Radiography (2006) **12**, 96–104

ELSEVIER

THE SOCIETY AND COLLEGE OF RADIOGRAPHERS

Can high frequency ultrasound predict metastatic lymph nodes in patients with invasive breast cancer?

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Received 4 May 2004; accepted 1 April 2005
Available online 13 May 2005

KEYWORDS
Sonography;
Axilla;
In vivo;
Sentinel node;
Surgery

Abstract **Purpose** Use high frequency ultrasound to predict the presence of metastatic axillary lymph nodes, with a high specificity and positive predictive value, in patients with invasive breast cancer. The clinical aim is to improve the surgical management and possible survival rate of groups of patients who would not normally have conventional axillary dissections.
Materials and methods The ipsilateral and contralateral axillas of 42 consecutive patients with invasive breast cancer were scanned prior to treatment using a B-mode frequency of 13 MHz and a Doppler frequency of 7 MHz. The presence or absence of an echogenic centre for each lymph node detected was recorded, measurements were also taken to determine the *L/S* (long axis/short axis) ratio of the node and the widest and narrowest part of the cortex. Power Doppler was also used to determine vascularity. The contralateral axilla was used as a control for each patient.
Results In this study of patients with invasive breast cancer, where ipsilateral lymph nodes had a cortical bulge of $\geq$3 mm and/or at least two lymph nodes had absent echogenic centres, all had disease spread to the axillary lymph nodes (10 patients). Sensitivity and specificity were 52.6% and 100%, respectively, positive and negative predictive values were 100% and 71.9%, respectively, the *P*-value was 0.001 and the Kappa score was 0.55.
Conclusion This would indicate that high frequency ultrasound could be used to accurately predict metastatic lymph nodes in a proportion of patients with invasive breast cancer, which may alter patient management.

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1078-8174/$ - see front matter
doi:10.1016/j.radi.2005.04.001

Introduction

The incidence of breast cancer in England and Wales has been steadily rising in recent years[1] although there has been a decrease in the mortality rates of older women in the UK partly as a result of the National Health Service Breast Screening Programme (NHSBSP).[2] Breast cancer, however, remains a major cause of premature death in women and in the year 2000 the overall mortality rate for England and Wales was 11,380.[3]

Current treatment options for patients with invasive breast cancer in the majority of cases involves either mastectomy or wide local excision and in both cases an axillary dissection is carried out to remove all or some of the lymph nodes.[4] The axillary lymph nodes are vital in assessing appropriate treatment regimes for individual patients.[5–6] The size and grade of tumour together with node involvement have been shown to be good prognostic indicators for survival[7] and are used to indicate which patients would benefit from further treatments such as cytotoxic chemotherapy and radiotherapy.

Complications of axillary node clearance are lymphoedema of the breast and arm, due to insufficient drainage of the lymphatic vessels,[8] reduced movement due to a reduction in tissue volume and sensory disturbances as a result of damage during surgery to the intercostobrachial nerve.[9] These side effects can cause significant morbidity. The routine practice of axillary dissection is sometimes avoided in the elderly in an attempt to avoid the associated morbidity in a group of patients not likely to gain significant benefit from this procedure.[10]

In the NHSBSP the majority of breast cancers detected in women screened regularly, are small. The vast percentage of these women are unlikely to benefit from an axillary node clearance, as their tumour is less likely to have metastasized.[11–12]

A technique has been developed to pinpoint the first lymph node a breast cancer drains to, the so called sentinel node. This technique is currently the subject of an MRC trial.

It is widely speculated that sentinel node procedures could dramatically reduce the number of patients undergoing axillary dissections. If, however, a patient has a positive (metastatic) sentinel node, further axillary surgery is required and the patient will have two operations under general anaesthesia instead of one.

Ultrasound of the axilla has been studied in recent years as a possible alternative to axillary dissection. All studies have shown false negative results, which have eliminated this option. If, however, the aim of axillary ultrasound was to screen for patients who are unsuitable for a sentinel node procedure or a ''wait and see'' policy, used by some centres in the old and frail, i.e. patients with lymph nodes strongly suspected of containing metastatic disease, there could be significant benefit, both financially and clinically.

Both ''In Vitro'' and ''In Vivo'' studies of lymph nodes have been carried out with ultrasound. These studies have used a range of transducer frequencies and have not always been restricted to the axillary lymph nodes of breast cancer patients.[13–25] Table 1 details these studies.

It can be seen from these studies that there are some features that are common to benign lymph nodes and some more common to malignant lymph nodes. Malignant lymph nodes seem to be more round, have concentric or eccentric cortical widening or demonstrate total loss of their echogenic centre. Benign lymph nodes were found to be oval with a thin cortex and have an echogenic centre.

The only study using frequencies above 10 MHz was that of Bruneton et al.[19] This was a relatively large study group of well volunteers and used an EsaoteBiomedica AU4 Ideal with a 13-MHz linear array transducer. The study looked at subject's necks. Normal lymph nodes were seen in 67% of subjects and 86.2% of nodes seen had an L/S ratio of ≥ 2.

Colour Doppler has been used to study the vascularity of breast tumours for some time.[26] One of the drawbacks to this technique in tumours is the random formation of vessels during neovascularisation.[27] This results in slow turbulent flow making detection difficult. Power Doppler simply detects flow in any direction. This has been found to be far more sensitive in detecting vessels in breast tumours than Colour Doppler.[28] Power Doppler is virtually angle independent and depicts density rather than velocity of red blood cells, this makes detection of flow in random and often blind ending vessels easier and eliminates aliasing artefact. The overall Doppler gain can also be increased by 10—15 decibels, again making visualisation of small vessels easier. The major disadvantages of Power Doppler are motion artefact, decreasing sensitivity with depth, and no ability to measure flow.[29–31]

Several studies have been carried out investigating the vascularity of lymph nodes using spectral Doppler in order to differentiate benign and malignant nodes.[32–37] The methods and results of these studies varied considerably. Ho et al.[38] attempted to analyse the methods and results of