Annals of the Royal College of Surgeons of England (1986) *vol.* 68

The accuracy of ultrasound in the diagnosis of breast disease

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Key words: ULTRASOUND; BREAST DISEASE

Summary

The accuracy of breast ultrasound using all purpose static β-scanning equipment has been compared with mammography. Ultrasound was found to be both more sensitive (93% : 82%) and specific (95% : 89%) in a large retrospective series of 1000 patients undergoing investigation for symptomatic breast disease. In a smaller prospective and consecutive series of 142 patients undergoing surgery where histological proof was obtained ultrasound was also found to be more sensitive (91% : 81%) and specific (81% : 69%).

In both studies, the greater accuracy of ultrasound was attributed to its ability to diagnose lesions hidden in X-ray dense breasts and where mammography had revealed featureless asymmetical densities of uncertain nature. In these instances ultrasound may have a significant role to play as an adjunct to mammography in the preoperative assessment of breast lesions.

Introduction

The accurate diagnosis of breast lesions without resort to formal biopsy is highly desirable both for patients who can be quickly reassured or counselled and the clinician who can reduce unnecesary surgery *(1)*. Mammography, although invaluable in a screening role, is not 'specific' enough for making a definitive preoperative diagnosis *(2)*. In suspected cases of carcinoma this usually requires histological proof by either a Tru-cut or an excision biopsy. More recently the less traumatic technique of aspiration cytology, long accepted abroad, has been gaining in popularity. Several centres will now make a firm diagnosis of malignancy on a positive cytology alone *(3)* or as part of a triple assessment *(1,4)*.

The failure of mammography as a definitive diagnostic technique is usually due to problems associated with breast density *(5)*. The unilateral featureless breast density leads to false positive diagnoses, reducing specificity, whilst an homogeneously dense breast may hide a carcinoma thus leading to false negatives, reducing sensitivity. The nature of such limitations stimulated our interest in breast ultrasound, an imaging modality less affected by tissue density.

Since Wild and Neal *(6)* first described breast ultrasound in 1951 there have been a number of studies from Japan *(7)*, Europe *(8)*, Australia *(9)* and the USA *(10–12)* with varying results. This has undoubtedly reflected the differing techniques of both static and real time ultrasound used, but in general ultrasound has been inferior although complementary to mammography in diagnostic accuracy. Only two reports have suggested that ultrasound may be more accurate *(13,14)*. Apart from an early report from this centre *(15)* there has been no large published series from the United Kingdom assessing the comparative accuracy of these two imaging modalities. We report the results of a large retrospective series of patients studied by both techniques and a smaller prospective and consecutive series where imaging accuracy was confirmed by formal histology.

Patients and methods

The retrospective series was composed of the first 1000 patients who underwent both breast ultrasound and mammography for symptomatic breast disease in the Southampton breast clinic. This was not a purely consecutive series and since some early selection of patients occurred they were split into two groups of 500 patients. The first group was partly selected as ultrasound was originally performed on patients who had masses and/or very dense breasts on mammography. The majority, however, underwent ultrasound within a week of mammography. In the

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second group of 500 almost all patients referred for mammography underwent ultrasound as a result of expansion of the ultrasound facility; only those under 35 years in whom mammography was not undertaken and those excluded by rare logistic or technical failure were excluded.

As some selection was apparent in the first group and histology was not always available as final proof, a prospective and consecutive series of 142 patients presenting with a breast lump were also studied. Both imaging examinations were performed within the week before operation.

METHODS

Breast ultrasound was performed and reported by one of two radiologists experienced in general purpose scanning who also read the x-ray mammograms in addition to a third experienced radiologist. With the exception of the first 500 patients all reporting of the imaging results was performed blind without knowledge of the other modality findings. The imaging results were reported as showing malignant, benign or equivocal features, thus permitting the sensitivity (proportion correctly diagnosed as malignancy), specificity (proportion correctly diagnosed as benign) and overall accuracy (proportion of positives and negatives correctly diagnosed) of each technique to be expressed.

The prospective data was collated at a weekly multidisciplinary breast meeting where in addition the histology of all cases was reviewed by an experienced pathologist.

Ultrasound of the breast This was performed using a Philips 7,100 static B-scanner with a 7.5 Mhz transducer. Olive oil was applied to the breast skin to facilitate sound transmission and with the transducer applied gently both longitudinal and transverse scans were taken at 5 mm intervals and also at 2 mm intervals over mass lesions or suspicious areas. The time taken to examine one breast averaged 5 minutes.

Mammography X-ray mammography was performed using a Senograph X-ray Set and Kodak Min-R film. Standard lateral and supero-inferior views were taken of both breasts.

Results

RETROSPECTIVE SERIES

The distribution of breast lesions between the first and second 500 patients was unequal; there were 35% more malignant lesions in the latter group which reflects the more stringent measures taken to examine all patients requiring surgery. The sensitivity of ultrasound for breast cancers improved marginally with time but in both groups was found to be superior to mammography (Table I); the overall sensitivity for ultrasound being 92.5% and for mammography 81.5% (Table I). This difference lay not in the

TABLE I *Sensitivity and specificity of ultrasound (US) and mammography (MAMM), retrospective series*

Imaging technique		*Sensitivity*	*Specificity*
A	US	91%	95%
	MAMM	81%	93%
B	US	94%	94%
	MAMM	82%	84%
C	US	93%	95%
	MAMM	82%	89%

A First 500 patients.
B Second 500 patients.
C 1000 total patients.

false negative rate but in the higher number of unequivocal cases found with mammography (21 : 3), (Table II). In 10 of these 21 patients this was a result of breast density hiding lesions, all of which were visualised by ultrasound; asymmetrical featureless density in 8 cases and uncertain lesions in 3 cases.

Ultrasound identified abnormalities in all its 10 false negatives and 3 equivocals but misinterpreted them as

TABLE II *Results of imaging malignant tumours: retrospective series*

Imaging techniques		*Correct*	*False negative*	*Equivocal*
A	US	62	6	1
n = 69	MAMM	55	3	10
B	US	88	4	2
n = 94	MAMM	77	6	11
C	US	150	10	3
n = 163	MAMM	132	9	21

A First 500 patients.
B Second 500 patients.
C 1000 total patients.

benign, usually fibroadenomas, or was unable to make a distinction (Table II). The 9 false negative mammograms were due to lesions hidden in dense breasts in 3 cases, benign appearing in 4 and misinterpretation of microcalcification in the remaining 2.

The specificity of ultrasound for benign disease was constant for both groups of 500 patients with an overall figure of 95% (Table I). The equivalent figure for mammography was more complex as the specificity in the second group of 500 patients was markedly lower (93.5% : 83.5%; Table I), with an overall specificity of 87%. This was due to a large number (57) of equivocal diagnoses (Table III), in

TABLE III *Results of imaging benign lesions: retrospective series*

Imaging technique		*Correct*	*False positive*	*Equivocal*
A	US	409	12	10
n = 432	MAMM	404	24	4
B	US	383	13	10
n = 406	MAMM	339	10	57
C	US	793	25	20
n = 838	MAMM	743	34	61

A First 500 patients.
B Second 500 patients.
C 1000 total patients.

most cases arising from bilaterally dense breasts where no lesion could be identified (40) and to a lesser extent by the more frequent reporting of asymmetical featureless densities as equivocal rather than possibly malignant. Such a change stemmed from the false positive rate of 24 cases in the first group which in 19 was associated with a featureless asymmetrical density.

The false positive rates for ultrasound remained constant in both groups with an overall number of 25 or rate of 2.5% (mammography 34 or 3.4%). In 16 patients the lesion turned out to be fibrocystic disease.

PROSPECTIVE SERIES

This consecutive series of patients admitted for surgery comprised 90 cases of carcinoma and 52 patients with benign disease. Ultrasound was both more sensitive and more specific than mammography (Table IV) with overall accuracies of 88% and 71% respectively; the relatively lower

TABLE IV *Results of imaging accuracy prospective series*

	Carcinomas n = 90			
	Correct	*Sensitivity*	*False negative*	*Equivocal*
US	82	91%	5	3
MAMM	73	81%	6	11
	Benign lesion n = 52			
	Correct	*Sensitivity*	*False negative*	*Equivocal*
US	42	81%	6	4
MAMM	36	69%	6	10

sensitivity and specificity of mammography resulted from a high equivocal rate. The 11 mammographic equivocals in patients with carcinoma were due to lesions lost in bilaterally dense breasts in 4 cases and featureless asymmetical masses in the remaining seven; nine of the 11 were firmly identified as cancers by ultrasound. Similarly, in cases with benign disease firm mammographic diagnosis could not be made (equivocals) owing to generalised density in five cases and featureless asymmetical density in four cases.

Ultrasound was associated with 5 false negative diagnoses—in 4 cases a carcinoma was thought to be a fibroadenoma; of the six false positive diagnoses five were confused with areas of fibroadenosis. Four of the six mammographic false positives and five of the six false negatives were due to ill-defined asymmetical densities.

Ultrasound and mammography were complementary to some extent in that ultrasound correctly diagnosed 17 of the 21 mammographic equivocals and 6 of the 12 misdiagnoses (false positives and negatives). In contrast, mammography correctly diagnosed only 3 of the 18 lesions where ultrasound was either equivocal or incorrect.

Discussion

In a critical review of currently available breast imaging techniques Moskowitz *(16)* stressed the need for a more stringent control of studies where the accuracy of a new technique was being directly compared to the gold standard of X-ray mammography; in addition the gold standard employed should be with the best technology available and any conclusion drawn must include evaluations for screening in breast cancer.

In this study we have attempted to be 'realistic' by comparing mammograms produced by standard equipment available in most hospitals with static ultrasound scans produced by units employed for general purpose β-scanning. We recognise that the accuracy of mammography can be improved with recent technological refinements but this works similarly for ultrasound where greater accuracy is claimed by the use of sophisticated breast immersion techniques which improve sound transmission.

The sensitivity of ultrasound for carcinoma was consistently higher than mammography; the figures of 92% and 81% respectively for both retrospective series strongly suggest that if some selection did occur earlier on, this failed to alter the overall result. The reasons for the greater accuracy of ultrasound also remained consistent, there being more equivocal results throughout the study with mammography, but no differences in the false negative rate. In the retrospective study the equivocals were due to 10 cases of tumours hidden in dense breasts and 8 cases of asymmetrical featureless density. The equivalent figures from the prospective study were 4 and 7. Ultrasound demonstrated its major value in this situation by diagnosing carcinomas in 28 of these 32 overall equivocals on X-ray.

The ultrasound false negatives, 6% in both series, were due to the misdiagnosis of fibroadenomas in 10 of the 15 cases. The sharing of ultrasound features between some carcinomas and fibroadenomas has become well recognised in several large series *(17,18)* and has been described by ourselves in an earlier publication from this centre *(15)*.

Although the specificity of ultrasound was also superior to mammography in all parts of the study, analysis of the data was more complex. The specificity for both imaging techniques was lower in the prospective study because many of the patients were partially preselected owing to difficulty in diagnosis. As with sensitivity the inferior results of mammography with benign disease were due to higher numbers of equivocals (61 mamm.: 20 US). In 42 cases this was due to bilaterally dense breasts where a carcinoma could easily be missed and in 12 cases the mass was unilateral but featureless and classified as equivocal following the high false positive rate associated with this phenomenon in the first 500 patients (Table III).

The false positive rate for ultrasound was slightly lower in the retrospective series but where asymmetrical breast density had been deemed equivocal on X-ray as in the second group of 500 patients and prospective series, the figures for both imaging techniques were the same. Of the 31 false positive diagnoses with ultrasound, in 19 cases the lesion excised was either fibroadenoma *(3)* or fibrocystic disease *(16)*. The presence of echos within a cyst due to reverberation or partial volume effect and distal acoustic shadowing can make the lesion appear highly suspicious; similar findings have been reported by Harper *(14)*, Maturo *(19)* and Fleischer *(13)*.

Ultrasound is unable to identify microcalcification which clearly limits its role in screening *(19)*. One intraduct carcinoma in the prospective series was picked up by mammography merely on microcalcification with no abnormality seen on ultrasound. Microcalcification, however, led to 2 false positive diagnoses in this group but it nevertheless remains as the cornerstone in identifying sub-clinical malignancy. The need for a radiologist to perform the ultrasound examination which may take 10–15 minutes for both breasts also mitigates against a screening role except perhaps in the young or pregnant patient where X-rays are undesirable.

Ultrasound has potential in several further roles all of which have been exploited at some time in our practice. In the very difficult patient with lumpy fibroadenotic breasts where mammography has identified multiple dominant masses, ultrasound can initially assess their innocence which can then be confirmed by serial ultrasound examination. Finally, ultrasound is ideal for needle guided biopsy and for identifying lesions at the breast periphery which may be missed with biplanar radiology.

As with any new diagnostic technique the indications for its use or 'utility' are difficult to define, particularly where economics are concerned. In this comparison of a conventional ultrasound technique with standard mammography we have found the former to be more accurate in the diagnosis of breast lumps particularly where the breasts are generally dense or a featureless density has been recognised on X-ray. It is in this situation that the use of ultrasound needs to be more widely assessed as part of the currently accepted diagnostic cascade. Furthermore, in those centres where facilities permit the use of a triple assessment on which our surgery is based, its efficiency may be enhanced by the addition (or substitution) of ultrasound to mammography. This is currently being assessed in our own practice.

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Notes on books

Normal Surface Anatomy by Bruce Keogh and Stephen Ebbs. 264 pages, illustrated. Heinemann. London. £14.95.

This new book on surface anatomy is well set out with illustrations on the right hand side and text on the left hand side of an opened page. Full use is made of radiographs, photographs and line drawings to emphasize the clinical applications of anatomy.

Scott: An Aid to Clinical Surgery Edited by H A Dudley. 3rd edition 306 pages, illustrated, paperback. Churchill Livingstone, Edinburgh. £4.95.

It is difficult to know how much of surgery the average medical student should know. This book makes an excellent attempt to cover the important points. Like its predecessor this edition has got the balance just about right.

Intra-Renal Surgery edited by J E A Wickham. 323 pages, illustrated. Churchill Livingstone, Edinburgh. £27.00.

The exciting field of intra-renal surgery has developed very rapidly and in this book international experts display the benefits of meticulous conservative renal surgery. Practising urologists will welcome this review.

Cancer in South Australia. 353 pages, paperback.

This is the fifth in the Cancer Series and displays the incidence, mortality and survival from 1977 to 1982 and the incidence and mortality during 1982 from the South Australian Central Cancer Registry Unit.

Biomedical Significance of Peptide Research edited by F A Laszlo and F Antoni. 278 pages. Akademiai Kiado, Hungary. £17.50.

As the editors point out Hungarian peptide research has great traditions. This is the proceedings of the meeting in 1983 on various aspects of peptide research in Hungary.

Intravascular Infusion Systems by R K Ausman. 199 pages. MTP Press, Lancaster. £24.95.

The vast increase in intravenous infusion in the past 30 years does not need to be emphasised. This book reviews the whole subject of design of infusion systems, the organisation of an iv service and various substances available for infusion together with a review of parenteral nutrition. The last part of the book deals with new technology.

The Theatre Nurse and the Law by Eileen Dixon. 141 pages, paperback. £8.95.

Most surgeons assume total responsibility both morally and legally in the operating theatre but the nurses also have legal responsibilities. This book deals with nursing aspects of consent, litigation, liability and accidents to patients in a simple and readable style.