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Diagnosis and Screening in Breast Cancer; a Review

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ONE OF the dogmas of medicine, as taught to students everywhere, I believe, is that of the importance of early diagnosis. Patients are constantly told not to delay with their symptoms, but seek medical advice as soon as possible. The rationale behind this is, of course, that cure may become impossible if treatment is delayed. My feeling is that to some extent doctors use this reasoning to put the blame on the delaying patients when treatment attempts fail. This is a kind of double talk because now it should be apparent that in many, perhaps most, chronic diseases early treatment in no way alters the biologic course of events. In those cases late diagnosis should be preferable. However, in some cancer sites the known facts about their biology still provides hope that early intervention may alter an otherwise ultimately fatal course. Breast cancer is one of these.

By early breast cancer diagnosis we mean a diagnosis made before the point in time when the woman herself would seek a doctor for a lump she had discovered herself. Interest in early diagnosis spread around 1960, when it was shown that clinically unsuspected small cancers could be detected by the soft-tissue X-ray technique, mammography.

Based on the knowledge that long-term prognosis was clearly correlated to the size of lesion at diagnosis, the rather simple concept of saving lives by finding a cancer while relatively small gave a strong impetus to the development not only of better mammography techniques but of other possible diagnostic methods. This all happened in the 1960s. At the same time the men behind the HIP-study were far ahead in planning their randomized controlled study, which aimed at finding out whether early diagnosis by screening non-symptomatic women by mammography and physical examination could lower the mortality in breast cancer. This, of course, was, and is, the crucial and all-important question. Their early and still persistent finding that it did is the motor behind all subsequent efforts of refining methods and corroborating their evidence, in the face of very strong headwinds of partly uninformed negativism and partly well-founded and intelligent objections regarding negative side-effects and drawbacks of early diagnosis and especially screening—more about this later.

Let us first concentrate on the deceptively simple question of finding an optimum means of diagnosis. Mammography was available, though we can now state, in a definitely primitive form. Reports in the 1960s showed that although mammography could detect small cancers, it also missed quite a number which could easily be detected by palpation, and besides, the radiation dose was on average so high that ultimately doubts about whether risks outweighed possible benefits were very strongly expressed. However, the mammographic technique very quickly developed on two fronts. Image quality improved by leaps and bounds as evidenced by reports of accuracy rates from well-conducted trials, which rose from about 60% to around 95%. Radiation doses lowered to fractions of what they had been and are now not considered to entail significant risks.

Two other diagnostic methods were early in the race. The traditional physical examination is, like the others, a very subjective method in which experience counts for all. Even in the best circumstances this method is not suitable for mass screening, because it cannot appreciably contribute to early diagnosis in the sense we mean, though it is an indispensible part of diagnosis.

Thermography appeared around 1965 and got an overenthusiastic reception as the non-invasive wonder method. That, combined with its commercial success, caused the first critical reports on blind method evaluation to be ignored. These came from Sweden, where thermography was tested in clinical and screening contexts and

fell flat in both. The sensitivity and specificity were both insupportably low. Among the negative findings was the nearly 30% false-positive rate, causing a vast dose of unnecessary mammographies, clinical visits, biopsies and, perhaps most important, anxiety.

In the last few years ultrasound has made considerable progress in general medical diagnostics. In its present state of development it has very little place in breast cancer diagnosis. Ultrasound can discriminate solid tumours from cysts, a feat which can be accomplished much faster and at a far lower cost by fine-needle biopsy.

This all boils down to the fact that the best method we have at our disposal to-day for early breast cancer diagnosis is mammography. Its role in screening has largely been defined in Sweden, first by developing the method of single-view mammography, and the organization which has made mass-screening possible in that country at least, and by the follow-up randomized controlled studies aimed at establishing its impact on mortality, if any.

I must now address the complicated question of breast screening *per se*, define some concepts which tend to confuse the issue and touch on some demands which should be met by the conscientious screener.

I have already mentioned sensitivity and specificity. It is self-evident that a high *sensitivity* is necessary and more words need not be wasted on this. *Specificity* is perhaps a more double-bottomed concept: when screening tens of thousands of women, even a specificity-drop of less than 1% has a significant impact. Numerous women will be drawn into lengthy investigations and suffer untold anxiety. This is one of the most important issues in screening: the injuries caused to many individuals in the hope of helping a few. A low specificity may be caused by a deficient method; by using several modalities with overlapping false-positive areas; and by screeners who cannot make up their minds.

The *acceptability* of a screening is a concept with several faces. Normally it is taken to mean whether the general public accepts the screening, and then acceptability is demonstrated by the attendance rates. A low attendance rate means that the screening organization has not been successful in persuading its target population of the usefulness of its task. Acceptability can also mean the degree of risk entailed and finally whether it is economically acceptable. One face of acceptability may influence the other: a low attendance rate means low effectiveness, which in turn means a bad cost–effectiveness relationship. The high attendance must continue through many repeated screenings.

Those were some practical viewpoints. We now turn to the confounding factors which tend to make a screener's inner life miserable. Firstly, there is *lead time*, the concept that gave survival a near-zero value. Is screening in some instances only prolonging the time of consciousness of disease—meaning a lowered quality of life? Yes, this must indeed be the case, especially when detecting slow-growing carcinomas that would never have killed their host anyway. At least, in Sweden only 40% of breast cancer patients died from their disease before screening was instituted. Clearly the cancers that are important to detect early and influence by treatment should be those 40%, the killing ones, since the other 60% manage well without screening. Here we are also touching on the concept of *length bias*, meaning that screening tends to detect the slow-growing cancers much earlier than the fast types. This is unfortunate, to say the least. It means that screening intervals have to be spaced to catch the fast-growing cancers, which we want to influence. The majority of potential patients will be screened too often, and this has a negative influence on costs. If screening is done too often, even the enthusiastic women in Sweden may tire, and attendance will go down.

Screening is not a simple and straightforward issue. It has many faces and resembles one of these Russian wooden dolls. When you open the first, there is another within, and another, and another. This ensures an exciting life for an active screener.

I would like to finish this paper on a positive note. The randomized screenings in Sweden are forging along well and will hopefully produce results in a few years. In Canada Tony Miller is also sure he has found a way to demonstrate screening's effects on mortality. I am certain that whatever the outcome, breast screening has or will influence treatment in a very positive way. Some logic finally seems to be seeping into the mess of opinions which has confused everyday surgeons to the point where they take for granted that whatever they do it will not influence the outcome. And to be on the safe side, too much is done. Mammography and early diagnosis are already pointing the way to a sensible and moderate view of treatment which does not entail amputation for every breast cancer, however good the prognosis.