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SYMPOSIUM

New approaches in axillary management

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INVITED

Lymphatic mapping and sentinel lymphadenectomy

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In October of 1991, our group began to study the feasibility of lymphatic mapping and sentinel lymphadenectomy in breast cancer. With no prior experience with the technique in this disease, a period was required to define technical aspects of the procedure.

In our 1994 study, we reported the results of our first 174 sentinel node procedures. 172 patients were included. All patients underwent lymphatic mapping and sentinel lymphadenectomy followed by level I and II axillary dissection and surgical treatment of the primary lesion. Sentinel nodes were identified in 114 (66%) of procedures overall. Axillary lymph node status was correctly predicted by sentinel node in 109/114 (96%) of cases. The 5 false negative results occurred in the first 87 procedures, 2 of which were in the first 10 procedures. One patient had micrometastases in the sentinel node using anti-cytokeratin stains. We have employed routine immunohistochemistry to detect occult metastases since that time.

In the last 100 patients undergoing lymphatic mapping and sentinel lymphadenectomy followed by axillary dissection, we identified the sentinel node in 94% of patients. There were no false negative results, indicating a sensitivity and specificity of 100%. We attribute our increased success to refinement of the technical details and extensive experience with the technique. Based upon these results, we began a trial to investigate lymphatic mapping and sentinel lymphadenectomy alone in patients with negative sentinel nodes in October 1995. This approach allows women without axillary metastases to be spared the expense and morbidity of a complete axillary dissection. Prospective clinical trials are being performed to further study sentinel node biopsy in breast cancer.

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INVITED

FDG-PET in breast cancer staging and biological characterization

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134 patients with breast lesions scheduled for surgery and, if indicated, ALND, were studied with FDG-PET. A comparison was made between histopathology and FDG-PET findings. The clinical stage was: N0 (58pts), N1a (47pts), N1b-2 (29pts). The results of postoperative histopathology were as follows: 117 lesions were carcinomas (80 pure ductal carcinoma) and 17 were dysplasias. The 117 breast cancer patients underwent ALND; the mean number of dissected nodes was 23 (range 9-49). Histology diagnosed 56 cases as benign pN+ and 61 as pN-. The overall FDG-PET results are as follows:

Sensitivity	89%	(50/60)
Specificity	87%	(68/78)
Accuracy	88%	(118/134)
Positive Predictive Value	83%	(50/60)
Negative Predictive Value	92%	(68/74)

The possible role of FDG-PET in the prognostic evaluation was investigated on 86 patients with T1-3 (TNM classification) breast tumours before surgery. The tumour FDG uptake, calculated as a Standardized Uptake Value (SUV), was compared with postoperative histopathological findings, steroid-hormone receptor status of the tumour, thymidine labelling index (LI) and tissular expression of p53. SUV was significantly higher in infiltrating ductal carcinomas (n=68; median SUV=5.6) than in lobular ones (n=18; median SUV=3.7) and in grade 3 carcinomas (n=26; median SUV=5.8) than in grade 1-2 ones (n=60; median SUV=4.4). Moreover, SUV was significantly higher in carcinomas with high levels of p53 (n=12; median SUV=9.5) than in those with low p53 levels (n=48; median SUV=4.25). By contrast there was no significant correlation between SUV and the steroid-hormone receptor status and LI of tumors.

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INVITED

Breast conservation without axillary dissection

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Randomized trials that compared the classic Halsted mastectomy with conservative breast surgery plus complete axillary dissection (AD) and breast radiotherapy, demonstrated that such aggressive treatments did not improve patient survival but only worsened the quality of their lives. For a century AD has been an essential component of the surgical treatment of infiltrating breast cancer. However with the increasing frequency of small-size cancer and the demonstration that axillary involvement correlates closely with tumour diameter, the question as to the best way of dealing with the axilla, that involves neither undertreatment nor overtreatment has become a subject of study and debate.

Today, as breast cancer is diagnosed earlier, the average size of the tumour is smaller and the probability of axillary involvement has decreased, it is not surprising that some surgeons believe a clinically negative axilla should only be treated in some instances. Recently published data confirm the view; however many variables were involved in these studies (RT, type of surgery to the primary, mammographic detection) and it would be difficult if not impossible to draw up consensus guidelines as to when and when not to perform AD.

Another point is that disease aggressivity varies considerably with histotype, and this has convinced us that AD can be avoided for example in intraductal carcinoma, and also in elderly women, as the results of large scale analyses show. Furthermore, as reported by our colleagues, AD may be safely foregone when the sentinel node is negative. Another possibility is that axillary radiotherapy may sufficiently lower the risk of axillary metastases. An ongoing multicentric study, co-ordinated by the IEO aims to evaluate this possibility in patients over 45 years undergoing conservative breast surgery for invasive carcinoma of ≤ 1.2 cm. The study will determine whether RT to the axilla can reduce the risk of axillary metastases from the expected 10% without axillary treatment to around 3%.

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INVITED

Predictors of axillary lymph node metastases

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For patients with invasive breast carcinoma, axillary dissection is routinely performed as part of treatment for operable disease in most institutes. The axillary dissection is mainly a staging procedure and patients with lymph node metastases receive systemic adjuvant treatment. In addition to being a staging procedure, the axillary dissection is considered to contribute to obtaining regional control.

The percentage of patients without lymph node metastases is approximately 50% and for these patients lymph node dissection could have been omitted from the treatment. For this reason, it would be of benefit to have methods to predict which patients have lymph node metastases (or are very likely to have lymph node metastases).

The most promising technique for predicting the presence of lymph node metastases is the sentinel node procedure and it is likely that many institutes will introduce this technique into treatment protocols.

In addition, characteristics of the primary tumor predictive of the presence of lymph node metastases may be used in clinical practice. At present, the best predictive factors are lymphangio-invasive growth and size. Additional predictive information may come from the knowledge of inactivation of tumor suppressor genes and activation of oncogenes.