In Korea, breast cancer ranks the 3rd most common female cancer and accounts for 12% (1). The prevalence of breast cancer is 10.9 per 100,000 women (2) and incidence is reportedly increasing (1,2).

Breast self examination, clinical examination, and film mammography are known to be the best methods for early detection of breast cancer. Although the mammographic sensitivity for breast cancer detection was quite low in early 60’s and 70’s, by the development of imaging diagnostic tools and techniques, the rate of minimal cancer detection is increasing, however, surgeon’s role for cancer diagnosis is still remaining.

We retrospectively reviewed files of 14393 women who visited Yonsei Health Center and took mammogram for screening during a period of August 1994 to July 1998. We also analyzed records of patients who visited breast clinic at Yonsei University Medical Center for screening without subjective symptom and took clinical breast examination (CBE) with a mammogram during a period of January of 1997 to December of 1998.

Of these 14,393 Health Center-based screening women, 4th decade (30.3%) was the most common and then 6th (29.8%), 5th (27.4%), 7th (11.2%), and 8th (1.4%) was the least. Among them 96 were disclosed category IV (93 cases) or V (3 cases) on mammogram and only 67 women were referred to our breast clinic and underwent CBE. On CBE 18 lesions were palpable and 7 turned out malignancy. CBE was negative for the remaining 49, however, ten were finally diagnosed as malignancy. The overall cancer detection rate was 1.18 per 1,000 women. During the same period, we found one mammogram-missed breast cancer patient who was 52 years of age.

In contrast to Health Center-based screening we analyzed 489 OPD-based screening patients. 255 cases were negative on both CBE and mammogram. The other 234 cases showed abnormal findings either on CBE or mammogram or on both of them. Among 234 patients with abnormal findings, 31 were detected by both CBE and mammogram, 183 by mammogram, and 20 by CBE alone. Among 183 abnormal findings detected by mammogram alone, benign mass (66 cases) was the most frequent finding and then benign calcification (63 cases) and the other 54
cases (32 microrcalicification, 9 microcalcification with mass, and 13 mass without microcalcification) suspected as malignancy. Interestingly, 13 (26%) of 50 benign mass lesions showed normal ultrasonographic findings. Most of benign-suggesting lesions were recommended to follow-up except 10 cases which were excised and turned out fibroadenoma or fibrocystic disease. We performed tissue diagnosis for the 54 malignant-looking lesions, 25 of them were cancer, 29 fibrocystic disease or fibroadenoma. Twenty-four of 25 cases of malignancy showed microcalcification (15 pure microcalcification and 9 microcalcification with mass) on their mammograms. These results suggest that microcalcification with mass is one of the most reliable finding to diagnose malignancy, and confirm that mammogram is the most sensitive tool to detect microcalcification, which is one of the earliest sign of breast cancer and ultrasonogram can be used as a complementary tool.

Among 20 cases of mammogram-missed lesions detected by CBE alone; 5 were found in 20s’, 5 in 30s’, 9 in 40s’, and 1 in 50s’. Six of them, found in patients aged 36, 38, 40, 41, 43, 45, and 52 years, were cancer and all of them showed dense breast pattern. Fourteen of them were benign. Therefore, false negative rate of mammogram was 45.5% for 20s’, 8.9% for 30s’, 6% for 40s’, and was 2.9% for 50s’. There was no case in women aged over 60 years. We performed ultrasonogram for the patients who showed negative results on both mammogram and CBE. Among 202 of 255 women, 134 cases showed negative result on ultrasonogram as well, but 68 cases showed abnormal ultrasonographic findings. Among those 68, 12 cases were excised because of malignant suspicion, and those were turned out fibroadenoma (7 cases) or fibrocystic disease (5 cases). Ultrasonogram detected some abnormal findings in 50% of 20s’ and 30s’, 29.2% of 40s’, 35% of 50s’, and 11.1% of 60s’ who showed no abnormal findings either on CBE or mammogram. These data support others’ reports that mammogram is less sensitive to detect abnormal lesions in younger women and suggest that the incidence and possibility of false negative result by mammogram is higher among younger aged group (under age of 50 years) than among older age of over 50. These results strongly suggest younger breasts need more careful clinical breast examination and additional diagnostic tool like ultrasonogram to prevent false negative results.

The death rate among women over 50 years of age was reduced by about 30% by carrying out regular screening mammography (3, 4). Smart et al (5) reported the breast cancer death rate was reduced by 24% in women in their 40s who underwent clinical examination and mammography annually. In 1997, however, National Institute of health Consensus Development Conference concluded that the data currently available do not warrant a universal recommendation for mammogram for all women in their forties (6). Moreover, Elmore et al (7) described a high rate of false positive results of breast screening. Over a period of 10 years, nearly one third of the women screened had at least
one false positive mammogram or clinical breast examination. However, the way to reduce the rate of false positive results would consequently increase the rate of false negative results. Smart et al (8) described that because 40% of all the cancers diagnosed were detected in the first screening with mammogram, the cost-effectiveness of subsequent screening is similar for women aged 45 to 49 years compared with women older than 50 years. Survival was slightly more favorable among younger women than among older women, which may be caused by the shifts in extent of disease at the time of diagnosis.

Most mammographic breast screening programs showed a very similar recall rate of 8 to 10.6% and cancer detection rate of 3.8 to 6.2 per 1,000 women (9-13). Interestingly, a study of breast screening by CBE alone in Japan showed 2.8% of recall rate and 0.06% of cancer detection rate (14). Satomi et al (15) reported that a higher cancer detection rate of 0.22% by a combination of mammogram and CBE in comparison to that of 0.10% by CBE alone.

In addition to film mammogram, a careful clinical breast examination by an expert would be an integral part for the screening procedure. BCDDP report that the rate of cancer diagnosis with PE alone was 10.8% among women aged 40 to 49 years, 5.2% among women aged 50 to 59 years, and almost same among women aged over 60-69 years, supports the necessity of clinical examination.

The Korean Cancer Registry reported that over 20% of all breast cancer in Korea have occurred in women under 40. Therefore, the usage of mammography for these women might be limited.

In conclusion, mammogram is one of the best method for breast screening and a careful CBE is also essential to reduce false negative results. In certain case, ultra-mammogram would be an additional tool for the breast screening.

References

10. The comparative value of mammographic screening for women 40-49 years old versus women 50-64 years old. AJR 164: 1099, 1995
There is widespread agreement among medical organizations and practitioners that routine mammographic screening is beneficial for women age 50 and older, primarily due to the strong scientific evidence demonstrating statistically significant breast cancer mortality reduction among women invited for screening in multiple randomized controlled trials. However, the role of mammographic screening for women age 40-49 remains somewhat controversial, primarily because the evidence of benefit is less consistently convincing.

**Evidence of Mammographic Screening Benefit**

A full understanding of the controversy must start with a review of the scientific evidence, principally that involving the several population-based randomized trials of screening efficacy. Results of all 8 individual trials show consistent evidence of reduced breast cancer deaths in screening versus control groups, the mortality reduction due to screening being statistically significant in several of the trials. These findings apply to the entire studied populations, with the lower limit of age ranging from 40 to 45 and the upper limit of age ranging from 64 to 74. When the data are analyzed as the trials were designed, this evidence indicates the existence of a screening benefit, extending from age 40-45 through age 64-74.

Controversy begins with the retrospective analysis of results by age subgroups, a method of evaluation unanticipated in the design of all but one of the trials, which were planned with statistical power sufficient only for whole-group examination of data. As a means to judge the end results of the trials, such retrospective subgroup analysis, by reducing the power of the results, considerably increases the likelihood that an observed benefit will not achieve statistical significance. The limitation is most substantial for women age 40-49, because breast cancer incidence (hence the breast cancer death rate) is lower among these women than older women, and because a relatively small proportion of women in the randomized trials were in their forties. Therefore, although an ample screening benefit indeed has been observed in 5 of the 8 trials for women age 40-49, with breast cancer mortality reductions ranging from 22% to 49%, it is hardly surprising that only two of these trials show a statistically significant result. The trials simply were not designed with sufficient power to show a statistically significant difference for women age 40-49.

A widely accepted method to clarify such an equivocal situation is to combine the data from the randomized trials, by meta-analysis, in an attempt to increase statistical power. The most recent meta-analysis indicates an 18% mortality reduction in the screened versus control group for women age 40-49, with results achieving statistical
significance (p < .05). However, meta-analysis is most meaningful if it evaluates trials that are similar in design. Seven of the 8 trials have somewhat similar study design in that women from defined populations were randomized, individually or by community, and then were offered or not offered screening. The Canadian National Breast Screening Study (CNBSS), on the other hand, involved self-selected subjects (volunteers), all control-group women had an initial screening clinical examination, and randomization took place after this clinical breast examination. For these reasons, the most recent meta-analysis also presents results excluding the CNBSS data, showing a 24% mortality reduction in the screened versus control group, an even more statistically significant result (p < .01). Demonstration of statistical significance is remarkable indeed, given the numerous deficiencies in design and execution not just in the CNBSS but in all the trials. These deficiencies likely have lessened the demonstrated benefit, perhaps substantially.

Because mammography in the randomized trials was for the most part completed at least 10 years ago, and because of subsequent major advances in mammographic imaging, some investigators have supplemented evidence from the trials with reports of intermediate screening outcomes in large service screening programs using more modern mammography. These results, although limited by the absence of matched populations of unscreened women and unavailability of mortality data, show that the major prognostic factors (median tumor size, axillary lymph node status, tumor stage) of screening-detected breast cancers for women age 40-49 are at least as favorable as those for women age 50-64, the age range for which screening is widely accepted.

In summary, for women age 40-49, data from randomized trials (limited by retrospective subgroup analysis, reduced statistical power, and use of older mammographic techniques) show a statistically significant but somewhat lower reduction in mortality than for older women. Furthermore, data from modern mammography demonstration projects (limited by lack of control group comparison and unavailability of mortality results) show evidence from which screening benefit also can be inferred, with the magnitude of benefit equivalent to or exceeding that already proved for older women.

Other Factors Affecting the Endorsement of Mammographic Screening

There are factors other than scientific analysis which also contribute to the decision of whether to endorse the routine mammographic screening of women age 40-49. One such factor is economic, specifically, the weighing of cost versus benefit. A common criticism of mammographic screening involves the costs induced by false-positive interpretations, especially the cost of interventional procedures for otherwise undetected lesions that prove to be benign. However, recent advances in mammographic imaging now permit substantial reductions in the number of benign surgical biopsies for screening-detected lesions. The efficacy of periodic mammographic follow-up as an alternative to biopsy for “probably benign” lesions (those having a very low likelihood of malignancy) has been demonstrated by large-scale prospective studies; this approach increases the positive predictive value for open surgical biopsy from 20%-25% to approximately 40%. Percutaneous imaging-guided tissue sampling (by fine-needle aspiration or core biopsy) also can serve as an alternative to surgical biopsy. This approach usually is used for nonpalpable lesions that carry a higher level of suspicion for
malignancy; it has been reported to increase the positive predictive value for open surgical
biopsy to 60%-85%. Increasing acceptance and utilization of these reduced-cost
approaches is developing as we enter an era of managed care and capitation payment.
Estimates of the current cost-effectiveness of mammographic screening are
favorable. Because of differences in cost estimates and methods of measuring benefits, it
is difficult to compare the wide range of findings from various published studies. The few
reports which describe age-related differences consistently show that mammographic
screening is less cost-effective at ages 40-49 than in women age 50-69. However, the
marginal cost per year of life saved for the age 40-49 group is similar to that of other
widely accepted medical prevention and treatment programs, including screening and
treatment of hypertension, coronary artery bypass surgery, and hemodialysis for renal
disease.
Political factors also affect the decision of whether to endorse routine
mammographic screening at ages 40-49. These apply primarily to those individuals
controlling government agency policies, who must make the difficult decisions of how to
allocate limited funds for health care, but who also are accountable to an electorate that
expects more in government-supported services than it is willing to pay for in taxes (since
mammographic screening is less cost-effective at ages 40-49 than in older women,
withdrawal of support for screening at younger ages appears to be an attractive means of
reducing costs). In the United States, the federal government also supports screening
women in their forties, in the form of guidelines set forth by the National Cancer Institute,
and in practice through the Medicare program.
Suggested Reading


Breast cancer is the commonest cancer and the commonest cause of cancer death in Australian women with >2500 women dying of the disease each year. It is a disease of increasing age and the lifetime risk (75 years) of developing breast cancer for an Australian woman is approximately 1 in 13. How to prevent breast cancer is unknown, and despite changes in breast cancer management, the survival rates in Australia have not significantly altered over the last 50 years. With this knowledge in mind, 11 breast cancer screening projects were established in Australia between 1987 and 1990. The results of their evaluation and of a review of international screening studies led the Australian Commonwealth, State and Territory Health Ministers to agree on a National Program for the Early Detection of Breast Cancer (now called Breast Screen Australia). This National Program began in 1991 and is funded jointly by the Commonwealth, State and Territory Governments.

The basic unit of the National Program is the Screening and Assessment Service (SAS). The SAS consists of a single Assessment Centre to which multiple Screening Units (fixed and mobile) are attached. All such services are managed by the State or Territory Coordination Unit. These State and Territory Coordination Units are under the central management of the National Coordination Unit.

BreastScreen Australia is a well integrated and coordinated program with planning and monitoring in areas including data management, quality assurance and accreditation.

The BreastScreen aims are outlined in the National Accreditation Requirements and include:
1) to maximise the early detection of breast cancer in the target population
2) to ensure significant reductions in breast cancer morbidity and mortality
3) to ensure screening is provided in dedicated, accredited Screening and Assessment Services
4) to ensure equitable access for the target population
5) to ensure the services are acceptable and appropriate to the needs of the eligible population.
6) to achieve high standards of management, service delivery, monitoring, evaluation and accountability.

To ensure that these aims are achieved the National Program carries out a detailed accreditation and monitoring process. Free screening by 2 view mammography only is available every 2 years for all women over 40 years of age. However the target population is women 50 to 69 years ie. the group at high risk of breast cancer and proven to benefit from mammography screening. While a doctor's referral is not essential,
GPs are encouraged to be involved in all aspects of screening. Screening films are read by 2 readers, at least one of whom is a radiologist. Any woman with a screen detected abnormality is recalled to the Assessment Centre for evaluation by a multidisciplinary team including radiologists, pathologists and surgeons. The Screening and Assessment Service is financially responsible for all activities up to the point of diagnosis and therefore funds cytology, core biopsies and surgical diagnostic biopsies. Treatment funding and quality control however are not included within the National Program.

With full participation it is anticipated that approximately 1 million women will be screened annually at a cost of approximately $100 million per year. Between 1 January 1995 & 31 March 1997 just over 1.2 million women were screened. This represents a biennial participation rate of 20% for women aged 40-49, 54% for 50-69, and 23% for 70-79. Each quality-adjusted-life-year-saved by mammographic screening is estimated to cost approximately $11,000. This is considered a relatively small cost in comparative health terms, and well worthwhile in view of the major cost of breast cancer to the Australian community.

References


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THE RISE AND FALL OF SWEDISH MAMMOGRAPHY SCREENING

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The Swedish National Board of Health and welfare started to recommend mammography screening in 1986. The decision was based on the positive results from the WE-trail (Tab recommended for all women between 40 and 74 years, some years later this recommendation was modified to 50 - 69 years. This decision was based on the lesser effect on breast cancer mortality observed in the younger age group. For the elderly women the attendance rate was considered too low.

Other well designed Swedish screening studies have been able to reproduce the first positive results. Up to date a significant reduction in mortality has been achieved, also for women less than 50 years of age.

However, in the future there will be several threats to the national screening program and there are many indications that the successful program may collapse. One important reason is the economical situation for many counties that may lead to reduction of the screening programmes. Another problem is the future shortage of radiologist specialised in mammography.
Expected Screening System for Breast Cancer in Japan

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Breast cancer is one of the major cancers in females in Japan. The mortality of breast cancer is ranked in the forth in the major cancers in females, but the incidence of it is in the first rank now. For primary prevention of the breast cancer it is proposed to avoid high risk factors, such as excess fat and calorie intake and high maternal age at the delivery of the first child. But these may not necessarily be easy from socioeconomic view points. So, the secondary prevention; breast cancer screening has been promoted.

Now, I want to make a short report of the present breast cancer screening in Japan and introduce a new current using mammography. Furthermore I want to make mention on the screening methods for women under fifty years old.

History of the breast cancer screening in Japan and its estimation

In Japan, breast cancer screening using palpation has been done since 1987, and it has been granted national assistance by law.

The examinees amounted to 3,125,516 (7.66% of women aged 30 years or older in Japan), of whom, 130,669 required further examination in 1995. 2,762 patients with breast cancer were found, and detection rate of breast cancer was 0.09% (1).

Now, the breast cancer screening using palpation has been held for this twelve years. It is the time the effect of the breast cancer screening must be evaluated.

A very important report for cancer screening was published in March 1998. It was written by the study group in the evaluation of the effectiveness in the various cancers screening system, that was supported by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare of Japan. In the report, it was said that “in the breast cancer screening using palpation, the effectiveness in the reduction of the mortality risk can be recognized in asymptomatic examinee in the study of comparison of the survival rate. And as trustworthy evidence of effectiveness in breast cancer screening using mammography is recognized, it is recommended that breast cancer screening using mammography must be realized as soon
In this manner, screening using palpation has been done in recent twelve years. On the other hand, the investigation about the induction of the mammography has been continued by a chain of investigation group supported by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare for these 12 years.

In the early years, comparison of the screening methods was done. Next, a trial study of the breast cancer screening using mammography was done. And in the last 4 years, materials and interval of mammographic screening were discussed. Furthermore, quality control of the mammographic apparatus, film reading, total control system and so on were discussed.

The objects of the mammographic screening are the women aged 50 years or more and the frequency of it is biennial. In addition, for women aged 40 years or more in the group of high risk for breast cancer, biennial mammographic examination is encouraged added to usual annual palpational examination.

This mammographic screening plan was made grounded on the data of Miyagi Trials (3).

Now, we make our effort to quality control of mammography and mammographic diagnosis. A short course of mammography for doctors and radiological technicians was planned and put into practice supported by Japan Association of Breast Cancer Screening.4) 5) And we made a mammography guideline supported by Japan Radiological Society and Japanese Society of Radiological Technology (4-6).

**Incidence of the breast cancer in Japan by age group and breast cancer screening**

The incidence of the breast cancer in Japanese women is high in the forties. And the mortality rate is also high in the forties. So, the appropriate selection of the screening methods for forties is very important. But, no special counterplan has not been decided by now for this age group.

Judging from the composition of the breast, it is said that the rate of dense breast is high in Japanese women than in western countries. So, it is estimated that the construction of effective breast cancer screening system is more difficult to obtain in Japan than in the western countries. And also it is especially difficult in the forties than aged group of 50 years or more.

On the one side, the mammographic screening method must be pursued with higher quality control, and the other hand, other screening method must be developed to adapt. Ultrasonographic examination is one of the most possible method.
The subject of the Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare of Japan concerned with breast cancer in 1999 was “the evaluation of the proper breast cancer screening methods under 50 years of age”. My study group applied to this theme and could be adopted. We are going to pursue the possibility of employment both ultrasonography and mammography. And Computer Aided Diagnostic System for both methods will be useful for screening abnormalities.

The problem of the screening system by ultrasonography

The ultrasonography is the excellent method in the screening of the abnormalities and diagnosis of the lesions. It can also presume the histopathological findings to certain degree and this advantage is most excellent compared with other methods.

But, regarding the mass screening, the other points of view is required. In the mass screening, there are various requests. For example, they are diagnostic ability, safety, objectivity, easy management, low cost for apparatus and management, easily trained, easy quality control and so on.

In these problems, next points are the most important problems.

1. Who is the examiner?
   Medical doctor or technologist?

2. Ultrasonographic apparatus
   Automatic scanner or not?

3. The selection of the recording methods
   Whole breast record or partial record?

These problems are interwined each other. If the technician is selected as examiner, whole breast information will be requested to diagnosis. On this occasion, too many images increase the difficulty in observation of the details. And one more problem is the apparatus to employment. If only the partial images were recorded, the objectivity is the problem. It is the same problem presented by palpation.

Prospection of the mass screening

In the breast cancer screening, proper and rapid judgement is proposed. If either of mammography or ultrasonography is used, many images will be presented to the diagnosticians. The quality of the judgement of the many images in the screening, the CAD may be useful, I guess.
The CAD for the mammograms has been developed in USA and in Japan. We have been attended to this work for about 10 years. The goal of our CAD is the appointment of the abnormalities by mass density and clustered calcifications. And the CAD for the ultrasonography has been also buckled down with the same attitude. Using ultrasonography, too many images can be offered. So, three-dimensional image will be useful for present the information of the abnormality, we consider.

References