

TUESDAY 16 SEPTEMBER 1997

## Proffered Papers

### Breast cancer, early disease

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ORAL

#### Can sentinel lymph node biopsy avoid axillary dissection in N0 breast cancer patients?

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All patients at our Institute who undergo breast surgery and total axillary dissection for breast cancer of any size but with a clinically uninvolved axilla enter the study. The objectives are: (1) to identify the sentinel node which is first node to receive lymph from the tumor area by lymphoscintigraphy following injection of  $^{99m}\text{Tc}$ -labeled human albumin subdermally overlying the tumor; (2) to mark the sentinel node thus identified by means of an indelible sign on the skin over the node; (3) to determine the feasibility of isolating this node surgically with the aid of a radioguided probe; and (4) to verify how often the node thus isolated is metastatic in comparison with involvement of the other removed nodes.

In a consecutive series of 163 women with operable breast carcinoma,  $^{99m}\text{Tc}$  was injected on the day before surgery, and scintigraphic images of the axilla and breast were taken 10 min, 30 min and 3 hours later. During breast surgery a hand-held gamma ray detector was used to locate the sentinel node, and facilitate its removal separately via a small axillary incision. Complete axillary lymphadenectomy was then performed. The sentinel node was tagged separately from all other nodes. Permanent sections of all removed nodes were prepared for pathological examination.

The sentinel node accurately predicted axillary lymph node status in 156 (97.5%) of the 160 patients in whom a sentinel node was identified, and in all of the cases (45 patients) with tumor  $<1.5$  cm in diameter. Of the 85 cases with metastatic axillary nodes, in 32 (37.6%) the only positive node was the sentinel node.

In the great majority of patients lymphoscintigraphy and gamma probe-guided surgery can locate the sentinel node in the axilla, obtaining important information on the status of axillary nodes. Breast cancer patients without clinical involvement of the axilla should undergo sentinel node biopsy routinely and may be spared complete axillary dissection when the sentinel node is free of disease.

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#### Prognostic impact of minimal residual disease in patients with early breast cancer (T1)

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**Purpose:** At the present time nodal status still is the best available prognostic factor in primary breast cancer. Immunocytochemical detection of tumor cells in bone marrow (TCD) is a marker of tumor dissemination, as axillary nodal status. Therefore TCD could replace nodal status in some subgroups of patients.

**Methods:** In a prospective study (1985-96) the intraoperatively aspirated bone marrow of 582 T1-patients were screened for micrometastatic cells. We used the monoclonal mucin-AB 2E11 (reactive with TAG 12) for cell detection.

**Results:** After a median period of 44 months follow-up results were statistically analyzed. 232 of 582 T1-patients were TCD-positive (39.8%). Distant metastases were found in 50 women. This subgroup displayed a 76% TC-detection rate, although only 56% of them have been nodal positive. 25 women have died during follow-up. Among these patients 70% were TCD-positive, but only 49% had axillary metastases. In a Cox regression model TCD was the best prognostic factor for disease-free and

overall survival. Complications of bone marrow aspiration were negligible compared to axillary dissection (15%).

**Conclusion:** As previously shown, tumor cell detection in bone marrow is an outstanding prognostic factor in breast cancer (JNCI, 1996, 1652). In the present analysis we could confirm this data in patients with small tumors. Tumor cell detection could be an alternative to axillary dissection in a future concept of outpatient treatment of early breast cancer. To prove this statement, in prospective randomized studies nodal status should be replaced by TCD.

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#### Use of Tc-99 labelled colloidal albumin for preoperative and intraoperative localization of non-palpable breast lesions

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Clinically occult breast lesions are found frequently now that mammographic and ultrasonic screening are widespread. Several methods are used to localize suspicious occult lesions prior to excision, including skin-projection and introduction of a hooked-wire; all suffer from limitations. We have developed a new localization technique in which mammographic or ultrasonic images are used to guide the injection of 0.05 mg of  $^{99m}\text{Tc}$ -labeled human serum albumin (6-8 MBq) directly into the lesion (cluster of microcalcifications and/or opacity) on the day before surgery. Subsequently a gamma ray detecting probe locates that lesion and guides its excision. Up to 31 July 1996 we had treated 115 patients with non-palpable breast lesions using this technique. In all cases the hot-spot was easily and quickly located both on skin projection and in the parenchyma. X-radiography and scintigraphy of removed specimens checked the presence and centrality of the lesion: in all cases the lesion was within the specimen, although in one case intraoperative re-excision was performed as activity was detected at a resection margin. Pathological examination revealed 69 cancer lesions and no case of carcinoma cell dissemination along the needle track; 68 of these patients were treated by breast conserving surgery, and one received a Patey mastectomy.

A limitation of the new technique is that tracer injection directly into the lesion cannot be verified before excision, and should therefore be performed by personnel experienced in the localization of breast lesions. In our hands the technique proved safe and accurate, allowing easy detection of the skin projection (permitting the surgeon to choose the best incision) and fast removal of the lesion, with the added advantage that resection margins could be checked during the operation. Our preliminary data indicate higher excision accuracy, better lesion centrality within the specimen and less need for margin radicalization compared to the hooked wire method.

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#### Tumor cell detection in breast cancer patients before and after neoadjuvant chemotherapy

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**Purpose:** The important goals of the neoadjuvant chemotherapy (NACT) concerns the operability of the primary tumor and the suppression of early 'tumor cell shedding'. The aim of our study was to investigate the influence of NACT on tumor cell detection (TCD) in bone marrow.

**Methods:** In 174 patients with primary breast cancer larger than 3 cm we performed a bilateral aspiration of bone marrow after NACT (3-4 cycles of Epirubicin/Cyclophosphamide). 174 patients without NACT with the same tumor size, hormone receptor status, grading and age (matched pairs) served as controls. In 42 women bone marrow puncture before and after