

but surgical biopsy revealed infiltrating ductal carcinoma with multiple foci of in situ carcinoma.

**Conclusion:** At present calcifications, particularly calcification clustering, that increase or appear, must make suspicious the radiologist. There are not still sufficient elements of analysis about calcifications that disappear. It is not possible draw definitive closures on single clinical case observed but it might represent an element of deserving reflection.

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POSTER

### The use of technetium-99m methoxyisobutylisonitrile (<sup>99m</sup>Tc-MIBI) breast scintigraphy to evaluate palpable breast masses

D.C. Yeh<sup>1</sup>, C.H. Kao<sup>2</sup>, C.C. Wu<sup>1</sup>, T.J. Liu<sup>1</sup>. <sup>1</sup>Department of Surgery; <sup>2</sup>Department of Nuclear Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

**Purpose:** The main purposes of this study is to assess the sensitivity and specificity of <sup>99m</sup>Tc-MIBI breast scintigraphy for tumor detection and to determine whether it could be used to differentiate malignancies from benign masses.

**Methods:** Thirty-eight female patients (age range: 31–79 years) with palpable breast masses which were detected by mammography and/or physical examination underwent <sup>99m</sup>Tc-MIBI breast scintigraphy in order to assess the value of <sup>99m</sup>Tc-MIBI scans in the detection of breast carcinoma and the differentiation of malignant from benign lesions.

**Results:** Twenty-seven of the thirty-two cases of breast carcinoma were detected by <sup>99m</sup>Tc-MIBI breast scintigraphy. In contrast, none of the six benign lesions could be detected by this method. The diagnostic sensitivity, specificity and accuracy were 84%, 100%, 87%, respectively, in the differentiation of malignant and benign breast masses.

**Conclusion:** We consider <sup>99m</sup>Tc-MIBI breast scintigraphy is useful in distinguishing malignancies from benign breast masses.

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POSTER

### The axilla – What can mammography offer?

F. Flanagan, P. Barton, J.T. Ennis. Mater Hospital, Breast Screening Unit, 46 Eccles Street, Dublin 7, Ireland

**Purpose:** This presentation will demonstrate the normal variations and pathological processes that can be seen in the axilla using standard routine mammography. It will also outline guidelines for further intervention or tissue sampling should they arise. This paper will discuss the potential role of other techniques used in imaging the axilla and compare them to standard mammography.

**Materials & Methods:** Over 30 consecutive cases were selected from 2 busy breast imaging practices where lesions in the axilla were reported on routine mammography examinations. In each case further investigations either by alternative imaging, clinical examination or tissue sampling was instigated on the basis of the mammogram.

**Results:** Masses, asymmetric densities and calcifications were the three main categories evaluated. The masses were subdivided into lymph node and non lymph node masses. In most cases tissue sampling proved unnecessary. Clinical examination of the axilla and a proper clinical history established the diagnosis in 75% of cases.

**Conclusion:** In most cases, the mammographic appearances of lesions in the axilla are typically characteristic requiring no further intervention. On occasion tissue sampling may be warranted.

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POSTER

### Correlation between sestamibi scintigraphy-mammography, mitochondria and neoangiogenesis in breast cancer

C. Vanoli<sup>1</sup>, R. Antronaco<sup>1</sup>, L. Giovannella<sup>2</sup>, L. Ceriani<sup>2</sup>, L. Cabrin<sup>3</sup>, G. Torrigiotti<sup>3</sup>, L. Colombo<sup>4</sup>. <sup>1</sup>Dept of Radiology; <sup>2</sup>Dept of Nuclear Med; <sup>3</sup>Dept of Surgery; <sup>4</sup>Centre of Senology-Univ Pavia in Varese, Italy

**Purpose:** Evaluation of SestaMIBI scintigraphy in the assessment of breast's microcalcifications without associated nodular lesion and the correlation between scintigraphy data and immunohistochemical detection of mitochondria and neoangiogenesis in tumour samples.

**Methods:** we evaluated 27 patients. All patients underwent mammography, US, <sup>99m</sup>Tc-SestaMIBI scan and stereotactic fine needle aspiration. Patients with positive cytological pattern, inadequate cytological sampling or suspect mammographic finding underwent surgical biopsy.

### Results:

Final Diagnosis	Mammography	Scan
Breast Cancer 8		4/8
• intraductal 5	- 5/5 dubious	1/5
• infiltrant Ca 3	3/3	3/3
Benign Lesion 19	14/19 (5 dubious)	18/19

**Conclusions:** <sup>99m</sup>Tc-SestaMIBI demonstrates a good predictive negative value and poor diagnostic specificity for DCIS; sestaMIBI uptake was related with mitochondria contents in the lesions.

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POSTER

### Preliminary results in the scintigraphic and radiosurgical identification of sentinel node (SN) in early stage breast cancer

L. Feggi, P. Carcoforo<sup>1</sup>, N. Prandini, A. Sartori<sup>1</sup>, S. Corcione<sup>2</sup>, D. Beccati<sup>3</sup>, D. Candini<sup>4</sup>, I. Donini<sup>1</sup>. <sup>1</sup>Nuclear Medicine; <sup>2</sup>Radiology; <sup>3</sup>Health Physics of Azienda Ospedaliera Arcispedale S. Anna; <sup>4</sup>Clinical Surgery; <sup>3</sup>Pathology of the University of Ferrara, Italy

Axillary lymph nodes dissection for breast cancer remains the most important prognostic factor and guide adjuvant therapy. We tested the scintigraphic and radiosurgical mapping of SN to verify if an adequate axillary staging and regional control is possible without radical axillary procedures.

**Material and Methods:** The study, began in October 1997, comprised 16 patients, aged between 35 and 78 (mean 60 years), with T1 tumor localized in 14 cases at the external superior region of the breast and in 2 case at the internal superior. All the patients underwent preoperatively two kinds of lymphoscintigraphy: 1- injection of <sup>99m</sup>Tc-colloid (30 MBq) the evening before the day of the surgery with scintigraphic imaging after about 15 hours; 2- injection of <sup>99m</sup>Tc-nanocolloid (10 MBq) in the morning of the surgery with scintigraphic imaging after 1 hour. We utilize a low energy LFOV camera with high resolution collimator for the scintigraphy (planar in two orthogonal projections); during the surgery we utilize a probe (Pol. hi. tech srl) specific for SN collimation. After induction of general anesthesia, Isosulfan blu vital dye was injected into the breast mass and surrounding breast parenchyma.

**Results:** The accuracy of lymphatic mapping was examined by comparing the histopathology of SN and non SN specimens. The SN accurately identifies axillary node status in all the patients. Only in 1 case (sensitivity 93.7%) it was not possible to identify the SN because the lymphatic drainage was dramatically modified by radical mastectomy 1 month before: the SN was found only by blu dye. In 1 patient the SN was identified only by probe and not with scintigraphy. In the two tumors localized in the internal superior region the SN was found not in the axilla but in the internal mammary chain. Finally in 2 case the SN was located in interpectoral region and in 2 cases in clavicular omolateral region.

**Conclusions:** This study is at the beginning and the number of the patients is too low for a conclusion but the experience indicates that lymphatic mapping by scintigraphic and radiosurgical technique can accurately identify the SN (wich is located in the axillary nodes only in 50% of our cases) and could guide to a less radical axillary procedure in the patients with tumour T1 N0, with obvious benefit for the patients and inducing a reduction in overall costs.

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POSTER

### In situ trap method for the cytological examination of breast cancer (preliminary report)

S. Nakayama<sup>1</sup>, M. Kusama<sup>1</sup>, H. Kaise<sup>1</sup>, T. Aoki<sup>1</sup>, Y. Koyanagi<sup>1</sup>, N. Yahata<sup>2</sup>, K. Ohyasiki<sup>2</sup>. <sup>1</sup>Department of Surgery; <sup>2</sup>Department of Internal Medicine, Tokyo Medical College, Japan

**Purpose:** We report our study on the usefulness of checking the activities of telomerase for breast cancer cytology using in situ TRAP with fluorescent primer.

**Material and Method:** Aspiration biopsy cytology were performed on our breast OPD patients.(ten breast cancer, two fibroadenoma, one phyllodes tumor, one mastopathy) The specimens were immediately de-erythrocyted at 4°C and were then fixed and dried on silane-coated slide glasses. In situ TRAP method with fluorescent primer (by Ohyasiki et. al.) were applied for cytology to check the activities of telomerase. The activities of telomerase were evaluated on slide glasses with primer through fluorescence microscope after PCR reaction.

**Result:** Fluorescence colorization were noticed on breast cancer cells. Besides it is easy to differentiate lymphocytes from cells of positive telomerase activity by way of morphology and color differences.

**Conclusion:** It is suggested that in situ TRAP method combined with cytologic diagnosis makes a great contribution to the improvement of diagnostic accuracy and the decrease of judged difference among persons and institutions.

Thursday, 1 October 1998

16:00-18:00

## PARALLEL SESSION

## Endocrinology

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INVITED

## Update on endocrine approaches in the treatment and prevention of breast cancer

M. Kaufmann. *Department of Gynecology and Obstetrics, Johann Wolfgang Goethe University Hospital of Frankfurt, Germany*

During the last 100 years endocrine procedures and agents became more and more important in the treatment and prevention of breast cancer.

The choice of endocrine drugs depends on the stage of disease, menopausal-status of the women, steroid hormone-receptors, and the toxicity profile of the drug.

In metastatic breast cancer patients endocrine therapy was the first effective palliative treatment and is also today's treatment of choice for low risk situation.

Along with adjuvant (post-operative) endocrine treatment with or without cytotoxic drugs it has been shown to improve disease-free and overall survival rates of primary breast cancer patients.

Neoadjuvant (primary or pre-operative) endocrine treatment is currently under investigation in the elderly patients to achieve more breast conserving surgery and better survival rates. Contrary to cytotoxic treatment endocrine therapy is active on tumor cells through distinct and highly selective mechanisms.

In the future endocrine treatment (e.g. tamoxifen, raloxifen, SERMS) will also play a major role for the prevention of breast cancer.

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ORAL

## Increased risk of recurrence for patients with EGFR and HER-p185 positive tumours when treated adjuvantly with tamoxifen for one year

A. Knoop<sup>1</sup>, S. Bentzen<sup>2</sup>, M. Nielsen<sup>1</sup>, B. Rasmussen<sup>3</sup>, C. Rose<sup>1</sup>. <sup>1</sup>Dept. of Oncology, University Hospital, Odense; <sup>2</sup>Dept. of Experimental Clinical Oncology, University Hospital, Aarhus; <sup>3</sup>Dept. of Pathology Roskilde County Hospital, Denmark

**Aim:** The aim of this study was to investigate interactions between treatment with tamoxifen and steroid receptor content and EGFR, HER-p185 and p53.

**Methods:** 1,716 high-risk postmenopausal breast cancer patients, who were all treated with irradiation, were randomly assigned to treatment with tamoxifen (868 women) or observation (848 women). The contents of the steroid receptors and expression of p53, EGFR, and HER-p185, were determined by immunohistochemistry. The follow-up time was 10 years. The endpoint was disease-free survival.

**Results:** Multivariate analysis demonstrated independent risk of disease for EGFR and HER-p185 positive high-risk patients and a decreased risk of disease in steroid receptor positive patients or patients with many positive lymph nodes when treated with tamoxifen. Patients with p53 positive tumours had an increased risk of disease, independent of adjuvant treatment with tamoxifen.

**Conclusion:** In patients with tumours positive for HER-p185 or EGFR another treatment than tamoxifen could be considered.

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ORAL

## Idoxifene antagonism of oestradiol-dependent MCF-7 breast cancer xenograft growth

S.R.D. Johnston<sup>1</sup>, M. Dowsett<sup>1</sup>, S. Riddler<sup>2</sup>, M. Jarman<sup>2</sup>. <sup>1</sup>Department of Academic Biochemistry, Royal Marsden Hospital; <sup>2</sup>Institute of Cancer Research, London, England

**Purpose:** Idoxifene is a novel selective oestrogen receptor modulator (SERM). We have previously shown idoxifene to have significantly greater inhibition of ER+ve MCF-7 xenograft growth in comparison with tamoxifen (TAM) when given in the absence of oestradiol (E2), (Br J Cancer 1997 75; 804-809). In our current study we compared the antagonist effects of idoxifene with TAM in MCF-7 xenografts whose growth continued to be supported with E2. In addition, we compared the activities of the cis and trans forms of idoxifene. Cis-idoxifene has a 50-fold lower relative binding affinity (RBA 0.25) for ER than either trans-idoxifene (RBA 12.5) or TAM (RBA 5).

**Methods:** 95 tumours were established with E2 support in ovariectomised athymic mice and after 4 weeks were randomised to either continued E2, cis-idoxifene + E2, trans-idoxifene + E2, TAM + E2, or withdrawal of E2. Drugs were delivered in equimolar doses by implanted silastic capsule changed every 8 weeks.

**Results:** Tumour growth continued with E2 and regressed exponentially upon E2 withdrawal, confirming the hormone-dependence of this model. Cis-idoxifene had no effect on E2-dependent tumour growth. In contrast, both trans-idoxifene and TAM significantly inhibited E2 dependent growth ( $p < 0.0001$ ), and tumour volumes remained static over the subsequent 12 weeks of the experiment. Uterine weights in animals treated with either transidoxifene + E2, or TAM + E2 were significantly ( $p < 0.009$ ) less than those treated with E2 alone.

**Conclusions:** These data show that idoxifene and TAM are equivalent in their ability to antagonise E2-dependent MCF-7 xenograft growth and therefore support the potential clinical utility of idoxifene in the treatment of breast cancer. Furthermore, these studies suggest that idoxifene's antagonist activity on tumour growth correlates well with its binding affinity for ER.

(Supported by SmithKline Beecham Pharmaceuticals)

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ORAL

## Ocular toxicity from standard dose adjuvant tamoxifen therapy

P. Dulle, A. Patel, M. Morgan, H. Bradpiece, I. Fawcett. *Breast Unit, St Margaret's Hospital, Epping, Essex, UK*

**Purpose:** Ocular toxicity due to Tamoxifen is a recognised side effect of the drug, but few studies have attempted to discover how common the problem is. The literature shows that most reports are in the form of individual case studies of symptomatic patients, whilst cross-sectional studies have used relatively small sample sizes, with a wide variability in incidence found (0-12%). This study was undertaken to determine the incidence of ocular toxicity in patients on standard dose adjuvant Tamoxifen therapy for breast cancer.

**Methods:** 840 patients have been examined for signs of characteristic keratopathy/retinopathy. Many aspects of visual function were assessed, including visual acuities and central visual fields.

**Results:** Ocular toxicity was found in 6.7% of patients: keratopathy in 3.7% and retinopathy in 3.0%. Visual function was affected in 22% of those cases. The cumulative dose required for ocular toxicity to occur varied from 3.6 to 75g, suggesting that the problem is not simply dose related.

**Conclusion:** It was found that signs of ocular toxicity can be seen in asymptomatic patients with good vision, suggesting the need for regular ocular examination in all patients on Tamoxifen. The evidence does not indicate the need to discontinue the drug, unless a reduction in visual function is found.

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ORAL

Estrogen receptor  $\alpha$  and  $\beta$  expression in human breast cancer tissues analysed by RT-PCR

S. Kobayashi, H. Iwase, Y. Omoto, Y. Hara, Y. Ando. *Surgery 2, Nagoya City University Medical School, Nagoya, Japan*

The details of correlation between estrogen receptor  $\alpha$  (ER $\alpha$ ) and  $\beta$  (ER $\beta$ ) expression in human breast cancers have not been clarified yet. We analyzed expression of both receptors by RT-PCR on 66 primary breast cancer