but not ultrasound.

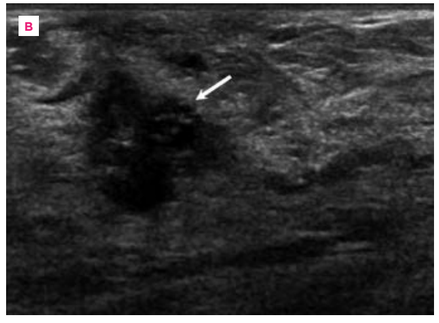
Magnetic resonance imaging

Contrast-enhanced magnetic resonance imaging (MRI) is recommended

FIGURE 3

Supplemental screening ultrasound detected breast cancer after negative mammogram (DBT). A) Bilateral digital mammograms show heterogeneously dense tissue which can hide masses. Even on tomosynthesis (3D mammogram), no abnormality was noted (not shown). B) Handheld ultrasound image from the left breast shows an irregular mass (arrow) due to 1.4cm invasive ductal cancer. Lymph nodes were not involved by cancer.





Images courtesy of Dr. Wendie A. Berg.

for supplemental annual screening in women of any breast density who are at high risk for breast cancer[16] (Figure 4). This requires intravenous injection of gadolinium-based contrast, a substance that helps to enhance the visibility of certain tissues in the resulting image. If MRI is performed, screening ultrasound is of no benefit. Not all women can tolerate MRI, due to claustrophobia, most pacemakers, other metallic implants, gadolinium allergy, or other reasons.

One study examined MRI in average-risk women of all breast densities after a negative mammogram and HHUS18. Among 1,705 MRI examinations, 54 (3.2%) showed suspicious findings and 18/54 (33%) were malignant, for an incremental cancer detection rate of 10.6 per 1,000 (Table 1). All cancers were lymph node negative. Importantly, in studies of high-risk women, MRI has been shown to shift stage at diagnosis to earlier, more curable stages and to reduce the number of findings categorised as late stage.

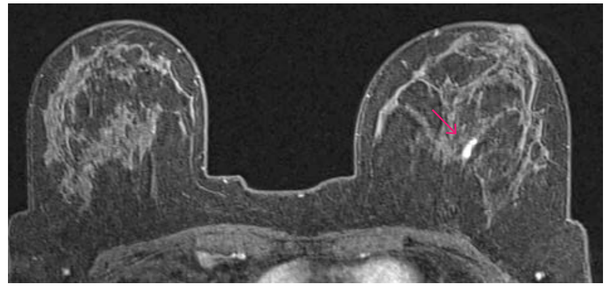
Although cost, patient tolerance, and accessibility are major barriers to using breast MRI to screen women with the sole indication of dense breast tissue, some investigators are developing abbreviated examinations that could be offered to the general screening population.

Molecular breast imaging

Single-centre studies have been performed using molecular breast imaging (MBI) for supplemental screening of women with dense breasts. MBI requires injection of radioactive material, ^{99m}Tc-sestamibi. The breast is positioned similar to a mammogram and stabilised with gentle compression (much less than a mammogram) between two detectors[23] or between one plastic paddle and a detector[24], and imaged for ten minutes per view (Figure 5). A typical examination takes a minimum of 40 minutes for both breasts. The typical dose of about 740 MBq (20mCi) has been considered excessive for use as a screening test[9]. In two recent studies using a lower dose of 300 MBq (8.1mCi) and encompassing more than 3,000 women, the incremental cancer detection rate of MBI after digital mammography in women with dense breasts was 8.8 per 1,000[25] and 7.7 per 1,000[26] respectively (Table 1). In both of these studies, the median cancer size was about 1.0cm and more than 80% were lymph node negative.

Importantly, radiation exposure is to the whole body and not just the breast with molecular breast imaging; effective dose (which considers radiation sensitivity of all exposed organs) is estimated at 2.5 mSv with an 8mCi dose of

FIGURE 4



Images courtesy of Dr. Jennifer A. Harvey.

Screening MRI of a woman at high risk for breast cancer. There is a small enhancing mass in the left breast (arrow). Biopsy showed invasive lobular carcinoma; the lymph nodes were negative. When lifetime risk is >20–25%, typically due to known or suspected disease-causing genetic mutation, annual breast screening MRI is indicated, regardless of whether or not the breast tissue is dense.

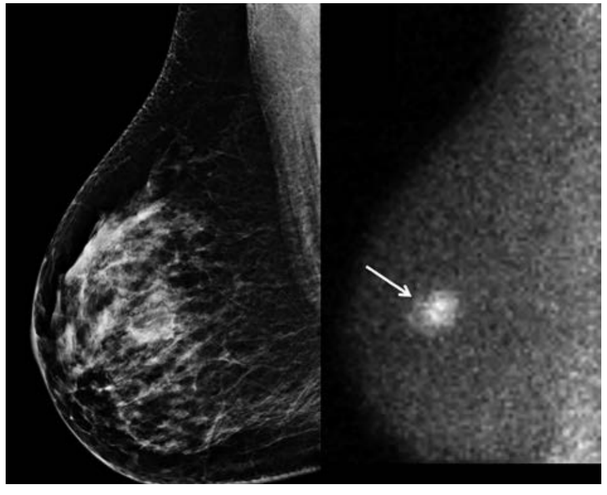
sestamibi, which is about five-fold that from digital mammography, about twice that from combination digital mammography and DBT, but less than background radiation of 3 mSv per year[27].

Contrast-enhanced mammography

Contrast-enhanced digital mammography (CEDM) is performed with a mammography machine adapted to obtain a low-energy and a high-energy x-ray exposure within a few minutes after the intravenous injection of iodinated contrast (as is used in computed tomography). A subtraction image is then created, showing only areas enhanced by the contrast. The risk of a fatal contrast reaction is extremely low; estimated to be less than 1 in 150,000 examinations, but less severe contrast reactions such as flushing are more common. Based on diagnostic work in women with known cancer[28,29], sensitivity is likely comparable to MRI and specificity may be higher.

FIGURE 5

Cancer seen only on molecular breast imaging (MBI) in a woman with dense breasts. A) Right mammogram with heterogeneously dense tissue which can hide masses. B) 10-minute MBI image obtained after intravenous injection of 8mCi (300 MBq) ^{99m}Tc-sestamibi shows intense radiotracer uptake (arrow) in mass due to 1.2cm invasive ductal cancer (courtesy of Mayo Clinic and www.DenseBreast-info.org/MolecularImaging.aspx accessed on 6/18/16). Lymph nodes were not involved by cancer.



Images courtesy of Mayo Clinic

SUMMARY

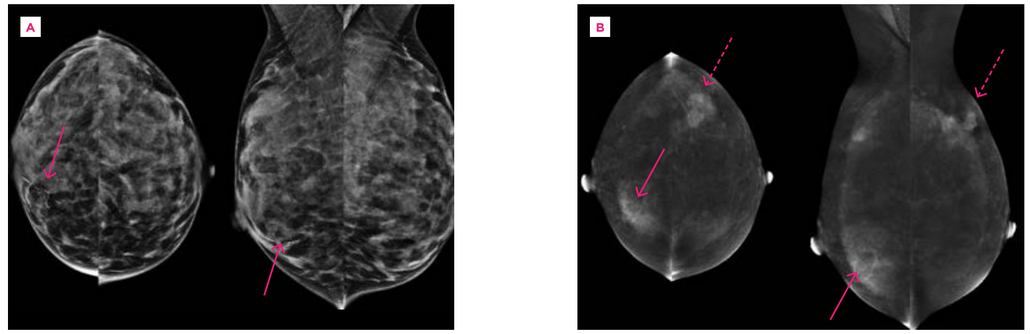
In summary, about 40% of women having regular screening mammography have dense breasts. Dense breast tissue increases the risk of breast cancer and impairs detection of cancers on mammography, and this can result in later stage at diagnosis with worse prognosis.

Digital mammography is better than film mammography in women with dense breasts. 3D-mammography improves cancer detection compared to standard digital mammography in women with heterogeneously dense breasts, but is less effective in women with extremely dense breasts due to lower internal contrast.

MRI is recommended for supplemental screening in women at high risk of breast cancer, regardless of breast density, but the cost is prohibitive for general screening.

FIGURE 6

Cancers on contrast-enhanced digital mammography (CEDM). A) This 45-year-old woman had calcifications in the right breast (arrows) that were due to ductal carcinoma *in situ*. B) CEDM shows enhancement in the right breast at the known cancer (solid arrows), but also has a large area of enhancement in the left breast (dashed arrows) that was multi-focal invasive ductal carcinoma, not seen on digital or 3D-mammography (not shown).



Images courtesy of Dr. Jennifer A. Harvey.

Ultrasound improves detection of invasive breast cancer and is the most frequently used supplemental screening modality in women with dense breasts. It appears that screening ultrasound is of benefit even after 3D-mammography, provided the woman is willing to accept an increased risk of false positives.

Fast MRI, molecular breast imaging, and contrast-enhanced mammography all show promise in improved cancer detection after mammography in women with dense breasts, but require broader validation. Surrogate endpoints of shifting to lower stage disease, reduced node-positive disease, and reduced interval cancer rates should be accepted as proof of benefit of supplemental screening[30].

REFERENCES

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IN SUPPORT OF SCREENING MAMMOGRAPHY

BY **FRANCESCO SARDANELLI** ET AL, ON BEHALF OF EUSOBI AND 30 NATIONAL BREAST RADIOLOGY BODIES

BREAST CANCER: A MAJOR HEALTH ISSUE AND THE ROLE OF MAMMOGRAPHY IN EARLY DIAGNOSIS

Breast cancer is a major issue for public health.

Increasing numbers of new cases and deaths are being observed in both developed and less developed countries, only partially attributable to an effect of increasing population age. Considering the 28 member states of the European Union, there were 361,608 new breast cancer cases in 2012, estimated to have increased to 373,733 in 2015 (+3.4%). The number of deaths were 91,585 and 95,357, respectively (+4.1%)[1]. The European Society of Breast Imaging (EUSOBI), together with a consortium of 30 national European breast radiology bodies, has summarised the knowledge and emphasised the importance of breast cancer screening using mammography in order to reduce breast cancer mortality.

Notwithstanding the intrinsic limitations in terms of sensitivity and specificity, mammography remains the main tool for population-based mass screening, with demonstrated effectiveness in reducing mortality and allowing for conservative treatment, as stated by EUSOBI[2]. The stage of a tumour at the time of diagnosis of breast cancer significantly impacts on overall survival, even in the current era of effective systemic therapy, so that early diagnosis remains crucial. This principle has been recently confirmed by a population-based study from the Netherlands Cancer Registry[3].

The evidence in favour of screening mammography has recently been summarised by the International Agency for Research on Cancer (IARC)[4]. According to results from randomised controlled trials, the reduction in breast cancer mortality due to screening mammography has been confirmed for women between 50 and 69 years of age. From cohort studies, a mortality reduction has been estimated for women aged 40–49 and 70–74, with 'limited evidence'. Available data did not allow the IARC working group to define an optimal screening interval. However, we should consider that the majority of European countries opted for biennial screening in women aged 50–69.

The average risk for a false positive recall has been evaluated by the IARC working group to be about 20% for women aged 50–69 who have ten screens in 20 years while the needle biopsy rate for a false positive finding is lower than 1% per round[4]. In addition, screening mammography allows for both downscaling of the clinico-pathological features of invasive breast cancers and reduction of loco-regional and adjuvant treatments[5-8].

The IARC working group accepted the estimation of overdiagnosis provided by the Euroscreen Working Group[9], equal to 6.5% (range 1–10%), calculated on the basis of the difference in the cumulative probability of a breast cancer diagnosis among women receiving or not receiving mammography. Notably, overdetection (a radiological issue) should be distinguished from overdiagnosis (which implies the essential involvement of pathologists)[10] and more efforts should be dedicated to the reduction of overtreatment.

RADIATION INDUCED BREAST CANCER: THE RISKS

For the 50–69 age range, the risk of radiation-induced breast cancer death has been estimated to be 1 per 100,000, taking into account a latency time of ten years and a dose of 2.5 mGy per screening round, which is at least 100 times lower than the probability of preventing a breast cancer death by early detection through screening. In other words, the chance of screening ultimately saving a life is 100 times higher than the risk of eventual death due to radiation exposure from mammography. Applying a mortality reduction rate of 43%, biannual screening mammography performed in 100,000 women saves 350 lives[11]. For the 40–49 age range, the problem of radiation effects must be more carefully considered and depends on the estimated magnitude of radiation induced breast cancers. Importantly, most radiation induced breast cancers will be cured[12]. The general conclusion of the IARC working group confirmed that the probability of avoiding a breast cancer death due to early detection via screening is at least 100 times greater than the risk of radiation-induced breast cancer due to screening mammography[4].

SCREENING MODELS AND OPEN ISSUES

On the basis of the available evidence, the consortium strongly supports mammography of the female population at average risk for breast cancer. Age selection and screening interval should be adapted to national demographics and local priorities. Importantly, the use of methods such as ultrasound alone, thermography or other digital optical imaging tools, for screening asymptomatic European women at average risk of breast cancer, as an alternative to mammography, is discouraged[13].

Preference should be given to population-based screening programmes on a regional/national basis with double reading rather than spontaneous mammographic screening with single reading, given the advantages of mammography in terms of higher specificity and positive predictive value[14,15], lower cost, structured quality controls and central data management.

In a wider framework, open debate in other contexts is acknowledged, such as in the United States, where the Society of Breast Imaging and the American College of Radiology support the use of screening mammography by informing women of the advantages of early breast cancer diagnosis[16]. The recent recommendations of the American Cancer Society[17] can be a useful reference for the U.S. context:

1. regular screening mammography starting at age 45 (strong recommendation);
2. annual screening mammography from 45 to 54 (qualified recommendation);
3. from 55, transition to biennial or continuing annually (qualified recommendation);
4. opportunity for annual screening from 40 to 44 years (qualified recommendation);
5. to continue screening mammography as long as the subject's overall health is good and they have a life expectancy of ≥10 years (qualified recommendation);
6. no suggestion for screening clinical breast examination at any age (qualified recommendation).

CHAPTER 1: **SCREENING & THERAPY**

TABLE 1

List of 30 national breast radiology bodies who signed a Memorandum of Understanding with the European Society of Breast Imaging and agreed on this paper

Austria	Workgroup of Mamma Diagnostic, Austrian Roentgen Ray Society, Österreichische Röntgengesellschaft (ÖRG)
Belgium	Senology Section of the Belgian Society of Radiology
Bosnia and Herzegovina	Association of Radiology of Bosnia and Herzegovina
Bulgaria	Bulgarian Society of Breast Imaging
Croatia	Croatian Society of Radiology Working Group of Breast
Czech Republic	Association of Czech Breast Radiologists
Denmark	Danish Society of Breast Imaging
Estonia	Breast Imaging Subgroup of Estonian Society of Radiology
Finland	Radiological Society of Finland/Breast Radiologists of Finland
France	Société d'Imagerie de la Femme (SIFEM)
Germany	AG Mammadiagnostik / Breast Imaging Working Group of the German Roentgen Society
Greece	Hellenic Breast Imaging Society
Hungary	Section of Breast Diagnostics, Hungarian Society of Radiologists
Iceland	The Breast Imaging Group of The Radiological Society of Iceland
Ireland	Irish Breast Radiology Group
Italy	Italian College of Breast Radiologists by SIRM (Società Italiana di Radiologia Medica)
Israel	Israel Breast Imaging Society
Lithuania	Lithuanian Radiology Association
Moldova	Department of Breast Imaging in the Society of Imagists of the Republic of Moldova
The Netherlands	Dutch College of Breast Imaging (DCBI)
Norway	Norwegian Society of Breast Imaging
Poland	Sekcja Diagnostyki Obrazowej Chorób Piersi; Polskie Towarzystwo Radiologiczne
Portugal	Breast Imaging Section of Portuguese Society of Radiology and Nuclear Medicine (SPRMN)
Romania	Romanian Society of Breast Imaging
Serbia	School of Breast Imaging
Slovakia	The Section of Breast Imaging of Slovak Radiologic Society
Spain	Spanish Society of Breast Imaging, Sociedad Española de Diagnostico e Interventencionismo de la Mama (SEDIM)
Sweden	Swedish Breast Imaging Society
Switzerland	Breast Screening representative of the Swiss Radiological Society
Turkey	Turkish Society of Radiology Breast Imaging Working Group

Moreover, the masking effect of increased breast density impacting on the sensitivity of screening mammography has been demonstrated[18]. Finally, the role of breast density as an independent risk factor for breast cancer must be taken into consideration, although this factor is frequently overestimated[19,20]. In studies with a control group representative of the whole population, the relative risk for women with dense breasts dropped to two or less[21,22]. At any rate, these societies consider the generalised adoption of digital mammography as the first priority, also to improve sensitivity in women with increased breast density.

THE POTENTIAL OF DIGITAL BREAST TOMOSYNTHESIS

EUSOBI and the 30 national European breast radiology bodies also consider the increasing evidence in favour of digital breast tomosynthesis (DBT) as a screening tool. Three prospective studies showed that DBT used as an adjunct[23-25] or alternative[26] to two-dimensional (2D) digital mammography (DM), allows for a superior diagnostic performance when compared to DM alone. Overall, DBT provides an increase in detection rate from 0.5 to 2.7 per 1,000 screened women, as well as a reduction in recall rate from 3.6 to 0.8 per 100 screened women[27]. DBT is now proposed along with synthetic 2D views, practically solving the problem of increased exposure to ionising radiation when DBT is performed as an adjunct to 2D DM[28-30]. All these aspects will probably confer to DBT the status of future 'routine mammography'. However, there should be evidence for a statistically significant and clinically relevant reduction in the interval cancer rate. An increase in overdiagnosis and costs, in the absence of the demonstration of the cost-effectiveness of DBT in screening, must be avoided. Initial results showing a reduction from 0.7 to 0.5 interval cancers per 100 screened women were recently reported[31], but further evidence is needed. Moreover, the probable increase in reading time associated with the use of DBT in screening[32] and its effects on the sustainability of screening programmes should be considered before routine implementation.

DIRECT DIGITAL OVER PHOSPHOR PLATE OR FILM-SCREEN MAMMOGRAPHY

Looking at the course of technological evolution of mammography in recent decades and at the current trend in favour of DBT, the adoption of direct DM (not phosphor plate computer radiography) instead of film-screen mammography in all countries is strongly supported. In fact, DM implies many substantial advantages, including lower dose, higher image quality, the possibility of post-processing, digital archive, image transmission, and no chemical pollution.

QUALIFIED RADIOLOGISTS ARE NEEDED!

Screening mammograms should be read by radiologists who are suitably qualified as screening mammography readers. Proficiency tests are encouraged in order to guarantee that radiologists achieve a standardised reading quality and can read a minimum numbers of screening examinations in a certain period.

A continuity of care from screening mammography to needle sampling and treatment planning should be obtained either with radiology units which perform both screening and diagnosis or with organisational models with screening units separated from diagnostic units. Whenever possible, radiologists should operate in the context of integrated breast centres. Quality assurance programmes regarding breast radiology units/sections are also encouraged in the context of forthcoming new European guidelines of breast cancer screening, diagnosis and treatment.

PREFERENCE FOR CORE OR VACUUM-ASSISTED BIOPSY

Preference should be given to needle sampling of breast lesions using core biopsy or vacuum-assisted biopsy instead of fine needle aspiration[33], considering the lower false negative rate and/or inadequate sampling, unless strict cooperation with a cytologist allows for a demonstrable equally high diagnostic performance. This does not apply for sampling of lymph nodes suspected to be metastatic at ultrasound of axillae, where fine needle aspiration has been shown to be effective[34].

WOMEN AT INCREASED RISK

The societies who endorse this paper are in favour of including, whenever possible, dedicated pathways for high-risk women (lifetime risk equal to or higher than 20%), offering breast MRI according to national or international guidelines and recommendations[35-37].

SUMMARY

EUSOBI and 30 national European breast radiology bodies strongly support mammography as a population-based mass screening tool which results in a relevant reduction in breast cancer mortality and leads to a favourable decrease in both loco-regional and adjuvant treatments in women attending these programmes. People and institutions questioning its validity, despite a large body of evidence accumulated in more than three decades, put women's lives at risk. Preference should be given to population-based screening programmes on a regional/national basis. Adoption of direct digital mammography is a priority, also to improve sensitivity in women with increased breast density. Suitably qualified radiologists should be involved. Digital breast tomosynthesis (DBT) will probably also become 'routine mammography' in the screening setting. Dedicated pathways for offering breast MRI to high-risk women, according to national or international guidelines and recommendations, are encouraged.

The authors support the adoption of screening mammography by national governments, policy makers, institutions, family doctors, and – last but not least – the general population.

ACKNOWLEDGEMENTS

This article is a summary of the paper *Position paper on screening for breast cancer by the European Society of Breast Imaging and 30 national breast radiology bodies from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland, and Turkey* by Sardanelli F, Aase H, Álvarez M, Azavedo E, Baarslag HJ, Balleyguier C, Baltzer PA, Beslagic V, Bick U, Bogdanovic-Stojanovic D, Briediene R, Brkljačić B, Camps Herrero J, Colin C, Cornford E, Danes J, de Geer G, Esen G, Evans A, Fuchsjäger MH, Gilbert FJ, Graf O, Hargaden G, Helbich TH, Heywang-Köbrunner SH, Ivanov V, Jonsson A, Kuhl CK, Lisencu EC, Luczynska E, Mann RM, Marques JC, Martincich L, Mortier M, Müller-Schimpfle M, Ormandi K, Panizza P, Pediconi F, Pijnappel RM, Pinker K, Rissanen T, Rotaru N, Saguatti G, Sella T, Slobodníková J, Talk M, Taourel P, Trimboli RM, Vejborg I, Vourtsis A, Forrai G, which was submitted to the scientific journal *European Radiology* in June 2016.

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RADIOTHERAPY IN BREAST CANCER

BY **LORENZO LIVI, ISACCO DESIDERI, ICRO MEATTINI,** ON BEHALF OF THE ESTRO – EUROPEAN SOCIETY FOR RADIOTHERAPY AND ONCOLOGY

> Breast cancer is the most common cancer occurring in women and it is the second leading cause of cancer-related deaths in women.

Breast cancer and benign breast tumours can also rarely occur in men, adolescents and children. Strenuous work among different figures in the scientific community has led to the conclusion that breast cancer actually consists of a heterogeneous group of diseases, with many different subtypes of both invasive and non-invasive cancers that have different treatment options and prognoses. Breast-conserving therapy (BCT) has become the standard therapeutic approach for women with early stage breast cancer over the past two decades, replacing mastectomy as the sole curative loco-regional treatment. BCT is defined as excision of the primary breast tumour with a rim of adjacent normal breast, with or without biopsy or dissection of axillary sentinel nodes (the first lymph node(s) to which cancer cells are most likely to spread from the breast tumour).

Irradiation of the whole remaining breast tissue after conservative surgery is a cornerstone of the breast conserving approach. In summary, the goals of BCT are 1) to eradicate microscopic foci of cancer that may remain in the breast after limited surgery to remove the primary tumour; 2) to provide local control and equivalent survival rates comparable to those of mastectomy; and 3) to maximise quality of life for the patient while minimising complications and achieving an acceptable cosmetic result.

Since the introduction of post-operative breast irradiation in the context of BCT, considerable technical innovations have been made in order to maintain the benefit of breast irradiation while minimising irradiation of healthy tissue near to the breast (e.g. breast skin, heart, and ipsilateral lung). Nowadays, computed tomography (CT)-based treatment planning is mandatory for appropriate radiation planning. Appropriate beam modification should be used (e.g. wedges, compensators, multileaf collimators [MLC]) to make sure that the whole breast is irradiated with an homogeneous dose, in order to minimise potential side effects. In particular, the use of dynamic wedges or MLC instead of physical wedges for beam

modification has become widespread in recent years, allowing the radiation dose to the opposite breast to be minimised. Adverse cosmetic results have been associated with the use of systemic therapy, higher total dose to the breast, and excess dose heterogeneity. Promising methods to reduce heart and lung dose include deep-inspiration breath hold, MLC, intensity-modulated radiation therapy (IMRT), and treatment in the prone position. In deep-inspiration breath hold, maximum inspiration is used to move the heart away from the chest wall, allowing the radiation beams to largely avoid the heart. Various commercial systems are available that allow the performance of breath-hold techniques. However, it is unclear whether breath-holding techniques truly lead to a decrease in cardiac morbidity, given the lack of prospective data covering a sufficient follow-up period. MLC can be used to conform dose to avoid the heart, either alone or in addition to other complementary techniques.

Examining patients in the prone position has been shown to reduce heart and lung dose when compared to treatment in the supine position. A randomised trial of large-breasted women reported improved dose homogeneity and reduced acute skin toxicity and pain in the prone position compared to supine. Finally, prone positioning can also reduce the patients' movement related to breathing during the radiation treatment. With the development of 3D treatment planning systems and the now widespread availability of linear accelerators with MLC capabilities, it has become possible to provide differential segmental blocking of the radiation beam through the treatment field to reduce hot spots in the dose distribution. This has led to an interest in administering radiation to the breast in several segmented fields. This technique has commonly been called 'breast IMRT'. It is noteworthy that this relatively simple technique, which is intended primarily to improve dose homogeneity, may lead to decreased rates of dermatitis and oedema. Because tens of thousands of women each year continue to require adjuvant radiotherapy after breast-conserving surgery, various alternative approaches to minimise the burden of treatment have been sought. Traditionally, radiation treatment after breast-conserving surgery has targeted the whole breast with total doses of 45 to 50 Gy administered in 1.8- to 2-Gy daily fractions, followed in many centres by an additional 10- to 15-Gy boost dose to the tumour bed (the breast portion where the breast tumour was originally located before being excised by the surgeon) leading to a total of five to six weeks of daily treatment; in this case the radiation treatment is delivered in what is commonly referred as 'normal fractionation'.

'Hypofractionation' of radiation treatment involves the use of larger daily doses of radiation and decreases the total number of fractions that must be administered. Several trials have investigated the use of hypofractionated regimens of irradiation to the whole breast, concluding that the oncological outcome of patients treated with a hypofractionated approach (e.g. local control, overall survival) are similar compared to the standard treatment, with a considerable reduction of overall treatment time. A further effort to tailor even better post-operative radiation treatment for operated women affected by early breast cancer was inspired by evidence that the majority of failures after breast-conserving therapy occur in the vicinity of the tumour bed. This led to the idea that it is possible to identify patients who have a low risk of residual disease remote from the lumpectomy cavity. Investigators have also begun to explore the possibility that an even more radically accelerated schedule of hypofractionated radiation might be tolerable if one treats only part of the breast. By further shortening treatment time, those developing these techniques of accelerated partial breast irradiation (APBI) hope that they may increase access to breast-conserving therapy for more women. Furthermore, it has been theorised that by decreasing the volume of irradiated tissue, these techniques might lead to a decrease in treatment-related toxicity. In addition, because chemotherapy is recommended for many patients with early stage disease, the potential for using APBI so that neither radiation nor chemotherapy is delayed appears appealing. Recently, many techniques have been tested in an attempt to administer adjuvant RT while reducing the burden for patients and RT departments. Various techniques are currently available to deliver APBI and comprise intra-operative radiotherapy (IORT), multi-channel brachytherapy, and external beam radiotherapy delivered either with a 3D conformal technique or an intensity-modulated technique (Figure 1). Although definitive data from a large prospective randomised trial are still awaited, current evidence obtained from brachytherapy experiences and external beam approaches encourage the use of APBI in appropriately selected patients.

An appropriate therapeutic choice for women operated for early breast cancer will be of utmost importance in the following years. The diagnosis of breast cancer is increasing, in part due to early detection of disease through imaging such as screening mammography, and this will inevitably lead to an increase in women operated for very low risk breast cancer, for whom a de-escalation of adjuvant therapies (both local and systemic) must be sought. In cases where mastectomy is unavoidable due to locally advanced breast cancer, patient selection for post-mastectomy radiotherapy is still debated. For patients at sufficient risk of harbouring residual disease in the chest wall and regional lymph nodes after mastectomy and systemic therapy, radiation therapy may not only prevent morbid local recurrence but also may improve survival, presumably by eliminating an isolated microscopic reservoir of residual disease from which distant metastases may be seeded or reseeded after initial elimination by effective systemic therapy. The intrinsic molecular biology of breast cancer also plays a major role in determining the risk for both local and distant relapses of breast cancer. Therefore, a key subject of research has been to identify which patients are likely to benefit from this type of treatment.

In conclusion, breast cancer radiotherapy has been established as one of the pillars of the management of women affected by this very common solid cancer, and a growing body of evidence will help to tailor the most appropriate treatment for every single woman in the near future. Technical improvements over the last two decades have also helped to further minimise the risk of both acute and long-term toxicity, while maintaining the clear benefit demonstrated in the previous years.

REFERENCES

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FIGURE 1

Accelerated partial breast using 3DCRT (A), and IMRT technique (B).

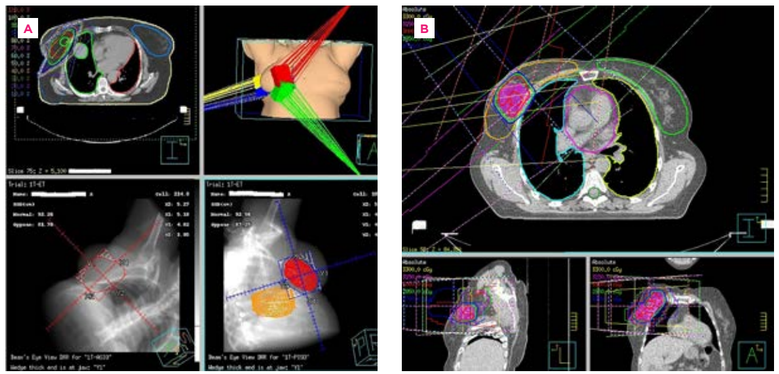


Figure 1A courtesy of B. Meduri, Radiotherapy Unit Modena Hospital

STANDARDS & QUALITY

BREAST IMAGING REPORTING AND DATA SYSTEM (BI-RADS): WHY IT IS SO IMPORTANT

THE IMPORTANCE OF THE MAMMOGRAPHY QUALITY STANDARDS ACT (MQSA)

BREAST EXPOSURE TO IONISING RADIATION

EUROPEAN COMMISSION INITIATIVE ON BREAST CANCER

BREAST IMAGING REPORTING AND DATA SYSTEM (BI-RADS): WHY IT IS SO IMPORTANT

BY **CAROL H. LEE**

> In the 1980s, growing recognition of the value of screening mammography in reducing deaths from breast cancer led to increased use of mammography.

However, it was realised early on that a number of significant problems needed to be addressed before mammography as a screening and diagnostic tool could be universally adopted. In addition to sometimes poor image quality, mammogram reports were often long, rambling, and impossible to understand. This was partly because the appearance of the normal breast is very variable from one person to another. In addition, findings that might represent breast cancer, such as calcifications, are not found in other parts of the body and there was no experience in describing or dealing with these findings. This meant that mammography reports often left the referring doctor with no idea whatsoever of what the mammogram showed or what to do for the patient.

In an effort to address this problem, the American College of Radiology Mammography Committee, headed by Dr. Gerald Dodd of MD Anderson Cancer Center in Houston, created a committee to develop a standardised reporting system. This committee was headed by Dr. Carl D'Orsi and included representatives from the National Cancer Institute, the Food and Drug Administration, the American Medical Association, the American College of Surgeons, and the College of American Pathologists. The result of the work of this committee was the Breast Imaging Reporting And Data System, known as BI-RADS. The BI-RADS atlas has revolutionised how breast imaging studies including mammography, breast ultrasound and breast magnetic resonance imaging are read and reported.

The first BI-RADS atlas was published in 1992 and was little more than a pamphlet. With time and experience, new editions refining the terms used and containing more information and detail were released. The 2nd edition was published in 1995 and the 3rd in 1998. In 2003 the 4th edition came out and for the first time included a lexicon of terms for breast ultrasound and breast MRI. Finally, in 2013, the 5th edition was published and for the first time an electronic version was available for download. This version attempts to be evidence-based and contains hyperlinks to references that refer to findings and their chances of representing cancer. The 5th edition also contains many actual images and is more than seven times larger than the 1st edition.

The BI-RADS atlas includes guidance on how the breast imaging report should be organised, a list of descriptions for findings seen on the exams, and a list of final assessment categories. The development of the descriptions for findings seen on mammography was done in a scientific manner that correlated imaging features with the likelihood of cancer. In the mammography lexicon, there are terms that should be used to describe mammographic findings such as masses, calcifications, asymmetries, and architectural distortion. For example, for masses, there are descriptions for the shape of the mass and for the edges of the mass (margins). For calcifications, there are descriptors for the way the calcifications are distributed in the breast and for the shape of the individual calcifications. Calcium deposits in the breasts are extremely common and the vast majority of them are not a problem. The BI-RADS lexicon includes terms and descriptions of typically benign calcifications that do not need any further testing, such as calcium deposits in blood vessels, scar tissue, benign growths, or tiny cysts. This knowledge is as important as recognising which calcifications might represent a problem, in order to avoid unnecessary biopsies.

For masses and calcifications seen on mammography, there are some features that are more likely to be benign and some that are more likely to be malignant and therefore the radiologist, by using these standard terms to describe them, can come up with a

FIGURE 1

Growth of BI-RADS

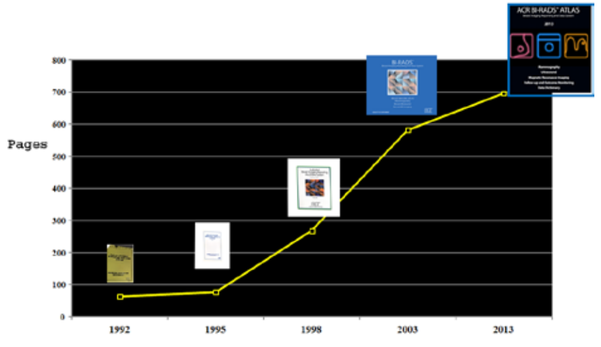
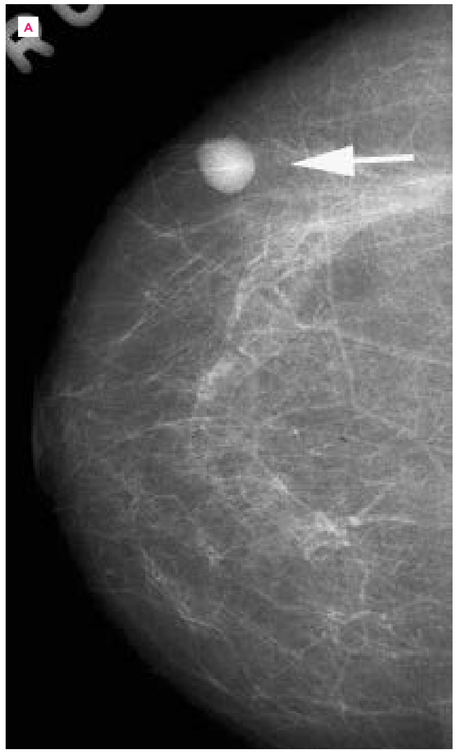


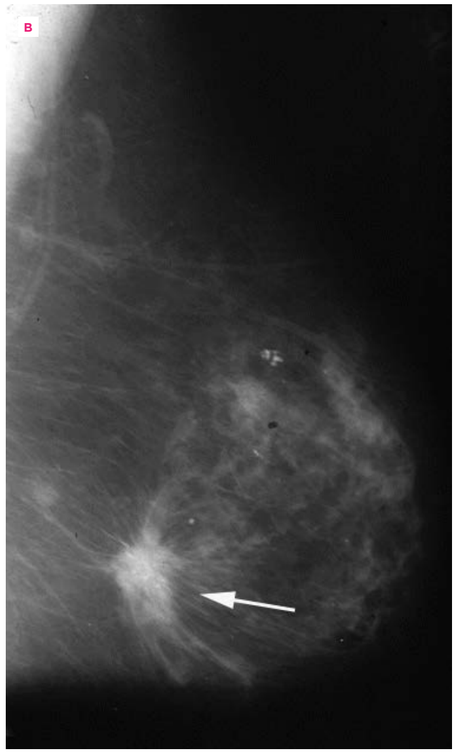
FIGURE 2

Masses

A: This mass (arrow) is round with circumscribed margins. These are descriptions that indicate this mass is less likely to be cancer.

B: This mass (arrow) is irregular with spiculated margins. These descriptions suggest that this mass is quite likely to be cancer.





final assessment category and the best recommendation for the next step.

The final assessment categories represent a vitally important part of the BI-RADS atlas. These categories sum up what the mammogram shows and what the most appropriate next step should be. The assessment categories range from 0 to 6. BI-RADS 0 is reserved for screening mammograms where two standard pictures are taken of each breast and then usually read after the patient has left the radiology facility. If there is a questionable or an abnormal finding BI-RADS category 0 is given and the patient is recalled for more mammogram pictures and/or ultrasound. The BI-RADS 0 category is reserved only for screening studies and not mammograms, ultrasound, or MRI where a complete evaluation is done at the initial patient visit.

'BI-RADS 1: Negative' is used when there are no significant findings. 'BI-RADS 2: Benign' is used when there is a finding that is definitely not suspicious or abnormal. For example, if there is a definitely benign calcification or a typical lymph node and no other finding, the examination could be given a BI-RADS 2 assessment.

'BI-RADS 3: Probably benign' is reserved for cases where there is a finding that is overwhelmingly likely to be benign. In order to receive a BI-RADS 3 assessment, a finding should have no more than a 2% chance of being cancer. The purpose of this category is to avoid biopsy of findings that are overwhelmingly likely to be benign, not definitely innocent. The way BI-RADS 3 lesions are managed is to get a repeat study in six months rather than waiting an entire year before the next examination, to be sure there are no changes. The most experience with this category is in mammography, where there are a number of very specific findings that have been shown to have a 2% or less chance of being malignant. This category is not meant to be used when the radiologist is uncertain about whether a lesion should be biopsied or not and wants to wait to see if it changes. It is meant to be used for those findings that are known through experience to most likely be benign, but in which close follow-up is desired.

BI-RADS 4 lesions are those that are suspicious for cancer and that require a biopsy. The likelihood of malignancy in BI-RADS 4 lesions ranges from 3% to 95%, which is a very large range, and there are subcategories 4a, 4b, and 4c that radiologists sometimes use in order to more precisely convey the likelihood that a finding might turn out to be cancer. Lesions categorised as 4a have up to a 10% chance of being malignant, 4b up to 50%, and 4c up to 95%.

BI-RADS 5 findings are those that are almost certainly cancer. These lesions have more than a 95% chance of being malignant. BI-RADS 6 is used for those cases in which there is a known cancer that has not been treated yet. For example, some women who have a new diagnosis of breast cancer have an MRI to see how much cancer is in the breast and those cases are usually given a BI-RADS 6 assessment.

All of the assessment categories are associated with a management recommendation. For BI-RADS 0 cases, more imaging is recommended. For BI-RADS 1 and 2, routine follow-up such as a mammogram in one year would be the recommendation. BI-RADS 3 cases usually have a repeat study in six months, and if there is no change, another study in another six months until two years of stability is shown. BI-RADS 4 lesions generally undergo biopsy, as do BI-RADS 5 findings. For BI-RADS 6 cases, appropriate treatment such as surgery or chemotherapy is recommended.

These final assessment categories represent a major advance and improvement in reporting of mammograms, breast ultrasound, and breast MRI examinations. In the United States, it is required by federal law that all mammograms have a final BI-RADS assessment. This means that all studies have a clear recommendation for the next step to be taken, either routine follow-up, short interval follow-up, or biopsy.

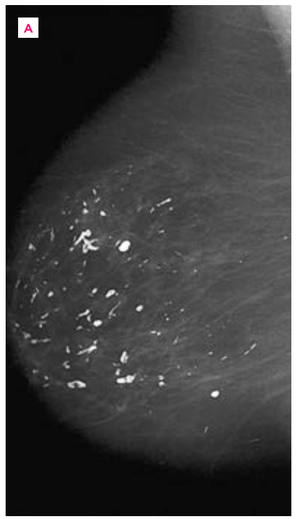
The development of BI-RADS has led to substantial improvements in the practice of breast imaging. By having standard terms to describe findings, research on how often these represent cancer has been possible. In addition, the descriptions of findings, when used correctly, help lead to the correct assessment and management recommendation. For example, if a mass seen on mammography is described

as being irregular in shape with spiculated margins, which are suspicious features, the appropriate assessment would be BI-RADS 5 and the appropriate management would be biopsy. By the same token, an oval mass with circumscribed margins, which are benign features, could possibly be given a BI-RADS 3 assessment and followed rather than biopsied.

Standard terminology also improves communication. Radiologists all over the world who use BI-RADS understand instantly what 'coarse calcifications' or 'milk of calcium' means. Prior editions of BI-RADS have been translated into a number of different languages including French, Spanish, Portuguese, Croatian, German, Russian, Mandarin Chinese, and Romanian, and the latest edition is being translated into Japanese as well.

FIGURE 3

Calcifications



A: These are large rod-like calcifications that are not a sign of cancer.
B: This is a close-up of grouped calcifications that are fine linear branching. These have a high probability of being malignant.

Having set terms also helps in teaching how to read mammograms. By being familiar with BI-RADS terms, those learning how to interpret mammograms and other breast imaging examinations are able to apply correct descriptions to findings and come up with appropriate assessment categories. Finally, having the lexicon and the final assessment categories allows radiologists and practices to track their results to see how they are performing in reading breast imaging examinations.

In summary, challenges in interpreting and reporting mammograms in the early days of mammography led to the development of the BI-RADS atlas which represents a remarkably useful tool that has improved the way mammograms, breast ultrasound, and breast MRI are read. Having a clear final assessment category and management recommendation is good for patients and their referring doctors. The structured reporting that is outlined in the BI-RADS atlas serves as a model for the rest of radiology in how to read examinations and there are additional reporting systems that are being developed for reading liver, thyroid, lung and other imaging studies. Breast cancer mortality has dropped since the introduction of widespread screening mammography and the BI-RADS atlas has contributed to improved accuracy of mammography interpretation that has helped to decrease deaths from breast cancer. Continued refinements and improvements to BI-RADS, as more experience is gained and more studies are conducted, are on-going.

THE IMPORTANCE OF THE MAMMOGRAPHY QUALITY STANDARDS ACT (MQSA)

BY **PRISCILLA F. BUTLER,** AMERICAN COLLEGE OF RADIOLOGY

> In 1987, the American College of Radiology (ACR) developed the Mammography Accreditation Program to address documented concerns for inadequate and varying mammography quality and radiation dose in the United States.

This voluntary programme provided a means for hospitals and clinics to demonstrate that they provided high-quality mammography by meeting the ACR's standards for mammography personnel, equipment, quality assurance, clinical (patient) images, phantom images (a plastic breast simulator, see Figure 1), and dose. If a hospital or clinic could not pass the accreditation criteria, the ACR would provide feedback from experts in mammography to guide the facility in making improvements. The ACR's accreditation programme gained wide acceptance among facilities and government agencies, even though it was voluntary. In 1991, approximately half of the estimated 10,000 mammography units in the United States had applied for accreditation; approximately one-quarter of the United States mammography units had successfully achieved accreditation.

Several U.S. states passed laws requiring mammography facilities to meet quality standards and submit to regular inspections by state inspectors. In 1990, the United States Congress passed a law authorising screening mammography to be covered by the national social insurance programme, Medicare. Facilities seeking Medicare reimbursement were required to register with the

Health Care Financing Administration and meet quality standards similar to those of the ACR's Mammography Accreditation Program. Federal inspections of Medicare-registered screening facilities began in 1992. Although the goal of quality mammography was the same, this assortment of state, federal, and voluntary private efforts created a patchwork of mammography requirements across the United States, and much of the mammography being performed at that time was not subject to quality regulations of any type. Consequently, quality remained inconsistent.

Recognising the need for uniform national standards that would apply to both screening and diagnostic facilities, the U.S. Congress passed the Mammography Quality Standards Act (MQSA) in 1992. This act requires all mammography facilities to meet minimum quality standards for personnel, equipment, and recordkeeping and to be certified by the U.S. Food and Drug Administration (FDA) or an FDA-approved state certifying body (CB) to legally operate in the United States. To become certified, facilities must be accredited by FDA-approved accrediting bodies. All mammography facilities in the United States had to be certified by October 1, 1994.

Although interim regulations were developed in time for the law to go into effect, a massive effort by the FDA and its advisory committee produced final MQSA regulations which were published on October 28, 1997. In brief, the final rule established personnel requirements, strengthened equipment standards, and outlined many performance-based equipment requirements for quality assurance. Furthermore, the new regulations required mammography facilities to provide patients with written results of their mammograms in language that is easy to understand. Also known as 'lay reports', these communications prevent situations where a woman would 'fall through the cracks' and never receive the results of her mammography examination as it was communicated by the mammography provider to her referring physician. The regulations also required that the mammography provider transfer original mammograms to the patient or the patient's physician at the patient's request. Finally, each mammography facility is required to have a consumer complaint mechanism to provide patients with a process for addressing any concerns.

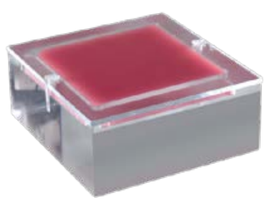
The majority of the final regulations became effective on April 28, 1999. Certain stricter equipment regulations became effective on October 28, 2002.

The FDA designated the ACR as one of four FDA-approved accrediting bodies. The other three are the states of Iowa, Arkansas, and Texas. These states may only accredit facilities within their own borders; facilities within these states have the choice of accrediting with the ACR or with their states. The ACR is the only body that accredits nationally.

The ACR's Mammography Accreditation Program process, which is directed by radiologists and medical physicists through the Committee on Mammography Accreditation, is summarised by the flowchart in Figure 2. A new mammography facility must first complete an online application to provide basic information on the facility, equipment, and personnel, and submit a summary of the pass or fail results from its medical physicists' equipment evaluation, along with an application fee. The facility must apply for accreditation on all active mammography units. If a facility fulfils the initial criteria, the ACR notifies the FDA who issues the new facility a six-month provisional certificate allowing it to legally perform mammography. The ACR then sends the facility a full application to obtain information on the qualifications of its radiologists, medical physicists, and radiological technologists; quality control results; and other requirements of the MQSA, along with the appropriate testing materials. Evaluating image quality is an integral part of the process.

FIGURE 1

American College of Radiology (ACR) mammography phantom



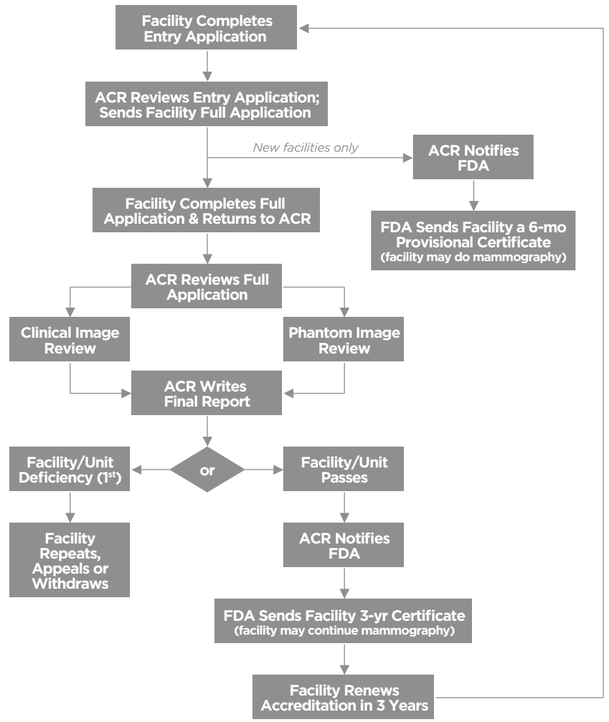
Each applicant must send ACR two sets of normal patient images for evaluation from each mammography unit: one set must be from a patient with fatty breasts and one from a patient with dense breasts. The clinical images are independently scored by two ACR-trained radiologist reviewers who evaluate them for adequate positioning, compression, exposure level, sharpness, contrast, noise, examination identification, and artefacts. In addition, each facility must submit one image from each mammography unit using a phantom (an object used to evaluate the performance of imaging devices in place of a patient). These images are scored by two ACR-trained medical physicist reviewers.

When all stages of the evaluation are completed, the ACR returns the original images and provides a final report (that includes specific assessments and recommendations) to the facility's lead interpreting physician. Those facilities successfully meeting all of the criteria are awarded three-year accreditation certificates for each approved mammography unit. The ACR notifies the FDA of each unit's accreditation approval so that it may issue the facility a three-year MQSA certificate (see Figure 3). The ACR lists each accredited facility on its website (www.acr.org) so that a list of such facilities is available to patients and patient referral organisations.

If a mammography unit does not pass, the ACR's final report provides specific recommendations for improvement so the facility may take

FIGURE 2

Process for the American College of Radiology (ACR) mammography accreditation and the U.S. Food and Drug Administration (FDA) certification.



corrective action on its own. After corrective action, the facility may reapply for accreditation by repeating only the deficient test or tests (e.g., clinical, or phantom). Facilities may appeal any denial of accreditation.

After two consecutive unsuccessful attempts, a facility fails accreditation, and the ACR strongly recommends that the facility take the unit out of service. The ACR works with each facility to help it improve its image quality and to achieve accreditation. The facility must submit a corrective action plan to the ACR for approval and follow-up with documentation supporting this corrective action to reinstate. Once a facility has reinstated, the FDA will send it a six-month provisional reinstatement certificate allowing it to resume mammography and reapply for accreditation.

If a mammography unit does not successfully obtain accreditation after three consecutive unsuccessful attempts, the ACR provides more personalised assistance and oversight before the facility may legally resume mammography. An ACR team (consisting of a radiologist reviewer, a medical physicist reviewer, and a mammography technologist who is a member of the ACR staff) conducts an on-site survey before reinstatement to assess the facility's independent corrective action and provide further advice on necessary improvements. This is an educational effort, and the ACR team works closely with the facility's radiologists, technologists, and medical physicists to achieve these goals. The facility may reinstate only after taking all corrective action recommended by the survey team.

On June 1, 2016, the FDA reported that there were more than 8,500 MQSA-certified facilities with more than 15,000 mammography units in the United States. Over 95% of the units are digital.

The ACR's Mammography Accreditation Program has been one of the most successful quality improvement programmes in radiology. Since its inception as a voluntary programme in 1987, it has improved the quality of mammography performed at facilities throughout the United States, as illustrated by increasing accreditation pass rates and the closure of facilities that could not pass mammography accreditation. This ensures that all women in the United States have access to quality mammography services.

FIGURE 3

Mammography Quality Standards Act (MQSA) certificate

FURTHER READING

Mammography Quality Standards Act of 1992. Public Law 102-539. As amended by the Mammography Quality Standards Reauthorization Act of 1998, Pub. L. No. 105-248, Title 42, Subchapter II, Part F, Subpart 3, § 354 (42 USC 263b), certification of mammography facilities. http://www.fda.gov/Radiation-Emitting-Products/MammographyQuality-StandardsActandProgram/Regulations/ucm110823.htm Accessed June 1, 2016.

Department of Health and Human Services. FDA Mammography Quality Standards, Final Rule. Federal Register, Vol 62, No. 208; Tuesday, October 28, 1997. Available at: http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/Regulations/ucm110906.htm#. Accessed June 1, 2016.

CHAPTER 2: **STANDARDS & QUALITY**

BREAST EXPOSURE TO IONISING RADIATION

BY **ZORAN BRNIĆ** AND **BORIS BRKLJAČIĆ**

> Breast cancer is the most commonly diagnosed cancer among women, accounting for 26% of all cancers, with increasing incidence.

Ionising radiation is well known as a factor that can induce breast cancer. Therefore breast radiation protection is imperative for all health service providers.

Knowledge about radiation carcinogenesis (radiation causing cancer) in the breast derives mainly from epidemiological studies of patients exposed to diagnostic or therapeutic medical radiation and of Japanese atomic bomb survivors, and supports a relationship in which the excess risk is proportional to radiation dose. Hence, breast cancer is a typical stochastic effect of radiation, and the ALARA (As Low As Reasonably Achievable) principle must be strictly adhered to when considering the dose of ionising radiation used in an examination. Radiation does not cause breast cancer immediately, but with a latency period of 10–12 years.

The risk of breast cancer induction per unit dose depends on the age of the patient at the time of exposure to radiation. The susceptibilty for carcinogenesis is increased when the mammary gland is not yet fully developed (intrauterine period, adolescence, pregnancy), with the second decade of life carrying the greatest risk. The risk for women exposed after the menopause is minimal[1]. Age at first full-term birth, the number of viable pregnancies, history of benign breast disease, and genetic factors all influence the risk of radiation-related breast cancer. BRCA genes are involved in the repair of DNA damage caused by radiation, and exposure before 30 years of age during radiation therapy for Hodgkin's disease is associated with an increased risk for women with BRCA 1 and 2 mutations[2].

The breast can be exposed to radiation directly, during imaging or radiation treatment, or indirectly by scattered radiation during other imaging studies. In breast imaging the radiation dose should be optimised, while breast exposure to scatter radiation in other examinations should be minimised.

Mammography is a large contributor to breast radiation exposure. Early detection is important for the successfull treatment of breast cancer and a good prognosis.

Mammography is a proven baseline technique which enables early detection in a large proportion of affected women, and is useful for diagnosis and screening. Randomised controlled trials have shown significant reductions in mortality from breast cancer as a result of screening mammography programmes. Unlike earlier machines, modern mammography machines use fairly low radiation doses to produce mammograms of high quality.

Breast radiation dose is not easily measured, and cannot be simply 'read out' from the mammographic unit. For the individual patient it can be calculated from the exposure (x-ray beam output), compressed breast thickness and percentage of glandular tissue in the breast. The quantity *mean glandular dose* (MGD) is defined as the average dose to the glandular tissue, based on the assumption that the glandular tissue is the most radiosensitive part of the breast.

The breast dose depends on the sensitivity of the image detector, technical parameters selected for the examination like peak kilovoltage (kVp) and milliampere seconds (mAs), and the size and density of the patient's breasts. To ensure the necessary *image quality* with *the lowest possible radiation dose to the breasts,* highly qualified radiographers select the optimum kV value (24 to 32 kVp) that provides a balance between breast penetration and absorbed dose. They also ensure the breast is adequately compressed to make it thinner, therefore requiring a lower dose of radiation.

Radiation dose is not an absolute criterion for the acceptability of the examination, and any encouragement for patients to go 'dose shopping' by searching for the facility with the lowest mammography dose should be avoided. Imaging with doses that are too low could result in missing cancers and having the risk of an additional radiation dose later on. The goal of the *optimisation* process – a compromise between the necessary image quality and as low a radiation dose as possible – can be achieved by sytematic implementation of a *quality assessment/control programme* in a mammography unit.

Systematic monitoring of equipment, technique and organisation is necessary to ensure the correct balance between the quality of mammogram and the dose, which should comply with international standards (eg. MQSA; *Mammography Quality Standards Act,* see separate chapter by Penny Butler). Unnecessary radiation dose should also be minimised by ensuring that as few mammograms as possible are repeated.

Two-view digital mammography has MGD of 3.7 mGy, associated with a *risk* of fatal radiation-induced cancer of 1.3–1.7/100,000 women. The risk of malignancy related to radiation dose is expressed with the *effective dose.* Since different tissues and organs have varying

TABLE 1

Adult effective doses for various radiology procedures in comparison to mammography (adapted from reference 4)

Examination	Average Effective Dose (mSv)	Values Reported in Literature (mSv)
Mammography	*0.4*	*0.10–0.60*
Posteroanterior and lateral study of chest	0.1	0.05–0.24
Lumbar spine	1.5	0.5–1.8
Pelvis	0.6	0.2–1.2
Head CT	2	0.9–4.0
Chest CT for pulmonary embolism	15	13–40
Abdominal CT	8	3.5–25
Coronary angiography (diagnostic)	7	2.0–15.8
Transjugular intrahepatic portosystemic shunt placement	70	20–180

sensitivity to radiation, the radiation exposure risk varies for different parts of the body. The term 'effective dose' is used when referring to the radiation risk averaged over the entire body. Knowledge of effective dose allows for the quantification of risk and comparison to more familiar sources of exposure that range from natural background radiation to radiographic medical procedures.

The effective dose for a two-view mammogram of each breast is 0.6 mSv for screen-film mammography (SFM) and 0.4 mSv for digital mammography (DM). People are exposed to an average effective dose from background radiation of 3 mSv/year, so the examination dose equals approximately two months of background radiation. For comparison, the dose from an airplane flight is 0.04 mSv, the annual dose from food is 0.3 mSv, and the annual limit for a radiation worker is 50 mSv. The effective dose of a chest x-ray is four times lower than that of mammography, while for abdominal CT it is up to 50 times higher, equivalent to several years of natural radiation (see Table 1).

Although radiation dose was much higher in the early stages of SFM, it has steadily decreased over time, especially after implementing full-field DM. The American College of Radiology Imaging Network (ACRIN) Digital Mammography Imaging Screening Trial showed breast doses from DM to be 22% lower than those from SFM, with MGD 3.7 mGy for two-view DM. With the use of 2007 ICRP breast tissue-weighting factor of 0.12, this MGD corresponds to effective dose of 0.44 mSv[3].

Digital breast tomosynthesis (DBT) is a promising new DM technology with improved diagnostic performance that has benefits in screening. The advantage of DBT is the elimination of the summation of shadows typical for conventional mammography and improved detection and characterisation of lesions in breasts with a high percentage of glandular tissue, improving sensitivity as well as specificity and decreasing recall rates, especially in patients with dense breasts who are younger than 50. It seems that the radiation dose with DBT may be up to two times the dose of DM only in women with predominantly fatty breasts with a low amount of glandular tissue, while in dense breasts the difference of the doses is lower. Radiation dose depends on whether DBT is implemented as one-view or two-view in addition to full-field digital mammography. Use of synthetic views reconstructed from original datasets of DBT could eliminate extra radiation dose due to mammography, and reduce the radiation dose by 40–50% without having an impact on diagnostic accuracy. In the future discussions of the role of DBT in screening, a moderate increase in radiation exposure per individual DBT exam must be weighted against the benefit of decreased recall rates (responsible for 10% of additional dose) which could reduce patient anxiety and radiation dose in general.

Nuclear medicine *breast-specific gamma imaging (BSGI)* and *positron emission mammography (PEM)* can be useful in the work-up of known breast cancer, or in women with very dense breasts. These methods are not suitable for routine screening, as single BSGI or PEM exams expose patients to a risk of radiation-induced cancer comparable to the risk from an entire lifetime of yearly mammograms starting at 40 years of age. The average effective dose from BSGI and PEM studies (6.2–9.4 mSv) equals two to three years of background radiation. While DM has a lifetime risk of inducing 1.3 breast cancers per 100,000 women aged 40 at exposure, the risk of a single BSGI or PEM was estimated to be 20–30 times greater.

In *CT examinations* where the breast is within the scanning volume, breast radiation dose is considerable. A chest CT examination for pulmonary embolism delivers 20–60 mGy to the breast, and CT coronary angiography 50–80 mGy. Even in abdominal CT, a breast dose of 10–20 mGy is considerable[4], seven times the dose of a standard two-view mammogram or equal to 50–100 chest radiographs. Since 1 mSv may induce five additional malignancies in 100,000 exposed people, a hundred additional cases of breast cancer can be assumed in 100,000 women exposed to chest CT. Especially for younger women, proper justification of procedures is strictly necessary, with shielding of the breasts with bismuth garments if feasible.

Radiation treatment to the chest for malignancy in childhood or adolescence substantially increases the risk of breast cancer. Young women irradiated for Hodgkin's lymphoma have three to seven times the risk of breast cancer compared to women with Hodgkin never treated with radiation. Although radiation therapy increases the risk of breast cancer later in life, the benefits of its use in the

treatment of potentially fatal malignant lymphoma far outweigh this risk. MRI based screening for breast cancer may be benefitial for these high-risk patients.

Randomised trials studying the *risk of cancerogenesis from mammography* do not exist for ethical reasons, so the levels of risk have been estimated based on data from atomic bomb survivors in Japan. Although many experts believe that low-dose exposure to radiation received by mammography minimally increases the risk of breast cancer, others warn that the damage from lower-energy x-rays, including mammography, cannot be predicted by estimating risk from higher doses, as they cause substantially greater damage to DNA than high energy sources.

The risk of radiation-induced breast cancer in properly organised and controlled mammographic screening is small compared with the expected mortality reduction, and the risk should not deter women from screening, even at the age of 40–50. Women older than 70 have a substantially reduced risk of radiation-induced cancer from screening, since the risk of cancerogenesis in breast tissue decreases rapidly with age. Mammographic screening should not generally be recommended for those women mainly because of the problem of overdiagnosis and potential harm. There are controversies regarding screening women at different levels of risks of breast cancer and the age at which screening should begin, particularly in women with dense breasts (which limits the sensitivity of mammography). Considering breast radiosensitivity in younger women, the U.S. Preventive Services Task Force (USPSTF) recommended in 2009 against the use of routine mammography screening for women under 50, and recommended two-year intervals for average risk women aged 50–75. The USPSTF concluded that for women aged 40–49, the benefits of screening do not outweigh the harm, particularly that caused by false-positive results with unnecessary biopsies and follow-up imaging, which lead to anxiety and distress.

The increased carcinogenesis risk at younger ages, the limited accuracy of mammography in dense breasts, and the high risk of cancer in BRCA-positive women, raises a dilemma about whether it is justified to begin with screening before the age of 40. Early screening of high-risk women might seem justifiable as many will develop breast cancer in their 30s or 40s, and early detection may save their lives. However, women with BRCA mutations who were exposed to radiation before the age of 20 had 2.5 times the risk of breast cancer. Even low doses associated with early annual screening mammography could jeopardise women with BRCA-mutations, as radiation exposure before the age of 30 increases the risk of breast cancers in a dose-dependent manner[2].

In conclusion, mammography is a fast, widely available, accurate, cheap and acceptably harmful method for diagnosis and screening of breast cancer. The main aim of mammographic screening is to reduce the mortality from breast cancer. The benefit of early diagnosis and treatment of breast cancer far outweighs the risk of the small amount of radiation received during a screening mammogram. The general conclusion of the IARC (International Agency on Research of Cancer) working group confirmed that the probability of saving a life by early detection with screening is at least 100 times greater than the probability of death caused by the radiation from screening. The possibility of inducing cancer by radiation is often sensationalised in the media, resulting in anxiety, and occasionally delays or avoidance of mammography, which may subsequently result in late diagnosed cancer. Many people overestimate the levels of exposure and the risks of ionising radiation from mammography, and fear radiation more than necessary – including some radiologists or referring physicians. Mammography screening has been considered one of the major medical advances of the past decades, and women need to be provided with the important information that mammography saves lives and that the radiation risk is minimal.

REFERENCES

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EUROPEAN COMMISSION INITIATIVE ON BREAST CANCER

BY THE JRC HEALTHCARE QUALITY TEAM:
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> The European Commission Initiative on Breast Cancer (ECIBC) is a person-centred sustainable initiative aiming to improve and harmonise breast cancer care in Europe.

ECIBC is coordinated by the Commission's Joint Research Centre (JRC) under the auspices of the Directorate General for Health and Food Safety. The JRC is the European Commission's in-house science service and provides an inclusive and transparent platform for engaging stakeholders. The JRC is independent of any national, commercial or private interests.

WHY IS THE ECIBC NEEDED?

According to WHO 2012 estimates, each year there are 2.6 million new cases of cancer in Europe (excluding non-melanoma skin cancers)[1]. Breast cancer is the most frequently diagnosed cancer in Europe, with 364,000 new cases each year. In women this figure represents almost one third of all diagnosed cancers. It is also estimated that breast cancer causes 91,000 deaths each year in Europe. Even though the prognosis of breast cancer is quite favourable, one out of every six women with cancer will still die from breast cancer.

Incidence rates (the number of new cases in a given period in a specified population) and mortality rates (the number of deaths in a given period in a specified population) for breast cancer vary widely between countries.

Although a higher mortality rate in some countries may be due to a higher incidence rate, in others it may be due to lower rates of survival of breast cancer patients. This lower survival rate may reflect major health inequalities, including those related to different health policies, but also those related to lower quality of care. Hence, there is considerable potential to reduce the burden of cancer, and inequalities in cancer diagnosis and care, at the European level.

The EU Member States acknowledged the need for a coordinated action to tackle the burden of cancer via the Council Conclusions of 2008[2]. As a consequence, the European Commission launched the ECIBC in 2012. It aims to ensure that all breast cancer care processes are performed with quality and appropriateness, based on the best available evidence, and are accessible to all citizens. The ECIBC is working towards this crucial harmonisation goal with the support of clinical and scientific experts, patients, and other stakeholders, and taking into account the existing guidelines and schemes.

FIGURE 1

The European Commission Initiative on Breast Cancer

ECIBC OBJECTIVES

The ECIBC covers all breast cancer care processes from screening of breast cancer until end-of-life care. The following six processes have been identified along the breast cancer care pathway (see also Figure 2):

1. screening
2. diagnosis
3. treatment
4. rehabilitation
5. follow-up and survivorship care
6. palliative care

The four specific objectives of the ECIBC are to establish:

1. A voluntary European quality assurance scheme for breast cancer services (the *European QA scheme)* addressing all care processes.

- The *European QA scheme* will define a common set of quality and safety requirements for breast cancer services in Europe.
- The scheme will cover all the relevant areas of healthcare provision for breast cancer and all processes of breast cancer care.
- It will be piloted among participant services in Europe in 2017, and thereafter it will be available to all by 2018.

2. Evidence-based recommendations supporting the *European QA Scheme:*

a. The European guidelines for breast cancer screening and diagnosis (the *European Breast Guidelines)*

- The *European Breast Guidelines* will provide recommendations for the screening and diagnostic processes of breast cancer services.
- Whenever possible and appropriate, the evidence-based approach is applied.
- The *European Breast Guidelines* will have a web-based format, and will be publicly available starting from 2016.

b. A platform of guidelines covering all care processes (the *Guidelines Platform)*

- Breast cancer guidelines produced by different entities and stakeholder organisations, such as professional societies, are being collected.
- Only those trustworthy guidelines fulfilling the carefully defined eligibility criteria will be included in the web-based platform hosted on the ECIBC website.
- This platform can be foreseen as a valuable resource of guidelines for professionals, policy makers, researchers, and guideline developers, as well as for citizens and patients, and will be available by 2017.

3. A European training template on digital breast screening for the competence and training requirements of the *European QA scheme*

- A concept for training on digital breast screening to be developed will be aimed at health professionals involved in screening programmes.
- The digital screening training template will include the essential requirements

FIGURE 2

The breast care pathway

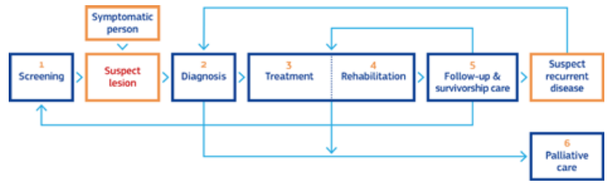
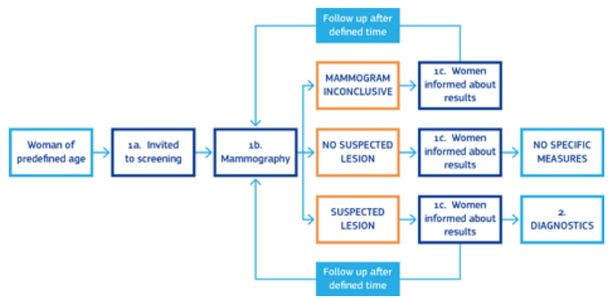


FIGURE 3

The screening pathway



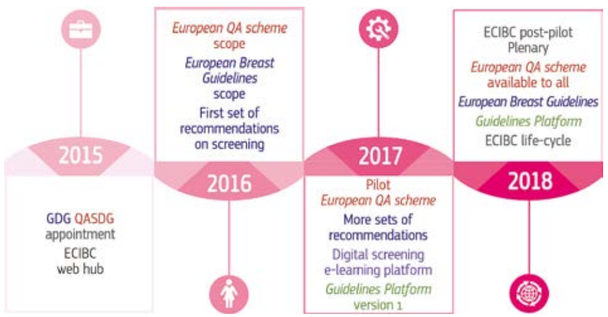
for professionals working for services adhering to the *European QA scheme.* It will be designed and disseminated in coordination with European key stakeholders.

- The digital screening template is expected to be ready by 2016. Thereafter, the model would be available and applicable to other professional profiles covered by the *European QA scheme.*

4. **A web interface, the *ECIBC web hub,* (ecibc.jrc.ec.europa.eu) offering complete public information on the ECIBC and its deliverables**
   - The site will host all the ECIBC objectives in the most updated version.
   - It will also provide a map of the certified breast cancer services accredited with the *European QA scheme.*
   - Key-information will be available in all official EU languages.

FIGURE 4

ECIBC Timeline



THE IMPACT OF THE ECIBC ON TRAINING – WITH SPECIAL EMPHASIS ON RADIOLOGY

Of particular importance from the radiological point of view is the screening and diagnosis of breast cancer, where different imaging methods and radiological interventions are needed. The schematic presentation of the screening pathway is shown in Figure 3.

The crucial importance of the correct and timely diagnosis is also emphasised by the ECIBC, of which one of the key objectives is related to development of the competence and training requirements for breast screening in general, and for digital breast screening in particular.

In fact, the European training template for digital screening will set essential training requirements for professionals working in breast screening activities, initially by developing a template tailored for radiologists and radiographers.

This training template will ensure that citizens going through breast screening will have it provided only by healthcare providers who have received adequate training. Moreover, the healthcare providers will be asked to fulfil some specific indicators which show that their work is admissible.

ECIBC TIMELINES

At the end of 2018 all key objectives will be fulfilled. The ECIBC will build on sustainable approach, and all project deliverables will be updated based on need. The timelines of the ECIBC are provided in Figure 4.

ECIBC WORKING MODALITY

To achieve these crucial objectives, the ECIBC does not work in isolation but counts on working groups consisting of professional and scientific experts, as well as citizens and patients, who work for the project voluntarily. The working group members have been selected through a transparent open call process.

To produce reliable outcomes, the requirements and the recommendations established within the project will be developed based on the best available evidence using explicit and transparent approaches. Thus, the outcomes will be based solely on scientific evaluation of the available data, independent of any national, commercial or private interests.

Other stakeholders, including patient organisations, professional societies and individual citizens, are able to contribute through public calls for feedback. This multidisciplinary, inclusive and transparent working method ensures feasible and wide implementation to truly impact on the quality of care.

ECIBC EXPECTED BENEFITS

By ensuring an essential level of quality and safety in breast cancer care, the ECIBC is expected to reduce inequalities and contribute to reducing the burden of breast cancer, and empower citizens and patients in breast cancer care in the whole of Europe.

The *European QA scheme* is designed to adhere to guidelines to facilitate the implementation of evidence-based recommendations and thus reduce unwanted variability in healthcare. Moreover, the continuous implementation of the scheme will be an effective way of keeping guidelines up-to-date.

The ECIBC model is being developed as a 'blueprint': it will be easily exportable to other cancers, diseases and healthcare areas.

CONCLUSIONS

Efforts are needed to ensure that all European citizens have access to healthcare services with an essential level of quality and safety.

The ultimate intended impact of the ECIBC is to improve quality and reduce unnecessary variability in healthcare services, and hence, to improve the outcomes of breast cancer patients in terms of morbidity, mortality, and quality of life.

More information: ecibc.jrc.ec.europa.eu

REFERENCES
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CHAPTER 2: **STANDARDS & QUALITY**

HISTORY OF BREAST IMAGING

FROM ‘MAMMOGRAPHY’ TO ‘BREAST IMAGING’: A HISTORY

FROM ‘MAMMOGRAPHY’ TO ‘BREAST IMAGING’: A HISTORY

BY **BONNIE N. JOE** AND **EDWARD A. SICKLES**

> What began as ‘mammography’ in the early days of x-ray technology has now evolved into the field of ‘breast imaging’.

Why did the name change? The history of breast imaging encompasses many years of improvement in mammographic techniques, entry into the digital age, and now includes breast ultrasound and magnetic resonance imaging as a standard part of breast imaging practice across the globe. The scope of this article allows only a brief glimpse into the rich history of breast imaging. Innovation, leadership, and commitment on the part of many over the past decades have contributed to making breast imaging the exciting field it is today.

MAMMOGRAPHY – THE BEGINNING

In 1913, Dr. Albert Salomon, a surgeon at the University of Berlin, first published his work using x-rays to study breast cancer *ex vivo* in 3,000 mastectomy specimens[1]. During the following decades, early attempts at in vivo imaging of the breast did not sustain interest, mainly due to poor visualisation of breast tissues (Figure 1). Fortunately, there were radiologists who continued to work on improving mammography techniques. Dr. Stafford Warren was able to successfully use direct x-ray technology to image the breast *in vivo* (Figure 2) and in 1930, published results of pre-operative evaluation of breast lesions for malignancy[2]. In 1948, Dr. Jacob Gershon-Cohen was able to demonstrate the feasibility of mammography to detect occult breast cancer[3] thus introducing the concept of screening mammography. In 1951 Dr. Raul Leborgne described the importance of the relationships between calcifications and breast cancers[4]. In 1960, Dr. Robert Egan’s description of a standardised direct-exposure mammographic technique sparked renewed interest in mammography[5]. Egan is credited with disseminating his direct x-ray technique for mammographic positioning and imaging, facilitating more widespread adoption of mammography. Around this time, Dr. Charles Marie Gros, in Strasbourg, France, developed the first dedicated mammography unit, the CGR Senographe, which became available in the 1960s[6].

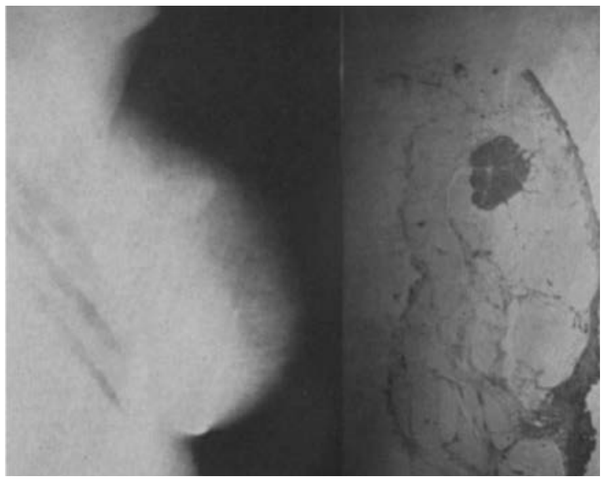
By today’s standards, direct-exposure film images (Figure 3a) are not considered of diagnostic quality. Nevertheless, the landmark results of the Health Insurance Plan of Greater New York, published in 1973 and known as the ‘HIP study’, showed a statistically significant reduction in breast cancer deaths among women offered screening compared with a control group of women not offered screening[7]. Subsequent randomised controlled trials and results of population-based service screening confirm the lifesaving benefit of mammography screening. Additional information can be found in the article devoted to screening mammography in Chapter 1.

XEROMAMMOGRAPHY

During the 1970s, thanks primarily to the efforts of Dr. John Wolfe, working closely with the Xerox Corporation, a

FIGURE 1

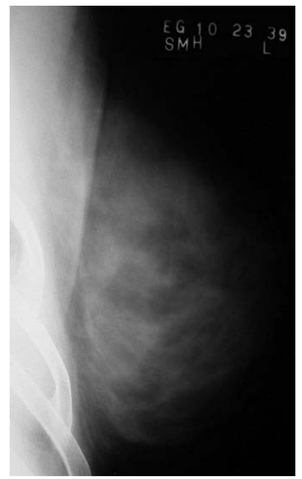
Example of a direct x-ray mammogram from 1934, showing an ‘infiltrating mass’ (left image) representing the breast cancer seen on the corresponding histologic section (right image). Note the difficulty in visualising the mass on this early mammogram.



Joe BN, Sickles EA. The evolution of breast imaging: past to present. Radiology. 2014 Nov; 273 (2 Suppl): S23-44

FIGURE 2

1939 direct exposure mammogram (lateral view) from files of Dr. Stafford Warren.



Courtesy of Dr. Lawrence Bassett. University of California, Los Angeles

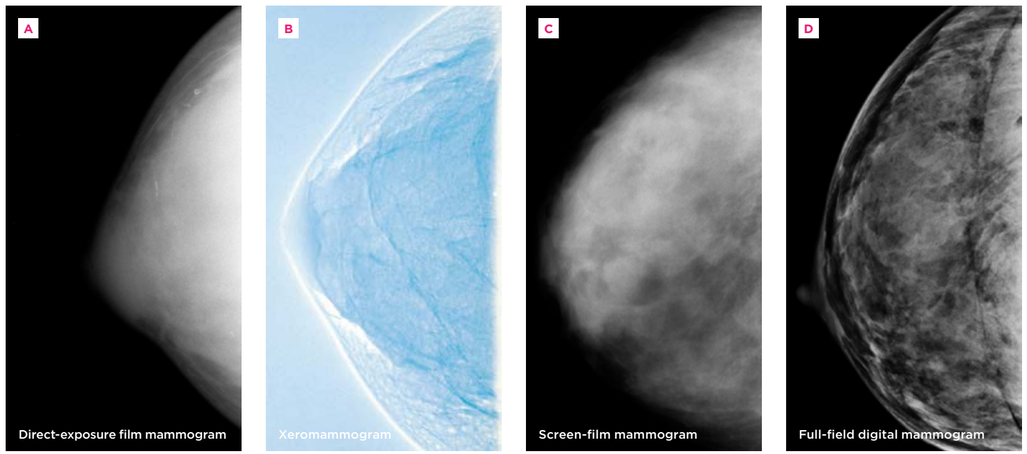
'new and improved' technology emerged called xeromammography. Xeromammograms were printed on paper with blue powder, using a technique adapted from the xerographic photocopying process, and were well-suited to imaging the breast (Figure 3b)[8]. However, there were problems with xerographic image processing such as paper jams and non-uniform toner (similar to those seen with modern-day copiers), and given the paucity of continuing innovation, xeromammography was ultimately replaced by screen-film mammography.

SCREEN-FILM MAMMOGRAPHY

Another major technological advance, screen-film mammography, was first introduced in 1973 by DuPont. Screen-film techniques allowed faster imaging times, improved contrast, and reduced

FIGURE 3

Comparison of negative CC view mammograms of dense breast tissue 1965 to present: A) direct-exposure film mammogram without compression. There was limited evaluation of tissue close to the chest wall because thicker tissue in this region could not be penetrated by the x-ray beam without overexposing thinner tissue near the nipple; B) xeromammogram illustrating improved depiction of breast tissue compared to A) due to the wide dynamic range of the xeroradiographic imaging process; C) screen-film mammogram obtained using dedicated a molybdenum-anode x-ray unit capable of uniform-thickness breast compression to allow proper exposure of tissues from chest wall to nipple; D) full-field digital mammography image obtained with uniform-thickness breast compression and selenium flat-panel detector.



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radiation dose compared with direct x-ray and xeromammography. With the addition of uniform thickness breast compression, breast tissue was spread out more evenly, allowing further reduction of radiation dose and better visualisation due to fewer motion artefacts[9]. Continued technological improvements in the screen-film process and advances in dedicated units for performing mammography led to continued improvements in breast image quality during the 1980s and 1990s (Figure 3c).

MAMMOGRAPHY OF TODAY: DIGITAL MAMMOGRAPHY AND DIGITAL BREAST TOMOSYNTHESIS

Breast imaging experienced another significant technological advance with the transition from analogue (film-based) mammography to digital mammography (Figure 3d)[10]. From the patient's perspective, digital mammography is performed the same as analogue mammography. However, because the images are 'read' from electronic signals by a computer rather than developed on x-ray film by a technologist, images are available to the radiologist in a much shorter time. Digital mammography has the added benefit of lower radiation dose compared with analogue (film-based) mammography. As radiologists traded in their light boxes for computers and workstations, the digital transition allowed workflow improvements such as integration of imaging with the electronic medical record and reporting systems.

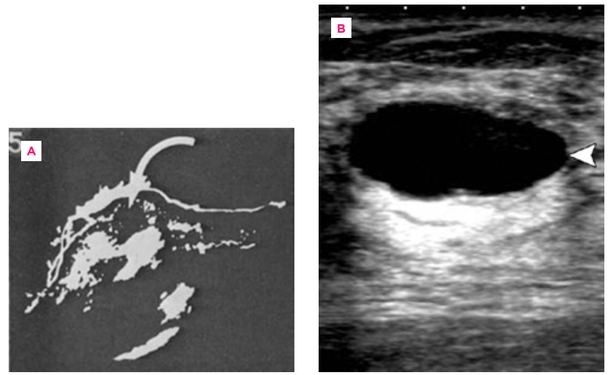
Building on advances in digital mammography, digital breast tomosynthesis (DBT) was the next major technological development in mammographic imaging[11]. DBT acquires multiple low-dose mammographic projections through the breast thereby improving the visualisation of overlapping tissues. DBT has been shown in studies to reduce false positive findings and improve detection of invasive cancers[12-14]. As a result, DBT is often called 'a better mammogram' and may soon become the standard for mammographic screening.

BREAST ULTRASOUND

Breast ultrasound is an indispensable tool in current breast imaging practice and provides complementary information to mammography. Similar to early mammograms, early ultrasound images would seem crude by modern standards (Figure 4a) but served to distinguish a mass as solid or cystic. Just as mammography has seen technological improvements, so has breast ultrasound.

FIGURE 4

A) Early grey scale ultrasound image of breast cyst (curved arrow) from 1970; B) grey scale ultrasound image of a simple cyst (arrowhead) from present time. Mass is anechoic with smooth margins and posterior acoustic enhancement. These features are diagnostic of a benign lesion that requires no additional workup.



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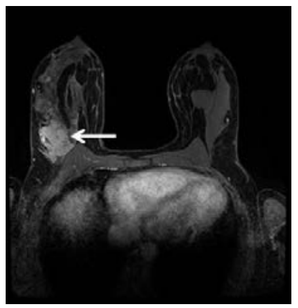
Adding ultrasound to mammography improves a radiologist's ability to distinguish benign from suspicious lesions, thus reducing the number of benign biopsies, for example, in the case of the simple cyst shown in Figure 4b[15,16]. Breast ultrasound for whole breast screening has been shown to detect small cancers that are not palpable and cannot be seen by mammography, particularly in dense breasts[17,18]. A high rate of false positive biopsies and operator dependence are acknowledged limitations of hand-held screening ultrasound[19].

FIGURE 5

Gadolinium-enhanced breast MRI showing cancer (arrow) in right posterior breast. Dense breast parenchyma may hide this cancer at mammography.



BREAST MRI

Breast MRI was not considered useful for breast cancer evaluation until gadolinium contrast became available. In the mid-1980s, Werner Kaiser and Sylvia Heywang-Köbrunner reported on the potential for contrast-enhanced MRI in the clinical evaluation of breast cancer[20,21]. During the next two decades, clinical applications for breast MRI expanded from diagnostic applications such as evaluation for unknown primary cancer in a patient with axillary adenopathy, extent of disease evaluation, and pre-surgical planning.

Breast MRI is the most sensitive means of detecting breast cancer (Figure 5) but is much more costly than mammography and results in more false positive biopsies than mammography. Thus, breast MRI is not currently recommended for screening the general population but reserved for supplemental screening (in addition to mammography) of high risk populations such as BRCA mutation carriers and patients with very strong family history of breast cancer.

BREAST INTERVENTIONAL PROCEDURES

Wire localisation

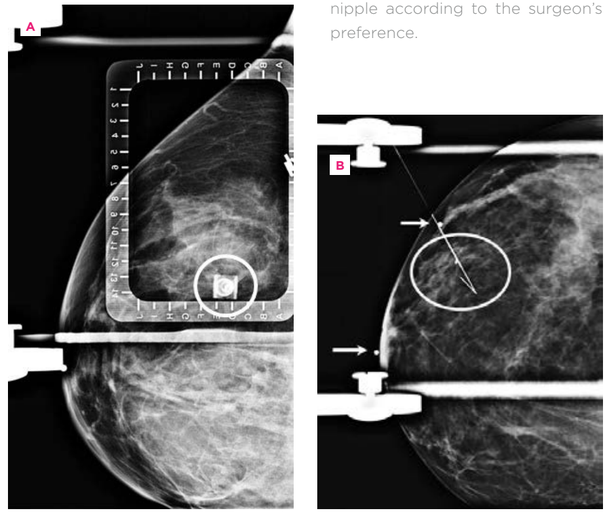
Breast localisation and minimally invasive biopsy procedures developed alongside mammography and other breast imaging technologies. Prior to the 1970s, suspicious breast lesions required surgical excision to obtain a diagnosis. As a result, several benign surgeries were performed to diagnose one cancer. For non-palpable lesions seen at mammography, a large amount of breast tissue was removed to ensure the lesion was included in the specimen. Pioneers such as Gerald D. Dodd, Jr. initially placed needles 'freehand' into the breast to guide surgeons to non-palpable lesions seen by mammography, but the needles could easily fall out[22-24]. Radiologist Ferris Hall, along with surgeon Howard Frank, reported a technique for hook-wire localisation through a needle in 1976[25]. The hook-wire held in place within the breast better than a straight needle. Additional improvements came with the development of needle localisation systems that allowed repositioning for more accurate placement of the wire, for example as developed by Daniel Kopans and Marc Homer[26,27]. Development of grid localisation devices, which allowed needle placement parallel to the chest wall (Figure 6), created a safer procedure for patients compared with the freehand technique, in which the needle pointed towards the chest wall and thus carried a risk of pneumothorax. The increased accuracy of wire localisation techniques allowed surgeons to remove less breast tissue and provide better cosmetic results for patients. Currently, localisation is performed under mammography, ultrasound or MRI guidance, even using localising devices other than wires, for example, radioactive seed localisation[28,29].

Percutaneous Biopsy

Development of image-guided percutaneous breast biopsy allowed a more rapid, less invasive, less expensive way to obtain a tissue diagnosis for suspicious findings and provided excellent cosmetic results for the patient with little, if any, scarring[30,31]. The role of the breast imaging radiologist now expanded to include tissue diagnosis with involvement of the breast surgeon only in cases of diagnosed malignancy or in cases where more tissue was needed for a definitive diagnosis. Percutaneous biopsy via fine-needle aspiration technique under stereotactic guidance for non-palpable breast lesions began in 1976 at the Karolinska Hospital in Sweden[32]. Fine needle aspiration biopsy was attractive as a minimally invasive procedure but suffered from a high rate of insufficient sampling under general use and also required available cytology expertise. Ultrasound-guided core biopsy was described by Carl D'Orsi and Ellen Mendelson in their 1989 review[33]. Core biopsy has advantages over fine needle aspiration biopsy in terms of larger tissue sample and ability to diagnose invasive disease based on histology. Currently, core biopsy is successfully performed under mammographic, ultrasound or MRI guidance. This minimally invasive technique is currently considered the 'first line' approach to obtain a diagnosis rather than surgical excision.

FIGURE 6

Wire localisation using a grid: A) Lateral view of the breast in grid after the needle has been placed parallel to the chest wall, targeting a biopsy clip. The needle hub is seen within the circle annotation; B) orthogonal view (CC) image after wire deployment. The stiff portion of the wire is centred at the biopsy clip (circle). BB markers (arrows) were placed at the skin entry site and on the nipple according to the surgeon's preference.



SUMMARY

Breast imaging radiologists today have more tools at their disposal and are a more integral part of patient care than ever before. Image-guided minimally invasive needle biopsies of the breast have virtually eliminated the need for surgical biopsies, decreasing patient morbidity and reducing healthcare costs for society. Advanced mammography remains central to early detection efforts and lower mortality rates from breast cancer.

REFERENCES
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CHAPTER 3: **HISTORY OF BREAST IMAGING**

RESEARCH

BREAST CANCER PATIENTS TO BENEFIT FROM EIBIR'S EU-FUNDED IMAGING RESEARCH PROJECTS

BREAST CANCER PATIENTS TO BENEFIT FROM EIBIR'S EU-FUNDED IMAGING RESEARCH PROJECTS

BY **MONIKA HIERATH, PAMELA ZOLDA, PETER GORDEBEKE, KATARINA KRISCHAK, MICHAEL CREAN**

> Breast cancer is the second most common cancer in the world, and kills more women than any other cancer type.

Between 2007 and 2013, the European Union (EU) invested €160 million in breast cancer research and that support continues under the current research and innovation programme until 2020. A number of EU-funded projects are taking up personalised medicine in their research approach, aiming to develop treatments adjusted to a patient's specific circumstances and condition.

As a result, patients will benefit from new findings that lead to better solutions for diagnosis and treatment of breast cancer. The EU's main goals are to get important research results from the bench to the bedside faster and to ensure that innovative technology is accessible to patients as soon as possible.

Since 2008, the European Institute for Biomedical Imaging Research (EIBIR) has coordinated and managed three major EU projects on personalised breast cancer diagnosis and treatment. EIBIR is a non-profit organisation founded by the European Society of Radiology which helps researchers and industry partners to coordinate biomedical imaging research throughout Europe and beyond. EIBIR provides expert advice, professional project management, coordination, dissemination (informing people of the results) and exploitation (ensuring the results are used) services for international collaborative research projects and clinical studies.

EIBIR's mission is to coordinate and support the development of biomedical imaging technologies and the dissemination of knowledge with the ultimate goal of improving the diagnosis, treatment and prevention of disease. EIBIR's support for several breast cancer research projects over the last decade is integral to this mission and this article presents three EU-funded and EIBIR-coordinated projects, highlighting their innovative ideas and results, as well as their potential benefits for patients across Europe.

The three-year (2008–2012) project Highly Accurate Breast Cancer Diagnosis through Integration of Biological Knowledge, Novel Imaging Modalities and Modelling (HAMAM) had the ambitious goal of improving methods for the early detection and accurate diagnosis of breast cancer and suspicious breast tissue. The aim was to tailor treatment procedures to the individual patient by integrating various types of medical images and patient information together into one clinical workstation.

When investigating a suspected case of breast cancer, clinicians prefer to use a range of imaging methods, which can include techniques such as mammography, 2D ultrasound, dynamic contrast-enhanced magnetic resonance imaging, digital breast tomosynthesis, positron emission mammography and automated 3D breast ultrasound. The HAMAM project set out to develop a new patient-centric workstation that incorporates these diverse and advanced image acquisition and corresponding image analysis methods into one user-friendly interface. This makes it quicker and easier to access the wide range of information needed for physicians to make accurate, early diagnosis of breast malignancy as a basis for reliable treatment decisions. A team of nine scientific institutes and companies from five European countries, plus the USA, contributed to the project, coordinated by EIBIR.

Among the key outcomes of the project were a number of tools designed to automatically correlate and interpret information from different sources. With conventional imaging workstations, extensive training is required before readers are able to identify instances of suspicious structures in 2D projection images, like mammography and 3D modalities. A major result of the HAMAM project is a set of new techniques that can automatically map corresponding anatomical structures across different types of medical imaging. The images can then be presented such that sizes, positions, and orientations match between these various types of imaging, giving the human reader a more complete and accurate picture of the lesion.

A new system was also developed to classify lesions as either benign or malignant using image descriptors from mammography with kinetic and morphological descriptors from magnetic resonance imaging (MRI). A second computer-aided diagnosis (CAD) system assists radiologists in characterising suspicious lesions in automated breast ultrasound (ABUS); a promising technology for screening women with dense breasts. In a reader performance study, this new CAD system outperformed most radiologists and, when used by radiology residents, significantly improved their performance compared to conventional ABUS reading. In addition, HAMAM generated improved knowledge of how the genetic risk of breast cancer can be used in clinical practice.

The methodological innovations were integrated into the patient-centric HAMAM workstation (see Figure 1), which enables readers to quickly access the various imaging studies, plus non-imaging information, and make fully informed, computer-assisted decisions about diagnosis and treatment. This offers the potential to dramatically improve the efficiency of breast cancer care.

The results from HAMAM encouraged the project team to apply for further EU funding and this led to the project Virtual Physiological Human: Personalised, Predictive Breast Cancer Therapy Through Integrated Tissue Microstructure Modelling (VPH-PRISM), which has continued with much of the work of HAMAM. VPH-PRISM aimed to develop personalised and predictive modelling of breast cancer which would allow treatment

CHAPTER 4: **RESEARCH**

stratification and prevent unnecessary and unsuccessful treatment. The rationale behind the VPH-PRISM project is that detecting breast cancer early and getting the right treatment started as soon as possible requires input and expertise from a number of medical specialists. These specialists include radiologists, gynaecologists, pathologists, surgeons, radiotherapists and oncologists, who all use different sets of tools in the diagnosis and treatment of breast cancer. For instance, radiologists read images from scans and pathologists examine tissue samples for signs of cancer. Surgeons and clinicians then use this information for diagnosis, as well as treatment and surgery planning, but they tend to receive this information separately from the various specialist disciplines, which also have their own specific 'language' when it comes to their findings.

The aim of the VPH-PRISM project was to develop a way to allow these specialists to essentially speak the same language. The team was made up of leading organisations in the fields of pathological imaging, radiological imaging, image processing and biophysical and statistical modelling from four European countries and two partner organisations from the United States. Researchers created a unique database that allows image data from a range of technologies such as MRI, mammography and ultrasound to be combined with pathology data and other information like patient age, patient lifestyle and genetics. This means the clinician would

FIGURE 1

The HAMAM Workstation which gives users access to various imaging studies and non-imaging data in one platform

FIGURE 2

Surgeon using VPH-PRISM surgery planning iPad application in the operating room

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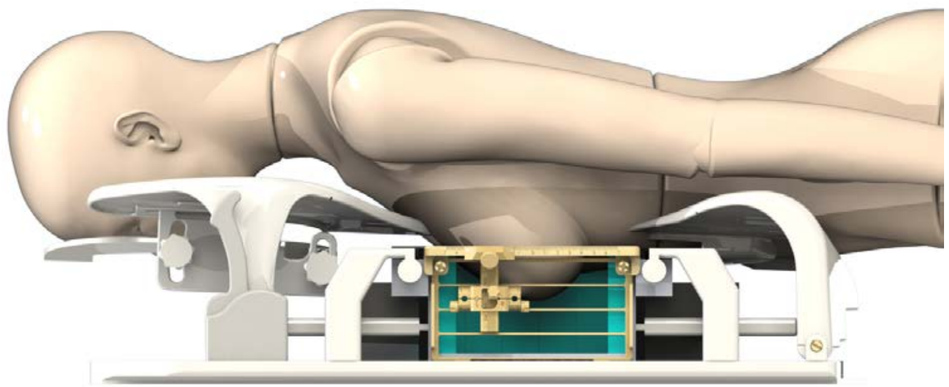
no longer need to try to make sense of all these different findings separately, but would have them together in one tool, which combines all this data for a more accurate assessment of the tumour characteristics, making therapy planning simpler and more objective.

The project also created new software and a clinical decision tool that can help surgeons in their planning. Together they constitute a surgery planning software suite that can make the planning process computer aided. The result is an augmented reality application that can be viewed by the surgeons in the operating room on an iPad (see Figure 2). By holding the iPad over the patient, the surgeon can see precisely where the tumour is located; the app corrects for deformities caused by the patient's position and the surgeon can view from various angles. Prior to surgery, surgeons normally review imaging data to ascertain the location of the tumour and then record this by hand on paper, which they then use to help them mark the patient's skin. With this app, surgeons have all the imaging data with them in the operating room, which has been automatically correlated to produce a three-dimensional computer graphic that can be displayed, rotated and changed, and viewed in-real time in the actual patient by using the iPad's built-in camera. This has the potential to facilitate more accurate breast cancer surgery, which could in turn lead to less follow-up surgery. The app has undergone some initial testing and further research and development will continue after the project officially ends.

FIGURE 3

Planned HYPMED PET/RF insert



These new tools will also have a significant impact on breast cancer care as they will facilitate earlier and more accurate diagnosis, leading to improved outcomes, as well as better surgical outcomes through more accurate and efficient surgical planning.

The project team is confident that the project has served as a successful proof of concept for facilitating the development of improved surgery planning tools in breast cancer and enhanced treatment decision support for clinicians. The data collected during the course of the project will also be made available to other researchers and the unique data-hosting platform developed for the purposes of the VPH-PRISM project will be of value to other research projects which plan to collect a range of multimodal data. This means that the project will have a lasting impact on research in the field of breast cancer and eventually clinical practice, which will benefit from improved surgery planning and support in the treatment decision-support process.

In early 2016, yet another breast cancer-related project was launched. The Digital Hybrid Breast PET/MRI for Enhanced Diagnosis of Breast Cancer (HYPMED) Project will develop a hybrid system of two medical imaging modalities (MRI and PET) for improved diagnosis of breast cancer and personalised therapy control. A team of nine organisations coordinated by EIBIR, including major universities, research organisations and industry, are working to develop a device that can transform conventional MRI scanners into high-resolution PET/MRI hybrid systems (see Figure 3). This system can then be used to identify even the smallest breast cancer tumours and better characterise the cancer, as well as its response to therapy. This new device will allow for vastly improved imaging of breast cancer and allow minimally invasive MRI and PET-guided targeted biopsy. The impact of this technology on the diagnosis, prediction, and monitoring of treatment response in breast cancer will also be assessed through a clinical study with 250 patients. Imaging data will be correlated with established and new molecular biomarkers and the results will be compared to those obtained from more conventional whole-body PET/MRI and PET/CT. Patients will clearly benefit as the radiation dose of the new technology will, in contrast to other PET/MRI examinations, be much lower and comparable to a regular digital mammogram. Moreover, the HYPMED approach is also likely to be transferrable to other clinical applications, such as prostate cancer detection and hybrid cardiac imaging. This groundbreaking concept convinced the reviewers of the EU Horizon 2020 funding programme, who awarded the HYPMED project's proposal the highest evaluation score possible.

Medical imaging is an indispensable partner in the fight against breast cancer. Its technology and methods allow clinicians to find breast cancer earlier and less invasively, which gives them and their patients more options and a better chance of survival. This makes it vital that investment in biomedical research imaging continues and that the researchers get the support they need. The projects covered in this article may have taken different approaches to improving breast cancer care, from integrating data into decision support tools for clinicians to developing new PET/MRI technology. However, they all share the goal of equipping clinicians throughout Europe with new and improved tools to diagnose and treat breast cancer earlier and more effectively. Despite the highly promising results from all of these projects, more research and innovation is needed to ensure that they are brought into clinical practice and their full potential is realised. To ensure that happens, the EIBIR team remains committed to helping imaging researchers get more innovative projects funded through the Horizon 2020 programme, and it will continue to offer its support beyond the next decade.

EUSOBI RECOMMENDATIONS FOR WOMEN'S INFORMATION

MAMMOGRAPHY

BREAST ULTRASOUND

BREAST MRI

IMAGE-GUIDED BREAST BIOPSIES

EUSOBI
european society of breast imaging

MAMMOGRAPHY

BY **FRANCESCO SARDANELLI, EVA M. FALLENBERG, PAOLA CLAUSER, RUBINA M. TRIMBOLI, JULIA CAMPS-HERRERO, THOMAS H. HELBICH, GABOR FORRAI,** ON BEHALF OF THE EUROPEAN SOCIETY OF BREAST IMAGING (EUSOBI)

INTRODUCTION

Malignant tumours (cancers) and benign diseases are very common in the breast.

Aside from clinical history (disorders in the family, previous breast diseases/surgery, hormone therapy, personal well-being and complaints), inspection (external viewing) and palpation, which compose the so-called *clinical breast examination,* imaging procedures and especially mammography are of crucial importance in the detection and diagnosis of breast cancer and other breast diseases. Mammography is a specialised radiography of the breast using x-rays to generate images of the breast. Its purposes are: first, early detection of breast cancer before symptoms *(screening mammography);* and second, diagnosis in patients with symptoms such as a palpable lump *(diagnostic mammography,* also named *clinical mammography).*

This article – specifically aimed at summarising the most important information to be offered to women about mammography – updates a previous article published in 2012[1] by the European Society of Breast Imaging (EUSOBI), taking into consideration the most recent evidence in favour of mammography and of two mammographic techniques now available for clinical practice: digital breast tomosynthesis (or simply *tomosynthesis*) and *contrast-enhanced spectral mammography (CESM).* Here we also took into account the recent position paper on screening for breast cancer by EUSOBI and 29 national breast radiology bodies[2], which should be considered complementary to this article.

SCREENING AND DIAGNOSTIC MAMMOGRAPHY

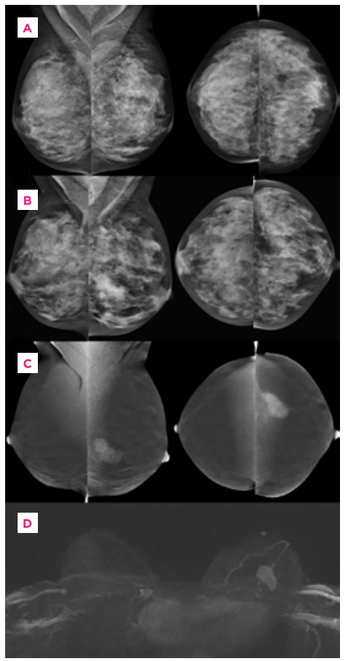
Mammography is the most important imaging procedure for breast cancer detection and diagnosis. The general aim is to enable early treatment of breast cancer, to improve survival rates and to reduce the need for aggressive treatment such as mastectomy[3-6]. It can be performed in a screening setting or a diagnostic setting. In both settings, whenever possible, preference should be given to full digital mammography (not phosphor plate computer radiography) instead of film-screen mammography, taking into consideration a number of relevant advantages for the women who get a mammogram and for the general population, including lower x-ray dose, higher image quality, possibility of post-processing, digital archiving, image transmission, and the absence of chemical pollution[2,7].

Screening mammography

Screening is performed periodically in order to find small cancers before they are detected through self-palpation or clinical breast examination. Mammography is performed every one, two, or three years from the age of 40–50 years until around 70–75, depending on regional screening programmes. Relevant differences in screening programmes across European countries, including ways of reporting, are due to differences in culture, technical circumstances, biopsy options, financial restrictions, and breast cancer prevalence. Women with a high frequency of breast cancer in their family should start even earlier with periodic imaging, possibly with protocols including contrast-enhanced magnetic resonance imaging (MRI)[8,9], after consulting specialised centres, since mammograms in those conditions may have very limited diagnostic power.

Screening mammography is a standardised procedure composed of four views (also named projections), two for each breast: the cranio-caudal projection and the medio-lateral oblique projection. In some countries, clinical breast examination is a part of the procedure, even though its added value in the screening setting, when mammography is performed, is negligible[4]. Screening mammography can be performed by a radiographer alone; the resulting images are usually read by two radiologists, independently, in separate sessions. If the exam is judged to not reveal any abnormality suspicious for malignancy, the woman receives a letter communicating this result. If something suspicious is found, the woman is recalled for a tailored further assessment that can be variably composed of additional mammographic views, tomosynthesis, ultrasound, MRI, CESM, or needle biopsy. When this assessment is concluded, a formal written report will be prepared by the radiologist and given to the woman during a dedicated interview.

FIGURE 1



Initial mammography (A), low-energy (B), and recombined image (C) of the contrast-enhanced spectral mammography (CESM) as well as as a maximum intensity projection (MIP) of the MRI (D) subtraction images 4 minutes after contrast administration in a 53-year-old patient with a 3cm palpable mass in the left breast. In mammography the tumour was not detectable. The low-energy image shows a probably slightly prominent area on the lower part on the medio-lateral oblique (MLO) view (left); on the recombined images and on the MRI the tumour can be clearly delineated because of a strong contrast uptake.

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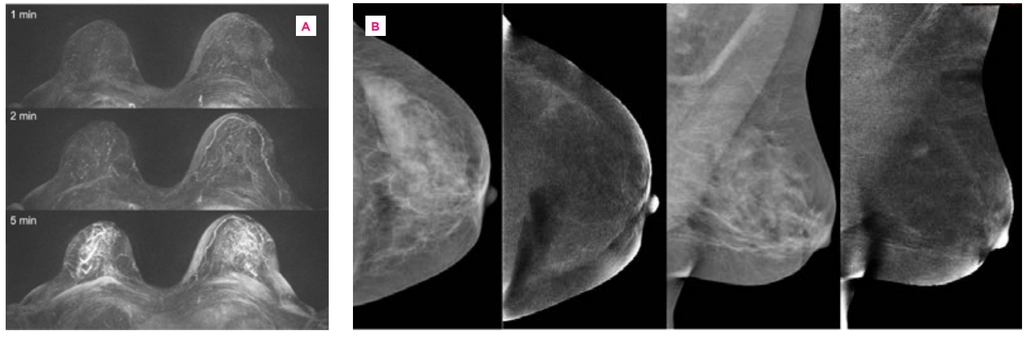
Diagnostic mammography

Diagnostic mammography is performed in patients presenting with clinical symptoms such as a palpable lump, nipple discharge, skin thickening or retraction, or nipple retraction, in order to diagnose or exclude breast cancer. Diagnostic mammography is usually performed by a radiographer and images are immediately available for the radiologist to assess. Before or after the bilateral acquisition of the two standard projections already mentioned for screening mammography, a full clinical breast examination is performed by the radiologist. This is particularly important when results of a full clinical breast examination recently performed by another doctor are not available. According to the radiologist's preference, palpable lumps, scars from previous surgeries or other abnormalities can be highlighted by positioning a marker on the skin. If necessary, additional views are acquired after the standard procedure and further assessment can be performed, as described above, for women with suspicious findings at screening mammography. A formal written report is always prepared by the radiologist, with conclusions, including recommended further steps.

Note A. *If you notice relevant symptoms in your breast, ask immediately for an appointment with your primary care physician in order to decide if you need a diagnostic mammography. Alternatively, you may also ask your breast radiologist directly for a prompt evaluation. This advice is also valid even if you have recently had a screening mammography that did not reveal suspicious findings. However, if you have symptoms and you are getting a screening mammography, inform the radiographer about them! The radiologists reading your images will decide whether you should be recalled based on these symptoms. In any case, if your symptoms do not disappear, you should consult your radiologist even if your mammography has been judged negative.*

FIGURE 2

A) MRI MIP (maximum intensity projections) images of the subtractions 1, 2, and 5 minutes after contrast injection in a patient with a 16mm invasive lobular cancer (ILC) in the left breast that was missed by MRI. Progressive enhancement of the lesion, resulting in a benign enhancement curve, as well as motion artefacts and background enhancement caused misdetection of the tumour. B) The same patient as in Figure A. The CESM images depict the ILC not detected by MRI in the upper outer quadrant.



SCHEDULING/PRECAUTIONS

The best time for a less painful mammography to be carried out is from day seven to day twelve after the beginning of the woman's last menstruation. No particular scheduling is required after menopause, implying that for the majority of mammograms performed in the context of population-based screening programmes, there are no limitations to scheduling. If the woman is pregnant, ultrasound is preferred as a first option.

Note B. *You should bring images and reports from previous mammograms (and from other recent breast imaging examinations) and give these to the radiographer or the radiologist before the procedure. This can be crucial for image interpretation, due to the fact that some cancers are diagnosed only on the basis of changes that have occurred since a previous examination.*

TECHNIQUE/PROCEDURE

Mammography is performed using a dedicated x-ray unit. A particular radiographic technique is used requiring the compression of the breast for 5–10 seconds in order to deliver a low radiation dose and to obtain high-quality images. As already mentioned, it is standard practice to take two views per breast and additional views in special cases. The procedure is performed with the woman's upper body undressed. All foreign objects (such as bras, necklaces, piercings, etc.) must be removed before the procedure. The woman will stand in an upright position in front of the machine. For each projection of each breast, the radiographer will place the breasts on the plate and will carefully apply a progressive compression for 5–10 seconds. During breast squeezing, women may feel some pain or discomfort[10]. It is important not to move during this short time. Immediately after acquiring the mammogram, the breast will be released from compression. The entire bilateral standard procedure, including preparation, takes approximately 5–10 minutes.

Note C. *To reduce pain or discomfort due to breast compression and to get the best mammograms, you should relax during the procedure; in particular, pectoral muscles should be relaxed. Follow the radiographer's instructions exactly, and bear in mind that heavier compression means a lower x-ray dose, higher image quality, and easier diagnosis. If you have previously experienced a painful mammography in the premenstrual phase, try to arrange the next one between day seven and day twelve of your cycle.*

AFTER THE PROCEDURE

When the procedure is over, the woman returns to the waiting room. In the case of screening mammography, she is usually only informed whether or not the acquired images are technically adequate. If no views need to be repeated, she may leave. She will receive a letter communicating that the mammogram is negative or she will be informed, usually by telephone, that further assessment is needed (recall). The first event is far more probable (over 90–95% of cases). In some countries, only positive screening exams (recalls) are communicated. In the case of diagnostic mammography, after checking technical adequacy, the radiologist immediately informs the patient either that the exam is completely negative or that further assessment is needed.

Note D. *If you are recalled after a screening mammogram or you are asked to have an ultrasound after a diagnostic mammography, this does not mean that you have a cancer. The most probable result of this second examination, especially in the screening setting, is a higher level of certainty in stating that you do not have cancer. Less than 10% of women recalled at screening are finally diagnosed with cancer. However, if a cancer were present, you would rightly like it to be diagnosed as early as possible.*

MAMMOGRAPHY REPORT AND CLASSIFICATION SYSTEMS

Diagnostic mammography and also diagnostic assessment of women recalled after mammography screening should be formally carried out by a certified breast radiologist. A detailed report should include a description of the clinical context, if relevant, as well as image findings, including breast density and structure according to different classification systems, interpretation of the described findings, and a final conclusion

with recommendations. In many European countries, standardised classification systems are used for the conclusions of mammography reports. A European system uses the five-level scale from R1 to R5, where R stands for radiography. R1 means no abnormalities, R2 benign findings, R3 equivocal findings, R4 suspected cancer, R5 strongly suspected cancer. A system developed in the United States – the Breast Imaging Reporting and Data System (BI-RADS) – but also used in many European countries, includes a similar scale, from BI-RADS 1 to BI-RADS 5. The main difference is for BI-RADS 3, which implies a very low probability of cancer (less than 2%), allowing the possibility of waiting for a short interval (usually three to six months) before a repeat mammogram. Conversely, the R3 category indicates a probability of cancer that is higher than that of BI-RADS 3. Moreover, the BI-RADS score system also includes BI-RADS 0 (examination insufficient for a diagnostic conclusion; further work-up needed) and BI-RADS 6 (evaluation of an already diagnosed cancer).

Note E. *In practice, if you have an R4–R5 or a BI-RADS 4–5 finding, needle biopsy is recommended. In case of R3 or BI-RADS 3, meet your radiologist and ask for a detailed explanation of this result, of the risks, and of the probabilities associated with different options.*

DIAGNOSTIC PERFORMANCE OF MAMMOGRAPHY

No diagnostic test is perfect. This rule also applies to mammography. When thinking about screening, women should be aware that about 28% of cancers can be missed[11,12], especially in pre-menopausal women and in those with dense breasts. This means that if we consider 1,000 women getting a screening mammogram, if eight to ten cancers are present, then two or three can be missed, mostly because they are not well distinguishable from normal breast tissue. Still, mammography is the best proven method for screening average risk women.

Note F. *Do not underestimate the importance of breast symptoms (especially a new palpable lump, skin/nipple retraction or nipple discharge), regardless of the timing of your last negative mammogram. Go to your radiologist and ask for a visit. Tell them your symptoms and they will decide the best course of action for you. Conversely, not all suspicious findings visualised on a mammogram are cancers: depending on the level of suspicion, cancer is confirmed in a highly variable proportion of cases. When the suspicion is confirmed after further assessment, image-guided needle biopsy is mandatory before planning any treatment.*

Note G. *A suspicious mammographic finding is not a confirmed cancer. However, do not postpone further assessment and, if necessary, needle biopsy.*

RADIATION EXPOSURE FROM MAMMOGRAPHY

The radiation exposure for a mammogram is low. A study[13] reported that undergoing repeated mammograms over a time period of 34 years (annually from age 40 to 55 and biannually from 56 to 74) entails a risk of radiation-induced breast cancer equal to one in every 1,000 women screened. The risk of breast cancer in the female population of western countries is equal to at least one in every ten women. The first risk is 100 times smaller than the second, while the reduction in breast cancer mortality thanks to early detection with screening mammography is about 40%[4]. Another study[14], applying a mortality reduction rate of 43% as an effect of screening mammography, also considering the 'minimal' risk of radiation-induced cancers, found that biannual screening mammography performed in 100,000 women age 50–69 saves 350 lives. Anyway, for the 40–49 age range, the problem of radiation effects depends on the estimated magnitude of radiation induced breast cancers in this younger age interval and must be more carefully considered. Importantly, even in the rare case of radiation-induced breast cancer, in a screening setting most of these will be detected early and treated.

OVERDIAGNOSIS

Not all the breast cancers diagnosed with screening are aggressive and fatal cancers. In the absence of screening mammography, some breast cancers – estimated to be about 6.5%, with a range from 1% to 10%[4] – would have remained totally free of symptoms, due to the very slow growth of these types of lesions, that do not tend to advance outside the breast[15]. However, these cancers cannot be distinguished from those that, if left undiagnosed and untreated, would be fatal. Thus, if we want to reduce breast cancer mortality, we must accept a rate of overdiagnosed cancers with the consequence of a rate of unnecessary treatment, mainly including surgery and radiation therapy. An effective representation of the balance between early diagnosis and overdiagnosis has been provided by the Euroscreen working group[16]: for every 1,000 women screening from 50 to 69 years of age, seven to nine breast cancer deaths are avoided, four breast cancers are overdiagnosed, 170 women have at least one recall followed by non-invasive assessment with a negative result, and 30 women have at least one recall followed by invasive procedures with a negative result. In practice, the probability of a life being saved is double that of a breast cancer being overdiagnosed.

NEW MAMMOGRAPHIC TECHNIQUES: TOMOSYNTHESIS AND CONTRAST-ENHANCED SPECTRAL MAMMOGRAPHY

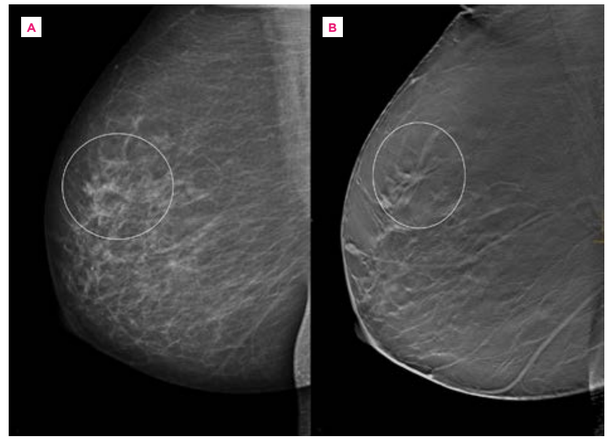
Two further developments of digital mammography have recently been introduced into clinical practice: tomosynthesis and contrast-enhanced spectral mammography (CESM). Both techniques are intended to overcome some limitations of mammography by reducing summation effects (tomosynthesis) or by increasing contrast differences (CESM), especially (but not only) in women with denser breast tissue. In these women, tumours can be masked due to overlying breast tissue, and lack of contrast to the adjacent normal breast tissue is common. So far, these techniques have mainly been proposed as an adjunct to mammography in women with inconclusive findings in their initial mammograms, with interesting results. Tomosynthesis has also been positively evaluated as a screening tool.

Tomosynthesis

Tomosynthesis is carried out with a mammographic unit that allows acquisition of either usual digital mammograms or tomosynthesis studies. The same cranio-caudal and medio-lateral oblique views are acquired for both examinations and the patient preparation

FIGURE 3

An asymmetry is seen in the superior quadrants of the right breast in a 66-year-old woman undergoing screening mammography (only MLO view shown) (A). On digital breast tomosynthesis (MLO view) a mass associated with architectural distortion is clearly visible (B). The lesion was identified on ultrasound (not shown) and image guided biopsy was performed. Histology showed an invasive ductal carcinoma.



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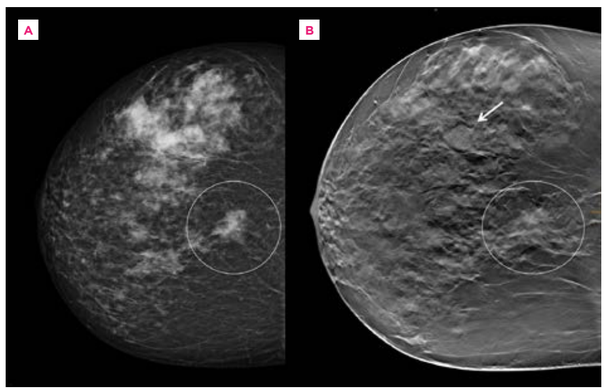
and positioning is the same. The most important difference is the use of a moving x-ray source in tomosynthesis. During a tomosynthesis examination, the x-ray source moves in an arch over the breast and acquires several projections. At the end, numerous images per view are obtained, each of them showing a slice of the breast[17-19]. Tomosynthesis can be acquired as an addition to the usual mammograms or it can be acquired alone. The latter protocol is possible because very similar images to the usual mammograms can be reconstructed from the tomosynthesis dataset: these so-called *synthetic mammograms* can avoid the need to acquire the original usual mammograms[18,20]. Depending on the device used, the radiation exposure is equal to or slightly higher than mammography, but it is still within the limits recommended by international radiation safety guidelines[21]. The results of different studies comparing mammography on its own against mammography with tomosynthesis have demonstrated that tomosynthesis is able to significantly increase cancer detection up to 30–40%[19].

FIGURE 4

A focal asymmetry is seen in the central, pre-pectoral area of the right breast in a 54-year-old woman undergoing screening mammography (only craniocaudal (CC) view shown) (A). On digital breast tomosynthesis (CC view) no suspicious findings are seen in the area detected by mammography (B). Further well-defined masses, non-suspicious, are seen in the external quadrants (B, arrow). Breast MRI (not shown) confirmed the absence of suspicious lesions and showed several cysts in the external quadrants.



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Tomosynthesis is already used as a screening modality in the United States. In Europe, only few centres perform tomosynthesis in organised screening programmes, mostly in the context of research programmes approved by ethical committees. The results of these studies are promising. Three prospective studies showed that digital breast tomosynthesis (DBT) used as an adjunct[22-24] or alternative[25] to the usual digital mammograms allows for a superior diagnostic performance when compared to mammography alone. Overall, tomosynthesis provides an increase in detection rate in the range from 0.5 to 2.7 per 1,000 screened women as well as a reduction in recall rate in the range from 0.8 to 3.6 per 100 screened women[26]. All these aspects probably mean tomosynthesis will become a routine procedure in screening, just as mammography is now.

However, before introducing tomosynthesis in breast cancer screening outside ethical-approved trials, there should be evidence for a statistically significant and clinically relevant reduction in the interval cancer rate. This cautiousness is due to the need to avoid an increase in overdiagnosis and costs. Initial results showing a reduction from 0.7 to 0.5 interval cancers per 100 screened women were recently reported from a large study in the United States[27], but further evidence is needed.

Note H. *During a breast examination performed outside the screening setting, it is up to the radiologist whether to perform only mammography, to associate tomosynthesis or ultrasound, or to perform tomosynthesis without standard mammography and to obtain reconstructed synthetic mammograms. This decision is based on various issues: the characteristics of the breast, the availability of previous examinations, the availability of technology, and also the radiologist's preference in relation to the specific case.*

Note I. *If you are invited to attend a screening programme where tomosynthesis is proposed in the context of a study or as routine practice, consider that the potential advantages of tomosynthesis in terms of increased cancer detection and reduced recall rate should overcome the modest increase in radiation dose.*

Contrast enhanced spectral mammography

As is the case for contrast-enhanced MRI, the basis of contrast-enhanced mammography is the fact that during the development and growth of a tumour, it develops its own new blood vessels, which can be a bit *leaky,* allowing an intravenously injected contrast agent to enrich the tumour. This enhances the contrast of the tumour compared to the surrounding tissue. To be able to show this tumour contrast uptake in a mammographic image, you have to acquire two exposures of the breast within the time of one compression, each of them with a different x-ray energy composition, a technical possibility available with some new mammographic units. This results in a low-energy image, identical to a normal mammogram, and a high-energy image containing information about contrast agent distribution in the breast; the use of different energies is the reason for the denomination *spectral* mammography. Depending on breast composition and thickness, this causes an extra radiation dose of approximately 20%, but both images together still imply an x-ray dose below the recommended dose for mammography[28-31].

Before the acquisition of the two images starts, iodinated contrast agent has to be intravenously injected. This is usually done while the patient is seated near the mammographic unit. Two minutes after the start of the injection, the patient is guided to the mammography system and positioned similarly as with a normal mammography examination. Within roughly five minutes, the usual cranio-caudal and medio-lateral oblique views of both breasts are taken bilaterally, each of them composed of a low-energy image and a high-energy image. The two images are combined using special software, creating a new image where the presence of contrast uptake is easily seen.

The diagnostic performance of CESM has recently been summarised by a systematic review and meta-analysis[32], i.e. a combination of the results of previous studies on CESM. The authors identified eight studies (four prospective and four retrospective) for a total of 920 patients with 994 lesions. The ability to detect existing cancers (sensitivity), estimated from all studies, was about 98% while the ability to recognise the normal condition in the absence of any false positive findings (specificity), estimated from six studies reporting raw data, was about 58%. The majority of included studies were judged to have studied very selected populations. The mean cancer size, reported only in three studies, was 21.2mm. The authors concluded that high-quality studies are required to assess the CESM accuracy. In practice, CESM still deserves evaluation and the results of this meta-analysis cannot be considered conclusive. Interestingly, two recent studies confirmed a high sensitivity of CESM (94–95%) with higher values of specificity: 81% in the symptomatic setting[33] and 74% in the post-screening assessment[34].

On the basis of preliminary results, CESM can be considered an alternative to contrast-enhanced MRI in the case of contraindications to MRI (including the presence of MRI-unsafe devices in the patient's body, claustrophobia, and obesity that prevents the patient from entering the magnet) or to gadolinium-based contrast injection as well as local conditions of limited MRI availability[8,9], due to interesting results obtained by comparing CESM and MRI in the same patients[37, 38].

Note J. *It is important to note that iodinated contrast agents are frequently used in clinical practice, mostly intravenously injected for contrast-enhanced*

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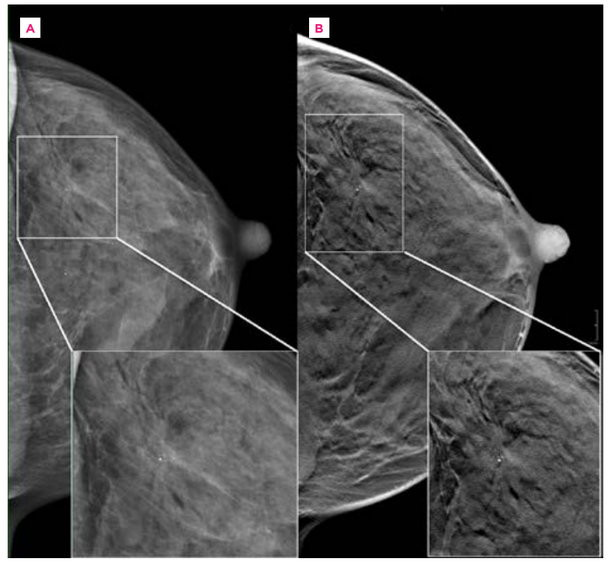
computed tomography. There are contra-indications (history of allergic reactions, renal failure) and possible side effects that require discussion with the patient and the signing of an informed written consent. Thus, the injection of iodinated contrast agents for mammography requires the same precautions used for other contrast-enhanced x-ray based examinations[35,36]. Before the examination, the radiologist will clarify the risks and benefits associated with the intravenous injection of iodinated contrast agents.

FIGURE 5

A cluster of microcalcifications is seen in the left breast of a 55-year-old woman undergoing screening mammography (only CC view shown) (A). On digital breast tomosynthesis (CC view) microcalcifications are clearly visible, and associated with a spiculated mass (B). Needle biopsy was performed under stereotactic guidance and final diagnosis was invasive ductal carcinoma with ductal carcinoma *in situ*.



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FREQUENTLY ASKED QUESTIONS (FAQS)

1. How painful is breast compression for mammography?
Mammography is well tolerated by the vast majority of women. In particular, it is painless for about 40–50% of women, a little painful for 40%, rather painful for 12%, and very painful only for 4%. Pain disappears immediately after the procedure for 76% of the women, while it lasts several minutes for 13%, several hours for 7%, and more than a day for 4%[10]. However, the advantages of compression are clear, and unnecessary pain may sometimes be avoided by suitable scheduling (see Note C). The radiographer will guide you through all the steps of the examination, and will take care of minimising the discomfort during breast compression.

2. When should the first mammogram be done? What are the time intervals for further examinations?
Different recommendations are issued by different radiological and cancer societies, as well as by health authorities and governmental bodies. There is a general agreement on the usefulness of screening mammography from 50 to 70 years of age, with a time interval depending on several factors described above. Extension from about 40–45 to about 75 is now adopted by several screening programmes. When starting at 40, a one-year interval can be recommended up to 45–50, considering the probable higher density of the tissue and the possible faster growth of the tumour. After 50, the optimal interval may be decided based on personal history and breast density. If you have symptoms, mammography may be necessary for you at any age. If you are a woman with an increased risk of breast cancer (gene mutation carrier, multiple breast/ovarian cancers in the family), screening should start before the age of 40, according to your personal calculated risk level, access to special screening programmes, and other factors.

Note K. *If you are invited to attend an organised screening programme, follow the programme's planned interval. If you have any doubts about this time interval, or the usefulness of ultrasound as a supplemental screening method, consult your radiologist. If there are a high number of incidences of breast cancer in your family, especially at a young age and before menopause, you may need to be screened with MRI[7-8]: consult your radiologist or a specialised centre (e.g. a family cancer clinic). Information on reasons to have an MRI scan is available in a special EUSOBI paper[9].*

3. What about screening mammography for women over 75?
The continuous increase in life expectancy prevents us making a clear cut definition of an upper age limit for screening mammography. A general suggestion is to continue screening with mammography for elderly women as long as their health is not significantly compromised by illness that drastically reduces life expectancy[39,40]. Discuss this decision with your radiologist.

4. Can women with breast implants or breast reconstruction undergo mammography?
Yes, in the majority of cases they can. Special views with back placement of the implant are commonly needed, as well as specific technical expertise from the radiographer. Exceptions where mammography cannot be performed are breast reconstructions after complete gland tissue removal. Limitations of mammography due to the presence of implants can be counteracted by an accurate clinical breast examination and breast ultrasound.

Note L. *Always tell the radiologist and the radiographer if you have breast implants.*

5. Is x-ray radiation from mammography dangerous?
The x-ray radiation associated with mammography is low. See the Section 'Radiation exposure from mammography' in this article for a comparison between the risk of radiation-induced breast cancer and the reduction of breast cancer mortality due to mammography.

6. What is the role of new technologies like tomosynthesis and CESM?
The role of these new technologies is to help in the detection and diagnosis of breast cancers. Tomosynthesis is commonly accepted as an effective tool for the evaluation of symptomatic patients and suspicious findings at screening mammography. Large studies in the screening setting have shown that tomosynthesis allows the identification of more cancers than mammography and potentially reduces the number of women recalled for benign findings.
So far, CESM has been evaluated in a limited number of small studies. It provides useful information on suspicious lesions, increasing the visibility of malignant lesions, particularly in women with dense breasts, and can be used as an alternative to contrast-enhanced MRI, especially in the case of contraindications to MRI or to gadolinium-based contrast injection, or when MRI is not available.

REFERENCES
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BREAST ULTRASOUND

BY **ANDY EVANS** ON BEHALF OF THE
EUROPEAN SOCIETY OF BREAST IMAGING (EUSOBI)

INTRODUCTION

Breast ultrasound is one of the four main methods for diagnosing breast diseases, together with mammography, magnetic resonance imaging (MRI) and image-guided needle biopsy.

It is based on the use of sound waves with a frequency too high for humans to hear. Ultrasound images are made by sending pulses of ultrasound into the breast tissue using a probe. The sound reflects and echoes off the breast tissue. These echoes are detected by the probe and converted into an image. Ultrasound does not expose the patient to potentially harmful ionising radiation.

The ultrasound probe is moved around the breast with the aid of contact gel, with the patient lying on their back or side. It does not require pressure, so ultrasound is usually painless.

In terms of invasive cancer detection, the performance of ultrasound is similar to that of mammography and is less hampered by dense breast tissue. It may therefore be particularly helpful in younger women, who tend to have dense breasts. However, it doesn't mean that ultrasound can replace mammography. Ultrasound is less sensitive than mammography at detecting breast microcalcifications, hence the sensitivity of ultrasound for the detection of ductal carcinoma *in situ* (DCIS) is less than that seen with mammography. Benign breast disease is very common, and ultrasound also detects benign lesions that may otherwise have gone unnoticed. Ultrasound is particularly useful in differentiating cysts from solid breast masses. Breast ultrasound examinations sometimes use Doppler and elastography, which are automated applications used to detect and measure blood flow and tissue stiffness respectively. However, these are not obligatory elements of a breast ultrasound examination. Breast ultrasound is inexpensive compared

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to breast MRI. However, compared to mammography, ultrasound of both breasts is time consuming and false positive test results are common. For this reason breast ultrasound examinations are often restricted to the breast of concern or even to the part of the breast which is symptomatic. Interventional procedures are easy to perform under ultrasound control, so biopsy of solid breast masses, even if they are palpable, are often performed under ultrasound guidance. Automated whole breast ultrasound is being developed and provides images which can be reported by a radiologist at a later time.

An impediment to the more widespread use of breast ultrasound for screening is the fact that with breast ultrasound – unlike all other breast imaging methods such as mammography, tomosynthesis and breast MRI – the vast majority of the examination is not captured, i.e. the images are not stored for later review, or for review by other breast imaging specialists. Usually, the examiner will only document abnormalities that they have noticed during the scanning process. If an examiner overlooks an abnormality during the ultrasound examination, that abnormality will not be visible on later reviews of that ultrasound study documentation. This, in turn, means that quality assurance for ultrasound is more challenging than it is for other breast imaging methods, where third parties have a chance to review the images of a given study and thus may identify insufficient reader or examiner performance. This is not, however, true for examinations using automated whole breast ultrasound, where the whole examination is recorded.

CONTRAINDICATIONS AND INDICATIONS

For breast ultrasound there are no absolute contraindications (reasons a patient could not undergo the procedure). The examination can be suboptimal in patients who cannot lie still, lie flat or move onto the examination couch. Examinations can be difficult in women with open wounds or damaged skin, and tissue behind breast implants is often obscured. The total examination time ranges from five to twenty minutes. In women with a suspected breast cancer, the whole of the affected breast and the axilla (underarm area) of the same side are usually examined. Ultrasound of the opposite breast in women with breast cancer is performed in some centres as there is a small chance of picking up a cancer in the opposite breast not seen on the mammogram. Definite indications for breast ultrasound are listed in table 1. Possible indications and non-indications are listed in tables 2 and 3 respectively.

TECHNIQUE/PROCEDURE

Breast ultrasound is performed using a clinical ultrasound scanner using probes of 10–13Mhz. Clear instructions and explanation regarding the entire procedure are provided by the operator performing the investigation. Breast ultrasound is usually performed with a chaperone in the room who will also

TABLE 1

Definite indications for breast ultrasound[23]

Focal palpable abnormality
Mammographic abnormality which is not definitively benign
Breast lesion detected on MRI which is not definitively benign
Local staging of a known breast cancer
Single duct nipple discharge
Recent nipple inversion
Skin tether
Breast inflammation
To guide biopsy/drainage/localisation of a breast lesion
Follow-up of women receiving neo-adjuvant systemic therapy for breast cancer
First examination for any abnormality in pregnant/breastfeeding women
First examination for any abnormality in young women

TABLE 2

Possible indications for breast ultrasound[24]

Patient feels a lump, normal clinical examination
Localised new breast pain
Screening in women aged 40–70 with dense breasts (in addition to mammography)
Follow-up in women with previous mammographically occult breast cancer treated with breast conserving surgery
Differentiation between fibroglandular tissue and other abnormalities in men presenting with gynaecomastia
Screening high risk women, especially if the patient is unable to have MRI

assist the operator in performing ultrasound-guided procedures. The procedure is performed with the upper body undressed, including the removal of undergarments. Contact gel is applied to the breast and the scanner probe is moved around the breast with minimal pressure. The axilla will be scanned in women with clinical abnormalities in the axilla and routinely in women with personal history of breast cancer. If large nodes are seen in the axilla, other nearby nodal basins may be examined, such as the neck and the regions directly below the clavicle. The procedure should be pain free. Images using advanced techniques such as Doppler and shear wave elastography are obtained using no pressure. Strain elastography requires very gentle quivering of the probe but not enough pressure to cause discomfort.

For the procedure, the patient lies on their back and extends the arm of the side being examined over the head to flatten the breast. Breast ultrasound can be performed in women who cannot lie flat or extend the arm above the head, but such examinations are more difficult to perform. Whether one area of one breast, the whole of one breast or both breasts are examined depends on the indication, mammographic breast density and local policies.

TABLE 3

Non-indications for breast ultrasound[25]

Non-focal breast pain
Diffuse breast nodularity
Screening in women under 40
Screening in women with fatty breasts
Screening mastectomy scars and axillae in women with a history of breast cancer

AFTER THE PROCEDURE

When the examination is completed the woman redresses and can go home. The report should be generated within a few days after scanning and requires correlation with clinical findings and results from other imaging tests.

THE ULTRASOUND REPORT

Evaluation of breast ultrasound scans should be performed by a dedicated breast radiologist or breast sonographer, according to local regulations. The report should contain the indication for the performance of the scan and other relevant clinical information. Reported image findings should include a structured description of relevant abnormalities, including abnormalities in the axillae and incidental findings.

Each report should end with a conclusion, a classification and recommendations. In most European countries a structured reporting and classification system is in use. The most commonly applied system is the Breast Imaging Reporting And Data System (BI-RADS) developed by the American College of Radiology. BI-RADS 1 means 'negative', no findings, BI-RADS 2, 'benign' findings; BI-RADS 3, 'probably benign' findings; short-interval follow-up recommended, BI-RADS 4, 'suspicious', tissue diagnosis, and BI-RADS 5 'highly suggestive of malignancy', tissue diagnosis. BI-RADS 6 means 'known biopsy – proven malignancy', and is reserved for ultrasound scans made for cancer staging or follow-up of neoadjuvant chemotherapy. BI-RADS 0 means 'incomplete – need additional imaging evaluation'. BI-RADS 4 and 5 findings require tissue diagnosis through biopsy. BI-RADS 3 findings require short term follow-up, but may also be biopsied[3].

SENSITIVITY OF BREAST ULTRASOUND

The sensitivity of breast ultrasound for breast cancer is approximately 85%, which implies that a fraction of cancers may be missed by an ultrasound examination[4]. Invasive cancers that are missed are in general either very small, directly behind the nipple or are difficult to distinguish from normal tissue or fibrocystic change. This is particularly true of lobular cancers, which account for about 15% of invasive cancers. Ductal carcinoma *in situ* (DCIS), a possible precursor of invasive breast cancer that is treated similarly to invasive cancers, is frequently not seen on ultrasound. DCIS is commonly depicted on mammograms as a cluster of microcalcifications. This means that significant clinical, mammographic or MRI findings should not be dismissed because an ultrasound scan is normal.

The sensitivity of mammography is affected by breast density; therefore

mammography is less sensitive in younger women. There is some evidence that ultrasound too is less sensitive in women with dense breasts but the effect of breast density on sensitivity appears to be less for ultrasound than for mammography[4].

Benign/malignant differentiation of solid breast nodules

Solid masses that have clear benign characteristics are probably benign (BI-RADS 3), and have a less than 2% risk of being a cancer, so short term follow-up is often performed rather than immediate biopsy[5]. New ultrasound techniques such as shear wave elastography may further improve ultrasound's ability to differentiate benign from malignant breast masses[6,7].

FIGURE 1

Complex cystic and solid lesion.

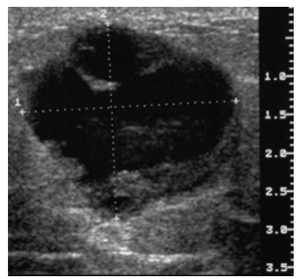
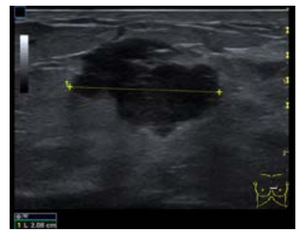


FIGURE 2

Highly suspicious mass lesion, BI-RADS 4 (irregular shape, ill-defined, angular margins).



BREAST ULTRASOUND FOR SCREENING

Many studies have shown that in women with mammographically dense breasts, adding bilateral whole breast ultrasound to mammography can help to identify additional invasive cancers, which tend to be small and node negative[8]. Most of these studies have been performed in women at increased risk of breast cancer[9] so the additional cancer detection in women of normal risk is unclear[10] and the few studies which have been carried out are from Asia, so their findings may not be valid in European populations. Nonetheless, the additional cancer yield in women with non-dense breasts is low.

Adding ultrasound screening to mammography in women with dense breasts has been shown to reduce interval cancers (those diagnosed in the interval between scheduled screening exams) occurring within one year of a negative screen[11]. This suggests that adjunctive ultrasound screening detects biologically important cancers and that such screening may reduce breast cancer mortality, although this is not proven. Ultrasound screening instead of mammographic screening is not recommended.

The down side of ultrasound screening is that it is very non-specific. Less than one in ten of biopsies prompted by ultrasound screening are malignant[12]. This means that ultrasound screening is less specific than both mammography and MRI. Ultrasound screening is also more time consuming than mammography for the patient and the radiologist. It takes about 20–30 minutes to perform. Mammography takes about 5–10 minutes to perform and two minutes to interpret.

In the future, additional ultrasound techniques, such as shear wave elastography, may reduce the number of ultrasound-detected lesions that require either short term follow-up or biopsy[13]. This may make adjunctive ultrasound screening more attractive.

Automated whole breast ultrasound allows ultrasound images of both breasts to be acquired in about 15–20 minutes. These images can then be read by a radiologist later. Reading such an examination takes about 5–9 minutes[14]. It is unclear if the sensitivity of this technique equals that of hand held ultrasound.

The false positive rate increases with automated whole breast ultrasound[15,16].

BREAST ULTRASOUND FOR BREAST CANCER DIAGNOSIS AND STAGING

Most breast cancers are detected by screening mammography or due to clinical symptoms. The standard way to assess suspicious lesions is with the so-called triple assessment: mammography, ultrasound, and image-guided needle biopsy. Ultrasound is used routinely in women with breast cancer to perform three tasks: to guide biopsy of cancer, to assess the tumour size and focality and to assess the axillary lymph nodes.

Guiding biopsy

Ultrasound is used to guide biopsy, where a sample of tissue is taken using a needle (usually 14 Gauge core biopsy) of suspicious findings, even if they are palpable, as the operator can see the needle pass into the lesion in real time, thus improving the accuracy of the procedure. The procedure is performed after injection of local anaesthetic into the skin and towards the lesion. Clips are sometimes placed under ultrasound control, to mark the site of cancer before neo-adjuvant chemotherapy (NACT) is given. Stereotaxic (x-ray guided) biopsy is reserved for those cancers not seen on ultrasound, as the procedure is more uncomfortable and more time consuming than ultrasound guided biopsy.

Tumour size and focality

Ultrasound is superior to mammography or clinical examination in assessing the size of invasive cancers and how many foci of cancer are present in the affected breast. Ultrasound is not as useful as mammography in detecting and sizing DCIS. MRI is the best method of assessing size and focality of breast cancer, but because of cost, availability, and the number of false positive results, MRI is reserved for those women where assessing tumour size is difficult.

FIGURE 3

Ultrasound image of axillary lymph node with highly suspicious morphology (rounded shape, ill-defined margins, missing hilus reflex).

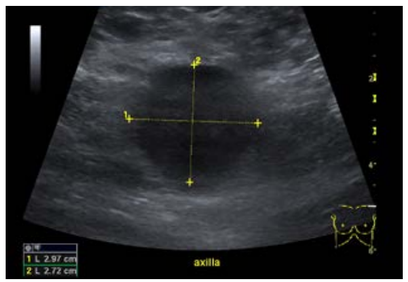
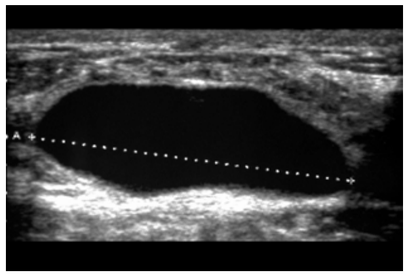


FIGURE 4

Simple cyst with characteristic anechoic (=black) internal appearance and posterior acoustic enhancement.



Usually the whole of a cancer baring breast is scanned to look for spread of the cancer to different parts of the breast[17]. This is particularly helpful in women who have dense breasts on mammography as in these circumstances extra foci of cancer remain commonly undetected by mammography. Ultrasound is particularly useful for seeing cancer that has spread from a tumour mass into a duct (intraductal extension).

In breast cancer patients, ultrasound of the other (contralateral) breast is performed to identify synchronous bilateral cancers (appearing in both breasts at the same time). Because false positive findings are common with whole breast ultrasound, whether contralateral ultrasound should be performed in women with a new diagnosis of breast cancer is debatable[18].

Second-look ultrasound

When a patient undergoes an MRI exam to stage a breast cancer, it is possible that MRI may detect additional lesions that have not been detected by an earlier staging ultrasound; therefore a second ultrasound exam, referred to as a 'second look' is indicated. This does not mean that the first staging ultrasound was not correctly performed: even in the most expert hands, small nodules or intraductal extensions can go unnoticed, and MRI, due to its superior sensitivity to breast cancer, depicts these lesions. In those cases in which these additional lesions are deemed important to characterise, because they may change the surgical treatment, a second-look ultrasound is indicated. This procedure will be most useful in additional mass lesions that are malignant and much less useful in non-mass lesions. If an additional lesion is not found in second-look ultrasound, the radiologist, together with a multidisciplinary team, will decide the next step, such as MRI biopsy or follow up[19].

Assessing the axilla

Until recently, ultrasound of the ipsilateral axilla was routinely performed in all women suspected or proven to have invasive breast cancer. If lymph nodes had a thickened cortex, were lobulated or were round rather than oval an ultrasound-guided biopsy was performed. Recent evidence suggests that core biopsy is more accurate than fine needle aspiration (FNA) in this clinical situation[20]. This allowed the pre-operative identification of nodal metastases in about 50% of cases. Most women with proven nodal metastases then underwent a surgical axillary clearance while those women without proven axillary node metastases would have had a biopsy of the sentinel node, i.e. the closest node or nodes that filter fluid draining from that specific area of the breast. A recent study has cast into doubt the need to treat all involved axillary nodes with surgery. So clinical practice in this area is in a state of flux. Research is underway to try and accurately identify the sentinel node(s) pre-operatively and remove them percutaneously (through the skin). In women with very large involved axillary lymph nodes, the supraclavicular and infraclavicular fossae (areas above and below the collarbone) should also be scanned to look for enlarged nodes.

BREAST ULTRASOUND IN PATIENTS WITH IMPLANTS

Breast ultrasound is usually the first imaging test performed on women with implants who develop a palpable breast lump. As well as benign and malignant solid breast masses and cysts, women with implants can have silicone granulomas as a consequence of extra-capsular rupture and leakage of silicone. Such granulomas have a characteristic 'snow storm' appearance on breast ultrasound images and the findings can be confirmed by ultrasound-guided biopsy. Almost all ultrasound-guided interventions (biopsy, preoperative localisation) may be performed on implanted breasts. Cancers arising behind implants and free silicone areas may be missed by ultrasound. Ultrasound is not an accurate tool for identifying intra-capsular rupture (where the silicone is contained by a pseudo-capsule of fibrous tissue). MRI is the best imaging modality for identifying intra-capsular rupture[21].

EVALUATION OF THE EFFECT OF NEOADJUVANT CHEMOTHERAPY

In advanced breast cancer, many centres have adopted protocols that include the reduction of tumour load with neoadjuvant chemotherapy before surgical treatment. In this setting, MRI and ultrasound are often performed to monitor early treatment response and for pre-surgical evaluation[22].

REFERENCES

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BREAST MRI

BY **RITSE M. MANN** ON BEHALF OF
THE EUROPEAN SOCIETY OF BREAST IMAGING (EUSOBI)

Below you will find the integral text of the paper *Breast MRI: EUSOBI recommendations for women's information.*

The paper was originally published in *European Radiology 2015 Dec;25(12):3669-78* and provides consensus recommendations from the European Society of Breast Imaging (EUSOBI) for information that should be given to women prior to MRI scanning. Although the paper provides suggestions for direct communication with women who might undergo breast MRI, the paper is specifically aimed at physicians referring patients to the radiology department for the performance of breast MRI.

Despite ongoing research, the big picture of breast MRI has not extensively changed. The technique is still the most sensitive modality for the detection of early breast cancer available, and still the most accurate in staging of breast cancer[a1]. Nevertheless, competing techniques such as contrast enhanced mammography and various nuclear breast imaging techniques now achieve performance levels only just below that of MRI, albeit mostly at the loss of 3D information, and might be a valid alternative when breast MRI is not available[a2,a3].

In recent years it was shown that, in patients who have undergone multiple MRI scans with a gadolinium based contrast agent, deposition of gadolinium in the basal ganglia of the brain may occur[a4]. This is complementary to the long recognised deposition of gadolinium in bones and skin. Both the European Medicines Agency (EMA) and the American Food and Drug Authority (FDA) are currently conducting evaluations on the safety of these contrast agents. Although a final verdict cannot be reached while these evaluations are ongoing, contrast agents containing gadolinium have been given to hundreds of millions of people, and currently no symptoms are associated with the finding[a5]. A recent publication, in fact, showed that there is no association between the administration of contrast containing gadolinium and Parkinsonism[a6]. Gadolinium based contrast agents are thus still regarded safe, and indications for the use of breast MRI remain unchanged. Also, the administration of contrast agents for research purposes is not discouraged, although clear patient information is of course mandatory.

For screening purposes, abbreviated and ultra-fast breast MRI protocols have attracted much attention[a7,a8]. These protocols limit the scanner time to below three minutes while maintaining high sensitivity and specificity, relying only on early enhancement of breast cancers. However, current published series contain only limited numbers of cancer cases and are not all conducted in true screening populations. Consequently, further research is essential before this can be offered to larger populations. However, in patients with severe claustrophobia who are unable to undergo a full-length breast MRI protocol, ultra-fast protocols might already present a viable alternative.

In breast cancer staging, preliminary results from the Multicenter International Prospective Meta-Analysis (MIPA) trial shed a different light on the often-reported increase of mastectomies due to preoperative MRI[a9]. It turns out that in most cases the indication for more extensive surgery is already present before the MRI is performed and the effect of the MRI itself appears to be bidirectional, i.e. sometimes leading to more extensive surgery, but just as often leading to a reduction in the extent of surgery. Nevertheless, the final results of this trial need to be awaited before recommendations may be altered.

INTRODUCTION

Initial results regarding magnetic resonance imaging (MRI) of the breast were published more than 30 years ago, but clinical use started during the 1990s after the introduction of contrast-enhanced (CE) protocols[1,2]. Breast MRI is today one of the main methods for diagnosing breast diseases, together with mammography, ultrasound, and image-guided needle biopsy. It is based on the use of (a) a strong magnetic field provided by a high-quality magnet; (b) low-energy electromagnetic waves (radiofrequency waves, similar to those of radio, television, and portable phones) radiated and received by special coils (antennas) inside the magnet and positioned close to the investigated body part. MRI can be used to differentiate lesions and abnormalities of the breast well. However, in order to diagnose or exclude a cancer, intravenous administration of a gadolinium-containing contrast material (CM) is needed[3,4]. Injection of CM is not required for evaluation of breast implant integrity. MRI does not expose the patient to potentially dangerous radiation, but other important precautions, contraindications, and potential side effects (including those regarding CM) should be considered.

REASONS FOR BREAST MRI EXAMS

Women's information is important not only for patient awareness about advantages and disadvantages of breast MRI, but also to be prepared for the examination. Patients need to be aware of the possible benefits and risks associated with breast MRI and of potential further investigations prompted by this exam. Moreover, technical quality of breast MRI is dependent on patient compliance.

In terms of cancer detection, MRI outperforms (but does not entirely substitute) both mammography and ultrasound. Its valuable diagnostic performance has been confirmed by many studies. However, benign lesions that would otherwise have gone unnoticed may be detected with MRI, leading to additional, otherwise unnecessary work-up. Costs must also be considered, as MRI is more expensive than mammography and ultrasound. The main reasons/indications for breast MRI exams[5-9] are listed in Table 1.

Other new indications have recently been proposed, such as nipple discharge[8] and evaluation of lesions with uncertain malignant potential (so-called high-risk or B3 lesions) detected with mammography or ultrasound and needle-biopsied under their guidance[9].

TABLE 1

Reasons/indications for breast MRI

Screening of women at high risk of breast cancer
Preoperative staging of newly diagnosed breast cancer (ipsilateral and contralateral)
Evaluation of the effect of neoadjuvant chemotherapy
Evaluation of women with breast implants
Occult primary breast carcinoma (searching for breast cancer in patients with metastases and negative mammography and ultrasonography)
Suspected local recurrence*
Problem solving (equivocal findings from mammography/ultrasonography)**

* When needle biopsy cannot be performed.
** When needle biopsy cannot be performed.

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PRECAUTIONS/ CONTRAINDICATIONS

An MRI system is a relatively narrow tube in which the woman lies face-down during a breast examination for 15 to 30 minutes. Patients with severe claustrophobia are unable to undergo the examination unless they are psychologically/pharmacologically prepared or sedated[11]. Because of the use of magnetic fields and radiofrequency waves, the presence of non-MRI compatible intracranial ferromagnetic clips for aneurysms and iron splinters in the eyes are absolute contraindications to MRI. In cases of doubt, an x-ray examination of the orbits can be performed to rule out the presence of iron splinters. Moreover, MRI is also contraindicated in patients with implanted electronic devices such as MR-unsafe pacemakers, implantable cardioverter defibrillators, and neurostimulators.

The patient should inform the radiologist or the staff personnel (technicians/nurses) if she has tattoos or permanent make-up. These may contain iron pigments, and especially when loop-shaped (like an antenna), they may heat up and cause local burns. Tissue expanders (e.g. for breast reconstructions) may not be MR-compatible. Women with intravascular stents or metal screws or plates for osteosynthesis can safely have a breast MRI six weeks after implantation. A list of acceptable and unacceptable implantable devices and precautions needed for MR imaging can be found on the internet[12].

As stated above, breast MRI without contrast material cannot be used to answer clinical questions[3,5–7], with the evaluation of breast implant integrity as the only exception. Women with allergic predispositions or earlier allergic reactions to any CM have a higher risk for allergic reactions to MRI CM. Moreover, in women with very poor kidney function (estimated glomerular filtration rate lower than 30 ml/min×1.73 m^2), contrast injection implies a real, but very low risk of a rare disease called nephrogenic systemic fibrosis[13]; contrast-enhanced MRI is also generally contraindicated in pregnant women, but this condition should be evaluated on a case-by-case basis[14].

Before entering the MRI room, the patient is asked to fill out a detailed questionnaire to rule out any contraindication to examination and to contrast media injection.

Note A. *If you think you may be claustrophobic, you can go to the MRI centre and ask to see the MRI scanner to get practical information. If you are seriously claustrophobic, discuss this with the referring physician, radiologist, and personnel of the institution where MRI is scheduled. This issue should be discussed and resolved before attending the examination. The use of a simple sedative medication to relieve the symptoms might be indicated.*

Note B. *If you have an implantable device such as pacemakers/defibrillators, metal implants, or breast expanders, discuss this with the referring physician, as these might imply that MRI could harm you or damage the device. In cases of doubt about contraindication, inform the radiologist and the personnel of the institution where MRI is scheduled. This issue should be discussed before the MRI takes place. If this information has not been provided in advance, inform the personnel before the examination.*

Note C. *If you have an important allergic predisposition (e.g. bronchial asthma) or you have had allergic reactions to drugs or contrast media before, discuss this with your referring physician. In cases of serious allergic symptoms, a balance between the potential advantages of MRI and the risk of allergic reactions has to be made. Where MRI has to be performed, precautions need to be taken, including the administration of corticosteroid and antihistaminic drugs prior to the investigation. In any case, consult your radiologist before the scheduled MRI date. We recommend informing the personnel of the institution where MRI is scheduled. This issue should be discussed before MRI takes place.*

Note D. *To avoid a risk from MRI CM in the presence of renal failure, different regulations are adopted in European countries. Your renal function can be checked using a simple blood test (performed up to 30 days from MRI) to evaluate your creatinine level and estimate the glomerular filtration rate. In any case, inform your referring physician and radiologist if you have a history of bladder or kidney disease, diabetes mellitus, cardiac or vascular disease, multiple myeloma, Waldenström disease, or if you use diuretics or non-steroidal anti-inflammatory drugs (e.g. ibuprofen/naproxen).*

SCHEDULING

In premenopausal women, contrast-enhanced MRI is preferably performed between the seventh and fourteenth days of the menstrual cycle, when the background enhancement of the normal fibroglandular breast tissue is low, and hence abnormalities are better detected and false positives less frequent[15–19]. During the remaining days of the menstrual cycle, lesions may be masked by enhancement of the fibroglandular tissue, potentially reducing the diagnostic value of the examination. If necessary, breast MRI may be performed in the third week of the menstrual cycle, taking into consideration that the results could be suboptimal. The use of oral contraceptives does not contraindicate CE MRI, but the above defined rules should be observed. Women with irregular menstruation (e.g., in the perimenopausal phase) may undergo blood sampling for serum progesterone to determine the optimal time for breast MRI, especially if earlier examinations have been non-diagnostic due to strong glandular enhancement[20]. Premenopausal women who only need implant integrity evaluation can undergo non-contrast breast MRI at any time. All postmenopausal women can undergo CE MRI at any time. In fact, postmenopausal hormone replacement therapy has recently been reported to have a negligible effect on parenchymal background enhancement[21]. In any case, optimal scheduling of breast MRI should not substantially delay therapy planning.

Note E. *If you are premenopausal and have an appointment for a screening CE MRI, check your menstrual cycle. If the exam scheduled is not between the seventh and fourteenth day after the first day of your period, contact the centre and try to reschedule your appointment. If CE MRI has to be performed for another indication, discuss this with your radiologist: speed is sometimes more important than adequate scheduling. Be aware that an MRI examination performed outside the most suitable phase of the cycle may cause both false positives (findings suspected to be malignant which turn out to be benign) and false negatives (apparently normal or benign findings when a cancer is present). Cycle-related scheduling is not required for the assessment of breast implants, and CM administration is not usually required.*

Note F. *If you have irregular menses (e.g. perimenopausal phase) or if you have had a hysterectomy before the age of 50, consult your radiologist to verify the need for blood sampling for serum progesterone to determine the optimal MRI scheduling.*

TECHNIQUE/PROCEDURE

Breast MRI is performed using MRI scanners working at 1.5 or 3 Tesla, which refers to the strength of the magnet within the machine. Clear instructions and explanation regarding the procedure are provided by a technician or a nurse. After a possible interaction with the radiologist on duty and completion of questionnaires, the woman is asked to sign a specific informed consent form if CM injection is needed. Thereafter, a small plastic cannula is inserted into the cubital vein of one arm, requiring a simple puncture comparable to that for blood sampling. During the examination, CM will be injected followed by a saline flush using an automated injector. The cannula will be removed after the procedure and the puncture site will be briefly compressed to stop bleeding.

The woman should keep still during the entire examination as patient movement can cause disturbances in the resulting image (known as 'artefacts'), which strongly reduce image quality and make interpretation difficult and sometimes impossible. A warm and sometimes tingling sensation can be felt in the arm that has received the injection. This may be more extensive and can possibly be felt throughout the body. A metallic taste may be noticed in the mouth, and a transient headache or nausea may occur in rare cases.

The procedure is performed with the upper body undressed and bra removed. Any clothing containing metal, any jewellery, and other foreign objects must be removed. Some centres require almost complete undressing and provide disposable clothing. The woman lies face-down on the MRI table with each breast in the openings of the special device used specifically for breast imaging, known as a 'breast coil', which contains the signal receivers. A technician or a nurse positions the breasts, avoiding folding of breast tissue on the edges of the coil. In some centres, slight breast compression is applied to reduce motion artefacts. Rubber ear plugs or headphones are

provided to reduce the scanner noise during image acquisition. Radiologists and technicians are able to communicate with the woman during the examination. An alarm bell is provided; when it is rung by the woman, the examination will be terminated immediately and she will be removed from the magnet. Thus, the woman can be sure that if needed, she will be assisted.

When the woman is optimally positioned, table and patient are moved into the magnet, so that her breasts are in the centre of the tube: the magnetic field is most homogeneous at that position allowing for optimal image quality. The procedure is noisy, even though ear plugs or headphones attenuate noise perception. During the examination, the staff are discouraged from talking to the woman, as this frequently induces movements and should be done only when really needed. Scan sequences produce different noises and different noise levels, more relevant being those for CE imaging (continuous buzzing sound), and for so-called diffusion-weighted images (high beeping sound). When breast implant integrity has to be evaluated, dedicated scan sequences are used, which make different noises.

When the examination is done, the table and the woman are taken out of the scanner, and the table is lowered. The woman is then asked to sit up to remove the venous access. The procedure commonly takes 15 to 30 minutes, except when additional sequences are done for clinical purposes. The radiologist can decide to postpone the removal of the venous access for 10 to 15 minutes before the patient leaves the department (see below).

Note G. *During the examination, it is of paramount importance that you keep still. When the scanner acquires data (the 'sequence'), you hear a relatively loud noise, reduced by the ear plugs or headphones. You may think that movements between the different sequences do not reduce image quality. However, as images acquired over time will be subtracted from each other, movements between different scan sequences should also be avoided.*

AFTER THE PROCEDURE

When the procedure is over, the woman gets dressed. If CM has been administered, outpatients may be asked to remain in the department for about 10 to 15 minutes to check for any very rare delayed reaction to CM. Prior to reading the images, they are sometimes co-registered (the various images combined into a coherent set) using special software, and the evaluation itself, which includes reference to previous examinations and clinical records, also takes time. The report is usually generated within a few days, but particular cases can require a longer time. In the case of artefacts or strong enhancement of background glandular tissue in women not examined in the best phase of the menstrual cycle or with unexpected other hormonal influences, a repeat breast MRI can be required. Depending on the findings and the indication for the examination, additional investigations may be necessary.

BREAST MRI REPORT AND BI-RADS® CATEGORIES

Evaluation of breast MRI should be performed by a dedicated breast radiologist. The report should contain the indication for the scan, relevant clinical information, and the type and dose of administered CM. In premenopausal women, the day or the week of the menstrual cycle on which MRI was performed should be stated. The techniques used should be very briefly summarised.

Reported image findings should include breast density, the amount of parenchymal background enhancement, and a usually structured description of relevant abnormalities, including those in the axillae (underarm area) or incidental findings in the imaged part of the thorax and abdomen, when visible. The side and location of any breast lesions should be described. Lymph node evaluation is not a specific aim of breast MRI, but it is possible that the exam reveals unsuspected nodal metastasis.

Each report should end with a conclusion, commonly associated with a diagnostic category and recommendations. In many European countries, a structured reporting and classification system is in use. The most commonly applied system is the Breast Imaging Reporting and Data System (BI-RADS®) developed by the American College of Radiology[22], also used with high-resolution 3 Tesla systems[23].

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Conclusive BI-RADS diagnostic categories are used as follows:

- 0 = incomplete, additional imaging evaluation is needed
- 1 = negative, no abnormalities
- 2 = benign findings
- 3 = probably benign findings (short-term follow-up within six months recommended; needle biopsy may be performed only in special cases, such as on patient request or for high-risk patients)
- 4 = suspected malignancy (needle biopsy recommended)
- 5 = highly suspected malignancy (needle biopsy recommended)
- 6 = already histologically proven cancer (typically reserved for MRI scans made for cancer staging or in the case of neoadjuvant chemotherapy)

See pages 34–38 for detailed information about BI-RADS categories

The recommendation of needle biopsy for BI-RADS 4–5 lesions is a general rule for isolated, newly diagnosed lesions. It could not be performed in the case of a lesion adjacent to or close to a lesion already known to be cancer. Around 60% of lesions initially detected at MRI are identified using second-look targeted ultrasound[24], even though this rate varies among studies. The term 'second-look' refers to the common event that a lesion undetected in a first ultrasound examination is detected at the 'second look', when the radiologist knows from MRI where to look. In that case, needle biopsy is performed under ultrasound guidance; a faster, less invasive, and cheaper procedure than MR-guided biopsy[25]. When the lesion is not detected with ultrasound and the indication for biopsy still stands, an MR-guided biopsy is indicated. It takes longer than a diagnostic breast MRI, and it is a special procedure, requiring dedicated targeting and sampling equipment, as well as trained personnel. In some countries it is necessary to apply for a specific reimbursement (this is a relatively new and expensive procedure).

However, in cases where MR-guided biopsy cannot be performed (e.g. dedicated equipment is not available; or the lesion site is not accessible, such as those very close to the thoracic wall), computed tomography-guided biopsy or MR-guided pre-surgical localisation may be performed.

Note H. *When a needle biopsy is indicated for an MR-detected finding, this doesn't mean you have cancer. Up to 50–70% of MRI findings that require biopsy turn out to be benign[26]. Targeted ultrasound, re-evaluation of mammograms, targeted mammographic views, or images obtained with digital breast tomosynthesis are useful, offering the possibility of a biopsy under ultrasound or mammography guidance. Thus, if a suspicious lesion (BI-RADS 4 or 5) is detected with MRI, an image-guided needle biopsy should be performed in almost all cases. Definition of the benign nature of an MRI-detected suspicious finding, using only other targeted imaging modalities, without biopsy, is only possible in very few cases.*

Note I. *In the case of MRI BI-RADS 4–5, even if targeted ultrasound and the above described mammographic approaches are negative, cancer cannot be excluded: an MRI-guided biopsy is required. Not all centres that perform breast MRI offer MRI-guided breast biopsy. However, your radiologist should be able to refer you to a centre where MRI-guided biopsy can be performed or should opt for needle sampling under computed tomography guidance or for MRI-guided pre-surgical localisation.*

BI-RADS 3 findings form a special diagnostic category[27], with a chance of malignancy below 2%[28]. However, the actual chance of an MRI-detected BI-RADS 3 lesion being malignant is sometimes higher, especially in high-risk women[29]. For a BI-RADS 3 lesion, short-term follow-up is recommended instead of biopsy due to the low probability of malignancy and the likelihood that the efficacy of treatment will not be reduced due to a slightly delayed diagnosis. This entails repeat MRI examinations within six months and potential further repeat MRI at one year and two years after initial detection. When, at MRI follow-up, an MRI-detected lesion has disappeared, shrunk, or remained unchanged in size, and does not show any new sign of malignancy, it can be downgraded to benign (BI-RADS 2) without biopsy. However, in some cases, mostly when the patient prefers an immediate conclusion of the diagnostic pathway, a needle biopsy can be performed for a BI-RADS 3 lesion straight away.

Note J. *In the case of an MRI BI-RADS 3 finding, you should discuss with your radiologist and/or referring physician whether watchful waiting with a follow-up breast MRI within six months should be preferred, or biopsy. Caution is advised to high-risk women: in*

these women a BI-RADS 3 finding has a higher probability of malignancy and biopsy is more frequently performed.

SENSITIVITY OF BREAST MRI

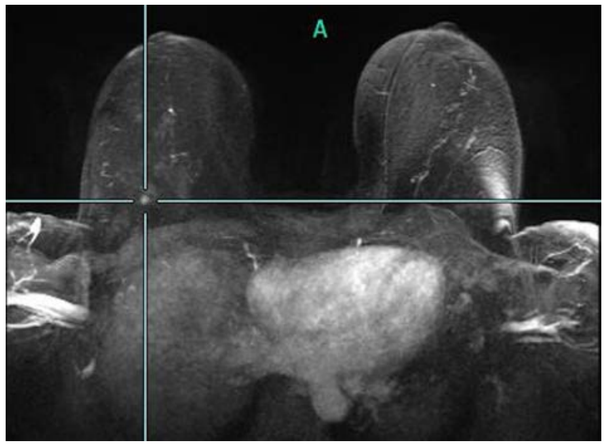
Overall sensitivity of breast MRI for breast cancer is approximately 90%, which implies that 10% of cancers may be missed. Missed cancers are in general either very small or do not have enough contrast enhancement.

Sensitivity for ductal carcinoma *in situ* (DCIS), a non-invasive lesion, possibly a precursor of invasive cancer and similarly treated, is variable; some of them, especially those with a lower pathological grade (G1) can be missed[30-32]. Occasionally, invasive cancers can also be hidden at MRI. DCIS may be depicted on mammograms as a cluster of microcalcifications, even if, in some cases, MRI findings are negative. This implies that findings from clinical examination, mammography, or ultrasound, even if only probably benign (i.e. BI-RADS 3), should be reviewed when MRI findings are negative[33]. Generally, if a needle biopsy is correctly indicated, a negative MRI finding cannot be considered an alternative to biopsy. Sensitivity also depends on technical prerequisites, clinical indication, and reader experience.

Note K. *If a needle biopsy based upon palpable abnormalities or mammography/ultrasound is indicated, you should have a needle biopsy to rule out cancer. Even though highly sensitive, breast MRI is not a perfect test and should not be used as an alternative for biopsy. Needle biopsies are performed to exclude the presence of cancer; as a consequence, when a biopsy is recommended, this does not mean that you have a cancer.*

FIGURE 1

Small screen detected ductal carcinoma *in situ* (DCIS) in the right breast.



BREAST MRI FOR SCREENING

Due to its high sensitivity, breast MRI is an excellent screening tool (Figure 1). In cohorts of women with a familial increased risk for breast cancer, and of women who are carriers of BRCA1, BRCA2, or other rare genetic mutations, the superior sensitivity of breast MRI compared to other breast imaging techniques has been shown[7, 34-39]. However, MRI also has a very high sensitivity for benign breast disease. This leads to additional investigations, including repeat MRI scans, targeted ultrasound, and biopsy, as stated above. This additional burden from MRI screening is greater in women with a priori lower breast cancer risk. Moreover, MRI is a relatively expensive examination, and the need for additional investigations further increases the cost. Consequently, the cost-effectiveness of MRI screening has been questioned for women who are not at increased risk[40]. Note that healthcare reimbursement of breast MRI screening varies from country to country.

Evidence for the substantial added value of MRI as a screening tool exists for women with proven BRCA1, BRCA2, or other rare genetic mutations[7, 34-39], for a proportion of women with an elevated risk based upon their family history, and for those patients who received thoracic radiotherapy before the age of 30[41-43]. A recent individual patient-data meta-analysis showed that for BRCA mutation carriers, the gain in sensitivity is also relevant over the age of 50[44]. Guidelines throughout Europe and the United States differ substantially for the risk level deserving breast MRI screening and the age for starting and ending MRI screening.

Note L. *If you have multiple cases of breast or ovarian cancer in your family, discuss the possibility of MRI screening with your referring physician and your radiologist. There are risk assessment systems available to estimate your risk. The referring physician or your radiologist could decide to refer you to a specialised centre for risk evaluation. The results thereof can subsequently be matched to your local or national guidelines. Note that healthcare reimbursement is variable among countries.*

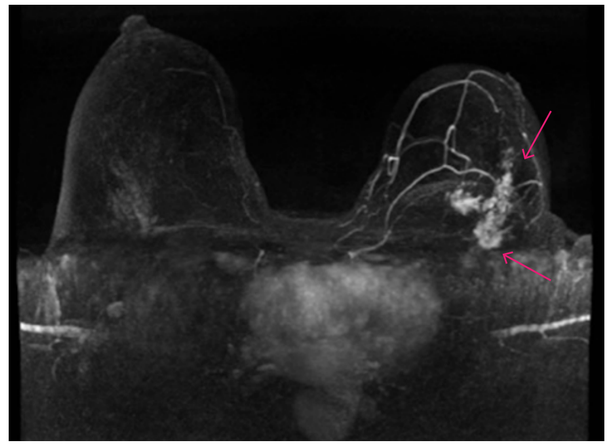
Note M. *If you have been treated with thoracic radiation therapy, discuss the need for MRI and mammography screening with your referring physician, radiation therapy specialist, and radiologist.*

BREAST MRI FOR BREAST CANCER STAGING

Most breast cancers are detected due to clinical symptoms or by screening mammography. The standard way to assess suspicious lesions is with the so-called triple assessment: mammography, ultrasound, and image-guided needle biopsy. MRI is not yet involved in initial cancer detection except in those women, usually at high risk, screened with MRI. When a breast cancer is detected, MRI may be performed to assess the extent of the disease, look for satellite lesions, and screen for other

FIGURE 2

Large screen detected ductal carcinoma *in situ* (DCIS) in the left breast. Large area of non-mass enhancement in the lateral and posterior aspect of the left breast (arrows).



cancers either in the affected breast or in the contralateral (other) breast (Figure 2). MRI is much more useful for tumour extent evaluation than either mammography or ultrasound, even though overestimation and underestimation of tumour size still occur in up to 15% of patients. Although better documentation of tumour size and extent could lead to a better tailored surgery, with a low rate of re-interventions for positive resection margins, randomised studies that evaluated the surgical outcome of preoperative MRI have yielded conflicting results[45-48]. In patients with invasive lobular carcinoma (a specific diffuse growing tumour type notoriously underestimated when seen with mammography and ultrasound) a reduction of re-excisions from 18% to 11% was observed[49], although this was not statistically significant in a meta-analysis[50]. Other suggested indications are discrepancy in tumour size among different modalities (including clinical examination) that may change the treatment strategy, breast cancer found in a high-risk woman, and eligibility for partial breast irradiation[7, 51].

Preoperative MRI is also used to detect many additional enhancing lesions unseen with mammography and ultrasound. Approximately 50% of them are cancerous (increased up to 75% in the breast harbouring an already known malignancy), indicating that pathological verification is necessary, especially when the additional lesions are distant from the already diagnosed cancer. When additional disease is detected, this logically leads to more extensive surgery. However, this must be regarded with caution. It should be understood that breast conserving surgery in breast cancer in over 40% of patients is primarily aimed at reducing disease extent rather than being completely curative[52]. This information should be presented to patients: treatment is mostly completed by radiation therapy, chemotherapy, and/or hormonal therapy. Consequently, additional MRI-detected tumour foci may be effectively treated by these adjuvant therapies. Extension of surgery indicated by MRI might, therefore, be unnecessary. So far, there is a lack of evidence of improved overall or disease-free survival due to preoperative MRI. In any case, the possible patient gain from preoperative MRI is also dependent on the experience of the radiologist reporting the MRI, the accuracy of mapping MRI-detected additional tumour extent, the capabilities of the treating surgeon using the results of this imaging technique, and thus on the interface between radiology and surgery.

In addition, MRI may reveal unsuspected cancer in the contralateral breast in approximately 3% of all women with unilateral cancer as found by conventional imaging[53], even though higher rates of otherwise undetected contralateral cancers were reported[54]. Since no radiation therapy is given to the contralateral breast, the detection of unsuspected contralateral cancer may be more relevant than detection of additional foci in the ipsilateral breast (the breast where cancer is already known to be). Although in most circumstances the eventual prognosis is mainly dictated by the size and grade of the largest cancer, early detection of second cancers is associated with a slight increase in survival, especially in patients below 50 years of age[55,56].

Note N. *In the case of a newly diagnosed breast cancer, preoperative MRI is a possibility for improving treatment of the already diagnosed cancer and also detecting cancer in the contralateral breast. This must be balanced against a risk that more extensive unnecessary surgery may be performed (e.g. mastectomy instead of a lumpectomy) as a consequence of MRI. Your radiologist and your surgeon can discuss with you potential advantages and disadvantages of preoperative MRI considering your particular case.*

BREAST MRI IN PATIENTS WITH IMPLANTS

MRI is the most sensitive technique for detecting breast implant ruptures when an appropriate protocol is performed[57]. This protocol includes specialised sequences without CM administration.

Notably, the breast's usual reaction to augmentation is to form a fibrous capsule around the implant. This capsule frequently keeps the silicone in place even after an implant rupture. In fact, up to 50% of old implants are leaky ten years after implantation[58], usually without any symptoms. Thus, screening for implant rupture is not needed[7]. In symptomatic patients, for example, those with an extracapsular rupture (i.e. with silicone outside the fibrous capsule), the leakage and spread of silicone in the breast can be very accurately depicted with MRI. MRI is able to confirm or exclude rupture when mammography or ultrasound are inconclusive. This may facilitate the decision of the surgeon to make a revision or to change the implants.

The presence of implants does not affect the sensitivity of MRI for breast cancer detection: other indications for CE breast MRI remain valid in the presence of implants.

Note O. *In the absence of symptoms, breast implants do not need to be screened for integrity with breast MRI. However, in cases of suspected rupture, MRI is the best technique for detecting possible leakage.*

Note P. *Breast implants do not affect the sensitivity of CE MRI for new or recurrent breast cancer.*

Note Q. *If you have breast implants and a breast MRI is planned, remember to bring with you detailed information about the model/type of the implants you have. If you don't have this information, please ask the surgeon to give you these data.*

EVALUATION OF THE EFFECT OF NEOADJUVANT CHEMOTHERAPY

In the case of advanced breast cancer, many centres adopt protocols for reduction of the mass with neoadjuvant chemotherapy before surgery. In this setting, MRI is proposed for either early prediction of response during chemotherapy[59] or for pre-surgical evaluation[60,61]. A baseline MRI evaluation should be performed prior to neoadjuvant chemotherapy, as MRI images cannot be compared to initial mammography or ultrasound studies. For both early response prediction and pre-surgical evaluation, MRI seems to be a better test than clinical breast evaluation, mammography, or ultrasound. However, women should be aware that if MRI is used to guide surgery at the end of chemotherapy, a fraction of patients (10–20 %) may have clinically relevant underestimation or overestimation of residual cancer[7].

OCCULT PRIMARY BREAST CARCINOMA

After the initial detection of metastases, breast cancer may be suspected, especially when axillary nodes are involved. However, in a small fraction of patients, in whom needle biopsy of lymph nodes confirms the breast origin of the disease, mammography and ultrasound are negative. This is occult primary breast cancer, accounting for up to 1% of breast cancers. In this clinical setting, MRI can be used to identify the primary breast cancer in about two thirds of cases, allowing for breast conserving surgery[6,7,62]. If breast MRI is negative, immediate surgery may be avoided. In cases of axillary metastases, patients are usually treated with radiotherapy to the ipsilateral breast. Follow-up MRI can be proposed[7].

FREQUENTLY ASKED QUESTIONS

1. Is MRI screening harmful?
MRI does not use ionising radiation, and consequently does not damage cells. There is no evidence that the magnetic fields and radiofrequency waves applied in MRI are harmful to humans. A little warming may occur, however this is by law restricted to a maximum of one degree core temperature. This potential effect is harmless. However, detection or exclusion of malignancy is only possible by intravenous injection of contrast media, which can lead to rare but severe side effects including life-threatening allergic reactions or nephrogenic systemic sclerosis (see above).

2. Should I bring my prior examinations and mammograms?
The availability of prior examinations improves the accuracy of the interpretation of breast MRI, resulting in increased sensitivity and decreased false positive rate. Therefore it is very important to take prior examinations (written reports and images, printed or on an electronic device) with you to the appointment for breast MRI (unless these are already present in the centre/hospital). This holds true for prior MRI examinations and for prior mammograms, ultrasound, histopathology results of needle biopsy or surgical interventions, and any clinical records relevant to your case. All

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this information creates the basis for obtaining the most detailed diagnosis and proper recommendations from your current breast MRI examination.

3. When should MRI screening in high-risk women start? How often should MRI screening be repeated?
The onset of MRI screening is highly dependent on the indication for MRI screening. In women with a strong family history of breast or ovarian cancer, in particular those with BRCA1 or BRCA2 mutations, MRI screening should start between the ages of 25 and 30. The proposed screening schedule is once yearly. This is more frequent than population-based mammographic screening due to the more rapid growth of breast cancers at a young age. Please note that one single case of breast cancer among your relatives, especially if it occurred after the age of 50, does not mean that you are at high risk. If you have any concerns in this regard, consult your family doctor or your breast radiologist. They will decide whether or not they should refer you to a specialised centre to evaluate your risk.

4. Does preoperative MRI also detect additional cancers in women with very fatty breasts and in women over 60 or 70?
MRI detects additional cancers unseen by mammography and ultrasound in a fraction of women with breast cancer, even though in women with very fatty breasts the added MRI detection may be lower than in those with very dense breasts. Breast MRI similarly detects additional ipsilateral and contralateral breast cancers in women at any age, even though the potential impact of such additional cancer on disease-free and overall survival may decrease with age. There is no clear cut-off for breast density or age. Consequently, the choice for preoperative MRI should also be based on the considerations about the risk-benefit balance described above.

5. Is there any special indication for breast MRI when partial breast irradiation is under consideration?
If you are offered partial breast irradiation in the context of or outside a clinical trial, the possibility of having a breast MRI in order to verify that you really qualify for reduction of the field treated with radiation therapy (i.e. that no tumour foci remain outside the treated field), should be evaluated by your physicians in a multidisciplinary meeting. Note that the reported rate of patients who are deemed not suitable for partial breast irradiation after a breast MRI is about 11%.

ACKNOWLEDGEMENTS

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REFERENCES

See page 168

IMAGE-GUIDED BREAST BIOPSIES

BY **ULRICH BICK** ON BEHALF OF THE
EUROPEAN SOCIETY OF BREAST IMAGING (EUSOBI)

INTRODUCTION

Increasing efforts to improve the early detection of breast cancer along with improved adjuvant therapy have led to a steady decrease in breast cancer mortality over the last three decades, despite a significant increase in breast cancer incidence over the same time period. Before the introduction of mammography screening more than 40 years ago, breast cancer was only found when palpable or when other clinical signs were present and was therefore traditionally treated with mastectomy.

Imaging-based early detection has made it possible to find breast cancer at an early, preclinical stage, which in the majority of cases can be treated with breast conserving therapy. However, both clinical breast exams as well as imaging-based early detection efforts will also find some breast abnormalities that are benign and do not require further treatment. To avoid unnecessary surgery for benign abnormalities and to allow optimal treatment planning, suspicious imaging findings detected in screening or during assessment of clinical abnormalities should therefore – if possible – first be subjected to minimally-invasive percutaneous biopsy. In their fourth edition from 2006, the European guidelines for quality assurance in breast cancer screening and diagnosis specify that at least 70% of patients with a clinically occult breast cancer should have the diagnosis confirmed preoperatively by percutaneous biopsy[1]. Ideally, this proportion should be much higher. The more recent European Society of Breast Cancer Specialists (EUSOMA) guidelines specify a target rate of 90% of women with breast cancer (invasive or *in situ*) with a definitive preoperative diagnosis[2].

A variety of different techniques are now available for this purpose[3]. Depending on the circumstances, the biopsy may be performed using different guidance techniques and needle types, all of which have specific strengths and disadvantages. It is important that the person choosing the optimal biopsy technique

is well versed in the full spectrum of available methods to be able to choose the optimal strategy for the specific patient. This article will discuss the strengths and weaknesses of the different biopsy techniques, including diagnostic accuracy and potential side effects.

RATIONALE BEHIND OBTAINING A DEFINITIVE PREOPERATIVE DIAGNOSIS THROUGH PERCUTANEOUS BIOPSY

Even with all the recent advances in imaging, a definitive diagnosis of malignancy can only be made through obtaining cells or tissue for microscopic histopathologic evaluation. There are a variety of benign abnormalities which can mimic malignancy on imaging and even the most suspicious imaging findings will never reach a positive predictive value of 100%. So the most obvious reason for performing a percutaneous biopsy prior to surgery is to prevent surgery, with all its associated morbidity and costs, for abnormalities that eventually turn out to be benign and which would not have required surgical treatment. However, in recent years another aspect has increased in importance. A whole range of surgical options, various primary and postoperative adjuvant systemic therapy concepts, and different local radiation therapy treatments are currently available for breast cancer patients. Adequate patient counselling and treatment planning is only possible if a definitive diagnosis of malignancy, including the type of cancer (e.g. *in situ* or invasive) and the biological tumour characteristics, is available prior to commencement of therapy[4].

CHOOSING THE OPTIMAL BIOPSY GUIDANCE TECHNIQUE

Percutaneous biopsy can either be performed freehand without imaging guidance or with the assistance of imaging techniques such as mammography, ultrasound or MRI, which are used to control the placement of the needle. Freehand biopsy is the least expensive and easiest method to perform, but it is the least accurate technique. It is usually reserved for performing fine-needle aspiration cytology (FNAC) on larger palpable abnormalities and

FIGURE 1

X-shaped hookwire in cannula for insertion for pre-operative localisation of non-palpable breast lesions.

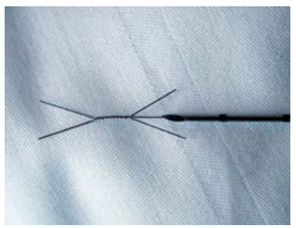
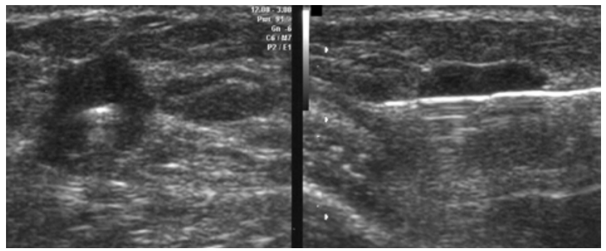


FIGURE 2

Ultrasound-guided core needle biopsy of a BI-RADS 4 lesion. Hyperechoic ('white') needle within hypoechoic ('black') mass lesion.



it is not suitable as guidance for more advanced biopsy techniques such as vacuum-assisted biopsy (VAB).

If a lesion is visible on ultrasound, the best choice is usually to perform the biopsy under ultrasound guidance[5]. Ultrasound is readily available, does not use radiation and allows for real-time supervision of the correct needle placement. Ultrasound-guided biopsies can be performed as a bedside procedure in bedridden patients and there are virtually no contraindications or anatomical restrictions for biopsy access to breast lesions. Typically, ultrasound-guided biopsy is performed as core needle biopsy (CNB) using a specialised biopsy gun, but ultrasound is also suited to guidance for VAB or advanced breast lesion excision systems.

Stereotactic biopsy using mammographic guidance is the method of choice for lesions detected with screening mammography which do not have a corresponding finding on ultrasound[6]. The majority of these lesions will represent microcalcifications and to a lesser extent architectural distortions and small masses. Stereotactic biopsies can be performed with dedicated prone tables or with upright mammographic add-on systems, with the patient usually sitting or lying on their side during the procedure. With the dedicated prone systems, vasovagal reactions can be avoided, but the upright add-on systems may have better access to lesions close to the chest wall. All stereotactic biopsies performed for microcalcifications should be followed by specimen radiography to document adequate sampling of the microcalcifications. A recent addition to mammographic biopsy options are systems which allow biopsies under tomosynthesis guidance[7].

FIGURE 3

Specimen radiography at vacuum-assisted breast biopsy of pleomorphic microcalcifications for verification of adequate lesion sampling.

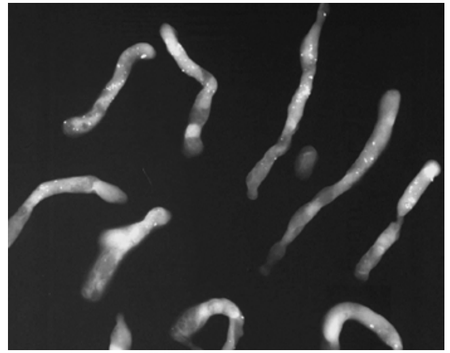
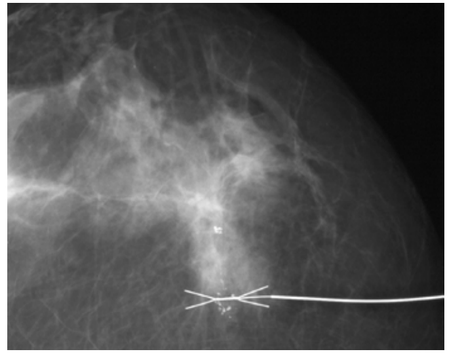


FIGURE 4

Mammography image after hookwire placement for pre-operative localisation of non-palpable pleomorphic microcalcifications.

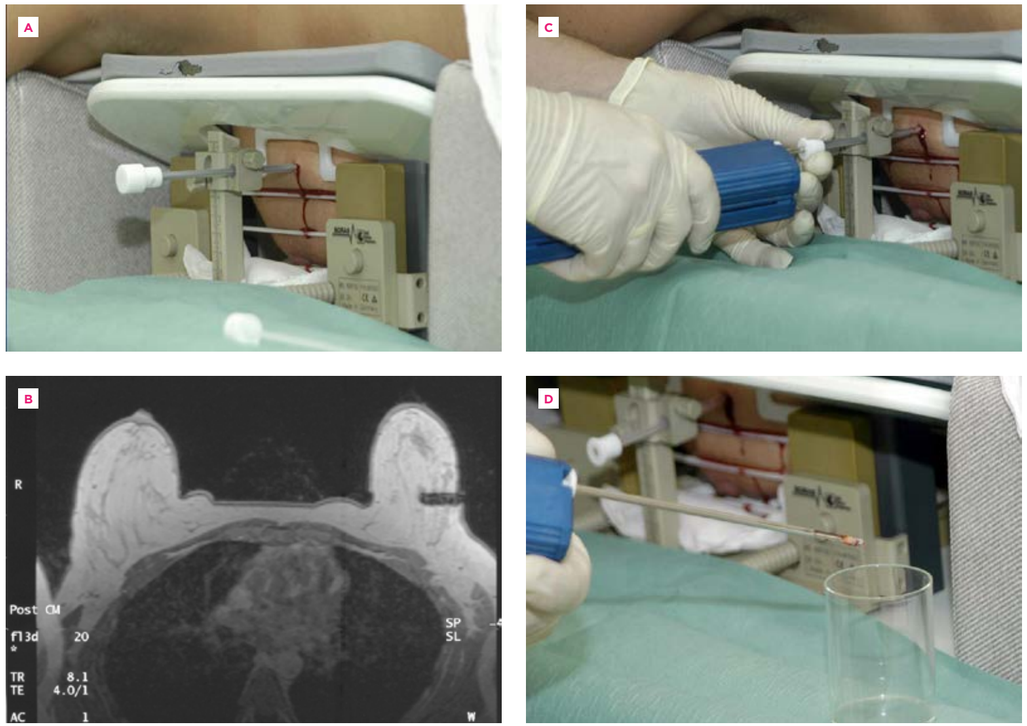


Figures 2–4: Images from: Raimund Jakesz, Manfred Frey (Eds.), Mammakarzinom. Operative Behandlungskonzepte, Chapter 2: Exakte Diagnosestellung – Voraussetzung zur optimalen Therapiewahl, 2007, p. 17–49, M. Fuchsjäger, N. Kropf und R. Jakesz, © 2007 Springer-Verlag / Wien. With permission of Springer.

FIGURE 5

MRI guided biopsy

A) Trocar in place.
B) MR image of trocar (black) in place in the left breast.
C) Biopsy with hand-held vacuum-assisted device.
D) Specimen (at needle tip) to be placed in tissue collection box.



Images provided by Dr. Lothar Ponhold

MRI-guided biopsies are usually reserved for lesions occult both on mammography and ultrasound[8]. In many cases, a careful second-look ultrasound[9] will be used to find lesions initially detected on MRI, thus allowing the biopsy to be performed under ultrasound guidance. For MRI-guided biopsy a special biopsy coil with a perforated compression plate is required to enable accurate needle placement in 3D. All MRI-guided biopsies should be followed by placement of a marker into the biopsy cavity to allow for easy preoperative localisation by ultrasound or mammography if necessary. Disadvantages of MRI-guided biopsies are relatively long procedure times, high costs, limited access to lesions close to the chest wall (depending on the biopsy coil setup), and the lack of real-time supervision of the needle placement. CT-guided biopsy may be an alternative in rare case of MRI-detected lesions which are occult both on ultrasound and mammography and in which MRI-guided biopsy cannot be performed for technical reasons[10].

If the correlation between the imaging findings and pathology is doubtful, a repeat biopsy may be necessary, guided by the original imaging modality used to detect the findings.

DIFFERENT OPTIONS FOR TISSUE SAMPLING

There are several different types of needles and other tissue sampling devices which can be used for percutaneous biopsy and which primarily differ in the amount of tissue obtained during biopsy. The least invasive technique is fine-needle aspiration cytology (FNAC), where very thin needles – typically with needle diameters between 21 and 25G – attached to a syringe are used to aspirate cells for cytological examination. This procedure is easy and fast to perform, the associated costs are low, and with a cytopathologist on site, results may be available immediately after the procedure[11]. However, the success of the technique is highly dependent on the skills of the physician performing the procedure as well as the pathologist interpreting the results, and even in experienced hands, this technique has a high rate of inadequate or false-negative results[12]. In addition, FNAC cannot be used to reliably distinguish between *in situ* and invasive malignant changes, and immunohistological tumour characteristics required for optimal treatment planning are largely unavailable[4].

This is the reason why FNAC has in recent years increasingly been replaced by core needle biopsy (CNB)[13,14]. With CNB, needles with a diameter ranging between 12 and 18G (most commonly 14G) mounted in a reusable or disposable, spring-loaded biopsy device (or 'gun') are used to obtain cylindrical tissue samples ('cores') with a length of somewhere between 11 and 22mm, depending on the system setup. These tissue cores will allow for accurate histopathological diagnosis including biological markers necessary for treatment planning. CNB is the most common type of biopsy in solid lesions under ultrasound guidance. Although in principle a single high-quality core obtained from the lesion in question is sufficient for making the diagnosis, usually multiple cores (at least three) are obtained to assure adequate sampling[15,16]. CNB has a low false-negative rate[17], but there is a certain risk of underestimating lesions due to the fact that only a small portion of the lesion is sampled. Depending on the underlying histological abnormality, 10–50% of lesions characterised as high-risk by CNB will eventually turn out to be malignant[18], and around 25% of lesions diagnosed as *in situ* by CNB will have an invasive component on final surgery[19].

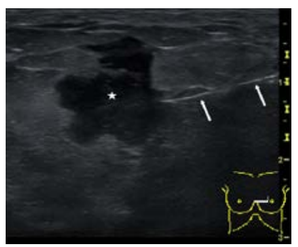
To reduce this underestimation rate, especially for lesions associated with microcalcifications, new vacuum-assisted biopsy (VAB) devices using needle diameters between 7 and 12G have been developed. These allow for rapid removal of much larger amounts of tissue (more than one gram or cubic centimetre of tissue per biopsy[20,21]) to reduce the risk of underestimation. With VAB systems, multiple (usually at least 12 for a needle size of 10G or 11G[16]) consecutive tissue cores can be obtained just by rotating the needle without the need for needle removal and reintroduction as in CNB. Small lesions (e.g. less than 1cm in size) may be completely removed by VAB, in which case a marker should be placed in the biopsy cavity to allow for subsequent surgery if necessary. In addition to reducing the underestimation rate, the larger amount of tissue removed with VAB is able to compensate for possible slight inaccuracies in targeting and needle placement in stereotactic and MRI-guided biopsies, where real-time supervision of correct needle placement is not possible[6].

In the past, several attempts have been made to develop systems which allow the complete removal of small lesions in one single contiguous specimen under

imaging guidance to further increase biopsy accuracy[6]. These include the earlier advanced breast biopsy instrumentation (ABBI) system[23] and the SiteSelect™ system[24], both of which are no longer marketed and were designed as add-ons to regular stereotactic biopsy tables, as well as the newer Intact® breast lesion excision system (BLES), which uses radiofrequency to facilitate the excision of the specimens and can be performed under ultrasound or stereotactic guidance[25,26]. So far however, none of these systems have shown clear advantages over existing VAB systems.

FIGURE 6

Ultrasound-guided biopsy. Core needle (arrows) approaching the highly suspicious mass lesion (asterisk) for the right hand side.



POTENTIAL SIDE-EFFECTS AND COMPLICATIONS

Percutaneous breast biopsies in general are a very safe procedure and severe complications requiring treatment are exceedingly rare[4,27]. The most common side effect of a breast biopsy is some degree of bleeding or haematoma formation at the biopsy site. The risk of bleeding will increase somewhat with the needle diameter and the amount of tissue sampled. Bleeding after biopsy is usually self-limited and may produce mild discomfort at the site of biopsy for several days. Severe bleeding requiring surgical intervention can be prevented almost completely by careful screening for bleeding disorders in preparation for the biopsy, avoidance of bigger, especially arterial vessels when choosing the needle track, and by adequate compression of the biopsy site after the procedure. As with any percutaneous intervention, a certain risk of infection exists and adherence to sterile working conditions is important. The risk of infection may be higher in patients with diabetes or a compromised immune system.

Although studies have shown that mechanical displacement of malignant cells along the biopsy tract can occur with percutaneous biopsy, reports of actual recurrences along the needle tract from seeding are very rare[27,28], likely because the displaced tumour cells are usually not viable[29]. A severe, but extremely rare complication of a breast biopsy is the development of a pneumothorax, which may occur with freehand or ultrasound-guided biopsy (in particular FNAC), especially if an inexperienced examiner uses an improperly steep angle for access[30]. This risk does not exist with stereotactic biopsy, where the needle is introduced parallel to the chest wall. As administration of contrast material is necessary for MRI-guided biopsy, there is a very low risk of a contrast reaction, although this will be quite negligible if the patient has had a prior diagnostic contrast-enhanced MRI without any kind of reaction.

PREPARATION FOR BIOPSY

To reduce the risk of bleeding, patients scheduled for percutaneous breast biopsy should be screened for bleeding disorders and any anticoagulation medication should preferably – if medically safe – be discontinued prior to biopsy, even though breast biopsies can safely be performed in patients receiving anticoagulation treatment, if necessary[16,31]. Stereotactic and MRI-guided biopsies are usually not performed during pregnancy and patients planned for MRI-guided biopsy should undergo the usual precautions including screening for MRI-incompatible implants, prior contrast reaction, or renal function impairment. The planned procedure, including the rationale for performing the biopsy, possible complications and the likely outcomes, should be explained in detail to the patient and (usually written) informed consent should be obtained[5,6].

The patients should also be informed about the possible necessity of placing a marker clip in the biopsy cavity, as well as about the rare need for re-biopsy or surgical excision in cases with poor radiological-pathological concordance or for certain risk lesions with uncertain malignant potential[32,33].

Efforts should be made to reduce the patient's anxiety prior to the biopsy, as the anticipated pain strongly correlates with the level of pain experienced by the patient during the procedure[34]. No other special safeguards are necessary prior to the procedure and the patients do not have to fast on the day of the procedure. Patients undergoing breast biopsy should be informed that the administration of local anaesthesia may, in rare cases, impair reaction times and the patients should be encouraged not to drive themselves home after the procedure.

PATIENT EXPERIENCE DURING BIOPSY

After selecting the best and safest needle access route to the lesion, the patient is properly positioned for biopsy, which in the case of stereotactic or MRI-guided biopsy will include mild compression of the breast for immobilisation. Next, the skin in the area of the planned needle entrance will be cleaned and disinfected. Whereas for FNAC the use of local anaesthesia is optional, since the size of the needle used is similar to an anaesthesia needle, all other types of percutaneous breast biopsy are usually performed under local anaesthesia. For superficial anaesthesia, lidocaine buffered in sodium bicarbonate may be used to reduce the initial stinging sensation of the lidocaine injection[5,16,35] and for the deep anaesthesia epinephrine may be added to reduce the risk of bleeding[5,16]. Even with optimal local anaesthesia, some discomfort or pain may be felt during needle insertion and tissue sampling, which will vary significantly from patient to patient[34].

Following the biopsy, a marker clip may be placed in the biopsy cavity to facilitate future localisation, if surgery will be necessary based on the histological results of the biopsy. This is especially important for MRI-guided biopsies and in cases where the imaging finding is small and the risk exists that the lesion will no longer be visible after biopsy. Upon conclusion of the biopsy, local compression as well as cooling may be applied to the biopsy site to achieve haemostasis and to minimise the amount of bleeding. In addition, the application of a circular compression bandage (for VAB only) after the procedure, which should stay in place until the next morning, can reduce the risk of bleeding. For all biopsies with clip placement, a post-biopsy mammogram has to be performed, either immediately following the procedure or later, e.g. at the time when the biopsy results are discussed. This mammogram is useful for confirming correct lesion targeting and clip placement and serves as a comparison for future follow-up exams.

POST-PROCEDURAL RECOMMENDATIONS AND COMMUNICATION OF RESULTS

Following the biopsy procedure and after achieving haemostasis, the patients can be discharged from the department with appropriate instructions, which should also preferably be given to the patient in writing. The wound should be kept clean and dry, and complete immersion in water (e.g. tub bath, swimming) as well as strenuous exercise should be avoided for at least three days following the biopsy. If possible, biopsy results as well as recommendations for further management (e.g. treatment, follow-up) should be discussed with the patient in person. With the exception of FNA, where biopsy results may be available immediately after the biopsy, this will occur during a second follow-up visit. Timing of the follow-up visit must strike a balance between minimising the waiting time for the patient (and its associated anxiety) and the necessity to allow for enough time to have final pathology results (if necessary, including additional immune-histological stains) available at the time of the follow-up visit. Ideally, the follow-up visit should – if applicable – already include the results from the multidisciplinary conference, at which concordance of imaging and histological findings is confirmed.

REFERENCES
See page 170

CHAPTER 5: EUSOBI RECOMMENDATIONS FOR WOMEN'S INFORMATION

EUROPA DONNA GUIDE

EUROPA DONNA GUIDE
TO BREAST HEALTH

EUROPA DONNA GUIDE TO BREAST HEALTH

EUROPA DONNA – The European Breast Cancer Coalition is an independent, non-profit organisation whose members are affiliated groups from throughout Europe. The Coalition works to raise awareness of breast cancer and to mobilise the support of European women in pressing for improved breast cancer education, appropriate screening, optimal treatment and care and increased funding for research. EUROPA DONNA represents the interests of European women regarding breast cancer to local and national authorities as well as to institutions of the European Union.

WHY IS BREAST HEALTH SO IMPORTANT?

- How we live our lives affects our health in the long term and certain **lifestyle factors** have been shown to increase the risk of getting cancer. WHO has reported that at least one-third of all cancer cases are preventable and up to 30% of cancers are probably related to diet and nutrition.
- Breast cancer is the **most common cancer** in women worldwide. In Europe it still claims the lives of more women than any other cancer.
- Although much remains to be learned about the causes of breast cancer*, some specific factors have been shown to influence risk:
  - Living a healthy, **active lifestyle, avoiding weight gain** and obesity can help maintain healthy breasts. Studies show that about one-third of breast cancer cases can be attributed to increased weight and physical inactivity.
  - **Limiting alcohol intake** can help keep breasts healthy, since high alcohol consumption can double the risk of breast cancer.
  - **Having children at a younger age,** having several and breast-feeding them also has protective effects.
  - Combined **hormone replacement therapy** (HRT) is associated with an increased risk of breast cancer. Seriously considering the pros and cons of using HRT can have a future influence on breast health.
- Participating in **population-based mammography screening programmes** can help detect potential problems early. Studies show that women who attend screening have a greater chance of surviving a breast cancer diagnosis; deaths from breast cancer are reduced by about 35% in women aged 50–69 who participate in screening.
- While studies have shown that **breast self-examination** is not necessarily effective, being aware of our breasts and changes in them can alert us to potential problems.
- Above all, paying attention to specific lifestyle factors, being breast aware and participating in a screening programme set up according to EU guidelines are the first steps toward **prolonged breast health.**

Source of above data: IARC and WHO

*Genetic factors account for approximately 5–10% of breast cancer cases, but most of the remaining cases are sporadic.

EUROPEAN CODE AGAINST CANCER

EUROPA DONNA encourages women to follow the recommendations resulting from the study supported by the European Community's Europe Against Cancer programme. Individual lifestyle choices may influence our health and decrease our chances of developing cancer.

Certain cancers may be avoided and general health improved if you adopt a healthier lifestyle

- Do not smoke; if you smoke, stop doing so. If you fail to stop, do not smoke in the presence of non-smokers
- Avoid obesity
- Undertake some brisk, physical activity every day
- Increase your daily intake and variety of vegetables and fruits: eat at least five servings daily. Limit your intake of foods containing fats from animal sources
- If you drink alcohol, whether beer, wine or spirits, moderate your consumption to two drinks per day if you are a man and one drink per day if you are a woman
- Care must be taken to avoid excessive sun exposure. It is specifically important to protect children and adolescents. For individuals who have a tendency to burn in the sun active protective measures must be taken throughout life
- Apply strictly regulations aimed at preventing any exposure to known cancer-causing substances. Follow advice of national radiation protection offices
- Women from 25 years of age should participate in cervical screening. This should be within programmes with quality control procedures in compliance with European Union Guidelines for Quality Assurance in Cervical Screening
- Women from 50 years of age should participate in breast screening. This should be within programmes with quality control procedures in compliance with European Union Guidelines for Quality Assurance in Mammography Screening
- Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality assurance procedures
- Participate in vaccination programmes against Hepatitis B Virus infection

www.cancercode.org, third version (2003)

BE BREAST AWARE

*While recent studies indicate that breast self-examination does not reduce deaths from breast cancer, EUROPA DONNA encourages women to be familiar with their breasts and to seek medical advice if they detect any unusual changes**

Check for unusual changes

It is quite normal for most women to notice changes in their breasts during their monthly cycle – but only you know what is normal for you. It makes good sense to be Breast Aware and check your breasts periodically. You can take convenient opportunities such as bathing or dressing to become familiar with your breasts by looking at them and touching them. This will help in noticing any changes or abnormalities (usually a lump) sooner and you will increase your general awareness of what is changing in your body and know what to have checked.

Check for

- A change in size or contour, or position of the nipple
- Obvious lumps or thickening, puckering or dimpling of the skin
- Veins which are more prominent than usual
- Inflammation or rash on the breast
- Blood or discharge from the nipple
- New sensation – particularly if only in one breast

Check it out

If you notice anything unusual, see your doctor. Remember, 9 out of 10 lumps are harmless. The breast is often naturally lumpy as a result of normal glandular changes.

*For women between the ages of 50 and 69 participating in a mammography screening programme set up according to EU guidelines is the most important method of early detection.

LIFESTYLE AND BREAST CANCER

There is growing evidence of the link between lifestyle factors and breast cancer. EUROPA DONNA encourages women to take charge of their own health and to make lifestyle choices now that could protect them later. Healthy living helps protect us against numerous diseases.

Women should pursue a health strategy that will reduce the known breast cancer risk factors as much as possible, including avoiding obesity and weight gain, increasing physical activity and managing lifestyle choices. IARC estimates that excess body weight and physical inactivity account for approximately 25–33% of breast cancer cases.

Obesity and weight gain

Recent studies indicate that women who avoid being overweight reduce their risk of postmenopausal breast cancer. This risk is independent of the effect of physical activity. It is important for women to limit their weight gain in adult life and maintain a body mass index (BMI) of 18.5–24.9 (see BMI chart below). Postmenopausal overweight/obesity is associated with an increased risk of breast cancer.

- A large amount of abdominal fat may increase the risk of breast cancer.
- Obese women tend to have more abnormal mammography readings than non-obese women.

Body mass index (BMI)

Being overweight with a BMI (see chart below) of 25 or higher, or obese with a BMI of 30 or greater, points to an increased risk of developing postmenopausal breast cancer. Women who have already had breast cancer may help reduce their risk of further problems by keeping their weight within the normal range.

Physical activity

Growing evidence supports that there is a protective association between physical activity and breast cancer, preferably over a lifetime, but probably beneficial even if begun after menopause.

- Regular physical activity reduces the risk of breast cancer
- Inactivity is estimated to cause 10–16% of all breast cancer cases
- Inactivity coupled with excess body weight account for nearly 33% of all breast cancer cases*

Women should:

- Stay healthy and active
- Engage in moderate exercise for at least 30–60 minutes every day

* The benefit of physical activity in reducing the chance of developing breast cancer is independent of the risk factor associated with body weight.

TABLE 1

Calculating your body mass index

BMI = weight in kgs/ height in metres^2		
	Underweight	**<18.50**
	Normal range	**18.50 – 24.99**
	Overweight	**≥25.00**
	Obese	**≥30.00**

Restricting alcohol intake

- Restrict alcohol intake to not more than one drink per day (i.e., 10 grams or less per day. A glass of beer, wine or spirits corresponds to 8–10 grams of ethanol)

Nutrition

While studies have not linked specific diets to breast cancer risk, nutrition is still important.

- Eat a well-balanced diet (daily intake of fat should not exceed 30%)
- Include fresh fruit and vegetables in your daily food choices
- Eat the right amount to maintain a healthy weight
- Limit red meat consumption

Other considerations

While there has not been a direct link found between active smoking and breast cancer, not smoking cigarettes and minimising exposure to second-hand smoke is beneficial for multiple health reasons. Smoking is directly linked to numerous types of cancer and other illnesses.

HORMONE REPLACEMENT THERAPY (HRT), CONTRACEPTIVES AND BREAST CANCER

*A number of published studies show an increased risk of breast cancer in women who use HRT. EUROPA DONNA has published a **Statement on HRT** and believes women should be informed of these risks and should discuss any decisions related to taking HRT in detail with their physicians. Younger women should also be aware of the risks of taking oral contraceptives.*

About HRT

Hormonal Replacement Therapy (HRT) is a common therapy offered to women to treat menopausal symptoms. HRT reduces the symptoms that are caused by menopause, maintains bone density in post-menopausal women and decreases the risk of bone fractures caused by osteoporosis during period of use.

HRT and breast cancer risk

Based on evidence from various studies, the Women's Health Initiative (www.nih.gov/PHTindex.htm or www.whi.org) and the Million Women Study (www.millionwomenstudy.org), there is a very clear connection between HRT and the risk of developing breast cancer. The Million Women Study found that current users of HRT at recruitment were more likely than never users to develop breast cancer (adjusted relative risk 1.66) (see Lancet 2003; 362: 419-27). The above mentioned studies indicate that the breast cancer risk increases the longer HRT is taken.

An IARC evaluation of cancer risk and HRT concluded that combined oestrogen-progestogen therapy is carcinogenic. This is based on the numerous studies consistently reporting an increased risk of breast cancer in women who currently use or have recently used combined oestrogen–progestogen therapy.

For women who do not have a history of breast cancer it is advisable to discuss the risks and benefits of taking HRT with your doctor in order to make an informed decision as to whether HRT is right for you. It is further recommended that you review your current treatments with your doctor on a regular basis to know if they are still your best option. If you opt for HRT, ask to take the lowest effective dose for the shortest amount of time needed to treat your symptoms.

HRT is generally not recommended if you have a history of breast cancer as HRT may increase your risk of a recurrence of breast cancer (see *Lancet 2004; 363: 453-5)*. Any decision to take HRT should, therefore, be discussed in detail with your physician.

Oral contraceptives and breast cancer

An IARC evaluation of the cancer risk with oral contraceptive use concluded: "There is sufficient evidence in humans for the carcinogenicity of combined oral oestrogen–progestogen contraceptives. This evaluation was made on the basis of increased risks for cancer of the breast among current and recent users only."

ABOUT MAMMOGRAPHY SCREENING

EUROPA DONNA advocates for population-based mammography screening programmes adhering to the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis. Attending screening has been shown to reduce the number of deaths from breast cancer by up to 35% for women between the ages of 50 and 69.

- Mammography is widely accepted as the best method to spot breast cancer early, before it becomes detectable to the touch. When you have a mammogram, a radiographer

places your breast between two large plates on the mammography machine. These plates compress the breast while an x-ray is taken. Although compression can be uncomfortable, it is necessary to create good, readable images, to reduce blur, to spread out the tissue and to reduce the dose of radiation. The radiographer should take two pictures of each breast, one from top to bottom and the other from side to side.

- Once the mammograms are taken, they are read by a radiologist. The *European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis* recommend that each mammogram should be read by two separate radiologists.
- Mammograms can be taken on film, like a photograph, or using a digital system, where your files can be stored in a computer. If you have already had a mammogram, the radiologist should compare the previous films or files with the current ones to check for any changes in your breasts.
- Ultrasound may also be used to obtain further images, particularly if you are younger or have dense breasts.
- If you are between the ages of 50 and 69, you should receive an invitation for mammography screening every two years as part of a screening programme offered by your public health system. This is stipulated in the *European Guidelines* and is in keeping with both IARC recommendations and the European Council Recommendation on Cancer Screening.
- Mammography screening should be carried out in conjunction with a specialist breast unit, as stipulated in the *European Guidelines,* to ensure access to a multidisciplinary team for diagnosis and treatment if necessary.
- The *First Report on the Implementation of the Council Recommendation on Cancer Screening* published in June 2008 states that in 2007 population-based screening programmes were running or being established in 22 EU Member States (Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovenia, Spain, Sweden, and the United Kingdom). The full report can be found at http://ec.europa.eu/health/ph_determinants/genetics/documents/cancer_screening.pdf.
- If population-based mammography screening does not yet exist in your country or area, you should discuss your options with your physician.

Some questions women should ask when having a mammogram

(This list is certainly not comprehensive, but can be used as a guide in preparing your own list of questions)

1. Does the mammography facility follow a quality assurance programme that meets EU quality standards* or the equivalent?
2. How many mammograms does this facility perform each year?
3. Will my mammogram be conventional (x-ray film) or digital?
4. Are all mammograms read by two separate radiologists?
5. Is the person who takes the mammogram a registered radiographer specialised in mammography?
6. Does the radiologist who reads the mammograms have extensive experience, i.e., does he/she read at least 5,000 mammograms per year?
7. Is the mammography equipment technically controlled and calibrated on a regular basis (i.e., at least once a year)?
8. How and when will the results be available? (Ideally they should be ready in less than 5 working days.)
9. If the results indicate a problem, will I be notified, and if so, within what time frame? (Ideally this information should be provided in less than 5 working days in person in the presence of a nurse counsellor.)
10. Is there another procedure, other than a mammogram, that is more reliable for my specific situation (e.g., pregnancy, breast implants, under the age of 35)?

*As described in the *European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis*, 4th Edition, published by the European Commission, 2006.

WOMEN UNDER 40 AND BREAST CANCER

EUROPA DONNA recognises the need to raise awareness concerning younger women and breast cancer.

Since approximately 5–7% of breast cancers occur in women younger than 40 years of age, young women should be informed about the risks of breast cancer and be aware of the recommendations listed in the European Code Against Cancer.

It is important that women, from an early age, become breast aware (see Be Breast Aware section). You can take convenient opportunities such as bathing or dressing to become familiar with your breasts by looking at them and touching them. This will help in noticing any changes or abnormalities (usually a lump) sooner. Even though most breast lumps are harmless, it is important to inform your physician of any changes without delay. Starting at an early age you should have regular clinical breast exams performed by a health care professional.

A younger woman's body has hormonal and biological characteristics which differ from those of older women. A typical consequence of this is denser breast tissue, which makes mammography less sensitive and specific for detecting early cancer. Ultrasound might be more effective in the diagnosis of breast cancer in younger women.

Young women with a family history of breast and/or ovarian cancer should be aware of the higher risks of developing breast cancer and make arrangements with their physician for regular and appropriate check-ups.

10 questions young women should ask their doctor following a diagnosis of breast cancer:

1. How does breast cancer treatment differ in younger women?
2. What kind of breast cancer do I have and how aggressive is it?
3. Could this breast cancer treatment cause early menopause? If so, what are the consequences?
4. How can I preserve my fertility? Will I be able to have children of my own in the future?
5. If I wish to get pregnant after breast cancer, when is the best time to consider this?
6. What are the treatment options if breast cancer is diagnosed during pregnancy?
7. Will breast cancer during pregnancy or its treatment affect my unborn child?
8. Will I be able to breast-feed?
9. Should I have genetic testing to determine if I carry a breast cancer gene?
10. Are there any clinical trials for young women and would I be eligible to participate?

Some questions women diagnosed with breast cancer might want to ask their doctors

Being diagnosed with breast cancer is a difficult, life-altering experience, and the treatment options can seem overwhelming. Below are some questions that may help you in preparing your own list of questions.

1. What kind of breast cancer do I have and is it invasive?
2. What are my treatment options and what treatment do you recommend?
3. Is the treatment you are recommending standard practice in cases such as mine? How quickly do I need to begin treatment and can I get a second opinion?
4. Will I require further treatment after surgery, e.g., radiation therapy, chemotherapy, hormonal therapy, rehabilitation therapy or a combination of these or other therapies?
5. What are the risks associated with each type of treatment and what are the possible side effects?
6. Can I be treated in a specialist breast unit by a team that includes a breast surgeon, medical oncologist, breast nurse, radiation oncologist and psychologist?
7. If no such specialised unit is available to me, how many breast cancer patients are treated annually in the hospital you are recommending?
8. How will treatment affect my ability to function in everyday life and when will I be able to resume normal activities such as work, etc.?
9. What literature, websites, and support groups would you recommend?
10. How do clinical trials work? Would you recommend I participate in one?

These texts are excerpts from a PDF provided by EUROPA DONNA on their website, which can be found here: www.europadonna.org/wp-content/uploads/GuidetoBreastHealth-ED.pdf

ABOUT EUROPA DONNA – THE EUROPEAN BREAST CANCER COALITION

By Susan Knox, CEO Executive Director

EUROPA DONNA – The European Breast Cancer Coalition (ED) is an independent, non-profit organisation whose members are affiliated groups from countries throughout Europe. The Coalition works to raise awareness of breast cancer and to mobilise the support of European women in pressing for improved breast cancer education, appropriate screening, optimal treatment and care and increased funding for research. EUROPA

DONNA represents the interests of European women regarding breast cancer to local and national authorities as well as to institutions of the European Union. ED was founded in 1994 and now has 47 fora (national country organisations) across Europe. The strength of our organisation lies in uniting women of many countries, cultures, and backgrounds in fighting breast cancer and seeking common goals toward that end.

EUROPA DONNA ten goals

1. To promote the dissemination and exchange of factual, up-to-date information on breast cancer throughout Europe
2. To promote breast awareness
3. To emphasise the need for appropriate screening and early detection
4. To campaign for the provision of optimum treatment
5. To ensure provision of quality supportive care throughout and after treatment
6. To advocate appropriate training for health professionals
7. To acknowledge good practice and promote its development
8. To demand regular quality assessment of medical equipment
9. To ensure that all women understand fully any proposed treatment options, including entry into clinical trials and their right to a second opinion
10. To promote the advancement of breast cancer research

EUROPA DONNA is an evidence based advocacy organisation and all our information and advocacy programmes are based on scientific evidence that has been agreed upon by European scientific experts in all the specialist fields. Since 2000 we have worked with the European Breast Cancer Network and EUSOMA – The European Society of Breast Specialists and these partnerships have resulted in the publication in 2006 by the European Commission of the *European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis.* This document now forms the basis for much of our advocacy work as it outlines the breast cancer services that all women should have a right to receive. ED has published a 'Short Guide' to these guidelines to enable women and the lay public to understand the main points contained in this scientific document. These can be downloaded from our website http://www.europadonna.org/short-guide/a-short/ and have been translated into 16 languages in addition to English so far.

INTERVIEWS

BREAST IMAGING TODAY: A ROUNDTABLE INTERVIEW

BREAST IMAGING TODAY: A ROUND-TABLE INTERVIEW

A panel of renowned breast imagers from all over the world took part in IDoR 2016 to make the benefits of medical imaging clearer to the public. They explained what exactly imaging can do in the detection, diagnosis and treatment of breast diseases, the role played by radiologists in healthcare and what patients should know before undergoing a breast examination.

European Society of Radiology: *Breast imaging is widely known for its role in the detection of breast cancer. Could you please briefly outline the advantages and disadvantages of the various modalities used in this regard?*

Michelle Reintals: Biennial mammography (breast x-ray) is considered the gold standard for screening for breast cancer in women aged 50–74. Breast Screen Australia has been providing mammographic screening for over 20 years, with proven benefits shown by improved survival rates from the early detection of breast cancer. If an abnormality is found on a mammogram or a woman has a symptom, then ultrasound is routinely performed for further investigation.
Mammograms can be used to identify mass lesions, distortion of normal structures and calcifications, whereas ultrasound is used to characterise the abnormality by determining for example if it is solid, cystic, infiltrating or vascular.

CHAPTER 7: **BREAST IMAGING TODAY: A ROUNDTABLE INTERVIEW**

As it is operator dependant and time consuming, ultrasound may not detect pre-malignant calcifications in the breast that may only be seen on mammography, and some small cancers may not be appreciated. In addition, ultrasound may detect many benign lesions such as inflamed cysts and this may result in the patient having unnecessary biopsies to prove they are benign.
As with any technology, there are advantages and disadvantages.
The pitfalls of mammography include slow growing lesions where stability is reassuring for a benign lesion and lack of detection of certain types of breast cancers, which may be difficult to perceive due to the nature of their biology and growth pattern.
Another limitation of mammography that is becoming topical amongst breast professionals is breast density. The ability to detect breast cancer depends upon subtle differences in contrast density between the normal breast tissue and the cancer. It is for this reason that women with high breast density are amongst the most difficult mammograms to read, as the cancers may be hidden by the normal background dense tissue.
To compound this dilemma, we also know that high breast density is associated with an increased risk of breast cancer. So not only are the mammograms more difficult to read, as the cancers are camouflaged by the normal surrounding tissue, but these women also have reduced detection of breast cancer on routine screening.
For this reason, and also applicable to women with a strong family history of breast or ovarian cancer, additional imaging technologies may be suggested for screening. These adjunct technologies include digital breast tomosynthesis (DBT) and breast magnetic resonance imaging (MRI).
Tomosynthesis obtains a series of low-dose x-rays through the breast at various angles, reducing the problem of summation effect, which is common in women with dense breasts. Its benefits include increased cancer detection rates, a reduction in the number of extra mammography views and a reduction in the use of ultrasound where the mammography abnormality is cleared.
The disadvantage is the extra radiation dose if it is performed in combination with mammography and the extra compression and discomfort for the women. The radiologist's reading time is significantly increased, as over 400 images are typically generated, compared with the standard four images with a mammogram.
Breast MRI is independent of breast density; it relies upon both the character of the tissue and the blood supply and enhancement pattern of an abnormality within the breast. It is highly sensitive in the detection of breast cancer.
The disadvantages of MRI are that it may detect many benign lesions that require further work-up with ultrasound and the possibility of biopsy, all contributing to patient anxiety. It requires an intravenous injection of contrast media and is therefore an invasive procedure. Also, recent reports have shown that the intravenous contrast medium used has the potential to accumulate in certain parts of the brain. Whilst gadolinium injection is not specific to breast MRI, the dilemma is that it is as yet unknown if this is significant or has long-term repercussions for the patient, and if so, what they may be. Given breast MRI is often performed routinely every year for women at high risk of breast cancer and in many circumstances from a young age (e.g. 25 years old) if known BRCA gene carriers, this has raised concerns. As a consequence of these recent findings, it is recommended that a cyclic structure gadolinium chelate is used in preference to a linear structure agent.

Miguel Angel Pinochet Tejos: Currently, mammography is still the most important technique when it comes to the early diagnosis of breast cancer. The technological advances of 2D and 3D digital mammography (tomosynthesis) have allowed an increase of sensitivity at the time of detection. The great disadvantage in Latin America is its implementation.
Ultrasound is highly accessible and used in daily medical practice. Its use in the region is very important in diagnosis as an auxiliary method to mammography. Magnetic resonance imaging (MRI) is very useful in the staging of diagnosed cancer, and its use is becoming more frequent every day. Additionally, it is a routine procedure performed on high risk patients. Its disadvantage is the high cost of the test itself and its accessibility in Latin America. The use of molecular imaging is very recent in the region.

Elizabeth Morris: Breast imaging is rapidly evolving. Our ability to detect breast cancer has improved markedly

over the past three decades. We have many new tests that cannot only detect anatomic abnormalities but can also detect functional abnormalities. Traditional mammography is being rapidly replaced by 3D mammography, which improves cancer detection and decreases the chance that the mammogram is called abnormal. Ultrasound screening is performed for women with dense breasts. MRI screening is performed in women with a high risk of breast cancer.

ESR: *Early detection of breast cancer is the most important issue for reducing mortality, which is one reason for large-scale screening programmes. What kind of programmes are in place in your country and where do you see the advantages and possible disadvantages?*

Gabor Forrai: Hungary was among the first countries to introduce nationwide organised screening, in 2001. The programme operates on an invitation basis and is free for all women. One special advantage is the lower-than-usual starting age (45), and a disadvantage is the quite low upper limit (65). Physical examination (palpation) is included, and is performed by trained radiographers. The goal of the programme is also to raise awareness, as well as to avoid as many invasive lobular carcinomas and non-calcified ductal carcinomas *in situ* as possible. The 15 years of practice have made the screening system robust, but it still needs continuous feedback and fine-tuning: this is a very important task in every country in order to achieve even better treatment selection (surgery, radiation therapy, chemotherapy, hormone therapy, etc.) and results.

Michelle Reintals: Australia's population-based screening programme, Breast Screen Australia (BSA) has been in existence since 1991. The programme invites women of the screening target group between the ages of 50–74 to attend for a biennial screening mammogram. Statistics have shown a benefit from screening with a significant reduction in mortality rates. In 1991, when BSA commenced, 68 women per 100,000 died from breast cancer, compared with 44 per 100,000 in 2012. The BSA Evaluation 2009 programme report demonstrated mortality reduction of 21–28% in the target aged women, in line with earlier randomised controlled trials undertaken in Europe.

Australia has six states, and each state provides an individual screening programme, which is held accountable to a high standard of practice by the National Accreditation Standards, under the jurisdiction of the national screening programme BSA. The challenges that a population-based screening programme experience are numerous, and a country the size of Australia introduces many additional challenges that are unique, including access for rural and indigenous populations and satisfactory participation among the target-aged, resident female population. Mobile bus units travel around Australia, which assists in breaking down the barriers of accessibility. Participation is centred around breast cancer awareness, which the Australian government promotes through the national screening programme. Participation rates are typically around 55% for the screening target group. Other non-government programmes, such as the McGrath Foundation, contribute significantly to the awareness of breast cancer through sponsored events and October Breast Cancer Awareness month. The benefits of a screening programme have been demonstrated with a reduction in mortality rates, but potential disadvantages of a population-based screening programme also exist. These include reduced accuracy of cancer detection in women with high mammographic breast density. It is recognised that women with a high risk of breast cancer due to their family history or those women who are BRCA gene carriers, are eligible for annual mammographic screening. So this raises the question, should we be reporting routinely on breast density? Should we be offering personalised screening pathways, incorporating family history, breast density, etc.? Should we be offering magnetic resonance imaging to women with high mammographic breast density? This is a complex issue, with concerns relating to funding and resources, and patient anxiety.

Elizabeth Morris: In the United States, there is no national screening programme, which is different than many European countries. Therefore, it is up to the woman to remember to have her mammogram as she does not receive a reminder letter in the mail. It is estimated that approximately

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60–70% of American women undergo screening mammography. Screening guidelines are recommended by many societies. The Society of Breast Imaging recommends that women be screened every year starting at the age of 40 to obtain the maximal benefit of screening mammography. It is recommended that the patient continues screening as long as she has at least a ten-year life expectancy.

Miguel Angel Pinochet Tejos: In Latin America, there are no screening programmes for the population as in Europe. The only programmes performed are opportunistic screening programmes, which can be found in Mexico, Brazil, and Ecuador. The biggest challenge is to raise awareness among governments for the implementation of screening programmes for the population.

ESR: *The most common method for breast examination is mammography. When detecting a possible malignancy, which steps are taken next? Are other modalities used for confirmation?*

Miguel Angel Pinochet Tejos: Once a possible malignant lesion has been detected with mammography, a crucial step is to perform an ultrasound study to define the lesion and locate any other associated findings. Then, a percutaneous biopsy (core biopsy, stereotactic biopsy) is performed to evaluate if it is cost-effective. Once breast cancer has been diagnosed, an MRI examination must be performed to stage the tumour, evaluate its size, extent, multicentricity, and bilaterality to apply the most effective treatment.

Elizabeth Morris: In the United States, for every 1,000 women screened approximately 100 are asked to come back for additional imaging, which would be specialised mammographic views and possible ultrasound. Of these, approximately 80 will be called negative at that point. The other 20 will be recommended for a needle biopsy either using ultrasound or mammography (stereotactic biopsy). Five of these women will turn out to have breast cancer. Rarely, an MRI will be used for further workup.

Gabor Forrai: When detecting a possible malignancy, the next step is an ultrasound examination to detect any

Elizabeth Morris, MD, FACR, is a radiologist who has dedicated her career to advancing early breast cancer detection through improvements in breast imaging. She developed the Breast Magnetic Resonance Imaging (MRI) service at Memorial Sloan Kettering Cancer Center (MSKCC) where she is currently Chief of the Breast Imaging Service.

Dr. Morris was educated at University of California San Francisco medical school, completed her radiology residency at Cornell Medical College and is a Fellow of the Society of Breast Imaging and Fellow of the American College of Radiology. Dr. Morris currently serves as President of the Society of Breast Imaging. She is Chair of the 2nd Edition of the Breast MRI section of the Breast and Imaging Reporting Data System (BI-RADS®). She has been principle investigator of several IRB protocols including: 'Breast MRI Positioning, Localization and Biopsy Device,' 'Breast MRI using a Bilateral Sequence,' 'Breast MR Spectroscopy' and 'Breast MRI High Risk Screening.' A grant from the Susan B. Komen Foundation was instrumental in allowing her to pioneer the work on breast MRI screening and breast MRI biopsy. Along with others, Dr. Morris has found that breast MRI is exquisitely sensitive in the detection of breast cancer and allows better characterisation of known cancers along with better detection of early cancer in high risk groups of women.

Dr. Morris is considered one of the leaders in the field of breast imaging both nationally and internationally and has been an invited speaker at more than 300 meetings throughout the world and has authored or co-authored more than 100 papers. Her bestselling book on breast MRI has become the standard in the field. Dr. Morris hopes that one day breast cancer can be detected early enough to be treated without radical therapies. Her future research will be in this direction.

Gábor Forrai MD, PhD, completed his studies at Semmelweis Medical University, Budapest, Hungary. He later served as a staff radiologist for ten years at the National Institute of Oncology, Hungary (1987–1996), as assistant professor and head of department at the Haynal Imre Postgraduate Education University, Budapest (1998–2007) and as head of the department of Radiology at the Military Hospital/State Health Center/Teaching hospital University Semmelweis (2007–2014). He is currently head of the department of radiology at Duna Medical Center in Budapest, Hungary and head of the breast screening centres in Vác and Eger County Hospitals.

He also gained experience abroad in Köln, Nürnberg, and Erlangen, Germany (1990), as well as Rehovot, Israel (1998), Nottingham, United Kingdom (1999) and Düsseldorf University, Germany (1993–1994). He also held a post as staff radiologist at the Hôpital Tenon, Paris, France (1994–1995).

An experienced lecturer (with 227 presentations in French, English and Hungarian), Prof. Forrai has published a book, 29 book chapters, 24 full articles and 56 scientific congress abstracts. He wrote his PhD thesis on the subjects of breast core biopsy and breast MRI.

Prof. Forrai has been the president and organiser of several national and international courses and congresses, such as the French-Hungarian Radiology Symposia (annually since 2001), Central European PACS School, Central European eHealth Academy, EUSOBI Schools and ESOR events.

He is the current President of EUSOBI (2015–2018), and was Chair of the Breast Subcommittee of the European Congress of Radiology 2014, Secretary General of the Hungarian Section of Breast Diagnostics of the Hungarian Radiological Society, and vice-president of the French-speaking Radiology Educators' Society (GREF). His contributions to French-Hungarian scientific cooperation have been recognised by the French Republic, which awarded him Knight of National Order of Merit (2012).

potential further findings and to assess the option of ultrasound-guided biopsy, which can be performed for any lesion visible on ultrasound. Biopsy with ultrasound guidance is a short procedure which is performed with the patient lying on their back. If the lesion is only visible with mammography (microcalcifications), biopsy will be performed through stereotactic guidance. Because of scanner availability, duration and costs, MRI-guided breast biopsy is only performed for lesions detected with MRI.

Eugene Jooste: Additional views are obtained in order to confirm or exclude the presence of suspicious findings. Ultrasound will be performed in order to obtain additional information and to do guided biopsy if required. Breast MRI can be performed to further characterise the abnormality and to assess the area of involvement and possible additional abnormalities (including in the other breast).

Michelle Reintals: The imaging guidelines recommended for standard practice include the use of multiple modalities, and the individual application depends upon many factors, including the nature of the lesion detected.
A standard mammogram that reveals a lesion will be further investigated with spot compression views if the abnormality is a mass, density or distortion, or with magnification views if calcification. Typically ultrasound will then be performed to assess for a mass or infiltrative lesion, evidence of skin or chest wall involvement and if there is lymph node spread.
Fine needle aspiration or core biopsy may be performed, usually under ultrasound guidance, however, if the abnormality is not visualised on ultrasound (e.g. calcifications), then it is common practice to perform vacuum-assisted core biopsy on calcifications under mammogram guidance.
A radio-opaque site marker may be placed at the time of biopsy, where appropriate, in order to mark the site of biopsy and assist in localisation if excision of the lesion is required. They are typically used when a lesion is almost completely excised at biopsy or difficult to see under all imaging modalities. The site marker is a few millimetres in size, typically made of titanium or stainless steel, and is safe to remain within the breast long-term if the calcifications are benign.
Once the diagnosis of breast cancer is made, staging investigations are carried out to identify any

spread of disease to lymph nodes or organs. The treatment will depend upon this pre-operative staging.
The staging investigations depend upon the size of the primary breast cancer.

1. Breast MRI may be performed for staging the size, extent of breast tumour burden, whether it is multifocal (multiple lesions within a breast quadrant) or multicentric (multiple lesions scattered throughout the breast), and if there is involvement in the contralateral (opposite) breast.
2. Chest x-ray, liver ultrasound or CT scan of the chest, abdomen and pelvis may be performed to assess for any spread to liver, lungs, or bone.
3. Whole body bone scan (WBBS) to assess for spread to bones.
4. Sentinel Node Biopsy (SNB) is performed on the day of surgery to identify the draining node from the site of the cancer, and this or the group of nodes are removed at the time of mastectomy or partial mastectomy. If these nodes prove to be malignant, then a second operation is required to remove any remaining nodes accessible in the axilla.

ESR: *Diagnosing disease might be the best-known use of imaging, but how can imaging be employed in other stages of breast disease management?*

Miguel Angel Pinochet Tejos: Nowadays, without a doubt, there are different types of breast imaging that assist us in handling other stages of the disease.
In advanced tumours that require chemotherapy, MRI is the best choice for evaluating the *in vivo* response.
In the future MRI should be implemented as a follow-up for breast cancer patients who have already been treated, to search for a high negative predictive value and to improve the patient's quality of life.
A breakthrough has been the use of MRI in patients who may develop the disease, such as women with high risk factors, given its higher sensitivity than mammography.
In elderly patients with cancer, who cannot undergo an operation and who do not respond to hormonal therapy, ultrasound can also help as a guide for radiofrequency ablation.

Elizabeth Morris: Using imaging can be very helpful when the patient is diagnosed with breast cancer. Imaging is relied upon to detect the entire extent of disease within the breast and axilla, and to exclude the possibility that the cancer has moved to other parts of the body.

Michelle Reintals: Imaging is used for screening for breast cancer and the diagnosis and staging of the extent of disease. There are circumstances where non-surgical treatment is administered.
Neo-adjuvant treatment is used in advanced cancers where the size of the tumour or the extent of lymph node spread is reduced with chemotherapy prior to surgery. This approach may also be used to reduce tumour size to allow breast conserving surgery.
Similarly, in frail or elderly patients who are not amenable to surgery, neo-adjuvant treatment, where the tumour is hormone sensitive (ER, PR positive), an aromatase inhibitor is used to locally control or reduce the primary cancer.
In all these instances, the tumour burden and extent of nodal disease is monitored at regular intervals, to ensure that the treatment is effective and the disease is responding to the chemotherapy or hormone treatment. If the tumour burden is increasing, then hormonal or chemotherapy agents can be altered. The imaging options available to closely monitor the tumour and nodal response are mammography, ultrasound and MRI. If there is distant spread of disease to common sites such as liver, bone, lung, or brain, then tumour response is typically monitored by CT scans.

Gabor Forrai: In Hungary, an Interdisciplinary Consensus Conference has been held regularly, where a protocol document is created, discussed and published, which includes updates of all diagnostic and therapeutic aspects of breast cancer. Staging and follow-up protocols, and nuclear medicine (e.g. use of PET/CT) are a part of the radiological chapter.

ESR: *What should patients keep in mind before undergoing an imaging exam? Do patients undergoing radiological exams generally experience any discomfort?*

Elizabeth Morris: Breast cancer screening with mammography involves compression. Compression can be

Dr. Miguel Angel Pinochet Tejos is an Academic Radiologist subspecialised in Breast Imaging. He works at Clinica Alemana de Santiago, in Chile. He graduated from the Faculty of Medicine of Universidad de Chile where he also underwent his postgraduate radiology training. He has performed breast imaging studies at the UDIAT Diagnostic Centre, Barcelona. Currently he is Professor of the Faculty of Medicine of the Universidad del Desarrollo and of the Inter American College of Radiology (CIR). He has lectured as an expert in breast imaging in most Latin American countries. He has co-authored more than 40 peer-reviewed papers and over 90 conference abstracts and lectures. He holds a master's degree in Health Administration and Management.

Dr. Pinochet is an active member of the Sociedad Chilena de Radiologia, Sociedad Iberoamericana de Imagenes Mamarias (SIBIM), and the Inter American College of Radiology (CIR). He has also been awarded an Honorary Membership by the Spanish Society of Breast Imaging (SEDIM).

Dr. Pinochet has been President of the Sociedad Chilena de Radiologia and of the Sociedad Iberoamericana de Imagenes Mamarias (SIBIM). In September 2016, he became President of the Inter American College of Radiology.

painful for some patients. For those who have breast pain around their menstrual cycle, it would be important to schedule mammography after the menstrual cycle. For ultrasound, gel is used and therefore it is not painful. MRI does not involve compression; however, there is an injection of contrast media in the vein.

Michelle Reintals: A patient undergoing a breast imaging exam will usually be anxious about the process and the possible outcome. As health professionals, we are trained to recognise and manage patient anxiety, and show a personal yet professional side to the patient and express empathy.
It is important to be aware that some women experience significant discomfort during the mammogram and biopsy. It is important to explain the process and describe the experience when obtaining the patient's consent, allowing time for any questions the patient may have regarding the procedure.
There are some suggestions that can be made when a women books in for a routine screening mammogram, which may reduce the physical discomfort. This applies to pre-menopausal women, where exams may be better tolerated between days 7 to 14 of their menstrual cycle.
If the study is being performed for symptoms, then timing with the menstrual cycle is unimportant, and imaging as soon as possible is optimal.
It is vital that the health professional shows guidance and knowledge of the patient's circumstance and gives advice on the diagnosis and management.

Eugene Jooste: Fear of the unknown generally adds to the anxiety associated with breast imaging. Anecdotal feedback is mostly that of pain and discomfort.
If you experience breast pain at certain points in your menstrual cycle, keep this in mind when scheduling an exam.
Mammography will be painful if you have painful or sensitive breasts, but generally feedback after mammography is that the procedure was not as uncomfortable as expected and that other stories are exaggerated.
Ultrasound is associated with cold jelly on the skin. Warming the jelly goes a long way to making the investigation more manageable.

ESR: *How do radiologists' interpretations help in reaching a diagnosis? What kind of safeguards help to avoid mistakes in image interpretation and ensure consistency?*

Elizabeth Morris: It has been shown that double reading increases cancer detection rates and decreases recall rates. Double reading means that each woman's mammogram is read by two radiologists who specialise in breast imaging. Many practices use this approach.

Miguel Angel Pinochet Tejos: Radiologists must have continuous training for updates in the diagnosis and management of breast diseases. To avoid mistakes, the breast imaging radiologist must be specialised and very well trained. The work environment must be appropriate with the right amount of brightness, no disturbances and with high resolution workstations.

Michelle Reintals: The detection of a breast cancer is a team approach and influenced by three main factors. These factors include image and display quality, mammogram positioning, and interpretation and perception of mammogram.

1. The quality and display of the image is influenced by image contrast resolution, display algorithms, and resolution of the computer monitors.
2. The quality of the acquired image is a challenge for the radiographer.
   The radiographer has the challenge of positioning the woman's breast such that all quadrants/axillae/infra-mammary folds/nipple are viewed, with minimal to no skin folds on view. The National guidelines for mammography stipulate required standards. These standards are monitored by the College of Radiologists via a Mammography Quality Assurance Program or in-house if within the national screening programme, by routine review of images and by giving constant feedback and ongoing education to the mammographers in the quality assurance programme.
3. The reading of a mammogram by a radiologist is task that involves both perception and interpretation. Whilst failure to detect breast cancer can result from multiple factors, it is important for the radiologist to be aware of any potential missed or interval cancers, as they may be due to a perceptive or interpretive error.
   The larger the number of mammograms read by a radiologist, typically the higher their cancer detection rate and the lower the missed cancer rate.
   Regular quality assurance sessions to review missed and interval cancers, multidisciplinary meetings, and peer education meetings, are important methods of improving cancer detection and maintaining a high quality of reading skill.

Eugene Jooste: Breast cancer diagnosis should be made by the radiologist. Always do RadPath (radiologic pathologic concordance assessment) correlation when interpreting pathology results. Have regular interdisciplinary meetings where cancer and complicated cases are discussed. Do regular audits of the practice in order to ensure compliance with international standards.

ESR: *When detecting a malignancy, how is the patient usually informed and by whom?*

Elizabeth Morris: This depends on the practice. In most practices in the United States, the radiologist informs the patient of their diagnosis as they are the physician that performs the biopsy and has developed a relationship with the patient as the breast imaging expert. They are also able to determine whether the finding on the imaging test was appropriately biopsied (this is called radiologic pathologic concordance assessment).

Gabor Forrai: As the malignancies are mostly detected and proved in a radiological screening/diagnostic centre, the radiologist informs most patients about the imaging and biopsy result. It is obligatory to issue a written overall diagnostic summary report. The patient is then referred to the breast/oncology team for a therapeutic decision. Of course, the radiologist is a part of this team.

Miguel Angel Pinochet Tejos: Generally in our environment, the radiologist is the one who informs the patient of the detection of a suspicious finding,

raising the need for a biopsy which is required to accurately determine the nature of the lesion.

Michelle Reintals: The primary care giver typically informs the patient of their diagnosis of breast cancer. This will depend upon the circumstance and whether the imaging was screening or diagnostic. If screening was performed by the national screening programme, then the common scenario is that the patient attends a results clinic a couple of days after the assessment clinic workup and biopsy of the abnormality. Within the screening programme, the diagnosis of breast cancer is typically given by a breast surgeon. In the diagnostic setting, patients in Australia may be assessed within either the public hospital or private imaging practice setting. Typically the doctor referring the woman for assessment will deliver the final pathology result to the patient and arrange referral to a breast surgeon for management.

Eugene Jooste: Depending on circumstances, the patient is either informed by the referring doctor or by the radiologist. This is mostly done by telephone or the patient can be called in to be given the news and for possible management options to be discussed.

ESR: *Some imaging technology, such as x-ray and CT, uses ionising radiation. How do the risks associated with radiation exposure compare with the benefits? How can patient safety be ensured when using these modalities?*

Elizabeth Morris: Ultrasound and MRI do not use radiation at all. Mammography, including 3D mammography, uses ionising radiation and therefore there is exposure to the patient's breasts. However, this exposure is small and the benefit of undergoing mammography far exceeds the risk of radiation exposure. Molecular imaging techniques have the highest radiation exposure to the patient as radioactive material is injected in the vein and therefore the entire body is exposed to radiation, whereas with mammography it is just the breasts.

Michelle Reintals: Imaging should only ever be performed if there is likely to be a clear benefit, and that the potential benefit outweighs any possible risk from the procedure. There has been a clear benefit shown in the Australian screening programme, with a reduction in breast cancer deaths between 21–28%. Whilst this is significant, there is the potential issue of over-diagnosis. This refers to those cancers which may not result in patient death if untreated. Whilst a discussion point, it remains a dilemma, as currently there is no way of accurately determining pre-operatively which cancers are harmful versus those that are not harmful, if left untreated.

Gabor Forrai: CT is rarely performed for local diagnosis of breast cancer, but rather for staging prior to definite therapy or re-staging at follow-up. Mammography comes with radiation exposure, although it uses the lowest dose among all radiological methods and the risks associated with radiation are by far outweighed by the benefits. Most currently used equipment is digital, which means dose is reduced by approximately 30% compared to the previously used film technique. Patients' safety can furthermore be assured by adequate training of radiographers to avoid repeat mammography examinations due to positioning errors.

ESR: *How aware are patients of the risks of radiation exposure? How do you address the issue with them?*

Elizabeth Morris: We will not perform mammography on a patient who may be pregnant, in order to protect the foetus. Most patients are aware of radiation exposure. If there are any concerns, we are happy to discuss with them the relative degree of radiation. For example, in the United States the radiation from a mammogram would be akin to taking an airline trip from New York to San Francisco.

Eugene Jooste: Most patients are aware of the general risks associated with exposure to radiation. We follow the ALARA (As Low As Reasonably Achievable) principle with regard to radiation dose, but we do also reassure patients that the radiation associated with mammography is very low and the radiation is comparable with that received on a long-haul international flight, for example.

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Michelle Reintals: The internet provides general information on a range of topics, including medical information, and therefore many patients will research what procedure their doctor has requested, and inform themselves prior to their appointment. Radiation risk versus benefit is topical and is the subject of many questions from patients attending for a mammogram. It is the health provider's role to explain these risks and benefits and to allow the patient to ultimately decide what their preference is. The Royal Australian and New Zealand College of Radiologists has a teaching portal available to members and also a general consumer section for the public, called *Inside Radiology,* where there is information on such topics. Breast imaging information at *Inside Radiology* is searched by approximately 13,000 people per month from 180 countries, and the website has approximately 200,000 visits per month. The optimal service is one where the principle of ALARA is adopted: ALARA is the acronym for the phrase 'As Low As Reasonably Achievable', which refers to the practice of keeping radiation doses as low as is practical to achieve a useful quality image.

ESR: *How much interaction do you usually have with your patients? Could this be improved and, if yes, how?*

Elizabeth Morris: The greatest joy in my job is having interactions with patients. In our practice we have a lot of interaction with patients and enjoy this enormously. We discuss abnormal findings with all of our patients and inform them of results from any needle biopsies. We have many patients who return year after year for continued care. We would like to start a clinic to take care of patients who have questions about breast density and about their risk of developing breast cancer.

Miguel Angel Pinochet Tejos: Always, the most beautiful and important part of breast imaging is the interaction with patients. Contact usually occurs in ultrasound, and later during biopsies, and then when we let them know the histological results. We always make sure we treat patients with a very humane and personalised approach.

Michelle Reintals, MBBS, FRANZCR, is an Australian radiologist, specialised in breast imaging, having undertaken fellowships at BreastScreen South Australia and observorships and sabbaticals in breast imaging at Memorial Sloan Kettering Cancer Center NYC, Brigham Hospital Boston, Curie Institute Paris and the Brussels Screening Program, during her 14-year career.

Dr. Reintals has worked in both public and private breast practices in South Australia and Australia in clinical, educational and administrative capacities, holding the role of State Screening Program Radiology Coordinator at BreastScreen South Australia. She has recently relocated to Brisbane to work for IMED Queensland SouthernX Radiology as Director of Breast.

Currently she is the Chair of the Breast Imaging Reference Group (BIRG) of the Royal Australian College of radiologists and a Committee member of the Breast Imaging Group (BIG) and Mammographic Quality Assurance Program MQAP of the Royal Australian and New Zealand College of Radiologists and Australasian Society for Breast Disease (ASBD).

Dr. Reintals undertook a study into polyimplant prostheses in 2012 in South Australia with Prof. Michael Middleton MD, from San Diego. She has authored numerous papers on breast diagnostics and radiology techniques for Australasian conference presentations and publications, and assists in the tutoring and fellowships of young breast radiologists.

Dr. Eugene Jooste trained at the Bloemfontein Complex of Academic Hospitals in the Free State Province of South Africa. He qualified as a radiologist in 1997 and spent nearly fifteen years in private practice in Gaborone, the capital of Botswana.

In 2012 he joined Capital Radiology (private practice) based at the Life Groenkloof Hospital in Pretoria, where he became involved in breast imaging beyond the level of general practice.

Dr. Jooste is former Chairman of the Breast Imaging Society of South Africa (BISSA), a subgroup of the Radiological Society of South Africa, and has to date arranged two international conferences of which the most recent was held in May 2016 together with the Society of Breast Imaging.

Michelle Reintals: There is a distinction in service provision between population and personalised private breast screening.
In a population screening programme, there is no individualised service based on risk factors or personal contact with the patient. The patient undergoes their routine mammogram and receives her result via mail. If there is an abnormality seen by two readers interpreting the image, then the patient is recalled for assessment, at which time she will be given the results by a health professional in a results clinic setting.
In a personalised private breast screening programme, there is typically a clinical breast exam done by either a breast physician or breast surgeon and a mammogram read by a breast radiologist. If there is a symptom then further diagnostic workup will be done, which may include ultrasound, MRI, and biopsy.

Gabor Forrai: Breast imaging is one of the radiological subspecialties with the most pronounced personal interaction with patients, particularly for breast ultrasound and image-guided breast interventions, which even require the presence of a radiologist at all times. Furthermore, the radiologist is usually the first doctor who discusses the findings of diagnostic imaging procedures, as well as histopathology results after biopsy, with patients. Therefore, breast radiologists should be sufficiently empathetic, in order to deal with these psychologically difficult situations, and should have profound knowledge of breast pathology and oncology.

ESR: *How do you think breast imaging will evolve over the next decade and how will this change patient care? How involved are radiologists in these developments and what other physicians are involved in the process?*

Elizabeth Morris: Over the next few years, the breast imagers will take on a more central role in the care of breast patients. As cancers are diagnosed at an earlier stage, traditional surgery, chemotherapy and radiation therapy may not be necessary. Percutaneous treatment is likely possible in the near future, changing breast cancer from a surgical disease to a nonsurgical disease.

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Miguel Angel Pinochet Tejos: The future of breast imaging is in sight: a blood test that will let you select the group that needs breast imaging. Customised studies and therapies according to the molecular biology of the tumour will improve. Radiologists will continue to actively participate in research together with physicists, oncologists, pathologists, radiotherapists, surgeons, gynaecologists and all others on the multidisciplinary breast team.

Michelle Reintals: Breast imaging is continually undergoing significant changes, improvements and upgrades. For many years analogue mammography and ultrasound were routine.
In recent years there has been a transition to computer radiography (CR) and more recently to digital radiography (DR) with tomosynthesis and magnetic resonance imaging (MRI).
We have also seen the transition from fine needle aspiration biopsy (FNA) to core biopsy and vacuum-assisted core biopsy, due to advances in technology and biopsy equipment, and changes in management that require histopathology and receptor status of the tumour prior to the decision on surgery.
There are also software programmes available that assess the mammographic breast density, and with this awareness comes a consideration for adjunct screening such as tomosynthesis, MRI or ultrasound where deemed appropriate. These adjunct imaging techniques are also used in the setting of known risk factors such as family history and gene carrier status.
Screening imaging techniques are used to detect early, small, curable cancers.
Ultimately, despite these efforts, there remains a relatively high interval cancer rate, where cancers present between screening mammograms.
Whilst the mortality rates from breast cancer are decreasing, the incidence of breast cancer is increasing. Perhaps the future developments will look at how to reduce the interval cancer rates, by determining which are the cancers that cause this. We are already moving towards screening women based upon their breast density, having recognised this is a separate risk factor as well as a compounding factor in the reduced sensitivity of mammographic screening.
Should we be offering personalised screening pathways, incorporating family history, genetics, breast density, etc.?

Eugene Jooste: I believe that imaging modalities will become more comfortable for the patient in the future. Increased accuracy will lead to fewer false positives. Risk management and genetic counselling will play progressively more important roles as the different characteristics of breast cancers are identified, and this will also result in tailored approaches to treatment and follow-up options.

Gabor Forrai: Breast imaging and image-guided biopsy are such complex procedures, that in Hungary, we created the most comprehensive licence exam in the EU for radiologists. It is obligatory to pass it to obtain authorisation to perform these procedures alone, without supervision.
The exam includes a test, screening image reading, ultrasound exam practice, guided biopsy practice on a phantom (synthetic model) and an oral exam with real, complicated cases.
I think that radiologists will always be in a leading position in breast diagnostics and treatment. Image-guided interventional procedures will increasingly be a part of the local treatment of breast cancer – I guess it is not too far away that radiologists may take over a part of the therapy from the surgeons.

THE ROLE OF RADIOGRAPHERS IN BREAST IMAGING: A BRITISH PERSPECTIVE

INTRODUCTION AND BACKGROUND

INTERVIEW

INTRODUCTION AND BACKGROUND

As in all aspects of contemporary healthcare, the aim in breast imaging is to deliver evidence-based care to underpin pathways and inform decisions in the management of breast problems.

The UK National Health Service Breast Screening Programme (NHSBSP) currently invites all women aged 50 to 70 for a screening mammogram once every three years. The NHSBSP has published detailed and specific guidance for all professionals involved, based on the most recent evidence, and this enables standardised care to be delivered nationally[1].

The role of radiographers in breast imaging is central and extends to the following areas: patient safety, patient care and image quality optimisation.

The involvement of x-ray radiation in mammography, albeit at much lower levels compared to other conventional x-ray imaging examinations, makes the minimisation of radiation dose delivered to patients imperative and involves important decision making regarding the compression technique and imaging parameters used for each patient. There are great synergies here with the team of medical physicists, who have an influence on optimising the dose. Compression of the breast also needs to be tailored to the patient's pain threshold to allow for useful diagnostic images, a skill that is perfected in close collaboration and multidisciplinary team meetings with the consultant breast radiologists. Knowledge of the different projections, and the ability to thoughtfully use these to demonstrate the lesion, is not only science but radiography art and can impact on the diagnosis and therapeutic scheme. Radiographers, like all healthcare professionals, work to deliver the best evidence-based care, and therefore they actively participate in and often lead research projects in their areas of expertise, closely collaborating with other healthcare professionals in the field. Their involvement with research ensures the radiographers know and can apply the most relevant techniques for the benefit of their patients.

There are different agreed protocols in different departments but generally two-view mammography (mediolateral oblique and craniocaudal projections) is recommended. Digital mammography is the standard modality, due to its increased cancer detection performance, and double reading by suitably trained readers is recommended[2].

Ultrasound alone is not an effective screening tool but is associated with an increased cancer detection rate in women with dense breasts. However, it is considered to have poor specificity, so is not recommended routinely[3]. It is a valuable adjunct in the workup of mammographically detected lesions. As in the case of mammography, radiographers are central in delivering evidence-based care and optimal image quality.

Women in high risk groups often undergo additional screening with magnetic resonance imaging (MRI) due to its increased sensitivity and ability to detect mammographically occult lesions with an acceptable specificity. MRI may also be subsequently performed for the delineation of additional disease. As a technique it is extremely sensitive to soft tissue changes; however, it demands deep knowledge and understanding of MRI principles and techniques, which may extend beyond structure to function, such as diffusion MRI. As this is a fast expanding imaging capability, breast radiographers often attend and participate in continuing professional development activities to ensure they keep abreast of recent developments and offer the best service to their patients.

Breast radiographers therefore have a central role as ambassadors of patient safety, champions of personalised patient care and gatekeepers of image quality with regard to all breast imaging examination techniques: mammography, ultrasound and breast MR imaging. Teamwork in breast imaging, as in all other aspects of medical imaging, is vital in achieving the best patient outcomes.

REFERENCES
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CHAPTER 8: THE ROLE OF RADIOGRAPHERS IN BREAST IMAGING: A BRITISH PERSPECTIVE

INTERVIEW

INTERVIEWER: **DR. ANDREW ENGLAND,**
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INTERVIEW OVERVIEW AND ADAPTATION: **DR. CHRISTINA MALAMATENIOU,**
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Breast imaging is widely known for its role in the detection of breast cancer. Could you please briefly outline the advantages and disadvantages of the various modalities used in this regard, with emphasis on the radiography aspects, such as patient safety, patient care and technical complexity?

There are many advantages of mammographic screening, which is currently a first line imaging screening method for the detection of breast cancer. These include, but are not limited to 1) a high sensitivity for fatty breasts, 2) detection of microcalcifications indicative of *in-situ* disease, 3) the speed of examination, which is why this imaging technique is ideal for screening and 4) the relatively lower cost, compared to other modalities. There are, however, many disadvantages in using x-ray mammography. Although it involves low dose x-rays, it still involves some radiation dose, to which the patient is exposed during the examination. There are also issues with the acceptability of this imaging technique, as compressing the breast to optimise image quality may cause discomfort and even pain, occasionally. Additionally imaging of the posterior aspects of the breast can often become challenging with mammography. Lastly, due to the nature of the technique and the variation of imaging protocols within different clinical sites, often relating to compression techniques and imaging parameters, there may be inconsistencies relating to follow-up imaging, which makes longitudinal comparison of mammographic images challenging but certainly not impossible.
There are other modalities for breast imaging, such as ultrasound, which does not involve the use of radiation. It is ideal for imaging soft tissue and for further assessment of other abnormalities and allows for a speedy examination when performed by experienced hands. It may, however, be admittedly very much operator dependent, not suitable for mass screening but helpful as an adjunct imaging tool to x-ray mammography, although still unable to detect fine microcalcifications, which may be indicative of early invasive disease.
Lastly, and more recently, MRI has gained ground as a complementary imaging tool, counting among its advantages high sensitivity – particularly for dense breasts – and better accuracy in demonstrating multi-focal disease and in delineating the size of a tumour. On the other hand, MRI can be time consuming, more expensive and less accessible. It is also not always well accepted, particularly by people who are claustrophobic.

Early detection of breast cancer is the most important issue for reducing mortality, which is one reason for large-scale screening programmes. What kinds of programmes are in place in your country and where do you see the advantages and possible disadvantages?

The National Health Service Breast Screening Programme (NHSBSP) is currently in place in the UK, inviting all women between the ages of 50 and 70 for breast screening once every three years. Breast screening facilitates the early detection of breast cancer, and therefore reductions in morbidity and mortality rates, and it allows for high-risk patients to be screened and followed up. However, it may also carry the possibility of false positives, it can cause unnecessary morbidity and anxiety, and increased costs to healthcare providers, and it requires a multidisciplinary team of highly experienced healthcare professionals, so it is resource-intensive. In the UK, screening, including the use of MRI, is in place for all women deemed to be high risk either due to family history or previous radiotherapy treatment.

Do you know how many women take part (percentage)? Do patients have to pay for this?

In the NHSBSP the average is 65–70% of 50–70 year-olds across the UK taking part and it is paid for by the NHS, without incurring any charge to individual patients.

The most common method for breast examination is mammography. When detecting a possible malignancy, which steps are taken next? Are other modalities used for confirmation and how can radiographers maximise their contribution with regard to these new modalities?

Yes, the most common breast examination is mammography. After a malignancy is confirmed, the next steps include 1) additional mammographic projections to ascertain whether an abnormality is present, and may include 2) tomosynthesis imaging and other modalities including ultrasound or MRI, depending on accessibility to these techniques locally. Breast radiographers in the UK regularly attend seminars and workshops, and participate at national and international medical imaging conferences, to ensure they keep up to date with recent technological advances and are familiar with the new software and hardware of image acquisition and analysis.

What should patients keep in mind before undergoing an imaging exam? Do patients undergoing radiological exams generally experience any discomfort? How can radiographers facilitate an optimal patient experience?

It is important to understand that no imaging test is 100% accurate all of the time and to realise that disease can be asymptomatic and so may be found unexpectedly, often resulting in shock for the patient being imaged. Patients may also experience some discomfort due to general strain and positioning during the examination. This may be due to the nature of the scan and the tolerance will vary from person to person. Every patient is different and radiographers are there to ensure personalised, compassionate care for each patient. The environment is often intimate and emotionally charged and performing a successful diagnostic examination while listening to the patient's anxiety and attending to their needs is a masterclass of multitasking and part of what radiography is really about: person-centred care.

How do radiographers and radiologists work together to achieve accuracy of diagnosis?

Radiographers and radiologists work seamlessly together. Radiographers ensure the optimal image quality is achieved with their expert knowledge of the equipment and successful patient management. Radiologists are highly specialised in looking for subtle abnormalities in normal tissue, which can be a challenge. Artefacts in imaging

CHAPTER 8: **THE ROLE OF RADIOGRAPHERS IN BREAST IMAGING: A BRITISH PERSPECTIVE**

Judith Kelly has worked in the UK as a Consultant Breast Radiographer since 2005. She performs all aspects of breast radiology including intervention and interpreting breast MRI and is a member of the Advisory Committee on Breast Cancer Screening to the UK Department of Health. Ms. Kelly has a keen interest in the diagnostic quality of clinical mammograms. She first observed and reported on blurred mammograms following the introduction of Full Field Digital Mammography within her unit in 2010 and has collaborated with the University of Salford on various published work relating to mammography and image blurring. She has co-edited a recently published textbook on mammography clinical techniques (2015) and has presented at national and international conferences over the last ten years.

can hamper diagnosis, therefore radiographers and radiologists work as a team to ensure the quality of the diagnosis from start to end.

Some imaging technology, such as x-ray and CT, uses ionising radiation. How do the risks associated with radiation exposure compare with the benefits? How can patient safety be ensured when using these modalities and how can radiographers contribute?

Any radiological test requested should be justified in terms of answering a clinical question or as a screening tool. Radiographers checking patient identity and clinical information can further enhance safety measures. There are also departmental protocols for patient imaging pathways, which should be followed closely. Additionally, all equipment should adhere to all QA procedures and protocols and all radiographers should have up-to-date training to use the available equipment resourcefully and for optimal patient care and image quality examinations.

How aware are patients of the risks of radiation exposure? How do you address the issue with them as a radiographer?

It vastly depends on the patient. Overall there should be an honest and trusting environment established between healthcare professionals and patients: many patients are aware of issues because of the abundance of information online. As radiographers we are in position to explain the benefits of the imaging methods and that everything possible is done to ensure the test is as reliable and safe as possible. We also need to keep continuing professional development to stay up to date with recent advances in our professional field, to ensure all staff are well trained in radiation awareness, patient care and image quality optimisation.

How much interaction do you usually have with your patients? Could this be improved and, if yes, how?

In diagnostic breast imaging, interaction is usually focused and intense, but short. It is difficult, though,

to see how this could be improved, given the workforce shortages and demanding everyday schedule. This interaction often involves helping patients feel comfortable during positioning, explaining the procedure, and creating a trusting environment, but very often in the UK the interaction of radiographers might involve breaking bad news, so advanced communication and counselling skills are frequently used, since many patients are highly anxious. Many patients also have a fear of further biopsies or procedures, so calm and competent reassurance by the radiographer is key to guiding them through a safe examination. Effective communication is important not only for improving the patient experience but also for ensuring the quality of the images which will be reviewed. Communication between radiographers and patients lies therefore in the heart of breast imaging procedures.

How do you think breast imaging will evolve over the next decade and how will this change patient care? How involved are radiographers in these developments and which other healthcare professionals are involved in the process?

I believe screening will be more tailored to individual needs – for example for those with fatty or dense breasts – for the normal risk population (as well as those at high risk). Additionally, image-guided interventional techniques will dramatically reduce the need for open surgical procedures as equipment becomes more refined.

As radiographers remain at the frontline of communication with the patients for each breast imaging technique and capability, it is imperative to keep up to date with recent technological developments, to manage expectations, and to achieve high image quality standards and optimal patient care.

ABOUT THE AUTHORS

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Massimo Ambrosio, MSc, graduated in Food Science and Technology in 1999. He has worked in the European Commission for eight years and joined the EC Initiative on Breast Cancer (ECIBC) in 2015. He has worked in accredited laboratories, including the European Reference Laboratory for Mycotoxins, and as an analyst inspector, and has experience in the management of projects in the areas of food safety and toxicology.

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Prof. Ulrich Bick is Professor of Radiology and Vice-Chairman of the Department of Radiology at the Charité Berlin. He is an internationally renowned expert in breast imaging and spokesperson of the Centre for Hereditary Breast and Ovarian Cancer in Berlin. His main research interests are digital mammography, computer-aided diagnosis and high-risk screening. He has authored or co-authored more than 100 peer-reviewed publications and has given numerous invited lectures, tutorials and refresher courses at national and international meetings. From 2008 to 2014 he was chairman of the board of the breast imaging group of the German Radiological Society. He is currently on the board of the German Society of Senology and the European Society of Breast Imaging (EUSOBI).

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Giulia Bocchi, MA, graduated in Communications and holds a master's degree in European Affairs. She has worked in the area of public and institutional communication and as a Communication and Press Officer in various European Commission services between Brussels and Italy.

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Dr. Anke Bramesfeld graduated in Medicine in 1993 and was approved as a medical specialist for psychiatry and psychotherapy in 2000. She has a master's degree in Public Health, and *habilitation* in Public Health and Public Mental Health. She is an expert in health and mental health services and policy research. In 2009–2010 she was a Seconded National Expert to the European Commission's Directorate General Health and Consumers Affairs SANCO. Since 2012 she has worked for a research institution (AQUA-Institute) mandated with executing and developing the statutory quality assurance scheme of the German healthcare system.

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Dr. Boris Brkljačić is Professor of Radiology and Vice-Dean at the University of Zagreb School of Medicine (UZSM), Croatia. He graduated from UZSM in 1988 and has been a board certified radiologist since 1994. He completed educational programmes at the Thomas Jefferson University, Philadelphia and the Memorial Sloan Kettering Cancer Center, NYC. Since 2001 he has been the chairman of the Department of Radiology at the University Hospital Dubrava in Zagreb, Croatia. He was President of the Croatian Society of Radiology from 2008 to 2012. Since 2013 he has been Vice-president of the Croatian Medical Association, and since 2014 he has served as Chairman of the Communications and External Affairs Committee of the European Society of Radiology (ESR). He has also served as Chairman of the ESR's Finance and Internal Affairs Committee (2011–2014) and as a member of the Education and Professional Standards Committee of the European Federation of Societies for Ultrasound in Medicine and Biology (2008–2011). He has been Head of the Advisory Board of the Croatian National Breast Cancer Screening Programme since 2005. He is a fellow of the European Society of Urogenital Radiology and member of the European Society of Breast Imaging and the Cardiovascular and Interventional Radiological Society of Europe. Moreover, he is an honorary member of the Hungarian Society of Radiology. He is editor-in-chief of the *Journal of Ultrasound* and sits on the International Editorial Board of *Ultraschall in der Medizin*. He has published two textbooks, 59 chapters in textbooks and books, 101 papers in peer-reviewed magazines and has given more than 210 invited lectures internationally. His work focuses on breast imaging, cardiovascular and interventional radiology, and urogenital radiology.

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Dr. Zoran Brnić is Head of the Clinical Department of Diagnostic and Interventional Radiology at Sister of Charity Hospital, School of Medicine, University of Zagreb, Croatia. He is Professor of Radiology and is in charge of training graduate and postgraduate students and radiology technologists. He specialises in breast imaging, diagnostic and interventional ultrasound and radiation protection in medicine. He is involved in the organisation of the Croatian National Breast Screening Programme and quality control service.

Dr. Brnić is a member of the Croatian Society of Radiology and an active participant at many international meetings. He has authored 45 publications, five book chapters, and one book. His main research interests include radiation exposure in mammography, quality of images in mammography, prostate ultrasound and biopsy, dosimetry in interventional radiology and minimally invasive liver ablation techniques.

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Prior to this she was Assistant Vice President of Public Affairs and Director of Public Affairs at Amplify Public Affairs. In these roles, she developed communication and education strategies, media outreach initiatives and managed third-party stakeholder outreach and support for a variety of clients.

Before her roles at Amplify, she was a Program Associate for the American Academy of Nursing (AAN), where she monitored health policy trends including health information technology, workforce issues and nursing research for the AAN and advocated for nursing's contributions to health reform.

She is a graduate of James Madison University (BSW) and received her Master's Degree in Public Policy from the Johns Hopkins University.

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Priscilla F. Butler, MS, FAAPM, FACR, has devoted her career to quality breast imaging and assessment of patient radiation dose. She has been with the American College of Radiology (ACR) since 1998, is currently Senior Director and Medical Physicist in the ACR's Department of Quality and Safety, and is responsible for a growing number of dose-related projects (e.g. Image Gently and Image Wisely) as well as physics-related activities (e.g. quality control manuals) and BI-RADS®. For over 13 years, she was the Senior Director for the ACR's Breast Imaging Accreditation Programs, including Mammography, Stereotactic Breast Biopsy, Breast Ultrasound and Breast MRI. Ms. Butler served on the original FDA National Mammography Quality Assurance Advisory Committee during the development of the Mammography Quality Standards Act (MQSA) final regulations.

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Dr. Julia Camps-Herrero is a breast radiologist and Head of the Radiology Department at University Hospital de la Ribera in Alzira, Valencia. She trained in Alicante in general radiology and also in Boston (Massachusetts General Hospital) in abdominal radiology. Since 1999 she has been an active researcher in multimodality breast radiology, with a special interest in MRI. Under her supervision, the diagnostic breast section became the first unit in the Valencian community to set up breast MRI, MR-guided biopsies, tomosynthesis, and tomosynthesis-guided and ultrasound-guided vacuum assisted biopsies and pre-surgical localisations. Dr. Camps-Herrero is an active speaker in Latin America and Europe, where she has been invited to give more than 160 presentations. She is the author of 14 papers, seven book chapters and 75 scientific posters and oral presentations. She has been the editor of the breast section of EURORAD since 2007; was chair of the Breast Subcommittee for the 2012 European Congress of Radiology (ECR) and for the Spanish Senology Congress in 2015; served as a member of the Programme Planning Committee for ECR 2015 and 2016; and is a current member of the Executive Board of SEDIM (Spanish Breast Imaging Society) and Vice President of the European Society of Breast Imaging (EUSOBI).

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Dr. Paola Clauser, MD, is a board certified radiologist currently working at the Medical University of Vienna. Her interest in breast imaging grew during her residency at the Institute of Radiology of the University of Udine, Italy. As a researcher, her main topics of interest are tomosynthesis and multiparametric breast MRI. She also works in collaboration with her former University and with other Italian research centres specialised in breast imaging. She is currently a committee member of the European Society of Breast Imaging and the Italian College of Breast Radiologists of SIRM (Società Italiana di Radiologia Medica). Her main goal in these societies is to increase the number of initiatives dedicated to young radiologists in training and to favour their interest in research and collaboration. She has co-authored several peer-reviewed papers and conference abstracts, some of which have received awards at national and international congresses.

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Michael Crean, BA, is a project manager at the European Institute for Biomedical Imaging Research (EIBIR) and has been involved in two of EIBIR's three breast cancer projects. He was project manager on the Virtual Physiological Human: Personalised, Predictive Breast Cancer Therapy Through Integrated Tissue Microstructure Modelling (VPH-PRISM) project and is currently involved in the Digital Hybrid Breast PET/MRI for Enhanced Diagnosis of Breast Cancer (HYPMED) project as work package leader for dissemination, as well as assisting with project management.

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Dr. Silvia Deandrea graduated in Medicine (specialisation in Public Health) and obtained her Biostatistics PhD in 2011. She has worked in healthcare quality consultancy, in cancer epidemiology research and in organising and evaluating population-based cancer screening programmes as Quality Manager. She is the author of more than 20 research papers published in international peer-reviewed journals.

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Prof. Andy Evans is Professor of Breast Imaging at Dundee University. He is a world leading authority on shear-wave elastography of the breast. His other fields of expertise include breast cancer screening and ductal carcinoma *in situ*. He is a past chairman of the British Society of Breast Radiology, a member of the scientific committee of the European Society of Breast Imaging (EUSOBI) and a member of the Breast Imaging Subcommittee of the European Congress of Radiology. His research outputs include 152 peer-reviewed publications, 17 book chapters and three books. He also plays the French horn and is a successful composer of classical music.

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Dr. Eva M. Fallenberg undertook her general radiology training from 1998 to 2004 at the University of Münster, where she went on to work as the responsible consultant of breast imaging, organising the first courses for the German Breast Screening programme, held in the Reference Centre of Mammography Screening in Münster. Since 2007 she has worked as a consultant and team manager in breast imaging at Charité University Hospital, Berlin. Her main research interests are contrast-enhanced mammography and MRI in which she has performed several studies both in Berlin and also in collaboration with Clarisse Dromain and the Institute Gustave Roussy in Paris, which have been published in several peer-reviewed journals including *Radiology, Investigative Radiology, European Radiology, Breast Cancer Research*, and *Breast Cancer Research and Treatment*.

Since February 2014 she has been Head of Clinical Instruction of Medical Students for the Radiology Department at the Charité Campus Virchow Klinikum. She obtained a doctorate degree in medicine in 2001, and in February 2015 finalised her *habilitation* (tenured professorship) on 'contrast-enhanced imaging of the breast – challenges, limitations and technical innovations'. Dr. Fallenberg is also very interested in teaching and training, and in 2011 became a founder member and examiner for the European Diploma in Breast imaging (EDBI).

In addition, she has been the breast sub-section editor for *Acta Radiologica* since August 2015. She is a member of the Breast Scientific Subcommittee for the European Congress of Radiology (ECR) 2016 and 2017, member of the board of German breast radiologists and President of the Congress of the German Society of Senology 2017.

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He also gained experience abroad in Köln, Nürnberg, and Erlangen, Germany (1990), as well as Rehovot, Israel (1998), Nottingham, United Kingdom (1999) and Düsseldorf University, Germany (1993–1994). He also held a post as staff radiologist at the Hôpital Tenon, Paris, France (1994–1995).

An experienced lecturer (with 227 presentations in French, English and Hungarian), Prof. Forrai has published a book, 29 book chapters, 24 full articles and 56 scientific congress abstracts. He wrote his PhD thesis on the subjects of breast core biopsy and breast MRI.

Prof. Forrai has been the president and organiser of several national and international courses and congresses, such as the French-Hungarian Radiology Symposia (annually since 2001), Central European PACS School, Central European eHealth Academy, EUSOBI Schools and ESOR events.

He is the current President of EUSOBI (2015–2018), and was Chair of the Breast Subcommittee of the European Congress of Radiology 2014, Secretary General of the Hungarian Section of Breast Diagnostics of the Hungarian Radiological Society, and vice-president of the French-speaking Radiology Educators' Society (GREF). His contributions to French-Hungarian scientific cooperation have been recognised by the French Republic, which awarded him Knight of National Order of Merit (2012).

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Dr. Michael Fuchsjäger is Professor of Radiology, Division Head of General Radiology and Vice-Chair of the Department of Radiology at the Medical University of Graz. Dr. Fuchsjäger received his MD degree from the University of Vienna and completed his residency at the Medical University of Vienna's Department of Radiology and was a research scholar at the Department of Radiology at the Memorial Sloan-Kettering Cancer Center, New York. He also served as Chair of the Clinical Imaging Institute at the Al Ain Hospital in Abu Dhabi, UAE. Dr. Fuchsjäger's clinical work and research is dedicated to diagnostic and interventional breast radiology. He serves on various committees for national and international radiology and senology societies, first and foremost the European Society of Radiology, where he is the Committee Chair for Finance and Internal Affairs on the Executive Council, as well as chair of evaluation on the Programme Planning Committee for the European Congress of Radiology. Furthermore, he is a member of the executive boards of the European Society of Breast Imaging, the Austrian Roentgen Society and the Austrian Society of Senology. Dr. Fuchsjäger is a member of the editorial boards of several of the most prestigious radiology journals including *European Radiology* and *Radiology.* Previously a guest editor for the 2005 special editions on breast imaging of *Investigative Radiology,* he has published more than 60 peer-reviewed scientific manuscripts, review articles and book chapters. He has also presented more than 350 educational lectures over his career.

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Peter Gordebeke, MSc, is a project manager at the European Institute for Biomedical Imaging Research (EIBIR) with a background in medical biology. He has been involved in managing Framework 7 projects on gastrointestinal stromal tumours and breast cancer. He is currently project manager of a Horizon 2020 project on dementia and stroke co-occurrence.

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Jennifer A. Harvey, MD, FACR, is Professor and Vice-Chair of Faculty Development at the Department of Radiology and Medical Imaging of the University of Virginia, in Charlottesville, Virginia. Her primary research interest is in the influence of breast density on breast cancer risk. She has more than 60 peer reviewed publications to her name, is co-author of the popular text *Making the Diagnosis: A Practical Guide to Breast Imaging,* serves on many national committees and editorial boards, and has been invited to speak worldwide on breast imaging and breast density. She has received many awards and is a fellow of the American College of Radiology and the Society of Breast Imaging.

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Thomas H. Helbich MD, MSc, MBA, Professor of Radiology, received his medical degree at the Medical University of Vienna in 1989. From 1990 until 1996 he was trained as a radiologist at the Department of Radiology at the Medical University of Vienna. He was a research fellow at the Department of Radiology, Center of Molecular Imaging of the University of California in San Francisco from 1996 to 1998. In 1999 he became Associate Professor of Radiology. In 2005 he became Vice Department Chair of the Department of Radiology/Surgical Division. From 2007 to 2008 he was Division Head of the Breast Imaging Department of the University of Toronto and Full Professor of Radiology of the University of Toronto. Since October 1, 2008 he has been Professor of Molecular Imaging and Vice Chair of the Department of Radiology of the Medical University of Vienna. His main fields of research interest are clinical and experimental investigation on a cellular and sub-cellular level to diagnose cancer, in particular breast cancer. His working group has developed and optimised several methods on the basis of MRI, various molecular imaging tools, as well as minimally invasive diagnostic techniques. He is author or co-author of more than 200 scientific articles. He is an advisor to both the Minister of Health of Austria and the Mayor of the city of Vienna for the national breast screening programme. He has been honoured with several national and international awards. He was President of the European Society of Breast Imaging (EUSOBI) from 2010 to 2012.

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Monika Hierath, MA, has been executive manager of the European Institute for Biomedical Imaging Research (EIBIR) since its foundation in 2006 and has ten years of experience coordinating international research projects within the EU's Framework Programmes 6, 7 and Horizon 2020. She oversees all EIBIR's support for funding proposals and ongoing projects.

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Bonnie N. Joe, MD, PhD, is Professor in Residence and Chief of Breast Imaging at the University of California, San Francisco. She is co-leader of the Breast Research Interest Group in the Department of Radiology and Biomedical Imaging. Dr. Joe received a PhD degree in electrical and computer engineering and bioengineering from Carnegie Mellon University (Pittsburgh, PA) and an MD degree from the University of Pittsburgh. She completed residency and fellowship training at the Mallinckrodt Institute of Radiology (St Louis, MO). Dr. Joe serves on committees for national and international radiology organisations including the Radiological Society of North America, the Society of Breast Imaging, the American College of Radiology, the American Board of Radiology, and the International Society for Magnetic Resonance in Medicine. Dr. Joe was guest editor for the 2013 edition of *Magnetic Resonance Imaging Clinics of North America: Breast Imaging.* Dr. Joe has published over 95 peer-reviewed scientific manuscripts, numerous review articles and book chapters, and presented more than 200 educational lectures. She is a Fellow of the Society of Breast Imaging.

Daniel B. Kopans
Cambridge, USA

Daniel B. Kopans, MD, FACR, is a *cum laude* graduate of Harvard College (1969) and an AOA graduate of Harvard Medical School (1973). He trained at the Massachusetts General Hospital and joined the staff in 1977. He is a Professor of Radiology at the Harvard Medical School and founded the Breast Imaging Division at the Massachusetts General Hospital, where he was Director of the Breast Imaging Division from 1978 to 2006. He has received numerous awards and honours, including the Gold Medal from the Society of Breast Imaging, which is its highest honour.

Dr. Kopans defined the field of breast imaging with a landmark article in the *New England Journal of Medicine* in 1984 recognising the value of multimodality breast evaluation. With more than 250 publications and one of the leading textbooks to his name, Dr. Kopans helped develop breast imaging as a specialty.

He invented a guide wire and techniques that made it possible to accurately direct surgeons to areas of concern found by mammography, making it possible to aggressively pursue small lesions with a minimum of trauma to the patient using local anaesthesia in an outpatient setting with a high degree of accuracy. Accurate localisation and early intervention facilitated the diagnosis of very small cancers that led to the major decrease in breast cancer deaths that has been seen in the United States since 1990.

He was co-chairman of the original BI-RADS committee and his organised approach to image interpretation and reporting is the basis for the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS).

Dr. Kopans is the leading expert on screening for women in their forties and it was in large part due to his efforts in defining the scientific issues, analysing the data, and pressuring the National Cancer Institute in the 1990s that women aged 40–49 have access to routine annual mammography screening. He continues to support the fundamental scientific basis of screening while exposing the flawed analyses that are being generated to try to reduce access to screening.

Dr. Kopans holds several patents on devices to improve breast cancer detection and diagnosis. He is the inventor and patent holder of Digital Breast Tomosynthesis (DBT), sometimes called 3D mammography. DBT permits high resolution tomographic breast evaluation that has been shown to significantly increase the detection of small cancers while also reducing the recall (false positive) rate.

Dr. Kopans is a clinician, educator, investigator, author, and inventor. He is a member and Fellow of the American College of Radiology (ACR) and is Chairman of the Fellows Committee of the Society of Breast Imaging.

Katharina Krischak
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Katharina Krischak, MA, is a project manager at the European Institute for Biomedical Imaging Research (EIBIR) with past experience working at the European Commission and the Council of Europe in Strasbourg. She is currently involved in the management of two Horizon 2020 projects on better thyroid cancer screening and an innovative glucose-based imaging method for cancer.

CHAPTER 9: **ABOUT THE AUTHORS**

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Carol H. Lee, MD, is Attending Radiologist at Memorial Sloan Kettering Cancer Center in New York and is also Professor of Radiology at Weill Cornell Medical College. Dr. Lee has specialised in breast imaging for more than 30 years and has served as Chair of the American College of Radiology (ACR) Breast Commission and as President of the Society of Breast Imaging. She is currently a member of the National Mammography Quality Assurance Advisory Committee, which advises the Food and Drug Administration on regulatory issues. She is also head of the ACR Breast Imaging Reporting and Data Systems (BI-RADS) committee. She is a recent recipient of the Gold Medal from the Society of Breast Imaging.

Donata Lerda
Moncalieri, Torino, Italy

Dr. Donata Lerda graduated in Chemistry in 1987. She worked in public administration in Italy for more than 20 years and started working at the European Commission in 2007. She is an expert in quality assurance, accreditation, auditing and management of networks; she also has a deep knowledge of the European Commission working rules. She coordinates the European Commission Initiative on Breast Cancer.

Lorenzo Livi
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Dr. Lorenzo Livi graduated in Medicine and Surgery in 1997. He specialised in radiation oncology in 2001 and in medical oncology in 2002. He served as Assistant Professor of Radiation Oncology at the University of Florence from 2002 to 2011. In 2012 he became Full Professor of Radiation Oncology and since 2013 he has been Chair of the Radiation Oncology Department of the Florence University Hospital. He has an extensive interest in radiation oncology and its interplay with systemic therapies, in particular: breast cancer, urogenital cancer and soft tissue sarcoma. He has been listed as an author or co-author in more than 100 peer-reviewed papers and as is the author of various book chapters. He is an active member of the Italian Association of Radiation Oncology (AIRO), the European Society for Radiotherapy and Oncology (ESTRO), and the European Organisation for Research and Treatment of Cancer (EORTC).

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Jesús López Alcade, MD, graduated in Medicine in 2004 and specialised in Preventive Medicine, Epidemiology and Public Health in 2006. He is an expert in guideline development methodologies and side processes like literature review (scientific evidence), health technology assessment, methodological research on biases in systematic reviews and guidelines, and the implementation and dissemination of research findings.

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Dr. Ritse Mann, MD, PhD, is an academic breast and interventional radiologist at the Radboud Universitair Medisch Centrum (Radboudumc) in Nijmegen, the Netherlands, and screening radiologist at Bevolkingsonderzoek Oost. He is an active researcher, and scientific leader of the clinical breast research line at the Radboudumc radiology department, aiming at clinical validation of novel strategies for breast cancer detection and treatment. Ritse Mann is a member of the executive board of the European Society of Breast Imaging (EUSOBI) and its scientific and young club committees. In addition he is a member of the EuroAIM working group on evidence-based radiology. He is course director of the Nijmegen advanced breast imaging course and actively involved in numerous other teaching courses. Ritse Mann is breast section editor of the *European Journal of Radiology,* and a member of the e-learning editorial board of the European Society of Radiology.

Icro Meattini
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Dr. Icro Meattini completed his medical studies in 2005, and specialised in Radiation Oncology in 2009 at the University of Florence, Italy. During his specialisation he undertook a fellowship at the Radiation Oncology Unit of the Royal Marsden Hospital, London, UK, in 2008. He became Consultant at the Radiation Oncology Unit of the University Florence Hospital in 2011, where he currently works as a Clinical Oncologist; he is chair of the Radiation Oncology Unit breast working party (BWP) at the Florence University Hospital. His major fields of interest are radiation therapy development, clinical trials, biological and systemic treatments, and breast cancer research. He has published more than 80 papers in peer-reviewed journals. He is an active member of the European Society for Radiotherapy and Oncology (ESTRO), the European Organisation for Research and Treatment of Cancer (EORTC), the Italian Association for Radiation Oncology (AIRO), and the Italian Association for Radiobiology (AIRB). He has been the young co-Chair of the BWP of the Radiation Oncology Group (ROG) of the EORTC since 2015, and counsellor of the non-profit Florence Foundation for Radiation Oncology (FFRO) 2013–2018.

CHAPTER 9: **ABOUT THE AUTHORS**

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Luciana Neamțiu, PhD, graduated in Mathematics and Physics in 1996 and obtained her PhD in mathematics (numerical analysis, optimisation and computer science applied to medicine). She worked for more than ten years in the area of Cancer Registries and Screening Databases and collaborated on the setting-up of the population based cancer screening programmes and regional population based cancer registry in her own country.

Liisa Pylkkanen
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Dr. Liisa Pylkkanen graduated in Medicine in 1986 and obtained her PhD in 1992. She is a specialist in Clinical Oncology (1995), Health Administration (2001) and Palliative Medicine (2010) and has held an Adjunct Professor position since 2001. She has worked in clinical oncology for more than 25 years and in different management positions both in academia and the pharmaceutical industry. Since 2012 she has worked as Chief Medical Officer at the Cancer Society of Finland. Her scientific interest has focused on breast cancer (including screening), prostate cancer, bone active compounds and patient support.

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Dr. Murray Rebner, MD, FACR, is a board-certified radiologist and Professor of Diagnostic Radiology and Molecular Imagining at Oakland University William Beaumont School of Medicine. He is also the Director of the Division of Breast Imaging at Beaumont Health System's Royal Oak Campus in Royal Oak, Michigan.

He graduated from McGill University Faculty of Medicine and completed his residency at the University of Michigan, where he also completed a fellowship in diagnostic radiology. Dr. Rebner specialises in diagnostic radiology with expertise in breast imaging. He is the Immediate Past President of the Society of Breast Imaging.

Francesco Sardanelli
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Dr. Francesco Sardanelli is Professor of Radiology and Director of the Postgraduate School in Radiodiagnostics at the University of Milan. He received his Medicine Graduation in 1982 and Postgraduation Diploma in Radiodiagnostics in 1986 at the University of Genoa. He was staff radiologist at the San Martino Hospital, Genoa from 1987 to 1999, and Adjunct Professor of the Postgraduate Course in Radiodiagnostics at the University of Genoa from 1992 to 2000. From 2001, he was Director of the Radiology Department at the Research Hospital Policlinico San Donato, Milan, then Adjunct Professor of the Postgraduate Course in Radiodiagnostics, University of Milan from 2001 to 2005. He became Associate Professor of Radiology (2006–2014), then Full Professor of Radiology (from 2015) at the University of Milan. He was Director of the Postgraduate School in Nuclear Medicine at the University of Milan (2008–2010). In 2015 he became Director of the Postgraduate School in Radiodiagnostics at the University of Milan. He was a consultant for the *Istituto Superiore di Sanità* (Italian Health Government Department), for the national radiological coordination of multicentre studies on MRI, including screening of women at high genetic/familial breast cancer risk (1999–2011). He is a founder and member of the Board of Directors of *Breast Centres Certification* according to EUSOMA guidelines, and Vice President of the *Quality Assurance Scheme Development Group* of the *European Commission Initiative on Breast Cancer* (2015–2017).

He is a member of the Editorial/Advisory Boards of *European Radiology, The Breast, La radiologia medica* (Associate Editor), *American Journal of Roentgenology* (Assistant Editor, Women's Imaging Section), *Insights into Imaging,* and *Clinical and Translational Imaging*. He is the Editor-in-Chief of the forthcoming journal *European Radiology Experimental,* and has served as a reviewer for 49 other medical journals. He is currently on the research Committee of the European Society of Radiology and the Advisory Board of the European Institute for Biomedical Imaging Research (EIBIR). He is Director of the EIBIR/European Network for Assessment of Imaging in Medicine (from 2009); Past-President of the European Society of Breast Imaging; and President of the Italian College of Breast Radiologists of the Italian Society of Medical Radiology.

He has received honorary membership of the British Society of Breast Radiology and the Iranian Society of Radiology. He has published six books and 46 book chapters; more than 350 full articles, and more than 700 congress abstracts. He has also given more than 500 oral presentations and lectures at medical congresses and courses.

Zuleika Saz Parkinson
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Zuleika Saz Parkinson, PhD, graduated and received a master's degree in biochemistry in 1994 and 1996 respectively. She obtained her PhD in Preventive Medicine and Public Health in 2005. She has worked in Health Technology Assessment, with a particular interest in screening, cancer and genetics, for over ten years and also has ample experience in Research Management and Quality Management gained in working at the Spanish National Cancer Research Centre and in a health research institute in Madrid.

Edward A. Sickles
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Edward A. Sickles, MD, is Professor Emeritus of Radiology at the University of California, San Francisco (UCSF), School of Medicine and served as chief of the Breast Imaging Section at the UCSF Medical Center for almost 30 years. He is a prolific contributor to breast imaging education and the scientific literature. He has provided editorial services to twelve professional journals, has been the author or co-author of ten books and monographs, approximately 250 scientific articles, and almost 100 other scientific communications. He has presented papers at more than 250 scientific meetings and has been an invited speaker at more than 850 educational seminars and medical institutions in 43 states in the United States and in 32 other countries. He has also served on many breast imaging committees of the American College of Radiology (ACR) since 1980, has chaired the ACR Committee on Mammography Interpretive Skills Assessment since its inception in 1992, and currently chairs the ACR BI-RADS Mammography Subcommittee. In his commitment to improving the science and art of breast imaging, he has also served in a leadership position in 10 other professional societies and organisations and on over 40 committees both nationally and internationally. He is a founding member and past president of the Society of Breast Imaging. He has been the recipient of numerous awards and special recognitions for his dedication, service, and contributions to breast imaging, including the Gold Medal of the Society of Breast Imaging and honorary membership in four international radiologic societies.

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Dr. Rubina Manuela Trimboli, MD, is a radiologist at IRCCS Policlinico San Donato, University of Milan. Her main area of interest is breast radiology. She is involved in mammography, ultrasound, breast MRI, and needle biopsy under stereotactic and US guidance, and is an active researcher in breast cancer prevention and diagnostics, focusing on screening in high and intermediate risk women. She also holds a PhD in Biomedical Imaging and Research and acts as a tutor of medical students and residents in radiodiagnostics. She is a fellow of the European Society of Breast Imaging (EUSOBI). She has co-authored 14 peer-reviewed papers and more than 20 conference abstracts, and given ten invited lectures.

Aslı Ulutürk
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Dr. Aslı Ulutürk graduated in Medicine in 2000 and received her specialist degree in radiology in 2007. She has worked in the field of breast imaging, in particular within a screening and early diagnosis programme, and in the obstetrics ultrasound field.

Pamela Zolda
Vienna, Austria

Dr. Pamela Zolda is a former assistant professor at the University of Vienna with highly valuable and in-depth experience of international research projects. She is a senior European research project manager at the European Institute for Biomedical Imaging Research (EIBIR) and has coordinated and managed several Framework 7 projects. She is currently the coordinator of the Digital Hybrid Breast PET/MRI for Enhanced Diagnosis of Breast Cancer (HYPMED) project.

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It's time to stop the misinformation about breast cancer screening
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Breast density and supplemental screening

By Jennifer A. Harvey and Wendie A. Berg

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In support of breast cancer screening mammography

By Francesco Sardanelli et al, on behalf of EUSOBI and 29 national breast radiology bodies

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Radiotherapy in breast cancer

By Lorenzo Livi, Isacco Desideri, Icro Meattini, on behalf of the ESTRO – European Society for Radiotherapy and Oncology

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CHAPTER 2
STANDARDS & QUALITY

Breast exposure to ionising radiation
By Zoran Brnić and Boris Brkljačić

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By the JRC Healthcare Quality Team

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CHAPTER 3
THE HISTORY OF BREAST IMAGING

From 'mammography' to 'breast imaging': a history
By Bonnie N. Joe and Edward A. Sickles

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CHAPTER 5

EUSOBI RECOMMENDATIONS FOR WOMEN'S INFORMATION

Mammography

By Francesco Sardanelli, Eva M. Fallenberg, Paola Clauser, Rubina M. Trimboli, Julia Camps-Herrero, Thomas H. Helbich, Gabor Forrai, on behalf of the European Society of Breast Imaging (EUSOBI)

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By Andy Evans on behalf of the European Society of Breast Imaging (EUSOBI)

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By Ritse M. Mann on behalf of the European Society of Breast Imaging (EUSOBI)

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Image-guided breast biopsies
By Ulrich Bick on behalf of the European Society of Breast Imaging (EUSOBI)

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CHAPTER 8

THE ROLE OF RADIOGRAPHERS IN BREAST IMAGING: A BRITISH PERSPECTIVE

Introduction and background

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