PRACTICAL MODALITIES OF AN EFFICIENT SCREENING FOR BREAST CANCER IN THE EUROPEAN COMMUNITY

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Editor:

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FOREWORD

Breast cancer is the most common cancer in women. In Belgium it amounts to one third of all women's cancers. After the HIP Study, several other trials have shown that a 30% mortality reduction by systematic screening is possible. However, in most European countries screening is not yet systematically offered to women. In some European countries, however, – the Federal Republic of Germany, the Netherlands and the United Kingdom – screening on a regular service level is starting to be introduced on a nationwide scale.

At the beginning of the European year of information on Cancer, the international symposium organized by the Association Against Cancer (Belgium) made it possible to gather essential information about conditions for an efficient application of breast cancer screening in Europe.

Data from the Canadian National Breast Cancer Screening Study and the UK Trial on Breast Cancer Detection opened the debate about the role of physical examination in breast cancer screening.

Review of data from the Swedish Two County Study and the Florence Trial enabled the controversy of screening interval and age to be dealt with.

Since the 1960's, mammographic equipment and accessory techniques have been spectacularly improved, increasing sensitivity of radiographic screening from 60% to 97% while reducing radiation exposure. Technical requirements for optimal quality are illustrated by figures from Nijmegen (the Netherlands) and the United States.

Histological and cytological results from ongoing studies in the Netherlands, the United Kingdom and Italy make it possible to introduce the application of special techniques for work-up of suspected lesions, such as stereotactical fine needle aspiration and specimen radiography. These techniques permit increased specificity and sensitivity of the overall programme, thus reducing the number of women submitted to unnecessary procedures or falsely reassured.

Cost-benefit evaluations are very important in deciding about the introduction of national programmes. Data from Malmö (Sweden) show that preexisting diagnostic services and differences in mortality should be taken into account to evaluate the influence of planned screening. The necessity of regular monitoring of screening results is illustrated by its organization in the Federal Republic of Germany. Cost evaluations are introduced by data from the USA and the Netherlands.

In preparation for this conference, the Association Against Cancer (Belgium) invited specialists from all Belgian universities and scientific societies in order to discuss the application of breast cancer screening in Belgium. A postal inquiry was undertaken to study the availability of mammographic equipment and accessory techniques in Belgium. These data focus the discussion on the concrete situation in the field.

High participation in screening is essential for any quality programme to

achieve effectiveness in the population as a whole, as illustrated by data from the United Kingdom.

Suggestions formulated during this conference will help the Association Against Cancer (Belgium) in its fight to increase compliance of the population with the 10th rule of the European Code: 'Check your breasts regularly and, if possible, undergo mammography after age 50.'

Following this symposium, our Association will continue to help scientific organizations in Belgium (and also in other European countries, upon request) by providing logistic support for scientific research and by diffusing the principles of high quality screening in the medical profession. Our Association will also, on the basis of the results of this symposium, collaborate with the Belgian health authorities to develop an efficient screening policy. The Association will, especially, advise the public and stimulate its participation. Finally, it will help to set up an adequate data collection.

Finally, I would like to take advantage of this opportunity to thank the various speakers and other contributors to the symposium, in particular, my collaborators Mrs. Véronique Kreit-Bernard and Dr. Léo Pas, without whom this symposium could not have taken place.

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Although often recommended as an important component of screening for breast cancer, physical examination of the breasts by health professionals is not well evaluated in current medical literature. It is important to emphasize that screening is not diagnosis. Screening seeks to identify the probably abnormal in a population which is probably normal. Those labelled 'probably abnormal' can then undergo diagnostic tests.

Physical examination (PE) has been a component of a number of screening programmes and been excluded from others in favour of mammography alone. The possibility of an 'overdiagnosis' bias of screening, that is, the mammographic detection of so-called cancers which would never have presented clinically in the absence of screening, presents a problem in any comparison of physical and mammographic examinations. On the other hand mammography does not detect all breast cancers.

The Canadian National Breast Screening Study (NBSS) (1) offers a unique opportunity to evaluate sensitivity, specificity and positive predictive value (PPV) of physical examination of the breasts in the detection of breast cancer since 50 percent of the participants did not receive mammography (2). The NBSS recruited with informed consent 89,835 women aged 40 to 59 years between 1980 and 1985. To be eligible, women were required to be 40 to 59 years of age, not pregnant, not to have had breast cancer and not to have had a mammogram in the previous 12 months. Recruitment was achieved largely by general publicity in the media, by word of mouth, and in some centers, by personal letters of invitation (3).

The two major research questions were :

1) In women aged 40 to 49 years, what reduction in breast cancer mortality can be observed with combined annual screening (using mammography and physical examination of the breasts) compared to normal community care following a single physical examination of the breasts ?
2) In women aged 50 to 59 years, what is the added contribution of

annual mammography to breast cancer mortality reduction over and above that achieved by annual physical examination alone ?

Fifty percent of all participants were randomly allocated to receive four or five annual mammographic and breast physical examinations plus instruction in breast self-examination (BSE). The remaining 50 percent received only PE and BSE instruction as their screening modality. In this group, 25,620 women aged 40-49 on entry received PE and BSE instruction once and were subsequently followed by a mailed questionnaire. However, 19,965 women aged 50-59 were eligible to receive PE four or five times annually combined with BSE instruction. Total person years accumulated during the screening regimen by June 1988 was 356,283 years, half of which arose from the women who received physical examination alone. Table 1 displays compliance of NBSS participants with their schedules.

The NBSS operated from 15 screening centers in 12 cities in five provinces stretching from the Atlantic to Pacific oceans. At 12 centres there were 77 nurse screen-examiners who performed PE. In 3 Quebec centres, 58 part-time physicians, all but two female, were the screen-examiners.

Both the screen-examiners and NBSS surgeons were given a written protocol for breast examination. The surgeon trained the examiners. The physical examination protocol recommended included :

* Visual examination with subject seated or standing, first with arms relaxed and hanging, then with arms above head and finally arms akimbo with hands pressing into waist.
* Palpation of supraclavicular triangles and axillae in the upright position.
* Palpation of the breasts with subject in upright (except for large-breasted women), supine and oblique positions; use of the finger pads of the first three digits; a rotational movement at each point of palpation; and a spoke search pattern.
* Appropriate arm positions for the subject : in the upright posture, above the head; in the supine posture, first above the head for the medial breast examination and secondly at right angles to the body axis for the lateral breast examination; in the oblique position, ipsilateral hand to forehead.
* Inclusion of entire breast tissue, not just the cone.

In practice, the time required to do only the physical examination varied from five to ten minutes, depending on the size of the breasts and the reactions of the participant.

TABLE 1
NBSS COMPLIANCE WITH SCREENING PROTOCOL *

Screen year	Allocation		
	Mammography plus physical examination	Physical examination alone	Follow-up by annual questionnaire
Screen 2	89.8 (2.9)	89.1 (3.4)	93.3
Screen 3	88.6 (4.1)	87.9 (5.0)	93.7
Screen 4	88.1 (4.9)	87.1 (6.0)	94.3
Screen 5	75.8 (6.0)	75.0 (6.8)	82.8

* Expressed as percentage of those attending Screen 1.
( ) Bracketed numbers refer to the additional percentage of women who declined to be re-screened but who agreed to complete annual epidemiological questionnaires.

The study design required the examiners to decide on the basis of PE alone whether the subject required referral to the NBSS surgeon at a weekly "review clinic". Similarly, the result of the mammographic examination could be referral to review clinic by the radiologist. At review clinic, NBSS surgeons were encouraged either to recommend specific diagnostic procedures such as mammograms and biopsies or to reassure the participant that no further investigation was required. If diagnostic recommendations were made, they were forwarded to the women's physician for him/her to implement.

Three estimates of PE sensitivity and specificity were made, one for the screen-examiners, another for the NBSS surgeons and the third for the NBSS overall. Histologically proven breast cancer, verified by a reference pathologist, was the gold standard to which test results were applied.

1. SCREEN-EXAMINERS

A positive test was an examination which resulted in a referral to review clinic and a negative test, one which resulted in no referral to review clinic.

False negatives were interval cancers occurring within 12 months of the screen in women whom the screen-examiners had not referred to review. False positives included women referred to review with no

known breast cancer in the 12 months following the screen.

In Table 2 estimates for the screen-examiners are displayed for women allocated to receive no mammography. Women aged 40-49 were eligible to receive only one physical examination. Older women returned for annual re-screening. All three estimates are lower for women 40-49 years than 50-59 years. For the older women the low sensitivity at screen 3 was linked to probably false negative calls by examiners in one center for five interval cancers.

TABLE 2
SENSITIVITY, SPECIFICITY AND POSITIVE PREDICTIVE VALUE ASSOCIATED WITH SCREEN EXAMINERS IN NON-MAMMOGRAPHY ALLOCATIONS

Screen year	Sensitivity	Specificity	PPV
Age 40-49 yrs			
1	70.8	84.3	1.5
Age 50-59 yrs			
1	83.3	87.9	3.0
2	71.4	94.0	3.2
3	57.1	95.7	3.6
4	83.3	96.1	2.9
5	77.3	96.0	4.2

2. NBSS SURGEONS

The NBSS surgeons saw only the 5-10 % of participants who had been referred to review clinic for physical and/or mammographic abnormalities. A positive test was defined to be a recommendation made at review clinic. In the absence of cancer, a recommendation for biopsy was a false positive, but whether a recommendation for mammography should be included or excluded as a false positive becomes a matter of opinion. Specificity and PPV are lowered if a mammography recommendation is termed a false positive as is shown in Table 3.

The first estimate given in the columns for specificity and positive predictive value is that resulting when diagnostic mammography is ordered and termed a false positive; the second estimate results when diagnostic mammography is termed a true negative. Overall, the table shows that surgeon sensitivity is higher than for the screen