

SCREENING FOR BREAST CANCER

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INTRODUCTION

Breast carcinoma is one of the commonest cancers in the United Kingdom affecting about 1 in 13 women, $\frac{2}{3}$ of whom will die from the disease. This represents approximately 15,000 deaths a year. The effectiveness of the treatment available depends partly on the stage at which the disease is diagnosed and at least $\frac{1}{3}$ of cases now present with advanced disease. Therefore a scheme to promote detection of the disease at a preclinical phase is desirable.

In 1986 the Forrest report on Breast Cancer Screening¹ was published. This recommended a national breast screening programme using triennial mammography for women between the ages of 50 and 64 years.

The recommendation was based on the findings of a series of trials, completed and in progress. The two main completed randomised and controlled trials were the Two Counties study in Sweden² and the Health Insurance study in Greater New York³. These had both shown a 30% reduction in mortality from breast cancer in the screened groups at 10 years. They failed to show any benefit in women under 50 years or over 64 years. Since publication of the Forrest report two further trials have been completed, one from Malmo, Sweden⁴ and the other from Edinburgh⁵. These have only shown a 20% reduction in mortality from breast cancer in the screened group, a figure which falls short of statistical significance. The different studies however are not strictly comparable as different protocols have been used.

In the Edinburgh study the cancer detection rate was 6.2 cases per 1,000 women screened in the initial screen and 3 cases per 1,000 women in the subsequent screens. In all, 96% of the detected cancers were demonstrated mammographically and 22% were clinically palpable. One of the main problems in this trial appears to have been the failure of attendance in the group offered screening, only 61% of those invited attended initially and this declined further in the subsequent recalls. Moreover the mortality in non-attenders was higher than in the control group suggesting that these women included a group who were symptomatic and feared the diagnosis. If the U.K. programme is to be effective, a high rate of attendance is essential.

Screening is not effective in the younger and older age groups because mammography is less sensitive in premenopausal women and many older women fail to attend.

Despite the disappointing results in the more recent trials the evidence is still in favour of screening; the natural history of breast cancer from the earliest detectable focus of in-situ disease to death may be as long as 15 years and therefore the benefits of treatment for early cancer may take a long time to become apparent. The advances in mammography and

surgical management consequent on the experience gained in a coordinated national programme will further enhance these benefits.

LOCAL ORGANISATION

In the North Western Region three screening programmes have been established. The Manchester conurbation is served by the Nightingale Centre at Withington Hospital. West Lancashire and the areas immediately north and west of Manchester are served by centres based at Wigan and Bolton hospitals respectively. The Blackburn and Burnley districts will be served by a shared unit. Blackpool, Preston and Lancaster districts will be served by a unit at the Royal Lancaster Infirmary, the North Lancashire Breast Screening Centre. Much of the screening for these three districts will be done from a mobile van which will visit selected sites in each district. Screening will also be done in the Lancaster centre for the local surrounding area.

Much careful thought has gone into the Lancaster centre. Apart from providing the latest radiological and film processing equipment, it is hoped that the centre will offer a calm and relaxed atmosphere to help minimise anxiety, the fittings and furniture having been chosen in an attempt to avoid the traditional hospital ambience. Breast cancer counselling is an integral part of the service and provision has been made in the centre for this.

The associated mobile van which will do screening work will operate mainly in Blackpool and Preston, and has been built to the specific requirements of the local service. The van, which is 36 feet long, will have on board an X-Ray machine (a mammograph), as well as film handling equipment. There will be a waiting area and changing cubicles for the ladies. Having in mind the wet climate, a special air conditioning and heating system has been ordered.

THE BREAST SCREENING PROGRAMME

Women aged 50 to 64 years whose names are on the FPC register are to be invited for mammographic examination not normally more frequently than once every three years. Mammography can identify changes in the breast long before they can be detected by the woman herself and the purpose of screening is to detect those changes which need further investigation (and which might be cancer) at an early stage when treatment is most likely to be effective.

The programme can be divided into screening stages, a diagnostic stage and treatment. The stages are:

1. The invitation of a woman from the FPC register for examination by mammography.
2. A single medio-lateral oblique view of the breast to see if there is any radiographic abnormality which may be breast cancer.
3. Further investigation of screen-detected abnormalities by either further radiography and/or ultrasound:
or
Specialist intervention by a multi disciplinary team comprising the radiologist, the surgeon and the pathologist to confirm normality or to make a definite diagnosis of cancer.
4. Treatment.

THE CALL SYSTEM

It is recognised that good communication with and involvement of the primary care health team is vital to the success of the programme. So that general practitioners and their teams can play as full a role as possible in the programme, it is intended that staff from the screening centres will offer to visit each practice immediately before women on the list of that practice are called for screening. This health information team will comprise at least the superintendent radiographer, the screening office manager and a health education expert. The visit will allow staff to explain in detail how the calling system works and give an explanation of the literature which accompanies each invitation. It is intended that the programme will call women practice by practice, which means that each practice will be involved once in each three year cycle. This method has been shown to produce a better response than calling one third of eligible women from each practice each year.

The screening programme allows women over 64 to invite themselves for a screen examination but they will not be included in the automatic call-recall system. Women under 50 will not be invited but where a practitioner considers such a woman to be at special risk, for example where there is a history of premenopausal breast cancer in a first degree relative, arrangements should be made for the women to be examined through the normal diagnostic channels.

DIAGNOSIS AND TREATMENT OF SCREEN-DETECTED ABNORMALITIES

The breast screening programme medical team includes radiologists, surgeons and pathologists. The radiologist's role lies in organisation of the programme, primary detection of abnormalities and further radiographic diagnostic investigations. The pathologist also is involved in diagnosis and advises on treatment, whilst the surgeon makes the clinical assessment and is responsible for further management.

SURGICAL ASPECTS OF BREAST SCREENING

Experience from several well established breast screening units has shown that a significant proportion of patients attending for assessment, after mammography, will have palpable breast lumps. These patients will be investigated and treated by the same methods as would a patient presenting with a clinically obvious lump outside the screening situation.

Impalpable mammographic abnormalities present a diagnostic challenge. Many of the early mammographic signs of malignancy e.g. microcalcification, are not specific to malignant tumours and can be seen in a variety of benign lesions. Benign biopsies are, therefore, an inevitable part of any breast screening programme.

These biopsies can be regarded as unnecessary as patients, being asymptomatic, would not have come to surgery if a breast screening programme had not existed. If a great deal of unnecessary anxiety and morbidity is to be avoided the ratio of benign to malignant biopsies must be kept as low as possible. The experience of the screening team is critical in this regard and most important of all is the experience of the person reading the mammograms. A high recall rate to the assessment centre may well lead to an increased biopsy rate. The well established British screening centres are now obtaining benign to malignant ratios of 1:1. However in their early years benign to malignant ratios as high as 8:1 were obtained.

Swedish experience has shown that an increased overall biopsy rate can be expected during the early years of screening as the prevalent disease is detected. In Sweden this was accompanied by an increased biopsy rate in women outside the screened population; presumably because of an increased awareness of breast disease. Swedish studies have also shown that cytological examination of aspirates, obtained from areas of mammographic abnormality, can reduce the number of benign biopsies. As these lesions cannot be palpated, they have to be aspirated under ultrasound control or by stereotactically guided X-ray methods.

MARKER BIOPSIES

Once the decision has been made that an open biopsy is necessary, then localisation of the impalpable lesion is necessary, in order to guide the surgeon. Two of the most popular methods are the 'double dye' and hooked needle techniques. The double dye technique involves injecting a mixture of a radiocontrast and a visible dye into the breast tissue adjacent to the mammographic abnormality. The hooked needle technique involves inserting wires with flexible tips into the breast close to the mammographic abnormality. Both of these methods have to be performed under ultrasound or X-ray control. Further films of the breast are then taken. The surgeon can then find the lesion by relating the position of the visible and radio contrast dye staining the tissues or the hooked needle to the position of these markers relative to the lesion on mammography.

As many of these lesions will be benign, the surgeon should aim to remove the minimum amount of tissue consistent with removal of the mammographic abnormality. While the patient remains anaesthetised, specimen radiography is carried out. If radiography confirms that the specimen contains the mammographic abnormality, the radiologist marks the abnormal area and the specimen is sent for histological examination. The patient is awakened and the results of full paraffin sections are awaited. Frozen section studies should not be used, as paraffin sections enable better histological interpretation of what are often borderline lesions.

If histology reveals that the lesion is an invasive cancer, then it should be possible to conserve the breast in the majority of patients. Wide local excision of the tumour area followed by radiotherapy to the breast and adjuvant

Tamoxifen will be suitable for all but the most aggressive or centrally placed lesions. Mastectomy may still be indicated in the latter situations.

IN-SITU CARCINOMA

A histological diagnosis of carcinoma in-situ presents different problems. In in-situ carcinomas the proliferating cells fill and expand the ducts or lobules but do not breach the surrounding basement membrane. Despite evidence that most cases of carcinoma arise in the terminal duct lobular unit, it is classified into two types:— ductal carcinoma in-situ (DCIS) and lobular carcinoma in-situ (LCIS). The ductal type can be further subdivided according to histological pattern into cribriform, micropapillary and comedo types.

It was thought until recently that carcinoma in-situ was an uncommon condition accounting for 5% of breast cancer cases. However, the introduction of mammographic screening has resulted in an increased diagnosis of DCIS and they now comprise 15% of screen detected cancers. DCIS is usually detected mammographically as microcalcification. While there is good correlation between mammography and pathology for the size of the comedo variety, mammography may under-estimate the size of the lesions in cases of cribriform/micropapillary DCIS.

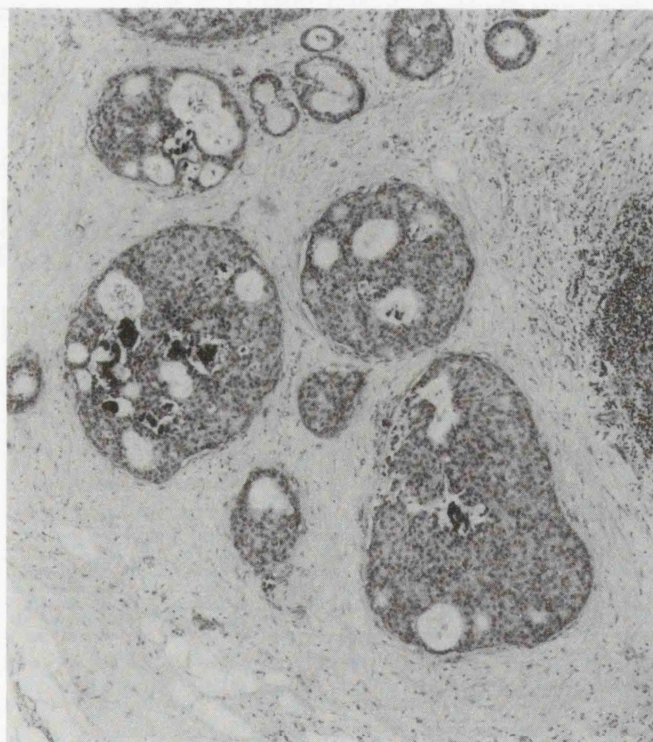


Fig 1 – Ductal carcinoma-in-situ of cribriform type

The natural history of DCIS is not fully understood, but studies have suggested that progression to invasive carcinoma occurs in 25-30% of cases. Results from the Royal Marsden Hospital have shown a recurrence rate of 55% at 7 years after local excision alone and 50% of these recurrences were invasive. Mastectomy, however, is curative in nearly all cases of DCIS. However, as DCIS only appears to progress to carcinoma in a minority of patients, mastectomy may represent overtreatment for the majority. This may especially be the case in small screen detected DCIS. The treatment of DCIS, therefore presents a dilemma, and until some definite answers are available these patients are best entered in the proposed United Kingdom trial. This randomised prospective study has a two by two multifactorial design and compares

wide local excision alone, against wide local excision with adjuvant Tamoxifen or radiotherapy.

Lobular carcinoma in-situ is usually an incidental finding in breast tissue removed for other reasons, and has no characteristic mammographic appearance. Studies have demonstrated that there is an increased risk of developing invasive carcinoma in either breast; the risk being approximately 1% per annum. Since LCIS is a marker for the development of invasive carcinoma in either breast, negative resection margins do not protect against development of invasive carcinoma elsewhere. Bilateral mastectomy is considered to represent overtreatment. Trials are now being conducted in LCIS comparing close observation following biopsy with observation plus adjuvant Tamoxifen 20 mgs. daily for 5 years.

It can be seen that there are many unknown factors in the surgical treatment of screen detected lesions. These problems will have to be resolved by prospective studies, as the National Breast Screening programme progresses.

THE PATHOLOGY OF BREAST SCREENING

Two procedures are especially recommended for breast screening; the use of fine needle aspiration cytology (F.N.A.) as a diagnostic procedure to minimise the number of open biopsies needed, and the marker biopsy for impalpable mammographic lesions.

F.N.A. can be used for both palpable and impalpable lesions, in the latter case the aspirator is guided by ultrasound or X-ray stereotaxis. For solid lesions a smear preparation is made and this can be checked for adequacy of cell content whilst the woman is in the clinic and repeated if necessary. Cyst fluid is also examined cytologically. The cytology is assessed in four main diagnostic categories, based on the appearances of the epithelial cells; carcinoma, suspicious (but not diagnostic) of carcinoma, benign and inadequate, the latter implying that there are insufficient epithelial cells present. Sometimes it is possible to suggest the benign process, fibroadenomas and fat necrosis may have characteristic patterns.

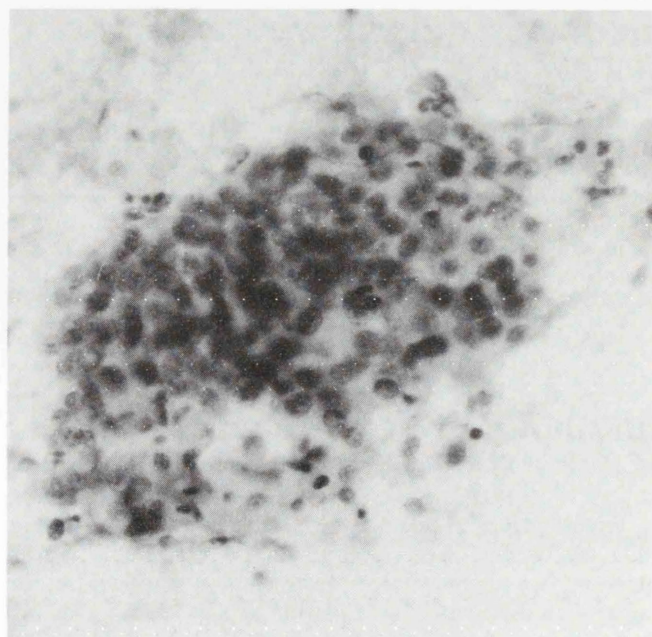


Fig 2 – Malignant cells in a breast FNA

This is a subjective assessment and should be considered alongside the clinical and radiological impression. This 'triple' approach to assessment is essential for diagnostic accuracy. Using this technique, the benign to malignant ratio of cases biopsied may be as low as 1:1 in experienced centres.

Marker biopsies are sent to the pathologist with the marker wire or dye in situ as already described. The specimen is serially sliced and radiographed, the resultant radiograph is then compared with the mammogram and the lesion is identified and sampled using conventional histological techniques.

The pathology of screen detected lesions is essentially similar to that seen in the symptomatic patient. Both benign and malignant lesions may show calcification on a mammogram. Benign lesions include fibroadenomas, papillomas, mammary duct ectasia, fibroadenosis and fibrocystic change. The presence of significant epithelial hyperplasia (epitheliosis) is noted as this is associated with a very small increased risk of cancer of the order of 1.5 to 2 times that seen in the general population⁶. This risk is further increased if features are seen borderline between in-situ carcinoma and benign hyperplasia. This is called atypical hyperplasia and is rarely seen but when present is an indication for close follow up.

Histologically breast carcinomas can be divided into in-situ and invasive groups. In-situ carcinoma has been discussed elsewhere. It is more commonly found in screen detected lesions, both in the initial prevalence screen and in subsequent screens, than in symptomatic patients.

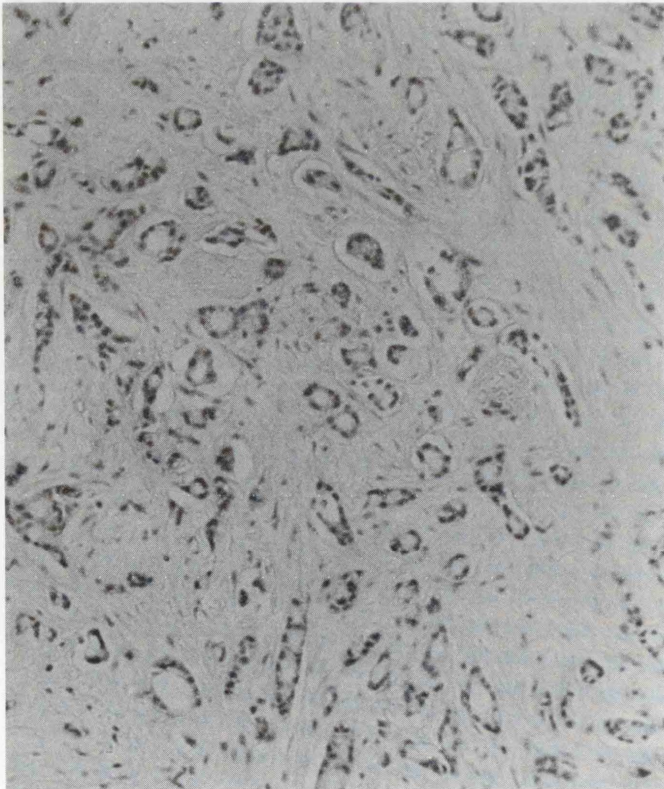


Fig 3 – Invasive carcinoma of tubular type

Invasive carcinomas infiltrate the breast stroma. They may be classified into ductal, lobular, mucoid, papillary, tubular and medullary types according to their histological pattern. Their prognosis depends on the size of the lesion, the degree of differentiation (resemblance to benign tissue) and the presence of lymph node deposits. Small well

differentiated carcinoma, with no lymph node deposits and measuring less than 2 cms across, have the best prognosis. All types of invasive carcinomas may be detected by screening but small well-differentiated tumours such as the tubular type are more common in the prevalence screen detected case than in the symptomatic patient⁷. The pattern in the subsequent screens is different; the new invasive carcinomas appear to be more aggressive presumably because to have appeared in such a short interval they must be rapidly growing.

QUALITY ASSURANCE

Possibly the most challenging part of the breast screening programme is that which deals with quality assurance (QA). This covers many areas but particularly uptake (by ensuring that as many women as possible respond), consumer satisfaction (minimising anxiety and maximising the acceptability of the service), maximising the detection rate, minimising the false positive rate, maintaining the highest quality of surgical and pathological service to ensure reliable diagnosis and treatment and maintaining the reliability and effectiveness of the information and management systems. Nevertheless, there will always be in any screening programme a proportion of both false positive and false negative results. The object of a good QA programme is to reduce these errors to the minimum.

The breast cancer screening programme is due to start in Lancaster early in 1991. The staff of the North Lancaster Breast Screening Service, many of whom are in post, are looking forward to this exciting challenge and will do their utmost to provide the women of the area with a service of the highest standard possible, one of which we can all be proud.

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