J HK Coll Radiol 2004;7:171-180

REVIEW ARTICLE

Update in Breast Cancer Screening

HS Lam

Department of Radiology, Kwong Wah Hospital, Hong Kong

ABSTRACT

Breast cancer screening by mammography has been practised in many countries on the basis of the results of published randomised controlled trials. Recently, there has been a lot of discussion about the validity of these trials. This review presents a history of the controversies surrounding mammography screening. The protocols in breast cancer screening in various countries are discussed, and limitations and risks of mammography screening are listed. Finally, several modalities that have the potential to improve the efficiency of breast cancer screening are highlighted. All told, mammography with or without clinical breast examination remains the gold standard for breast cancer screening, and mammography screening will reduce breast cancer mortality. However, its benefit decreases and harm increases as the incidence of breast cancer decreases. It is important that women be informed about the potential benefits, risks, and limitations when they undergo breast cancer screening.

Key Words: *Breast neoplasms; Clinical protocols; Mammography; Mass screening*

INTRODUCTION

Breast cancer is the most common cancer and leading cause of cancer deaths among women worldwide. The incidence varies in different countries but shows a rising trend.[1] Screening for breast cancer is based on the assumption that early detection of cancer improves survival. Treatment of breast cancer at a less advanced stage will also reduce the adverse effects of treatment. The decision of whether to screen or not rests heavily on the evidence from randomised controlled trials (RCTs). There are altogether 7 major RCTs (some authors may split the Malmo Trials, the Canadian Trials, or the Two-county Swedish Trial into 2 trials each). All except the Canadian Trials showed a significant reduction in mortality in the screened group (Table 1).[2-10]

THE MAMMOGRAPHY DEBATE

A heated debate about the value of mammography screening started after Gotzsche and Olsen (a pair of Danish investigators who are part of the Nordic Center for the Cochrane Collaboration, or Cochrane Library) published a paper that challenged the validity of the results from published RCTs. The sequence of events is described below.

January 2000

Gotzsche and Olsen published their paper in *The Lancet* in January 2000.[11] They stressed that the bias caused by suboptimal randomisation methods could be larger than the treatment effects that might be detected if a screening programme was beneficial. They reviewed the methodological quality of each RCT and reported that "baseline imbalances" were present in 6 of the 8 trials, and that inconsistencies existed in 4 trials in the number of women who were randomised. Furthermore, they highlighted an imbalance in age at baseline in the Swedish trials, and they criticised the methods of determination of mortality in the 6 "poor" trials, arguing that assessment of the cause of death was unreliable and biased in favour of screening. In the 2 "adequate" RCTs (the Canadian Trial and the Malmo I Trial), they found no effect of screening on breast cancer mortality. Hence, they concluded, screening for breast cancer with mammography was unjustified.

Nevertheless, all the trials that Gotzsche and Olsen had rejected showed a reduction in mortality, which ranged from 13% to 46%. In addition, they did not include the Malmo II Trial[12] (an extension of the Malmo I Trial), which reported a mortality reduction of

Correspondence: *Dr. HS Lam, Department of Radiology, Kwong Wah Hospital, 25 Waterloo Road, Kowloon, Hong Kong.*
Tel: (852) 3517 5107; Fax: (852) 3517 5454;
E-mail: hslam@ha.org.hk

Submitted: 10 January 2005; Accepted: 14 February 2005.

Table 1. Published randomised controlled trials on breast cancer screening.

Study	Age range (y)	Follow-up duration (y)	% Mortality reduction
HIP,[2] 1963	40-64	18	29
Malmo,[3] 1976	45-69	12	19
Swedish Two-county Trial,[4,5] 1977	40-74	12	18 (Ostergotland) 32 (Kopparberg)
Edinburgh,[6] 1976	45-64	7	16
Stockholm,[7] 1981	40-64	8	20
Gothenburg,[8] 1982	39-59	11	14
Canada, 1980:			
NBSS-1[9]	40-49	7	-3*
NBSS-2[10]	50-59	7	0

*The negative sign denotes an elevation.

36%. Their article aroused numerous responses in *The Lancet*.[13]

October 2001

In October 2001, the same 2 authors published a Cochrane review[14] and a research letter in *The Lancet*.[15] They stated that "a Cochrane review has now confirmed and strengthened our previous findings. The review also shows that breast cancer mortality is a misleading outcome measure. We use data supplemental to those in the Cochrane review to show that screening leads to more aggressive treatment." The editor of *The Lancet*, Richard Horton, supported the authors' argument in a commentary.[16] The same commentary, however, also noted that there were differences in view between the Cochrane Breast Group (which favoured screening) and the 2 authors.

December 2001

The issue on the usefulness of breast cancer screening was brought to the public's attention when Gina Kolata published a article about the work of Gotzsche and Olsen on the front page of *The New York Times* in December 2001.[17]

January 2002

More doubt was raised about the value of mammography screening as the Patient Data Query (PDQ) Editorial Board, after evaluating the RCTs, concluded that "screening for breast cancer does not affect overall mortality, and the absolute benefit for breast cancer mortality appears to be small". The PDQ Editorial Board is an independent panel of cancer experts that is responsible for producing and maintaining evidence-based, peer-reviewed cancer information summaries for the United States (US) National Cancer Institute (NCI). The PDQ Editorial Boards, however, are not formal advisory or policy-making boards of the NCI. The view of the PDQ Editorial Boards was reported by Gina Kolata in *The New York Times* in January 2002.[18]

The American College of Radiology reacted by issuing the following statement on its website[19]:

"The American College of Radiology strongly disagrees with the recent announcement by the Physician Data Query (PDQ) screening and prevention editorial board claiming there is insufficient evidence to show that routine screening mammograms help prevent cancer deaths….The panel has inexplicably decided to base much of its conclusion on last October's contested study by Gotzsche and Olsen published by the Nordic Cochrane Center in Copenhagen, a study based on flawed data and questionable statistical analysis….Not only does the panel's announcement conflict with well-founded clinical trials supporting the benefits of regular mammography screening, it contradicts the National Cancer Institute's long-standing position that women have regular mammograms starting in their 40s. Although the PDQ provides material for the NCI's online database, Peter Greenwald, MD, NCI's cancer prevention chief, has indicated that women should continue to be screened with mammography….The ACR, along with the American Cancer Society, the Society of Breast Imaging, the American Medical Women's Association and numerous other national women's groups, stands by its recommendation of annual mammography screenings and yearly clinical breast examinations beginning at age 40. This opinion is based on accepted and rigorous scientific analysis".

The NCI[20] also gave its stand by issuing the following statement on 31 January 2002:

"A recent report in the scientific literature has reawakened debate about the value of screening mammograms. The analysis, which appeared in *The Lancet* on October 20, 2001, reviewed the large, long-term mammography trials upon which the National Cancer Institute (NCI) and other groups have based their recommendations and

guidelines concerning mammography screening. This review cited a number of possible flaws in the conduct of the trials and the methods used to analyze the data. The NCI has carefully considered the issues raised in *The Lancet* review. It has also considered the recent deliberations of the PDQ Screening and Prevention Editorial Board and of the US Preventive Services Task Force and has consulted with a variety of experts in the field in order to determine whether a change in its position is warranted. After due consideration, NCI continues to recommend that:

- Women in their 40s should be screened every one to two years with mammography.
- Women aged 50 and older should be screened every one to two years.
- Women who are at higher than average risk of breast cancer should seek expert medical advice about whether they should begin screening before age 40 and the frequency of screening".

On 31 January 2002, 'An Open Letter to Women and Their Physicians' was published in *The New York Times*,[21] reconfirming the value of mammography screening and urging women to continue to attend screening. It was jointly written by the following medical organisations:

- American Academy of Family Physicians,
- American Cancer Society,
- American College of Physicians-American Society of Internal Medicine,
- American College of Obstetricians and Gynecologists,
- American College of Preventive Medicine,
- American Medical Association,
- Cancer Research Foundation of America,
- National Medical Association,
- Oncology Nursing Society, and
- Society of Gynecologic Oncologists.

February 2002

A different perspective about the Malmo study was given by the Canadian researchers Miettinen et al in the 9 February 2002 issue of *The Lancet*.[22] Miettinen and colleagues examined data from the Malmo trial (1 of the 2 studies regarded by the Danish writers as being of acceptable quality) for women aged 55 years or older at study entry. Miettinen et al found that compared with controls, screened women had a statistically significant reduction in breast cancer mortality that began 6 years after entry into the trial, and breast cancer deaths were significantly and increasingly lower from years 7 through 9, tapering to a 55% reduction by year 11. Miettinen et al pointed out the important fact that there was a time lag before any mammography benefits could be detected.

The debate in the US stopped as the Secretary of Health and Human Services reaffirmed the value of mammography screening.[23] The press release of 21 February 2002 quoted the recommendation from the US Preventive Services Task Force (USPSTF), which called for screening mammography with or without clinical breast examination every 1 to 2 years for women aged 40 years or older.

March 2002

The matter aroused the attention of the World Health Organization (WHO) in March 2002. A working group that was convened by the International Agency for Research on Cancer of the WHO met in Lyon, France, from 5 to 12 March 2002. This group, consisting of 24 experts from 11 countries, evaluated the available evidence on breast cancer screening. They reached the following conclusion[24]:

"The trials have provided sufficient evidence for the efficacy of mammography screening of women between 50 and 69 years. The reduction in mortality from breast cancer among women who chose to participate in screening programmes was estimated to be about 35%. For women aged 40-49 years, there is only limited evidence for a reduction. The quality of the trials that were used to make these evaluations was carefully assessed. The working group found that many of the earlier criticisms were unsubstantiated, and the remaining deficiencies were judged not to invalidate the trials' findings….The working group also concluded that there is insufficient evidence that clinical breast examination or self-examination reduces mortality from breast cancer."

Further support for the benefit of mammography screening was given when Nystrom et al[25] published an article in *The Lancet* on 16 March 2002. They updated the data of the Swedish RCTs (Malmo I, Malmo II, Ostergotland, Stockholm, and Gothenburg) up to and including 1996, and found a 21% reduction in breast cancer mortality. The benefit in absolute terms increased up to 12 years after randomisation and it was maintained thereafter. This paper countered the criticisms made against the Swedish trials by Gotzsche and Olsen.

June 2002

To settle the controversy regarding the efficacy of mammographic screening, the European Institute of

Oncology hosted a Global Summit on Mammographic Screening in collaboration with the WHO, the European Commission, the American Cancer Society, the American Italian Cancer Foundation, the European Society for Medical Oncology, the American Society for Clinical Oncology, the International Union Against Cancer, and the Centers for Disease Control and Prevention, in Milan, Italy, from 3 to 5 June 2002.

During that meeting, the design and recent results from the 7 RCTs were presented and discussed in detail in the light of each criticism put forward by Gotzsche and Olsen. The summit reached the conclusion that the work of Gotzsche and Olsen was unfounded and that the reduction in breast cancer mortality seemed to be between 21% and 23%. Women participating fully in screening programmes could expect greater benefit. The summit chairman concluded, "There was unanimity that with the current evidence from RCTs, taking full account of any limitations to their methodology, there were no grounds for stopping on-going screening programmes nor planned programmes".[26]

September 2002

The USPSTF is an independent panel of experts in primary care and prevention that systematically reviews the evidence of effectiveness and develops recommendations for clinical preventive services. The USPSTF first released their recommendations on screening for breast cancer on 21 February 2002.[27] In September 2002, they published further recommendations after incorporating the additional data on outcomes and methods of 4 mammography trials conducted in Sweden.[28] The new statement, however, differed minimally from those cited earlier in the year. The USPSTF found important methodological limitations in each trial, but rated only 1 trial as "poor". The USPSTF concluded that the flaws were problematic, but unlikely to negate the reasonably consistent and significant mortality reductions observed in these trials. They made the following statement:

"The USPSTF concluded that there was fair evidence that mammography screening every 12 to 33 months significantly reduces mortality from breast cancer. Evidence is strongest for women aged 50 to 69 years. For women aged 40 to 49 years, the evidence that screening mammography reduces mortality from breast cancer is weaker, and the absolute benefit of mammography is smaller because the incidence of breast cancer is lower. The USPSTF concluded that the evidence is also generalisable to women aged 70 and older (who face a higher absolute risk for breast cancer) if their life expectancy is not compromised by comorbid disease. The absolute probability of benefits of regular mammography increases along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminishes from ages 40 to 70. The balance of benefits and potential harms, therefore, grows more favorable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice. The USPSTF did not find sufficient evidence to specify the optimal screening interval for women aged 40-49."[29]

OTHER EVIDENCE

Gotzsche and Olsen had reviewed problems in the design of the RCTs. Are there any other pieces of evidence besides the classic RCTs, which may help elucidate the usefulness of mammographic screening? New evidence can be collected in the following ways:

(1) By designing new, 'more perfect' RCTs, although starting a new trial is a difficult task. For example, there are substantial implications for financial and human resources: a large number of women have to be screened to be statistically significant and these women have to be followed up for many years. To deny the controls their right to attend screening also represents an ethical problem. Until now, there have been no new RCTs.

(2) By conducting long-term follow-up in countries that had started the classic RCTs and are now practising population-wide screening. According to the view of Miettinen et al,[22] a longer follow-up duration would yield better results, because there is a time lag for the benefit of screening. New papers on the long-term follow-up of screening have been published.[30-35] Their results are summarised in Table 2. It can be seen that all RCTs, except for the Canadian Trial, show a further reduction in mortality. Extension of the classic RCTs, however, has a great limitation in that it evaluates the effect of mammography screening that was done decades ago, when the technology and technique were less advanced than those of today.

(3) By conducting service screening to compare the mortality before and after the introduction of mammography screening. Published work on such a topic also compared mortality among women invited to screening with those not screened during the screening period. The results of several large studies are

Table 2. Updated results of the randomised controlled trials on breast cancer screening.

Study	Age range (y)	Follow-up duration (y)	% Mortality reduction
HIP, 1963	40-64	18	29
Malmo, 1976	45-69	12	19
Swedish Two-county Trial,[30] 1977	40-74	20	32
Edinburgh,[31] 1976	45-64	14	21
Stockholm,[32] 1981	40-64	11	26
Gothenburg,[33] 1982	39-59	16	21
Canada, 1980:			
NBSS-1[34]	40-49	11-16	-3*
NBSS-2[35]	50-59	13	-2*
All trials combined	39-74	—	24

*The negative sign denotes an elevation.

Table 3. Summary of results of service screening studies.

Study	Summary
Malmo[36]	• Study period, 1961-1992; mammographic screening introduced in 1976 • Between 1977 and 1992, age-adjusted breast carcinoma mortality decreased in Malmo by 43% • Benefit was confined to the 45- to 65-year age group for which screening was offered • The benefit was 12% in the rest of Sweden during the same period
Two Swedish Counties[37]	• Study period, 1958-1997; women aged 40-69 years with mammographic screening introduced in 1978 • Mortality reduction of 16% when unscreened women were compared with women in the prescreen period • Mortality reduction of 44% when screened women were compared with women in the prescreen period
United Kingdom National Health Service[38]	• Study period, 1990-1998; women aged 55-69 years • Estimated 21.3% reduction in breast cancer mortality: 6.4% due to mammography and 14.9% due to increased awareness and improvements in therapy
Sweden[39]	• Study period, 1986-1997; women aged 40-69 years • Estimated mortality reduction consistent with other randomised controlled trials
The Florence Programme[40]	• Study period, 1990-1996; women aged 50-69 years • Mortality reduction of 55% for invited and 41% for non-invited women compared with the prescreen period in 1985-1986; mortality reduction attributed both to screening and treatment
Seven Swedish Counties[41]	• Study period, 1958-1998; women aged 40-69 years • Mortality reduction of 44% for women exposed to screening compared with the prescreen period • 39% lower mortality in women invited to attend screening (compared with those not screened) during the screening period • About two thirds of the observed mortality reductions were attributable to screening

summarised in Table 3.[36-41] Research on service screening has the advantage in comparing women who are exposed to the same level of technology and treatment. They can also estimate the relative contribution of mammography screening and other factors (e.g., breast cancer awareness and treatment) in the reduction in mortality.

HOW TO SCREEN

Many countries are currently involved in breast cancer screening (26 participated in the International Breast Cancer Screening Network). The breast cancer screening protocols that are used in various countries are listed in Tables 4, 5, and 6.[42-47] These are discussed below.

Two-view Mammography

Two-view mammography is used as the screening method in all countries. In the United Kingdom (UK), a comparison of screening units demonstrated a 42% increase in the detection of carcinomas measuring less than l.5 cm in units that used this approach (compared with 1-view). The effect was seen during subsequent screens as well as during the first screen.[48]

Clinical Breast Examination

The performance characteristics of clinical breast examination (CBE) are poorer than those of mammography. A meta-analysis conducted by Barton et al showed that CBE had a sensitivity of about 54%.[49] Thus, CBE cannot be used as a stand-alone method of screening. However, evidence has shown that CBE can detect some cancers that are not detectable by mammography.[2,31] When used in combination with mammography, CBE brings about an overall increase in sensitivity. However, addition of CBE to the screening programme also increases the cost of the programme. Both US and Canada, but no other countries, recommend CBE. Among Asian women, whose breasts are denser than those of women in the West, CBE is particularly helpful as an adjuvant to mammography.

Table 4. Tests used in breast cancer screening protocols in various countries.

Country	Screening programme started	Mammography	Breast self-examination	Clinical breast examination	No. of Views	Double-reading
United States	1988	Yes	No	Yes	2	Some places
Canada	1988	Yes	No	Yes	2	No
United Kingdom	1988	Yes	No	No	2	No
Sweden	1986	Yes	No	No	2	Yes
Netherlands	1989	Yes	No	No	2	Yes
Australia	1994	Yes	No	No	2	Yes
Singapore	2002	Yes	No	No	2	Yes

Table 5. Nature of breast cancer screening protocols in various countries.

Country	Age of women screened	Screening interval (y)	% Target population screened	Referral type	Financing method
United States	40-75	1-2	55-63	Doctor or self-referral	Government
Canada	50-69	2	54	Doctor or self-referral	Government
United Kingdom	50-70	3	76	Invitation	Government
Sweden	40-64 or 74	1.5-2	89	Invitation	Government
Netherlands	50-75	2	78	Invitation	Government
Australia	40-79	2	54	Invitation or self-referral	Government
Singapore	40-64	1-2	20	Invitation or self-referral	Co payment

Table 6. Quality assurance policies in various countries.

Country	Quality enforcement	Quality assurance site visits	Level of organisation
United States	National law (Mammography Quality Standards Act)	Yes	Medicare is national; otherwise based on state and private insurance provider policies
Canada	Voluntary accreditation	No	Province-level
United Kingdom	National accreditation requirements	Yes	National
Sweden	National law	Yes	County (Swedish counties are similar to states in the United States)
Netherlands	National law	Yes	National
Australia	National accreditation requirements	Yes	National
Singapore	National accreditation requirements	Yes	National

When CBE is done just before mammography, it offers a unique opportunity for the clinician to discuss with the woman the benefits and risks of mammography screening.

Breast Self-examination and Awareness

Breast self-examination refers to the systematic checking of the breasts at a specific time each month according to a set technique. The Shanghai trial[50] provided high-quality evidence of the lack of effect of teaching breast self-examination and confirmed the results of the early RCT on breast self-examination in Russia.[51] The Shanghai trial showed that the proportion of deaths due to breast cancer and the cumulative mortality were almost identical in the instruction group and in the control group, with more breast biopsies and diagnoses of benign lesions occurring in the instruction group. Breast self-examination is not advised by all countries.

On the other hand, breast awareness is advocated in many countries. Women are encouraged to be familiar with their breasts at different times of the month and at different ages, and to be aware of their breasts in everyday activities, such as bathing or dressing, and to report any obvious changes promptly.

Double-reading

Double-reading increases the cancer detection rate by 5% to 15%.[52-55] Furthermore, cancers identified by a second reader are detected at an earlier stage.[53] Consensus reading or reading by a super-reader will decrease the recall rate. Without such an arrangement, the recall rate increases by 10%. Double-reading also involves additional cost. The cost of double-reading can be reduced by asking a radiographer to be the second reader, or by using a computer. Some countries practise double-reading while others do not.

Age of Screening

The age of screening varies. Most countries screen women from ages 50 to 69 years because this is the age range for which the RCTs show benefit. Extending

the age range of screening would increase the cost of screening. The evidence on the usefulness of screening women older than 69 years is limited: only 1 RCT included women older than this age. There are certain considerations for screening older women. For example, they have a higher absolute risk for breast cancer. The decrease in breast density as one grows older also makes cancer detection easier. However, this benefit is counterbalanced by the effect of comorbidity and the reduction in life expectancy.

The USPSTF concluded that the absolute probability of benefits of regular mammography increase along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminished from ages 40 to 70 years. The balance of benefits and potential harms, therefore, becomes more favourable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice. Although most countries do not actively invite women older than 69 years to attend screening, they do allow them to voluntarily join the screening programme.

Regarding screening women between the ages of 40 and 49, the evidence so far is inconclusive. Altogether, there are 7 RCTs that have included women younger than 50 years, but these trials were not designed specifically to compare the benefit of commencing screening at 40 years with that of starting at 50 years, and they were done using old technology and techniques. The UK Age Trial[56] is the first RCT designed to compare the impact of commencing screening at different ages. The results will be available soon.

Screening Interval

Tabar et al[30] have estimated that 'tumour sojourn times' lengthen with increasing age. The mean sojourn time estimated for women is as follows: 2.4 years for 40- to 49-year-olds, 3.7 years for 50- to 59-year-olds, 4.2 years for 60- to 69-year-olds, and 4.0 years for 70- to 79-year-olds. Data also show that young women are likely to benefit more from annual screening than from screening at 2-year intervals. Shorter screening intervals would result in the detection of tumours at smaller sizes, thereby decreasing mortality. The cost of screening, however, would also increase. In most countries, the screening interval is 2 years. A RCT conducted in the UK,[57] however, showed that shortening of the 3-year screening interval in the 50- to 62-year age group would be likely to have a relatively small effect on breast cancer mortality.[57] The researchers suggested that improvements to the screening programme would be targeted more productively on areas other than the screening interval, such as improving the screening quality.

Percentage of Target Population Screened

It is generally accepted that a compliance rate of 70% or more of at-risk individuals is required for an effective breast cancer screening programme. The compliance in different countries varies. Countries that invite women to attend screening have a higher compliance rate than those that practise self-referral.

Financing Method

All screening programmes are financed by governments, except for that of Singapore, which uses a copayment method. The copayment method would relieve a part of financial burden of the government.

Quality Assurance

All countries that perform population screening have strict quality control measures. These measures include site visits and accreditation requirements that are organised at a national level. In some countries, quality enforcement is incorporated into national law.

LIMITATIONS AND RISKS OF SCREENING

Apart from its financial implications, mammography screening has limitations and risks. False-negative results occur in 10% to 15% of cases, which results in missed cancers. False-positive results also occur, requiring patients to undergo additional breast imaging (e.g., mammography views, ultrasonography) or breast biopsy examinations. This additional testing would also cause anxiety to the patient. Christiansen et al[58] found that the cumulative risk of a false-positive mammogram over time varies substantially. The risk of false-positives decreased with increasing age and increased with the number of breast biopsies, a positive family history of breast cancer, oestrogen use, time between screenings, a lack of comparison with previous mammograms, and the radiologist's tendency to call mammograms abnormal. By the ninth mammogram, the risk can be as low as 5% for women with low-risk variables and as high as 100% for women with multiple high-risk factors.

Another concern is overtreatment. Mammography screening leads to increased diagnosis of ductal carcinoma in situ (DCIS). Although DCIS is a significant

risk factor for invasive breast cancer and is believed to precede its development, a substantial proportion of DCIS cases will remain non-invasive and may never become life-threatening. Still, all cases of DCIS require full diagnostic investigation and treatment. The problem is not with mammographic screening itself, but with our ignorance to distinguish cases of DCIS that will become invasive and those that will not. With a better understanding about DCIS, we should be able to manage DCIS more appropriately.

There is also a risk of radiation, although with advances in technology, the risk of radiation-induced cancer is small compared with the benefit of breast screening. It should be noted that the health risk from screening increases and its benefit decreases as the incidence of breast cancer in the population concerned decreases. One should bear this in mind in the screening of Asian women, who have a lower incidence of breast cancer than western women.

NEWER MODALITIES IN SCREENING

New modalities in breast imaging emerge as technology advances. Can these add to the efficacy of mammogram in the screening of breast cancer? Can these new modalities replace mammogram in breast cancer screening?

Digital Mammography

Digital mammography can offer several potential advantages. The images can be stored and transferred electronically, and the method has a wider latitude than film-screen mammography and can be manipulated to correct for problems in exposure without producing another mammogram. Also, it can be used in combination with computer-aided detection (CAD). The difference in cancer detection rate between full-field digital mammography and screen-film mammography is not significant, but full-field digital mammography has a significantly lower recall rate.[59] A digital mammography machine is much more expensive than a conventional screen film mammography machine. This will limit its use in population screening.

Computer-aided Detection

It had been reported that the use of CAD in screening mammograms leads to as much as a 19.5% higher cancer detection than a single reading.[60,61] This method can therefore be used in place of a second reader to improve the sensitivity in screening. However, not all CAD systems have the same efficacy, and not all radiologists will benefit from CAD. General radiologists will find more benefit from CAD than breast specialists. In addition, CAD may also slow down the workflow because of extra steps needed to digitise films.

Ultrasonography

Ultrasound examination can detect lesions not seen in mammograms. It is especially useful for dense breasts. Ultrasonography has the advantage of not involving radiation. But it has high operator variability and is poor in detecting microcalcification. Furthermore, it demands too much of physicians' time and is thus expensive as a screening tool. Ultrasonography, however, is a useful adjuvant in the evaluation of clinically or mammographically detected breast lesions.

Magnetic Resonance Imaging

A recent report showed that magnetic resonance imaging (MRI) is useful in screening high-risk women.[62] Although it is more sensitive than mammography, MRI is less specific. It is also expensive — more expensive if one considers the generation of more false-positive results compared with mammography. In addition, MRI examination techniques are not yet standardised. As with ultrasonography, MRI does not involve radiation. But, also like ultrasonography, it is poor in the detecting microcalcification. Lesions that are solely detected by MRI can be followed up or undergo biopsy examination only with the use of MRI. The cost of MRI makes it unsuitable for population screening.

CONCLUSION

Mammography with or without clinical breast examination remains the gold standard for breast cancer screening. Mammography screening will reduce breast cancer mortality. However, its benefit decreases and harm increases as the incidence of breast cancer decreases. It is important that women be informed about the potential benefits, risks, and limitations when they undergo breast cancer screening.

REFERENCES

1. Ferlay J, Bray F, Pisani P, Parkin DM. Globocan 2000, Cancer incidence, mortality and prevalence worldwide. International Agency for Research on Cancer, World Health Organization. Geneva: IARC Press; 2001.
2. Shapiro S, Venet W, Strax P, et al. Periodic screening for breast cancer: the health insurance plan project and its sequelae, 1963–1986. Baltimore: John Hopkins University Press; 1988.
3. Andersson I, Aspegren K, Janzon L, et al. Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial. BMJ 1988;297:943-948.
4. Nystrom L, Rutqvist LE, Wall S, et al. Breast cancer screening

with mammography: overview of Swedish randomised trials. Lancet 1993;341:973-978.
5. Tabar L, Fagerberg CJ, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography. Lancet 1985;1:829-832.
6. Roberts MM, Alexander TI, Anderson TI, et al. Edinburgh trial of screening for breast cancer: mortality at seven years. Lancet 1990;335:241-246.
7. Frisell J, Eklund G, Hellström L, et al. Randomized study of mammography screening — preliminary report on mortality in the Stockholm trial. Breast Cancer Res Treat 1991;18:49-56.
8. Bjurstam N, Bjorneld L, Duffy SW, et al. The Gothenburg breast screening trial: first results on mortality, incidence, and mode of detection for women ages 39–49 years at randomization. Cancer 1997;80:2091–2099.
9. Miller AB, Baines CI, To T, Wall C. Canadian National Breast Screening Study: I. Breast cancer detection and death rates among women aged 40-49. Can Med Assoc J 1992;147:1459-1476.
10. Miller AB, Baines CI, To T, Wall C. Canadian National Breast Screening Study: 2. Breast cancer detection and death rates among women aged 50-59. Can Med Assoc J 1992;147:1477-1488.
11. Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? Lancet 2000;355:129-134.
12. Andersson I, Janzon L. Reduced breast cancer mortality in women under age 50: updated results from the Malmo Mammographic Screening Program. J Natl Cancer Inst Monogr 1997; 22:63-67.
13. Duffy SW, Tabar L. Screening mammography re-evaluated Lancet 2000;355:747-758.
14. Olsen O, Gotzsche PC. Screening for breast cancer with mammography. The Cochrane Database Syst Rev 2001;4: CD001877.
15. Olsen O, Gotzsche PC. Cochrane review on screening for breast cancer with mammography. Lancet 2001;358:1340-1342.
16. Horton R. Screening mammography—an overview revisited. Lancet 2001;358:1284-1285.
17. Kolata G. Study sets off debate over mammograms' value. New York Times; 9 Dec 2001:1.
18. Kolata G. Expert panel cites doubts on mammogram's worth. New York Times; 24 Jan 2002.
19. American College of Radiology, American College of Radiology website; 2002, <http://www.acr.org>.
20. National Cancer Institute (NCI), United States. Statement on mammography screening. NCI; 2002, <http://www.nci.nih.gov/newscenter/mammstatement31jan02>.
21. An open letter to women and their physicians. New York Times; 31 Jan 2002.
22. Miettinen OS, Henschke CI, Pasmantier MW, Smith JP, Libby DM, Yankelevitz DF. Mammographic screening: no reliable supporting evidence? Lancet 2002;359:404-405.
23. Department of Health and Human Services (HHS), United States. HHS affirms value of mammography for detecting breast cancer. HHS; 2002, <http://www.hhs.gov/news/press/2002pres/20020221.html>.
24. International Agency for Research on Cancer (IARC). Mammography screening can reduce deaths from breast cancer. IARC; 19 Mar 2002, <http://www.iarc.fr/ENG/Press_ Releases/pr139a.html>.
25. Nystrom L, Andersson I, Bjurstam N, et al. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. Lancet 2002;359:909-919.
26. European Institute of Oncology. Statement from the Chair. European Institute of Oncology; 2002, <http://www.ieo.it/inglese/didattica/state_1.htm>.
27. US Preventive Services Task Force (USPSTF). Screening for Breast Cancer. USPSTF; 2002, <http://www.ahrq.gov/clinic/uspstf/uspsbrca.htm>.
28. Agency for Healthcare Research and Quality. Screening for breast cancer. Recommendations and rationale. Agency for Healthcare Research and Quality; 2002, <http://www.ahrq.gov/clinic/3rduspstf/breastcancer/brcanrr.htm>.
29. USPSTF. Recommendations and rationale: screening for Breast Cancer. USPSTF; 2002, <http://www.ahrq.gov/clinic/3rduspstf/breastcancer/brcanrr.htm>.
30. Tabar L, Vitak B, Chen HH, et al. The Swedish Two-County Trial twenty years later. Updated mortality results and new insights from long-term follow-up. Radiol Clin North Am 2000; 38:625-651.
31. Alexander FE, Anderson TJ, Brown HK, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. Lancet 1999;353:1903-1908.
32. Frisell J, Lidbrink E, Hellstrom L, Rutqvist LE. Follow-up after 11 years: update of mortality results in the Stockholm mammographic screening trial. Breast Cancer Res Treat 1997;45: 263-270.
33. Bjurstam N, Bjorneld L, Warwick J, et al. The Gothenburg Breast Screening Trial. Cancer 2003;97:2387-2396.
34. Miller AB, To T, Baines CJ, et al. Canadian National Breast Screening Study-1: Breast cancer mortality after 11 to 16 years of follow-up. A randomized screening trial of mammography in women age 40 to 49 years. Ann Intern Med 2002;137:305-312.
35. Miller AB, To T, Baines CJ, et al. Canadian National Breast Screening study-2: 13-year results of a randomized trial in women aged 50-59 years. J Natl Cancer Inst 2000;92:1490-1499.
36. Garne JP, Aspegren K, Balldin G, Ranstam J. Increasing incidence of and declining mortality from breast carcinoma Trends in Malmö, Sweden, 1961-1992. Cancer 1997;79:69-74.
37. Tabar L, Yen MF, Vitak B et al. Mammography service screening and mortality in breast cancer patients: 20-year follow-up before and after introduction of screening. Lancet 2003;361: 1405-1410.
38. Blanks RG, Moss SM, McGahan CE, Quinn MJ, Babb PJ. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990-8: comparison of observed with predicted mortality BMJ 2000;321:665-669.
39. Jonsson H, Nystrom L, Tornberg S, Lenner P. Service screening with mammography of women aged 50-69 years in Sweden: effects on mortality from breast cancer. J Med Screen 2001;8: 152-160.
40. Paci E, Duffy SW, Giorgi D, et al. Quantification of the effect of mammographic screening on fatal breast cancers: The Florence Programme 1990-96. Br J Cancer 2002;87:65-69.
41. Duffy SW, Tabar L, Chen HH, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. Cancer 2002;95:458-469.
42. American Cancer Society. American Cancer Society guidelines for breast screening: update 2003. Atlanta, GA: American Cancer Society; 2003.
43. National Health Service (NHS), United Kingdom. The NHS cancer plan 2003. London: NHS; 2003.
44. Morison BJ. Screening for breast cancer (including 1998 rewording), Canadian Task Force on Preventive Health Care, 2004, <http://www.ctfphc.org>.
45. Wang SC. The Singapore National Breast Screening Programme: principles and implementation. Arm Acad Med Singapore 2003; 32:466-476.
46. BreastScreen Australia. BreastScreen Australia achievement report 1997 and 1998. Sydney: BreastScreen Australia; 2000,

<http://www.aihw.gov.au/publications/index.cfm/title/5991>.
47. International Breast Cancer Screening Network (IBSN). IBSN website, <http://appliedresearch.cancer.gov/ibsn>.
48. Blanks RG, Moss SM, Wallis MG. Use of two view mammography compared with one view in the detection of small invasive cancers: further results from the National Health Service breast screening programme J Med Screen 1997;4:98-101.
49. Barton MB, Harris R, Fletcher SW. The rational clinical examination. Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? JAMA 1999;282:1270-1280.
50. Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self–examination in Shanghai: final results. J Natl Cancer Inst Cancer Spectrum 2002;94:1445-1457.
51. Semiglazov VF, Moiseyenko VM, Bavli JL, et al. The role of breast self–examination in early breast cancer detection (results of the 5–years USSR/WHO randomized study in Leningrad). Eur J Epidemiol 1992;8:498-502.
52. Ciatto S, Del Turco MR, Morrone D, et al. Independent double reading of screening mammograms. J Med Screen 1995;2: 99-101.
53. Thurfjell EL, Lernevall K, Taube AA. Benefit of independent double reading in a population-based mammography screening program. Radiology 1994;191:241-244.
54. Beam C, Sullivan D, Layde P. Effect of human variability on independent double reading in screening mammography. Acad Radiol 1996;3:891-897.
55. Anttinen I, Pamilo M, Soiva M, Roiha M. Double reading of mammography screening films: one radiologist or two? Clin Radiol 1993;48:414-421.
56. United Kingdom National Health Service (NHS), Cancer Screening Programmes. Key research in breast screening. NHS; 2004, <http://www.cancerscreening.nhs.uk/breastscreen/research.html#age-trial>
57. The Breast Screening Frequency Trial Group. The frequency of breast cancer screening: results from the UKCCCR Randomised Trial. Eur J Cancer 2002;38:1458-1464.
58. Christiansen CL, Wang F, Barton MB, et al. Predicting the cumulative risk of false-positive mammograms. J Natl Cancer Inst 2000;92:1657-1666.
59. Lewin JM, Hendrick RE, D'Orsi CJ, et al, Comparison of full-field digital mammography with screen-film mammography for cancer detection: results of 4,945 paired examinations. Radiology 2001;218:873-880.
60. Warren-Burhenne LJ, Wood SA, D'Orsi CJ, et al. Potential contribution of computer-aided detection to the sensitivity of screening mammography. Radiology 2000;215:554-562.
61. Freer TW, Ulissey MJ. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. Radiology 2001;220:781-786.
62. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004;351: 427-437.