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Imaging Techniques in Breast Cancer: Workshop Report

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INTRODUCTION

THE WORKSHOP provided a full overview of breast imaging techniques and some points of controversy were identified. What have proved to be useful procedures in breast imaging are not that new, and the new procedures that were reported, while fascinating and showing great promise for the future, cannot at this stage necessarily be characterized as useful. In summarizing the procedures of the workshop, which included a total of 24 posters, short presentations and keynote addresses, we follow the pattern of Professor Maisey's review lecture [1] and will deal with imaging techniques in relation to the four areas of clinical problems which he defined: (1) diagnosis and screening, (2) evaluation of axillary node disease, (3) staging and follow-up, (4) response to therapy.

DIAGNOSIS AND SCREENING

Several studies were presented which demonstrated that the highest yields were probably provided by a combination of physical examination and mammography. Other procedures such as ultrasound, magnetic resonance imaging, computerized tomography and transmission spectroscopy may be considered as supplementary in selected situations but are not suitable for mass screening or primary diagnosis.

A presentation on Receiver Operated Characteristic (ROC) [2] curves was important in demonstrating the value of ROC curves to evaluate diagnostic procedures. In evaluating new techniques, this method allows comparisons between a new technique and a standard approach, such as mammography, and enables the selection of an appropriate cut-off point to optimize the balance of true positives over false positives. A procedure which increases the positive yield of a diagnostic imaging procedure while reducing the number of false positives may be characterized as having improved specificity. In the case of breast cancer that refers to the relative reduction in the number of patients with benign tumours who are subjected to biopsy procedures compared with the number of patients with malignant tumours. What is needed is a non-invasive test which can discriminate more accurately between benign and malignant tumours.

Presentations on magnetic resonance spectroscopy [3] and on the use of monoclonal antibodies pointed the way to the future using techniques which may also have value in assessing therapeutic response. Similar applications may apply in the use of magnetic resonance imaging and quantitation using T1 relaxation times. Using the latter technique, Richards presented work with lymphomas that may also prove to be applicable to breast cancer patients [4]. Chetty showed correlation of T1 relaxation times with the Wolfe classification of mammographic patterns [5].

Kasumi presented the results of ultrasound studies on 10,000 patients together with confirmatory laboratory studies using phantoms of agar, biogel and fine glass beads to demonstrate that microcalcifications may be identified on ultrasound images [6]. This is in contrast to prevailing opinions regarding the deficiency of ultrasonographic images in identifying microcalcifications.

Applications relating to clinical trials were reported by Cohen and Rankin who described the development of a questionnaire to be used in present and future EORTC clinical trials to provide a standardized system for the evaluation of mammograms [7]. In pilot studies they showed a high degree of reproducibility, and of intra- and inter-observer consistency. The need to use original radiographs rather than photographic copies was

emphasized as copies did not reveal the same clarity of features. The use of transmission spectroscopy (also known as lite scanning and diaphonography) in the diagnosis of breast lesions was reported [8]. They found similar sensitivity but lower specificity in comparison with X-ray mammography. Because the procedure is more time consuming and costly than mammography it does not appear to have a defined value in screening and diagnosis.

EVALUATION OF AXILLARY LYMPH NODES

The identification of metastatic breast cancer in the axillary lymph nodes represents an important aspect of the diagnostic work-up of breast cancer patients. At present, surgical removal of axillary lymph nodes is widely used to evaluate the extent of nodal metastatic disease and contributes significantly to improved selection of patients for appropriate treatment. The surgical procedure *per se* does not appear to contribute to therapeutic management, but may influence morbidity.

Several presentations addressed the topic through the non-invasive evaluation of axillary lymph nodes using radio-labelled monoclonal antibodies or radio-labelled colloidal particles injected subcutaneously. Leclef *et al.* reported on the use of a non-specific antibody [9] while Kubista *et al.* reported on three specific antibodies and noted the correlations with the pathology findings and controls using technician radio-labelled colloid [10]. The specific antibodies HMFG2 and 3C6F9 labelled with iodine-123 enabled them to increase the yield of lymph nodes in the surgical specimen by an average of 25% and increased the proportion of positive nodes to 49%, compared with 40% in the control cases. It was agreed that future studies were necessary with larger numbers of patients and should include the evaluation of the non-specific effect of monoclonal antibodies, the non-specific uptake of IgG and technical problems of clumping of colloid-forming particles. The future of this area depends on the development of tumour-specific antibodies which will have a low incidence of false positive results. Begent reported some results with advanced cases of breast and colon cancer using radio-labelled anti-CEA antibody and suggested that some degree of specificity can be achieved [11]. Further work in this area is necessary for the full potential of these techniques to be realized.

STAGING AND FOLLOW-UP

The sensitivity of bone scanning in the staging and follow-up of breast cancer patients was the major topic discussed in this section of the workshop. Coleman and Fogelman reviewed the range of positive findings of bone scanning for metastatic disease reported for different stages of breast cancer in numerous publications over several years [12]. This report on a carefully conducted study of over 1000 patients revealed no positive findings in patients with Stage 1 disease and extremely low yield in patients with Stage 2 disease. Further follow up at the end of 1 year still revealed no positive bone scan in the patients with Stage 1 disease and a slight increase in the patients who had presented with Stage 2 disease. It was suggested that while bone scanning was definitely the most sensitive method to screen for bone metastases the low yield suggested that it was not useful in patients with Stage 1 or 2 disease. A 'baseline' bone scan at the time of presentation was considered justified by some delegates on the basis of providing an opportunity to discriminate new from long-standing findings on subsequent bone scans. A lively discussion centred on this topic without consensus being reached. A possible use of non-imaging methods to predict the risk of metastatic disease was mentioned but the high sensitivity, moderate cost and lack of morbidity associated with bone scanning resulted in many participants supporting the need for a 'baseline' bone scan in all patients and the specific use of bone scans in patients with Stage 3 and 4 disease to define extent of metastatic involvement.

Coleman and Fogelman reported on a new bone scanning agent, dimethylaminodiphosphonate, which resulted in a better target to background ratio [12]. This may provide a higher yield of true positive images (higher pathology contrast) although the pictures did not show the normal skeleton as clearly as bone scans obtained with methylene diphosphonate presently in use.

Bourgeois *et al.* reported on the use of bone marrow scanning as a method of screening for metastatic disease and suggested that a small number of cases of metastatic breast cancer may be diagnosed as a result of this approach, although they did not suggest that the method competed with bone scanning in respect of sensitivity or specificity [13].

RESPONSE TO THERAPY

The presentations in this area were the most interesting and promising in suggesting real steps forward. Although some of these techiques may also have application in diagnosis and staging, it may be in evaluating response to therapy that they offer the greatest potential for future benefit. Johnson presented a discussion of the use of ultrasound techniques to assess the rate of tumour response [14]. The range of tumour regression rates, using physical examination techniques, suggests that breast cancers represent a wide range of response rates to treatment. It was suggested that early detection of a slow response to a particular method of treatment might be useful in discontinuing one method of

treatment and implementing another.

Richards reported on the use of magnetic resonance imaging using a colour scale display for quantitative differences in T1 relaxation time [4]. Quantitative readings suggested a correlation with therapeutic response in lymphomas and may also be applicable to breast cancer but much work remains to be done. Griffiths reported on the use of magnetic resonance spectroscopy with quantitative evaluation of the various phosphate peaks in the spectroscopic reading [3]. In a study with rodent tumours, he demonstrated a correlation of tumour volume with phosphocreatine/inorganic phosphate and ATP/inorganic phosphate ratios with the ratios differentiating well between tumours which responded or did not respond. Although macroscopic criteria were evident at the time that changes in the ratios were recorded, it is appealing to postulate that more sensitive spectroscopic techniques may result in this approach being used on a predictive basis. The possibility that the therapeutic efficacy of a clinical trial regimen might be evaluated within weeks or even days of implementing treatment is a very attractive prospect and may significantly reduce the duration of use of therapeutic regimens before they are judged to be ineffective. Conversely, appropriate choice of treatment might similarly be identified early in the course of a patient's management.

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