A number of abstracts accepted for poster presentation at the 1998 Annual Meeting of the Society of Nuclear Medicine were not presented at the meeting due to miscommunication between committee members and SNM staff. We do hope that the special inclusion of these abstracts to The Journal of Nuclear Medicine will give each applicant's work the recognition it deserves. The following pages should be included as part of the 1998 May Abstract Book Supplement to The Journal of Nuclear Medicine and have been numbered accordingly.

SNM Scientific Program Committee

No. 1200

USEFULNESS AND ADDITIONAL INFORMATION OF SCINTIMAMMOGRAPHY IN UNI- AND MULTIFOCAL BREAST CANCER. **D. François, J. Hermans, F. Bodart, JP. Fauconnier, C. Six, A. Schmitz, R. Gérard, M. Beauduin, Hôpital de Jolimont, Belgium.**

The aim of this study was to analyze the diagnostic performance and the additionnal information provided by scintimammography (SMM) in the diagnosis of breast cancer. Methods : 77 consecutive women referred to surgery for suspicious breast lesions were scanned before surgery. Ten min. after IV injection of 740MBq Tc-99m MIBI. anterior, left and right lat. views of the breasts were acquired for 10min in the prone position. The following visual criteria were applied : grade 1 (G1) : normal uptake; G2 : diffuse and mild uptake; G3 : well-delineated, but mild focal uptake; G4: well-delineated and intense focal uptake. G1 and G2 were considered as normal or benign; G3 and G4 were considered as malignant. Were also recorded : the presence of multiple foci of uptake in the same or in the controlateral breast, and the location of the uptake in the breast. Final diagnosis relied on the histology of the lesion.

Results :

	G1	G2	G3	G4
fibrocystic disease	9	1	1	
fibroadenoma	1	1	1	
adenosis	1		1	4
papillomatosis				1
cancer	5		2	49

1. The sensitivity is 91%, the specificity 62%, the positive predictive value 86%, the negative predictive value 72% and the accuracy 83%. 2. All false negative scans occured in cancers ≤1cm, meaning that all cancers >1cm were correctly identified. 3. In 4 women, the focal uptake was located against the chest wall : pectoralis muscle infiltration was present in all patients. 4. SMM detected multiple foci of uptake in the same breast in 6 women, that were all confirmed to be multifocal disease at histology. 5. Controlateral focal uptake was detected in 9 women : at this time, two are confirmed to be bilateral breast neoplasms.

Conclusions : 1. As previously shown, SMM is reliable in the diagnosis of breast cancer, particularly in lesions larger than 1cm. 2. Moreover, SMM provides additional qualitative information in 18% of breast carcinomas, such as chest wall infiltration, multifocal or bilateral breast cancer, that is relevant for the management of those patients.

No. 1201

L-[F-18] FLUOROETHYLTYROSIN (FET) SHOWS A HIGH AND RAPID UPTAKE IN SW707 TUMOR TISSUE. P. Heiss, S.Mayer, H.-J. Wester, M. Herz, G. Stöcklin, M. Schwaiger, and R. Senekowitsch-Schmidtke. Nuklearmedizinische Klinik der Technischen Universität München, Munich, FRG

It has recently been shown that [F-18]FET seems to be a promising F-18-labeled amino acid derivative for tumor imaging (Wester et al., JNM 1997;38: 175). The aim of the present study was to further investigate the uptake and transport behavior of L-[F-18]FET into human colon carcinoma SW707 in vivo and in vitro. Mice xenotransplanted with SW707 tumors were injected i.v. with 37 MBq [F-18]FET with and without unlabeled FET or tyrosine. The animals were sacrificed by cervical dislocation at 10, 30, 60, and 120 minutes p.i., and the radioactivity in various organs was measured using a γ-counter. The uptake was expressed as % injected dose per gram tissue (%ID/g)±SD (n=6). In addition SW707 cells were seeded in 24-well plates for two days. The cells were incubated with 185 MBq/ml [F-18]FET for 0, 0.3, 0.6, 1, 2, 4, 6, 10, 20, and 30 minutes at 37°C. After washing the samples three times with ice-cold PBS, the pellets were dissolved in 0.1 N NaOH plus 2% Triton X and counted in a γ-counter. To investigate the transport system for the FET uptake, cells were incubated with L-[F-18]FET and the transport inhibitors BCH, MeAIB and MeAIB in combination with serin for 5 minutes. The data of the biodistribution experiments demonstrated a high uptake of L-[F-18]FET into the tumor (at 30 and 60 minutes 6.42 ± 1.35% and 6.34 ± 1.70% ID/g). Only the pancreas had a higher uptake (18.9% ID/g at 30 and 60 minutes). The calculation of the tumor to plasma ratio showed a linear increase up to 60 minutes followed by a plateau ath a value > 2. Coinjection with unlabeled L-FET or L-tyrosine resulted in a reduction of [F-18]FET uptake into the tumor tissue. The transport inhibition experiments revealed that the uptake of [F-18]FET into the cells occurred mainly by the amino acid transport system L, similarly to the uptake of tyrosine. The in vitro kinetics showed a constant uptake rate up to 6 minutes followed by a plateau. This results encourage further studies with L-[F-18]FET for tumor imaging of solid tumors with PET.

Supported by Deutsche Krebshilfe e.V., Dr. Mildred Scheel Stiftung.

No. 1202

ACCUMULATION OF LIPOSOME-ENCAPSULATED Tc-99m-SESTAMIBI IN SENSITIVE AND MULTI-DRUG RESISTANT HUMAN TUMOR CELL LINES. M. Duran-Cordobes, A. Starzec, F. Benazzouz, V. De Beco, and J.L. Moretti. UPRES 2360, Université Paris-Nord, UFR L. De Vinci, 93000 Bobigny, France.

It is well established that accumulation of Tc-99m-sestamibi (MIBI) is much higher in sensible than multidrug-resistant (MDR) tumor cells. MIBI seems to be recognized by two transmembrane pumps involved in MDR, Pgp 170 as well as multidrug-resistance related protein (MRP) (Moretti, Duran-Cordobes, Starzec et al., J Nucl Med, in press). Thus, it is a good candidate to diagnose the MDR phenotype by *in vivo* imaging. But, the blood clearance of MIBI is too rapid to achieve its optimal accumulation in tumors and its uptake by liver, spleen, heart and muscle is too high to make it an excellent *in vivo* tumor tracer. One solution is using of liposomes which could prolong the MIBI circulation in blood and decrease its non specific accumulation. Since liposome-encapsulated doxorubicin is able to modulate cell MDR we explored, in the present study, whether association of MIBI with liposomes can affect its accumulation in three sensible and four resistant cell lines, two of them expressing Pgp 170 and two other overexpressing MRP. MIBI was incorporated into liposomes prepared by thin film hydration with phosphate buffered saline using distearoyl phosphatidyl choline, distearoyl phosphatidyl ethanolamine and cholesterol in ratio 1.85/0.15/1.00. Liposome size was 97.9±4.5 nm as determined by dynamic light scatering. The leakage of MIBI from liposomes to cell culture medium was rapid (up to 37% of the radioactivity after 90 min). The cells were incubated with liposome-encapsulated MIBI at 37C for 0, 30, 60 and 90 min followed by measure of intra- and extracellular radioactivity. To evaluate the possibility of specific liposome effect on MIBI accumulation the cells were incubated with free MIBI in the presence of empty liposomes. In both experimental cases the MIBI accumulation was similar to control (in the presence of only free MIBI) value: it was much higher in sensible than in resistant PgP-positive as well as MRP-positive cells. In conclusion, encapsulating in liposomes does not change the potency of MIBI to distinguish the sensitive and MDR tumor cells and can offer to this tracer better usefulness for *in vivo* imaging of tumors.

No. 1203

BRAIN TUMOR IMAGING WITH Tc-99m TETROFOSMIN SPECT: COMPARISON WITH Tl-201 AND Tc-99m MIBI SPECT AND FDG-PET. **J.Y. Choi, S.E. Kim, Y. Choi, Y.S. Choe, K.H. Lee, B.-T. Kim, H.J. Shin, Y.-L. Suh, J.H. Kim. Sung Kyun Kwan University College of Medicine, Samsung Medical Center, Seoul, Korea**

The uptake of Tc-99m tetrofosmin (TF) has been demonstrated in various extracerebral tumors. The purpose of this study was to investigate the feasibility of Tc-99m TF SPECT in the evaluation of brain tumors in comparison with Tl-201 and Tc-99m MIBI SPECT and FDG-PET.

Ten patients with histologically proven supratentorial tumors (5 high grade gliomas, 3 low grade gliomas, 1 lymphoma, 1 germinoma) were studied with Tc-99m TF SPECT. Tl-201 SPECT in 5, Tc-99m MIBI SPECT in 6, and FDG-PET in 5 of the 10 patients were concomitantly performed with Tc-99m TF SPECT within a 5 day interval. In both SPECT and PET studies, a standard ROI with preset size and shape (10.68 mm x 10.68 mm rectangle for SPECT, 3.75 mm diameter circle for PET) was positioned on the tumor areas having representative activities with an aid of brain MRI. In SPECT studies, the radiotracer accumulation in tumors was evaluated by the radioactivity ratio of tumor-to-contralateral nontumor region

(T/NT). FDG-PET tumor metabolic activity was expressed as the tumor-to-contralateral cerebellar ratio (Kim et al., J Neuro-Oncol 1991;10:85-91).

On visual examination of Tc-99m TF SPECT images, high grade gliomas and other malignant tumors exhibited a high Tc-99m TF uptake and were easily differentiated from low grade tumors. The T/NT ratios of Tc-99m TF uptake clearly separated malignant tumors (range 4.0-52.0) from low grade gliomas (3.0-4.2). Tc-99m TF uptake was significantly higher in high grade tumors than in low grade gliomas (T/NT 15.7 ± 16.9 vs. 3.5 ± 0.6, $p<0.05$). Tc-99m TF uptake in tumors was significantly correlated with Ki-67 labeling index ($r=0.975$, $p<0.01$) and %p53 expression ($r=0.97$, $p<0.01$). There were significant correlations between the uptake of Tc-99m TF and Tc-99m MIBI ($r=0.98$, $p<0.001$), Tl-201 ($r=0.87$, $p<0.05$), FDG ($r=0.91$, $p<0.05$) in tumor areas. Interestingly, a good agreement between the uptake of Tc-99m TF and Tc-99m MIBI was found (TF = 1.12 x MIBI - 3.14), suggesting that TF and MIBI may accumulate in brain tumors by similar mechanisms.

These preliminary results suggest that Tc-99m TF may be useful for the evaluation of brain tumors, comparable to other radiopharmaceuticals being currently used.

No. 1204

TECHNETIUM-99m TETROFOSMIN SPECT IN PRIMARY BREAST CANCER DETECTION AND AXILLARY LYMPH NODE STAGING.
A. Spanu, G. Dettori, A.Farris, C.Bagella, A.Porcu, S. Nuvoli, P. Solinas, P.Cottu, M.E. Solinas, P.Chiaramida, A.Masia and G. Madeddu. Depts. of Nuclear Medicine and Surgery. University of Sassari. Italy.

In order to evaluate the usefulness of TC-99m Tetrofosmin (T) SPECT in detecting primary breast cancer and in axillary lymph node staging, we studied 67 female patients, aged 40 to 83 yrs: 56 with suspected primary breast cancer following mammography which identified 65 breast lesions,10 of which non-palpable (Group A); and 10 with previously ascertained breast cancer following nodular excisional biopsy (Group B). In all pts, 15 min after 740 MBq i.v. injection of TC-99m Tetrofosmin, SPECT images were acquired using a dual rectangular head gamma camera. All pts were studied with their arms raised over the head with chest, mammary and axillary regions included in the field of view. In 48 Group A pts with breast cancer diagnosed by histology, T-SPECT identified 49/52 malignant lesions (sens. 94.23%). Of the 49 lesions detected by SPECT, 17 had a diameter <15mm and 11 of these <10mm, including 6 non-palpable lesions, one of which "in situ". However, T-SPECT was negative in another "in situ" carcinoma and in 2 palpable 15mm malignant lesions. In the remaining 9 Group A pts with 13 lesions all benign at surgery and 3 non-palpable, T-SPECT was true negative in 10 lesions (4 fibroadenomas, 4 fibrocystic dysplasia and 2 adenofibrosis), while it was positive in 3 fibroadenomas with a size of >20mm (spec. 77%). In Group B pts, T-SPECT was positive in 3/3 cases with residual breast tumor after excisional biopsy; it was true negative in the remaining 7 pts, concordantly with histological findings after mastectomy. In 57/58 cancer pts (47 Group A and 10 Group B) submitted to axillary lymph node dissection, T-SPECT had identified axillary lymph node metastasis in 24/27 cases (sens. 88.88%); it was true negative in 26 cases and false positive in 4 cases (spec. 86.66%).T-SPECT seems a reliable preoperative diagnostic tool in primary breast cancer and axillary lymph node staging. Moreover, it could be useful to identify residual breast cancer after excisional biopsy.

No. 1205

SESTAMIBI ACCUMULATION IN NASOPHARYNGEAL CARCINOMA CELL LINES *IN VITRO*.
J.R. Ballinger, J-H. Li, F-F. Liu, and I. Boxen. Experimental Therapeutics, Radiation Oncology and Nuclear Medicine, Ontario Cancer Institute, Toronto, Canada.

Sestamibi imaging has been found to be clinically useful to assess nasopharyngeal carcinoma (NPC) and to monitor therapy. This phenomenon has been further investigated by determining the *in vitro* accumulation characteristics of sestamibi in the NPC cell lines CNE-1 (C1) and CNE-2Z (C2Z),.

Sestamibi (1 MBq) was added to a single-cell suspension (3-10x10^5/mL) and aliquots were removed over 1 hr and centrifuged to determine cell-associated radioactivity. Further experiments studied the effect of addition of a P-glycoprotein (Pgp) modulator or alteration in plasma and/or mitochondrial membrane potentials.

Sestamibi accumulation reached similar plateau values in C1 and C2Z within 15-30 min of addition. Saturating concentrations of PSC833 (1 μM) or GG918 (0.2 μM) increased accumulation 1.9±0.5 and 1.9±1.1 fold (n=5) in C1 and C2Z, respectively. Hyper-polarisation of the mitochondrial membrane (nigericin, 5 μg/mL) increased accumulation 3.1-3.5 fold. In contrast, depolarisation of the plasma membrane with isotonic high potassium buffer reduced accumulation to 80% of control values and additional depolarisation of the mitochondrial membrane (valinomycin, 1 μg/mL) further reduced accumulation to 30-50% of control.

These results indicate that both cell lines contain a modest level of Pgp activity and that both are capable of further polarisation of the mitochondria. This suggests that hyperpolarisation of the mitochondria is not the explanation for high accumulation of sestambi in NPC. *(Sestamibi was donated by DuPont Pharma)*

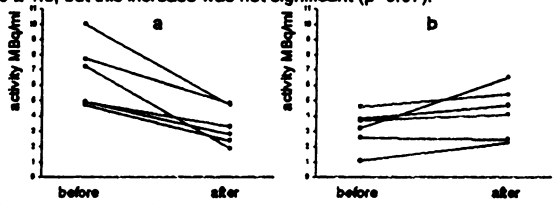
No. 1206

[O-15]-H2O-PET MAY PREDICT AND EVALUATE TUMOR RESPONSE TO THERAPY
A.C. Kole and W. Vaalburg. PET Center & Department of Surgical Oncology, Groningen University Hospital, Groningen, The Netherlands

Aim of this study was to explore the use of [O-15]-H2O-PET for the prediction of sensitivity of tumors to therapy, and the evaluation of response to treatment.

Twelve patients (4 bone tumors, 5 soft tissue sarcoma, 2 melanoma, 1 squamous cell carcinoma) underwent [O-15]-H2O-PET twice. After the first PET, patients were treated with high dose systemic chemotherapy or hyperthermic isolated limb perfusion with tumor necrosis factor-α and melphalan. The second PET was performed just before resection of the tumor remnant. A good histological response was seen in six patients and a bad response in the other six patients. A 951/31 ECAT positron camera (Siemens/CTI, Knoxville, USA) was used for data acquisition. 1850 MBq [O-15]-H2O was administered intravenously. An attenuation corrected emission scan was obtained for 3 minutes and the average radioactivity in the tumor was calculated.

All twelve tumors were clearly visualized with PET. Mean tumor activity before therapy was 4.9 MBq/ml (range 1.1-10.0). All patients with activity >4.6 prior to therapy responded well to that therapy, whereas all patients with less activity responded poorly (t-test, $p=0.007$). Tumor activity in good responders (a) decreased after therapy from 6.6 ± 2.1 (mean ± SD) to 3.3 ± 1.2 (paired t-test, $p=0.005$). Tumor activity in poor responders (b) increased from 3.2 ± 1.2 to 4.3 ± 1.6, but this increase was not significant ($p=0.07$).



This preliminary study shows that high tumor perfusion as measured with [O-15]-H2O-PET corresponds with a good response to subsequent treatment, and a lower perfusion with a poor response. The response to therapy can also be shown with [O-15]-H2O-PET. [O-15]-H2O PET may therefore be used to both predict and evaluate the response to anticancer-treatment in vivo.

No. 1207

EVALUATION OF TECHNETIUM-99m-(Tc-99m)-LABELED LIPOSOMES VERSUS Tc-99m-SULFUR COLLOID (SC) AND Tc-99m-HUMAN SERUM ALBUMIN (HSA) FOR LYMPHOSCINTIGRAPHY IN A RABBIT MODEL.
W.T. Phillips, T. Andrews, H.L. Liu, R. Klipper, A. Laundry and B. Goins, University of Texas Health Science Center, San Antonio, TX.

This study investigated the use of Tc-99m-liposomes for detection of the sentinel lymph node compared with the commonly used agents, regular-SC, 0.22 μ-filtered-SC, reduced heat old Tc-99m-0.22 μ-filtered-SC, and HSA. Liposomes had no surface modification (Neutral) or were coated with polyethylene glycol (PEG). Liposome formulations were prepared in various diameters ranging from 50 to 600 nm and were labeled with Tc-99m using HMPAO. Rabbits were injected subcutaneously in the hindpaw with each agent (0.3 ml; 11 MBq). Hindpaw was manually massaged for the first 5 min and leg movements performed for 1 min at 30 and 45 min to evaluate retention in the popliteal node. Images were acquired for the first 60 min and at 20 hr. Images were analyzed to determine the % of the agent which migrated from the injection site, the retention in the popliteal node at 30 min, retention in the popliteal node at 1 hr after leg movement, and the total migration from the injection site at 20 hr. All liposomal agents performed better than regular-SC and HSA. Regular-SC showed virtually no migration (< 0.5%) from the injection site while Tc-99m-HSA was poorly retained in the popliteal node after leg movement (<

1%). Both liposome formulations had an initial migration of ~ 5-10% from the injection site at 30 min with liposomes >100 nm (5%) while liposomes < 100 nm (8-10%). At 1 hr post-injection, PEG-liposomes had decreased retention in the popliteal node (1%) compared with Neutral-liposomes (2.6%). Filtered-SC showed good migration (15%) from the injection and good retention in the popliteal node (12%). Liposomes offer a potential advantage in allowing sufficient retention in the popliteal node while allowing visualization of secondary nodes.

No. 1208

COMPARISON OF TL-201 WITH Tc-99-m SESTAMIBI FOR DIAGNOSIS OF CNS LYMPHOMA IN AIDS. W. Erdman, D. Skiest, W. Chang, J. Fleckenstein, D. Mathews, M. Devous, F. Bonte. University of Texas Southwestern Medical School, Dallas, TX.

Purpose: To evaluate image interpretation criteria of TL-201 and Tc-99m Sestamibi brain SPECT in differentiating lymphoma from others CNS lesions. **Methods:** Twenty-five AIDS patients with CNS lesions underwent prospective TL-201 Brain SPECT. A subset of 20 patients also underwent Tc-99m MIBI SPECT. Images were subjectively interpreted as positive for lymphoma when lesion activity appeared to equal or exceed contralateral scalp and to exceed contralateral brain. Region of Interest (ROI) data for lesion to brain and lesion to scalp activity was generated by a blinded observer. **Results:** Final diagnosis was established in 15 patients (two biopsy, two autopsy, 11 clinical and other laboratory). Five patients had lymphoma, eight had toxoplasmosis and two had PML. Subjective TL-201 interpretations were positive in all lymphoma and negative in all non-lymphoma patients (sensitivity, specificity = 100%). Subjective MIBI interpretations were positive in two of four lymphoma patients and negative in 6/6 non-lymphoma patients (sensitivity 50%, specificity = 100%).

ROI Data	Lymphoma (Range)	Non-lymphoma (Range)	Two Tail *t*-Test
TL lesion/Brain	2.85 (2.38 – 3.25)	1.27 (0.99 – 1.85)	P < 0.001
TL lesion/Scalp	1.17 (1.03 – 1.54)	0.61 (0.29 – 1.12)	P < 0.001
MIBI lesion/Brain	7.8 (5.28 – 12.26)	1.6 (0.74 – 2.25)	P < 0.001
MIBI lesion/Scalp	0.49 (0.25 – 1.0)	0.16 (0.02 – 0.32)	P < 0.05

Conclusion: Subjective interpretation of Thallium Brain SPECT reliably (100% accuracy) diagnosed CNS lymphoma, while subjective MIBI interpretation had only a 50% sensitivity despite higher lesion to brain ratios. The confounding factor was that MIBI lesion to scalp ratios were significantly lower than Thallium lesion/scalp ratios and none of the lymphomas was greater than the scalp on MIBI SPECT. Diagnosis of lymphoma on MIBI images should be based on lesion to brain ratios >2.25.

No. 1209

COMPARISON OF A TECHNETIUM LABELED SSTR BINDING PEPTIDE (P829) AND F-18 FDG PET IN THE EVALUATION OF SOLITARY PULMONARY NODULES. H. Handmaker, J.E. Blum, and M.A. Lawson. Arizona Institute of Nuclear Medicine, CIGNA HealthCare of Arizona, and Good Samaritan Regional Medical Center, Phoenix AZ.

Many neoplasms, including small cell and non-small cell lung cancer are known to express Somatostatin Type Receptors (SSTR). Tc-99m P829 ("P829") is a unique peptide radiopharmaceutical under investigation for the noninvasive detection and staging of a variety of malignancies that are known to express SSTRs. In the course of a Phase 3 clinical trial to evaluate the ability of P829 scintigraphy to differentiate those SPN resulting from granulomatous diseases, including coccidioidomyocosis, from those due to malignancy, a subset of patients were concurrently studied with F-18 FDG PET and the results of both imaging studies compared to surgical pathology in each patient. **Method:** Following IRB approval, 8 patients with pulmonary nodules grater than 1 cm in size and previously entered into the Phase 3 trial underwent simultaneous Computerized tomography (CT), P829 scintigraphy, including Single Photon Emission Computed Tomography (SPECT), and F-18 FDG Positron Emission Tomography (PET). After obtaining written informed consent from the patients, 10-50 µgm of P829 labeled with 5-23 mCi (185-851Mbq) of Tc-99m was injected intravenously in to the patients. On a subsequent visit, 10 mCi F-18 FDG was administered in fasting patients with a blood glucose level less than 100 mg/dl. Planar anterior and posterior whole body images, as well as SPECT reconstructions were obtained for P829, and conventional emission and transmission PET scans obtained and SUV determinations performed for the FDG study. **Results:** 5 male and 3 female patients, ranging in age from 41 to 73 years (mean age-53.8 years) comprised the study population. All 8 patients underwent tissue biopsy, either transthoracic needle biopsy or thoracotomy. In 2 patients with malignancy (1 adenocarcinoma and 1 squamous cell carcinoma) there was uptake of both P829 and FDG. In 3 patients with necrotizing granulomatous disease consistent with cocci, there was no uptake of either P829 or FDG. In 3 patients with granuloma (2 consistent with cocci and 1 with Mycobacterium avium ("MAC") infection) there was concordant P829 and FDG uptake corresponding to the SPN seen on chest xray and CT scan. Of interest, the SUV for one cocci patient was 4.7, and the SUV for the MAC patient was 3.5, indicating metabolically active disease. **Conclusion:** These preliminary data suggest that P829 SPECT imaging compares favorably to FDG PET studies in the noninvasive evaluation of solitary pulmonary nodules. Both techniques appear to be sensitive but somewhat nonspecific in these patients. Comparison of the two procedures in a larger population seems warranted. The more convenient imaging requirements and projected lower cost of P829 SPECT may provide wider availability for this technique than does FDG PET.

No. 1210

COMPARISON OF A TECHNETIUM LABELED SSTR BINDING PEPTIDE (P829) AND MIRALUMA IN THE DIAGNOSIS OF BREAST CANCER . H. Handmaker, Arizona Institute of Nuclear Medicine, Phoenix AZ.

Early diagnosis of breast cancer is of utmost importance to increase survival rates. Various imaging techniques have been proposed to reduce the uncertainty associated with conventional mammographic techniques. Mammoscintigraphy using Tc-99m sestamibi ("Miraluma") has been evaluated in this setting, with a reasonably high degree of accuracy. It is well known that malignant cells from patients with carcinoma of the breast express various subtypes of somatostatin receptors on their cell surfaces. Several reports describe success with In-111 pentetreotide ("Octreoscan") in these patients. For this reason, a study was conducted to compare mammoscintigraphic data using a low molecular weight (1358), somatostatin type receptor ("SSTR") binding peptide, Tc-99m P829 ("P829") with concurrently performed Miraluma studies in the diagnosis and staging of patients suspected of having breast cancer **Method:** 18 studies were performed in 16 female patients (27-77 years of age, mean age-48.6 years) with either a prior histologic diagnosis of breast cancer or mammographic abnormalities requiring additional evaluation. After obtaining written informed consent from the patients, 10-50 µgm of P829 labeled with 5-23 mCi (185-851 MBq) of Tc-99m, and 20-25 mCi (740-925 MBq) Miraluma was injected intravenously on separate visits at least one day apart. Planar anterior and posterior whole body images, and 1-3 hour selected spot images, as well as single photon emission computed tomography (SPECT) reconstructions were obtained for P829, and conventional prone lateral and anterior planar Miraluma images. SPECT images were obtained in several Miraluma patients for correlation with P829 images. Comparisons were retrospectively made to independently interpreted conventional mammographic, computed tomography (CT), F-18 FDG PET imaging procedures, as well as, when available, surgical pathology. **Results:** There were 6 true positive (TP), 10 true negative (TN), 1 false negative (FN) and 1 false positive (FP) study with each radiopharmaceutical in this series. This resulted in a PPV of 85.7%, NPV of 90.9%, Sensitivity of 85.7%, Specificity of 90.9%, and an Accuracy of 88.9% for both tracers, all comparable to published data for Miraluma MMS. Significantly, however, one patient with intense P829 uptake in malignant foci on both an immediate postoperative study and a later study after definitive therapy had only minimal Miraluma uptake on both studies and was considered positive only after review of the P829 studies. One patient with a biopsy proven intrapulmonary metastatic lesion had neither P829 or Miraluma uptake, but had positive F-18 FDG uptake and a positive CT scan. **Conclusion:** Results of this preliminary study indicate that P829 is equivalent or superior to Miraluma in the detection of primary and metastatic breast cancer. The greater intensity of P829 uptake in several patients reflects a distinctly different mechanism of uptake from that of Miraluma. P829 binding to the expressed SSTRs in these patients suggests a potentially useful biologic marker with therapeutic implications.

No. 1211

DYNAMIC SPECT DEMONSTRATES DISCREPANCIES BETWEEN INITIAL UPTAKE AND RETENTION OF Tc-99m HMPAO AND Tc-99m ECD IN HIGH GRADE GLIOMA. F. Payer, F. Fazekas, K. Brodtrager, and H. Valetitsch. Karl-Franzens University, Graz, Austria.

In a small group of patients with recurrent high-grade glioma Tc-99m hexamethylpropylene (HMPAO) has been proposed an adjunct to thallium-201 chloride to distinguish between viable tumor and necrosis. However, recent studies have demonstrated differences in retention between HMPAO and Tc-99m ethylcisteinate dimer (ECD) in high-grade glioma.The purpose of this study was to determine the initial uptake and the retention of HMPAO and ECD in this setting. Seven patients (median age 68 yrs, range 35-72) with surgically established diagnosis of high-grade glioma (6 glioblastoma WHO IV and 1 astrocytoma WHO III) were studied with HMPAO and ECD. Measurements were performed with SPECT using a system consisting of an array of 4 rapidly rotating detector banks (Tomomatic 564, Medimatic, Denmark). For dynamic studies the data acquisition started immediately after i.v. injection of 10.36 MBq/kg body weight of either HMPAO or ECD. The time interval between the two examinations ranged from 1 to 3 days. The dynamic mode was performed in steps of 30 seconds providing 9 serial images. The static SPECT was started 30 minutes after injection. For analysis predefined regions of interest were placed on the basis of MRI studies on the tumor and the ipsilateral cerebellar hemisphere. Regional semi-quantitative ratios were performed and time-activity curves were calculated.

Initial relatively high focal uptake of both HMPAO and ECD was seen in 2 patients. The remainder demonstrated isoactive or slightly hypoactive initial uptake. Although the differences between HMPAO and ECD uptake (0.90 ±0.2, 0.86 ±0.3, respectively) were minimal, six out of 7 patients showed slightly higher initial uptake of HMPAO than ECD in the tumor. Time-activity curves were characterized by a minimal decrease of HMPAO (0.90 ±0.2, 0.84 ±0.2) within the first 30 seconds and an almost unchanged activity in the static study (0.83 ±0.1, $p<0.3$). ECD studies were characterized by focal decline of activity in 6 patients (initial:0.86 ±0.3,

30 seconds:0.67 ±0.1, static study:0.59 ±0.0, p<0.04). A constantly low tracer activity was retained in one tumor.
These preliminary findings suggest that ECD in contrary to HMPAO may not differentiate viable high-grade brain tumor from surrounding tissue and therefore may not adjunct other functional imaging studies.

No. 1212

MEDIASTINAL LYMPH NODE STAGING WITH TECHNETIUM-99m-MIBI SCAN IN PATIENTS WITH NON SMALL CELL LUNG CANCER (NSCLC): A COMPARATIVE STUDY WITH THALLIUM-201. S. Nagamachi, S. Jinnouchi, T. Ohnishi, Leo G Flores II, H. Nakahara, S. Futami, S. Tamura. Miyazaki Medical College, Japan

Aim: To compare the performance of CT, Technetium-99m MIBI (MIBI) and Thallium-201 (Tl) in the detection of metastatic mediastinal lymph nodes (MLN) in patients with non small cell lung cancer (NSCLC). **Methods:** 25 patients with operable NSCLC underwent spiral CT, MIBI-SPECT and Tl-SPECT scan within two weeks prior to surgical treatment. Spiral CT with bolus injection of contrast medium was performed on a Toshiba high speed scanner (slice thickness of 5 mm, pitch 1.6). MLN larger than 1.0 cm in the long axis was considered to be abnormal. MIBI and Tl dual isotope scan was done both 15 min (early) and 3 hr (delayed) after injection of tracers. All SPECT images were processed on Prism 2000 console. Transaxial images were visually evaluated.
Results:

	CT	MIBI SPECT		Tl SPECT	
		early	delayed	early	delayed
Sensitivity	73%	73%	27%	73%	55%
Specificity	64%	93%	100%	93%	86%
Positive predictive value	62%	89%	100%	89%	75%
Negative predictive value	75%	87%	64%	87%	71%
Accuracy	68%	84%	68%	84%	72%

Conclusion: Both MIBI and Tl SPECT are sensitive, non-invasive method for assessing mediastinal involvement in the preoperative stage of non small cell lung cancer and their diagnostic accuracy were better than that of CT. Although Tl was superior to MIBI on the delayed images, early SPECT images were comparable between MIBI and Tl in the diagnostic ability of mediastinal lymph node metastasis.

No. 1213

Positron-Emission-Tomography for Monitoring N-13-Cisplatin Uptake in Ovarian Cancer

S. Fenchel, V.J. Möbus*, R. Kreienberg*, S.N. Reske
Department of Nuclear Medicine and Department of Gynecology,*University of Ulm, Germany

Purpose: Resistance to platinum-containing chemotherapeutics is a major obstacle in the cure of advanced ovarian cancer. Mechanisms of resistance are decreased cellular drug accumulation, increased intracellular glutathione and metallothionein concentration and enhanced DNA repair. We performed positron-emission-tomography (PET) with N-13-labeled cisplatin in order to investigate individual tumoral cisplatin pharmacokinetics and to examine the connection between tumoral cisplatin accumulation and tumoral cisplatin sensitivity. **Methods:** 7 patients with suspected ovarian cancer (4 with histologically proven ovarian cancer, 1 with tubal carcinoma, 1 with corpus carcinoma, 1 with ovarian cancer and corpus carcinoma) were enrolled in the study. Dynamic FDG-PET imaging was performed for 50 min starting with the i.v. bolus injection of N-13 cisplatin (185-740 MBq, specific activity 37-74 GBq/mmol). Tumoral cisplatin uptake was evaluated by visual interpretation on integral images (0-90 sec, 90 sec-10 min, 10-20 min and 20-50 min) and by decay corrected time-activity curves in ROIs comprising the tumors. **Results:** In 4 out of 7 patients tumor masses (3 ovarian carcinomas, 1 corpus carcinoma) could be visualized by PET. N-13 cisplatin accumulation in the tumor region was visible on the perfusion images (0-90 sec) as well as on the following frames untill 50 min scanning time. Time activity curves showed a steep increase over 60-90 sec, reached a maximum at ca. 60-90 sec and remained more or less at the same level over the following 49 min without distinct changes. In 3 out of 7 patients no clear N-13 cisplatin uptake into the tumors could be detected, neither on the perfusion scans nor on the later images. **Conclusions:** N-13 cisplatin PET is suitable for measuring cisplatin accumulation in gynecological malignancies and for detection of differences in cisplatin pharmacokinetics in tumors. The clinical follow-up will show if PET by detecting accumulation differences between tumors is able to predict individual tumoral chemotherapy response.

No. 1214

VALUE OF INDIUM-^{111} OCTREOTIDE IMAGING IN PATIENTS WITH UNKNOWN PRIMARY CARCINOMA
E.S. Delpassand, M. Vaseghi, Lenzi R., D.A. Podoloff. U.T. M.D. Anderson Cancer Center, Houston, TX.

Patients presenting with cancer of unkown primary origin make up 3-15% of all malignancies seen in cancer referral centers. The initial biopsy of present-ing site (PS) is not contributory in 80% of the malignant neoplasm. We evaluated fifteen patients (pts.) with carcinoma of unknown primary referred to Department of Nuclear Medicine, M.D. Anderson Cancer Center from August, 1994 to January, 1997. **All pts. had exhaustive evaluation by other laboratory and imaging modalities (Histology,CT, MRI, U/S) that were unsuccessful in localizing the primary tumor.** There were 11 female and 4 males, ages ranging from 44 to 70 with average of 55. Imaging was performed following IV administration of 5.0 mCi of Indium-^{111} Octreotide. Wholebody and SPECT images were obtained at 4 and 24 hours. Patients presented with metastasis to the bones, lungs, liver and lymph nodes. Three patients had complete excission of PS prior to scan. Ten out of 12 PSs showed Octreotide uptake (83%). Histological type of cancer on visualized lesions were adenocarcinoma, clear cell carcinoma from follicular thyroid cancer, and neuro endocrine tumors. Pathology on non visualized PSs were metastatic adenocarcinoma of the lungs (lesions <1 cm) and unclassified malignant neoplasia in fibrous tissue. Octreoscan was able to identify or suggest primary (i.e. hilar uptake suggesting lung primary) in 7 out of 15 cases (46%).
The result is comparable to the yield of autopsy in patients with unknown primary carcinoma [1]. Based on the uptake in PS, identification, and/or suggestion of the primary cancer, pt. management was affected in 10 of 15 pts.(67%).
CONCLUSION: Indium-^{111} Octreotide is helpful when other imaging modalities fail to identify primary site of malignancy. Visualization of primary cancer or uptake in presenting site can make significant impact on pts. management and probably outcome.

REFERENCE: 1. Chevalier, T.L., Cvitkovic, E., et al. Early metastatic cancer of unknown primary origin at presentation. A clinical study of 302 consecutive autopsied patients. Arch Intern Med. 148:2035-2039, 1988.

No. 1215

[Tc-99m] SESTAMIBI SCINTIMAMMOGRAPHY TO EVALUATE RESPONSE OF BREAST CARCINOMA TO NEOADJUVANT CHEMOTHERAPY.
A.J.Joaquim, J.Y.Shinzato, C.D.Ramos, E.C.S.Camargo-Etchebehere, R.F.Vargas, F.A Severiche, M.Alvarenga, E.E.Camargo. Divison of Nuclear Medicine, Department of Radiology; and Division of Pathology, Department of Obstetrics and Gynecology, Campinas State University (Unicamp), Campinas, Brazil.

Accurate assessment of locally advanced breast carcinoma response to presurgical neoadjuvant chemotherapy is crucial in planning subsequent treatment. Conventional evaluation by clinical examination and mammography is not always reliable. [Tc-99m] sestamibi scintigraphy has been shown to be useful in the evaluation of response to therapy of several types of tumors such as bone and soft tissue sarcomas and brain tumors.

We have investigated the usefulness of this method to assess the response of breast carcinoma to neoadjuvant chemotherapy. Fifteen patients (35-69 years of age) with locally advanced breast carcinomas were studied with [Tc-99m] sestamibi scintimammography prior to the first cycle and 21 days after the last cycle of chemotherapy. We used prone planar images obtained 10 minutes after an intravenous injection of 925 - 1,111 MBq (25-30 mCi) of the tracer. Tumor uptake of [Tc-99m] sestamibi before and after chemotherapy was graded visually as absent, mild, moderate and intense.

Tumor response to chemotherapy was conventionally assessed by mammography, clinical evaluation and histopathological examination of the specimens in all patients. Seven patients who did not demonstrate significant change in tumor uptake were found to be poor responders to chemotherapy. Of the remaining 8 patients who were good responders to chemotherapy, 5 demonstrated significant reduction in tumor uptake and 3 showed no significant reduction in tumor uptake. The overall agreement between scintimammography and the conventional classification of tumor response, including mammography, clinical evaluation and histopathology, was 80%. The sensitivity of scintimammography for detection of good responders was 62.5%, with a specificity of 100%. On the other hand, its sensitivity for detection of poor responders was 100%.

Scintimammography with [Tc-99m] sestamibi seems to be an important adjunct in the assessment of response of locally advanced breast carcinoma to neoadjuvant chemotherapy.

No. 1216

PROGNOSTIC VALUE OF RESTAGING GALLIUM SCAN FOLLOWING CHEMOTHERAPY IN LYMPHOMA PATIENTS: 8 YEARS FOLLOW-UP.

M.Gasparini, *E. Bombardieri, *L.S. Maffioli, *L. Devizzi, M. Castellani, *C. Tondini, A. Bruno, V. Longari, R. Benti, P. Gerundini. Nuclear Medicine Depts. IRCCS-Ospedale Maggiore-Milan and *Istituto Nazionale dei Tumori-Milan; Italy

In lymphoma patients the response to chemotherapy represents one of the most important prognostic factors in the management of this disease. A significant percentage of these patients fail to achieve complete remission (CR) after treatment, or they relapse following initial therapy. The use of gallium scintigraphy (Ga-67) in relation to conventional restaging techniques is still controversial. In particular its role in detecting active disease after treatment may be of particular interest in the subsequent treatment planning. In order to evaluate the ability of Ga-67 to define residual disease after treatment, 41 lymphoma patients (22 Hodgkin's disease-HD and 19 non-Hodgkin lymphoma-NHL) were per-spectively studied (follow-up 99 months: range 7-99 months). We investigated if the positivity of the scan after chemotherapy could predict the clinical outcome. All patients underwent restaging 2-4 weeks after termination of 4-8 cycles of chemotherapy and were examined 48-72 hours after the i.v. injection of 185-300 MBq of Ga-67. Imaging included whole body planar imaging and in many cases SPECT of the involved region. The restaging workup included physical examination, laboratory assessment with complete blood count and chemistry, complete radiographic baseline studies including chest X-rays, CT scan and/or MRI and all diagnostic examinations performed at staging. The patients were divided into two groups according to the positivity or negativity of restaging Ga-67. In the first group 14 of 41 patients showed persistent uptake of gallium. Of these, 10 (71%) died (follow-up 7-31 mths, mean 17.9) and 4 were considered to be in CR (follow up 41-84 mths, mean 70.2). In the second group 27 patients resulted negative on restaging. Of these, 22 pts (81.4%) are alive without evidence of disease and 5 died (follow-up 16-58 mths, mean 36.0) dued to disease relapse. The mean follow-up was 70.4 months (range of 57-99 mths). Statistical analysis of the association between Ga-67 results and survival was performed using the log-rank test. There was a statistically significant association between scan result and survival ($P<.001$). The 8-year overall survival rate was 81.4% for pts with negative scans and 28% for gallium-positive pts. Restaging gallium scan seems to be an excellent indicator of residual viable tumor and accurately distinguish complete responders from induction failures.

No. 1217

INHIBITION OF *MDR1* Pgp-MEDIATED TRANSPORT OF Tc-99m-SESTAMIBI BY HIGH-POTENCY MODULATORS IS A MARKER OF INCREASED ESTERIFICATION OF PLASMA MEMBRANE CHOLESTEROL.

G.D. Luker and D. Piwnica-Worms. Washington University Medical School, St. Louis, MO.

Tc-99m-Sestamibi is a transport substrate recognized by *MDR1* P-glycoprotein (Pgp). Because *MDR1* Pgp may function in trafficking of sterols, we pulse-labeled plasma membrane cholesterol with ^{3}H-cholesterol and quantified esterification of cholesterol as a marker of transport from plasma membrane to endoplasmic reticulum. Correlation was made with Tc-99m-Sestamibi transport. After one hour of chase, esterification of cholesterol was greater in NIH 3T3 cells transfected with human *MDR1* Pgp than in parental cells (mean ± SEM: 0.68 ± 0.03 vs 0.42 ± 0.03 fmol(mg protein)$^{-1}$(pM$_O$)$^{-1}$, respectively). Differences between *MDR1* transfectants and NIH 3T3 cells also were observed after stimulation of esterification with exogenous sphingomyelinase (14.4 ± 2.4 and 7.89 ± 0.77 fmol(mg protein)$^{-1}$(pM$_O$)$^{-1}$, respectively). In NIH 3T3 cells transfected with a related transporter, the human multidrug resistance-associated protein (*MRP*), esterification without or with sphingomyelinase treatment did not differ from control cells. In NIH 3T3 cells transfected with human *MDR1* or *MRP*, steady-state accumulations of Tc-99m-Sestamibi were 0.93 ± 0.08 and 15.5 ± 3.1 fmol(mg protein)$^{-1}$(nM$_O$)$^{-1}$, respectively, compared with control cell content of 36.6 ± 4.8. In contrast, decreased net accumulation of Tc-99m-Sestamibi mediated by *MDR1* Pgp, but not *MRP*, could be fully reversed to control levels by high potency MDR modulators (such as LY335979). These data show that increased esterification of plasma membrane cholesterol is associated with expression of *MDR1* Pgp. Drug-induced enhancement of Tc-99m-Sestamibi cell content by high potency *MDR1*-directed modulators may be a specific marker of enhanced cholesterol esterification.

No. 1218

DIAGNOSTIC ACCURACY OF TL-201 SPECT IMAGING IN HIV POSITIVE PATIENTS WITH CNS LESIONS.

S. Miseljic, A.C. Civelek, J.D. Port, D.A. Wolk, J. McArthur, A. Mudun, B.B. Chin. Johns Hopkins Medical Institutions, Baltimore, MD.

Initial studies with smaller populations reported promising results in accurately diagnosing CNS lesions in HIV patients utilizing Tl-201 SPECT. The purpose of this study is to define diagnostic accuracy in a large patient population and to evaluate the accuracy of several methods of classifying lesions.

Of 76 patients with Tl-201 SPECT, 53 with complete followup were included. Final diagnosis was established by autopsy (n=4), biopsy (n=6), and clinical diagnosis by a HIV neurology team (n=43). 25 cases were CNS lymphoma. 16 were toxoplasmosis, 9 were PML and 3 were classified as others (septic emboli, stroke and meningitis).

To evaluate the best visual method, all studies were interpreted first without MRI correlation and then with MRI correlation at a low threshold (lymphoma defined as lesions greater than background). This process was repeated with a higher threshold (lymphoma defined as greater than twice background). All studies were blindly interpreted in random order by 2 experienced nuclear medicine physicians.

To evaluate the semi-quantitative methods, an operator (blinded to results) defined ROIs around the largest abnormal Tl-201 lesion (correlated with MRI) and background ROIs (small and large) to determine counts/pixel for lesion/background (L/B) calculations. ROC curves were generated to define the optimal threshold for each semi-quantitative method.

Visual	Sens	Spec
Low threshold, No MRI	86%	50%
Low threshold, with MRI	91%	65%
High threshold, No MRI	80%	79%
High threshold, with MRI	84%	96%

Semi-quantitative	Sens	Spec
Small BKG	68%	82%
Large BKG	88%	93%

The higher threshold interpretation using MRI correlation provided the most accurate visual results. Correlation with MRI added incremental diagnostic accuracy. The most accurate semi-quantitative method utilized larger background ROIs. Semi-quantification may be useful when visual interpretation is equivocal.

No. 1219

WEIGHTED GLEASON SCORE PROVIDES ACCURATE STRATIFICATION IN PATIENTS WITH RISING PROSTATE-SPECIFIC ANTIGEN AFTER PROSTATECTOMY

K. Lin, Z. Szabo, B.B. Chin, A.C. Civelek. The Johns Hopkins Medical Institutions, Baltimore, MD

In patients with rising PSA after prostatectomy the correlation of positive bone scan with clinical parameters i.e., Gleason score (GS), capsular penetration (CP), seminal vesicle invasion (SV), lymph node/vascular invasion (L/V), surgical resection margin (RM), and pathologic stage (T stage) is not well defined. We retrospectively studied 106 consecutive patients with rising PSA after prostatectomy who had bone scans. To better characterize the degree of malignancy, we describe and propose the use of a weighted (Wt) Gleason score: [(primary tumor grade) + (secondary tumor grade) + 4]. This equation corrects for the overweighting of the secondary grade in the conventional GS and more accurately reflects the true pathology of the tumor.

Six of 43 patients with PSA <2 ng/ml, 10 of 29 with PSA 2-10 ng/ml, 12 of 22 with PSA 10-50 ng/ml, and 10 of 11 with PSA >50 ng/ml had metastatic bone disease. Significant correlation was found with positive bone scan and GS, Weighted GS, PSA level, seminal vesicle invasion, lymph node/vascular invasion, and resection margin (but not with capsular penetration or T stage).

	CP		SV		L/V		RM		GS		Wt GS	
	pos.	neg.	pos.	neg.	pos.	neg.	pos.	neg.	≥8	≤7	≥4.8	≤4.3
Patients	76	30	35	71	26	80	44	60	43	63	61	45
B. Mts. +	25	13	20	18	14	24	22	16	22	16	31	7
P values	>0.05		<0.05		<0.05		<0.05		<0.05		<0.001	

Two of 2 patients (100%) with a weighted GS of 4.75 (GS 8) had bone metastasis, while only 2 of 9 patients (22%) with a weighted GS of 4.25 (also GS 8) had bone metastasis. In the group of GS 7, 11 of 26 (42.3%) with a weighted GS of 4.75 had bone metastasis, while only 3 of 20 (15%) with a weighted GS of 4 had bone metastasis. Conventional GS was unable to define these two subgroups, but the weighted GS separates them.

In patients with rising PSA after prostatectomy, high Gleason score, seminal vesicle invasion, lymph node/vascular invasion, and positive resection margin all are highly associated with bone metastasis. The weighted Gleason Score was a superior prognostic indicator which was able to identify low risk patients falsely included into high risk (GS 8) group and those high risk patients falsely included into intermediate (GS 7) risk group.

No. 1220

1-[C-11]-GLUCOSE AND FDG UPTAKE IN MALIGNANT GLIOMAS: RESPONSE TO RADIOTHERAPY. A.M. Spence, M. Muzi, M.M. Graham, F. O'Sullivan, A. Olshen, J.M. Link, K. Stelzer, S.D. Freeman and K.A. Krohn. Departments of Neurology, Radiology and Radiation Oncology, University of Washington, Seattle, WA.

This work examines whether quantitative metabolic imaging with PET correlates with treatment outcome in malignant gliomas. Determinations of the metabolic rates of glucose (MRGlc) or [F-18]-fluorodeoxyglucose (MRFDG) in normal brain or malignant gliomas with PET can be made independently with 1-[C-11]-Glc or FDG and can be combined to derive the proportionality factor, the lumped constant (LC_{FDG}).

Adults with malignant cerebral gliomas were imaged within two weeks before or two weeks after radiotherapy (RT). Four patients were imaged only before RT, thirteen only after RT and thirteen both before and after RT. Each was studied with 1-[C-11]-Glc followed by FDG, both with arterial plasma sampling. MRGlc and MRFDG were estimated by an optimization program based on 2 compartment, 4 rate constant models which yielded estimates of the kinetic parameters and MRGlc or MRFDG from which the LC_{FDG} was calculated as MRFDG/MRGlc. The percentage change in MRGlc, MRFDG, or LC_{FDG} from pre- to post-RT was calculated for the thirteen patients studied at both times. Survival was compared to historical controls in appropriate prognostic classes.

Low pre-RT MRGlc ($p<0.02$) or MRFDG ($p<0.04$), or an increase in MRGlc from pre- to post-RT ($p<0.06$) are correlating with increased survival (4 patients still alive).

Relatively low MRGlc or MRFDG before RT may be indicative of less aggressive disease. Alternatively these results may indicate that a favorable response to RT is associated with a shift from glycolysis (lactate production) to oxidative metabolism via the tricarboxylic acid cycle. (Supported by NIH grant CA42045)

No. 1221

DOES ITERATIVE SPECT IMPROVE THE DIAGNOSTIC ACCURACY OF PLANAR SCINTIMAMMOGRAPHY FOR THE DETECTION OF BREAST CARCINOMA? R. Tiling, R. Linke, H. Sommer, M. Pechmann, K. Gebauer, K. Tatsch, and K. Hahn. Departments of Nuclear Medicine and Gynecology, Ludwig-Maximilians-University of Munich, Germany.

As previously reported, reconstruction by iterative algorithms is preferable as compared to filtered backprojection for processing SPECT data of scintimammograms. The purpose of this study was to compare the results of planar scintimammography (SMM), iterative SPECT (ISA) and combined data evaluation aiming on the improvement of diagnosing breast cancer.

133 consecutive patients with unclear mammograms and histopathologically confirmed diagnoses (69 malignant, 64 benign) underwent SMM. Planar lateral and anterior scans were obtained using the common technique, following the injection of 740 MBq Tc-99m sestamibi. In addition SPECT was performed using a triple headed camera (imaging parameters: 360° rotation, 3°/step, 20 sec/step). SPECT data were reconstructed using iterative algorithms (8 iterations, lowpass postfiltering). Images were visually scored using 3 categories: positive (focal uptake), indeterminate (diffuse uptake) and negative (normal uptake). For statistical analyses indeterminate findings were called negative for carcinoma. Planar and SPECT images were read separately and combined, respectively.tii

The results are summarized in the table below. Four carcinomas rated as indeterminate on planar SMM were correctly identified by combined planar SMM plus ISA-SPECT. In case of positive planar SMM ISA-SPECT provided additional information with respect to better localization of sestamibi uptake, the tumor extent, the diagnostic certainty and the detection of axillary lymphnodes in 43/133 patients.

	Sensitivity	Specificity
Planar SMM	75%	86%
ISA-SPECT	70%	75%
Planar SMM +ISA-SPECT	81%	77%

In conclusion, combined reading of planar SMM and ISA-SPECT has shown to improve the sensitivity of tumor detection and provides important additional information to planar scans. However, the specificity of this approach is markedly lower as compared to planar readings. ISA-SPECT may not replace but complement planar SMM if the latter reveals positive and in particular indeterminate findings.

No. 1222

NON-INVASIVE GRADING OF GLIOMAS: A COMPARATIVE STUDY BETWEEN SPET WITH I-123-α-METHYL TYROSIN AND CONTRAST ENHANCED CT AND MR IMAGING. B. Riemann, T. Kuwert, G. Schuierer, P. Matheja, M. Schäfers, S. Palkovic, H. Wassmann, O. Schober. Department of Nuclear Medicine, Institute of Clinical Radiology, and Department of Neurosurgery, University of Münster, Germany.

Introduction: Using single-photon emission tomography (SPET) the radioactively labeled amino acid L-123-I-α-methyl tyrosine (IMT) has been applied to study amino acid transport in brain tumors. It was the aim to compare the ability of contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) with that of IMT SPET in non-invasive grading of untreated gliomas.

Methods: The study comprised 26 patients with untreated gliomas. Ten patients suffered from low-grade gliomas (WHO II) and 16 patients from high-grade neoplasms (WHO III-IV). Histopathologic diagnosis was based on specimen of stereotactic biopsies in 11 patients and of open surgery in 14 patients. The lesions were classified into low- and high-grade gliomas according to the contrast enhancement on CT/MRI. IMT SPET was performed using the triple-head camera MULTISPECT 3. IMT uptake was quantified as the ratio between amino acid uptake in the tumor over that in the contralateral hemisphere. A threshold value of 1.95 was used for differentiation between low- and high-grade gliomas.

Results: CT/MRI performed the grading with a sensitivity of 100% (16/16), IMT SPET with 81% (13/16). The corresponding specificities were 60% (6/10) and 100% (10/10), respectively. Accuracy values were 85% (22/26) for CT/MRI and 88% (23/26) for IMT SPET.

Conclusion: Contrast enhanced CT/MRI and IMT SPET showed similar accuracy in differentiating between low- and high-grade gliomas. However, with a slightly lower sensitivity IMT SPET was more specific.

No. 1223

FDG AND F-18-DIHYDROXYPHENYLALANINE IN PATIENTS WITH METASTATIC MELANOMAS. A. Dimitrakopoulou-Strauss, D. Schadendorf, H. Naeher, P. Mantaka, G. Irngartinger, F. Oberdorfer, L.G. Strauss. German Cancer Research Center, Heidelberg, Germany.

PET with F-18-Dihydroxyphenylalanine (DOPA) was used in patients with metastases from malignant melanomas in order to increase the specificity of PET for tumor diagnosis.

Eight patients with pretreated metastatic melanomas were studied twice with different tracers within one week. Dynamic PET multitracer studies with O-15-water (tissue perfusion) and F-18-Deoxyglucose (FDG, tumor viability) preceeded F-18-DOPA (second study). The dynamic acquisition times are: O-15-water, 8 min; FDG, 60 min; F-18-DOPA, 120 min. ROIs were applied and SUV calculated. The transport konstants k1 and k2 were evaluated for the perfusion series and the DOPA series using a two compartment model and the median uptake of a larger vessel was used for the input function. Parametric images of the influx and efflux of the tracer were reconstructed. The Patlak analysis was applied to the FDG data.

The FDG-scans showed an increased FDG metabolism in all subcutaneous metastases (n=3) and in 3/5 liver metastases. The DOPA-uptake was less than the FDG-uptake in 5/8 patients, equivalent to FDG in 1/8 patients, and higher than FDG in 2/8 patients. Two lesions with DOPA>FDG were treated with a combined immunochemotherapy and were false negative on the FDG scans. These lesions demonstrated an FDG-uptake of 2.45 and 1.94 SUV in comparison to 2.47 SUV for the normal liver parenchyma. The DOPA-uptake was 2.85 and 4.96 SUV for the lesions accordingly and 1.95 in the liver. A comparison of the transport constants for the O-15-water and the F-18-DOPA showed no statistically significantly correlation between these parameters. Therefore, the DOPA-uptake is not perfusion dependent. The lesion dependent sensitivity was 77 % for each of the tracers and 82 % for both radiopharmaceuticals.

These preliminary results demonstrate, that F-18-DOPA is a promising tracer for the diagnosis of malignant melanomas and can help to optimize the differential diagnostics and therapy management in patients with treated metastases.

No. 1224

VALUE OF ADDINING MEDIAL VIEWS TO ROUTINE BREAST IMAGING – EXPERIENCE WITH A SOLID-STATE (CdZnTe) GAMMA CAMERA I. Khalkhali, F. Mishkin, L. Diggles and W. Ashburn. Harbor-UCLA Medical Center, Torrance, CA and Digirad Corporation, San Diego, CA.

It is well known that higher target-to-background contrast is achieved when the lesion to be imaged is closer to the gamma camera. This would appear to be of particular importance in scintimammography as evidenced by our previously reported results in which only lateral and anterior images were obtained. In spite of a negative predictive accuracy of 96%, 3 of the 4 false-negative results were associated with lesions located in the medial region of the breasts. In a recent multi-center trial sponsored by DuPont Pharma, lateral and anterior views of the breasts were obtained. Preliminary results indicate that the sensitivity for Tc-99m sestamibi in non-palpable cancers located in the lateral regions of the breasts was 65.8% versus only 47.6% when the cancers were located medially. The sensitivity in palpable masses was 88.8% vs. 76.9% respectively for lateral vs. medially located cancers.

To overcome problems associated with cancers located in the medial aspect of the breasts, we used a solid-state, cadmium-zinc-telluride (CZT), multicrystal gamma camera (Digirad 2020*tc* Imager™) to image breasts in the medial as well as in the lateral projections. The 8x8 inch field-of-view detector head is less than 3 inches thick and has a non-imaging "dead space" of only ½ inch. This allowed the front edge of the detector to be positioned perpendicularly against the sternum. The detector was angled slightly so that it was tangential to the chest wall in order to image the deeper regions of the breasts. Imaging was performed with the patient in the prone position.

Results have shown that adding the medial view enhances lesion contrast in medially located cancers. Regions-of-interest placed over the areas of uptake in the medially located cancers and in the adjacent background region, showed enhanced contrast ratios between the lateral and medial views in the case of medially located lesions. Differences as small as 1.3:1 (lateral view) versus 1.6:1 (medial view) were associated with strikingly increased visual contrast for medially located cancers when viewed in the medial projection.

Conclusion: It appears that adding the medial view as part of routine breast imaging may increase the detection rate of medially located cancers.

No. 1225

11β-METHOXY-(17α,20Z)-21-[I-123]IODOVINYLESTRADIOL (MIVE2) AND Tc-99m MIBI SCINTIMAMMOGRAPHY: A COMPLEMENTARY ROLE IN THE CHARACTERIZATION OF BREAST TUMORS. O. Nachar, J. Rousseau, A. Rioux, B. Lefebvre, R. Ouellet, H. Ali, and J.E. van Lier. Faculty of Medicine, Université de Sherbrooke, Sherbrooke, Québec, Canada.

Technetium-99m labeled MIBI is routinely used for the characterization of breast malignancies. A positive MIBI scan does however not provide an indication on the status of the tumor estrogen receptors (ER). In the present prospective study we have compared MIBI uptake in 9 patient suspected of breast cancer with that of [I-123] 11β-methoxy-(17α,20Z)-21-iodovinylestradiol (MIVE2), an experimental ER-binding agent. The patients were referred following an abnormal mammography or detection of a suspect mass at physical examination. Tumor biopsies were obtained for pathologic examination and ER quantification. Patients were injected *iv* with 20 mCi of MIBI and subsequently with 4 mCi of MIVE2, images of the breast and of the axillary region were acquired 5 min and 1 h pi for MIBI and up to 4 h pi with MIVE2. The MIVE2 scintimammographies were acquired within 7 days of MIBI administration, and before commencing any treatment. The MIVE2 scintigrams were interpreted by nuclear medicine physicians which were unaware of the MIBI results.

No. of patients	MIBI uptake	MIVE2 uptake	Biopsy diagnosis
4	-	-	Fibrocystic disease
3	+	+	Malignant tumor (ER+)
1	+	-	Malignant tumor (ER-)
1	-	+	Non-conclusive (Follow-up in 3-6 months)

Results with this limited number of patients suggest that MIBI uptake is a prerequisite for the accumulation of MIVE2 by the breast tumors. The patient with an ER-negative tumor showed MIBI uptake only, in accordance with the absence of an ER-mediated mechanism in MIBI retention. Although confirmation of the observed relationships will require additional data, it is evident that ER imaging following a positive MIBI scan could contribute to a better characterization of the tumor and therefore improve selection of the most appropriate treatment protocol.

No. 1226

SCINTIMAMMOGRAPHY (SMM) WITH Tc-99m-MIBI FOR BREAST CANCER RECURRENCE : RESULTS OF A PROSPECTIVE FRENCH MULTICENTER TRIAL. C. Corone, D. Stevens, J.P. Muratet, O. Switsers, A. Boneu, P. Carpentier, F. Bonichon, J.C. Liehn, D. Mestas, V. Edeline, C. Soler, J. Fonroget, P. Cherel, V. Becette, A. Pecking, S. Petras, J. Hermans, J. Maublant. Rene Huguenin CLCC, Saint Cloud, France.

Tc-99m MIBI SMM has emerged as a new imaging technique for primary breast carcinomas. The aim of this study was to assess the performances of SMM to detect breast recurrent tumors and to compare it to MRI or CT enhancement imaging. From February 1996 to January 1998, twelve centers included 61 patients with clinical and/or radiological suspicious of recurrence. This study is due to end on February 1998. To date the raw data of 44 SMM have been blindly reviewed by 3 independent readers and will be presented. The median delay between initial treatment and suspicious recurrence was 4 years (1-25). 23 lesions were palpable. All patients had 10 min bilateral prone and anterior images after IV injection of 740-1100 MBq Tc-99m MIBI. Enhancement radiological imaging of the suspicious breast was done with MRI for 30 patients and with CT for 13. Final diagnosis confirmed by histology demonstrated 29 recurrences and 15 benign lesions. Results show :

	TP	TN	FP	FN	D	Sensitivity°	Specificity°
MRI + CT* (43)	18	11	3	4	7	81.8 %	78.6 %
SMM* (44)	13	12	0	12	7	52 %	-
SMM** (44)	15	12	3	14	-	51.7 %	80 %

* institutional reading ** blinded reviewing
° calculated without D = doubtful results

The major finding of this study is that the sensitivity of SMM seems to be much lower for the detection of recurrent than for primary tumors (which is generally around 80-90 %, as in the preliminary results of our multicenter trial unpublished data). This lack of sensitivity is not only related to the size since the FN lesions ranged from 2 to 30 mm. A weak uptake might be due to scar modifications by previous treatments. Another hypothesis might be that these FN recurrent tumors have chemoresistant characteristics with expression of the MDR1- Pgp which extrudes MIBI as cytotoxic agents. If this could be demonstrated, Tc-99m SMM might become an interesting tool to predict chemoresistance in breast loco regional cancer recurrences and to monitor therapy.

No. 1227

COMPARISON OF FLUORINE-18-DEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY (FDG-PET) AND IN-111 SOMATOSTATIN RECEPTOR SCINTIGRAPHY (SRS) IN THE EVALUATION OF PATIENTS WITH NEUROENDOCRINE NEOPLASMS. K. Lotfi, A. Alavi, F. Benard, D.C. Metz. University of Pennsylvania Medical Center, Philadelphia, PA.

Introduction: The role of SRS in patients with neuroendocrine tumors is well established. FDG-PET has been shown to provide invaluable information in patients with various malignancies. The role of FDG-PET in patients with neuroendocrine tumors is uncertain and this preliminary study was undertaken to explore its potential.
Methods: In 5 adult patients with neuroendocrine tumors FDG-PET and SRS were performed within 14 days according to standard protocols [1 patient with gastrinoma, 2 with carcinoid, 1 with medullary thyroid carcinoma (MTC), and 1 with glucagonoma]. Correlative MRI/CT studies were available in all patients. Average follow-up was 20+/-10 months.
Results: In a patient with gastrinoma, all 4 metastatic liver lesions were more clearly seen on SRS than on FDG-PET scan. In a patient with small bowel carcinoid, SRS showed 8 liver metastases while FDG-PET scan showed 2; also the primary right lower quadrant abdominal tumor was demonstrated on SRS but not on FDG-PET study. In a patient with MTC, SRS & FDG-PET imaging showed mediastinal and lung metastases equally in number and intensity. In a patient with appendiceal carcinoid, FDG-PET scan indicated a liver & a left axilla lesion while SRS was normal. FDG-PET results were proven false based on clinical follow-up & corroborative anatomic imaging. Both SRS & FDG-PET missed diffuse peritoneal carcinomatosis in this patient. In a patient with glucagonoma, SRS showed retroperitoneal lymphadenopathy not seen on FDG-PET imaging. In the liver, FDG-PET showed only 50% of metastases demonstrated on SRS, and FDG-PET was false positive in one patient. Liver lesions were much more clearly shown on SRS than FDG-PET scans. In extrahepatic sites, FDG-PET imaging detected only 40% of the lesions seen on SRS and FDG-PET was false positive in one case.
Conclusions: This pilot study demonstrates the superiority of SRS over FDG-PET in the evaluation of neuroendocrine tumors. These data corroborate the low sensitivity and specificity of FDG-PET in neoplasms with low metabolic rates and slow growth such as neuroendocrine tumors.

No. 1228

REVERSAL OF MULTIDRUG RESISTANCE (MDR) BY KR-30035, A NOVEL VERAPAMIL ANALOGUE: CELLULAR TC-99M-MIBI UPTAKE AND DAUNORUBICIN EFFLUX STUDY. J Lee, JS Suh, BH Lee*, SE Yoo*, KA Chun, IK Lee†, KB Lee, CK Kim‡. Kyungpook National University Hospital and Kyemyung University Hospital†, Taegu, Korea, Research Institute of Chemical Technology*, Taejon, Korea, and Mount Sinai School of Medicine‡, New York, NY.

Verapamil (VP), one of the most extensively characterized modulators of P-glycoprotein (Pgp) mediated MDR, reached clinical trial, but its plasma concentration required to reverse MDR can cause cardiovascular toxicity. Our newly synthesized VP analogue, KR-30035 (KR), showed 12-20 fold lower cardiovascular effects than VP, but more potent enhancing cytotoxic effects in vitro. We assessed the MDR reversing effect of KR by measuring Tc-99m MIBI uptake and flow cytometric measurement of intracellular daunorubicin retention (IDR) in (1) cancer cell lines (L1210) with Pgp expression [Pgp(+) cells] induced by either adriamycin or vincristine, and (2) L1210 alone [Pgp(-) cells], in the presence of varying concentrations of VP or KR (0 to 200uM for MIBI and 0 to 100uM for IDR).

MIBI uptake with varying concentrations of VP or KR

	0 uM	1 uM	10 uM	50 uM	100 uM	200uM
Pgp(-) with VP	8.9(100%)	13.7	25.1	26.5(298%)	25.7	23.4
Pgp(-) with KR	8.9(100%)	11.8	21	26.3(296%)	21.5	22.5
Pgp(+) with VP	3.5(100%)	3.3	3.7	4.8	6.0(171%)	8.8 (251%)
Pgp(+) with KR	3.5(100%)	3.7	4.0	5.3	6.3(180%)	8.0 (229%)

(The numbers in Pgp(+) group are the mean of the results of L1210-adriamycin and L1210-vincristine groups).

MIBI uptake in Pgp(+) cells was lower than that in Pgp(-) cells. There was no significant difference in MIBI uptake between VP and KR groups at any concentration. Considering MIBI uptake without VP or KR (0 uM) as 100%, MIBI uptake in Pgp(-) cells was approximately 300% at 50uM followed by mild decrease at higher concentrations. MIBI upake in Pgp(+) cells continuously increased with higher concentration in both VP and KR groups upto 230-250%. Likewise, IDR was also significantly increased in both VP and KR groups (359% and 283%, respectively). **Conclusion:** These studies show that KR-30035 can potentially be used as an active modulator of MDR, with its significantly lesser cardiovascular toxicity than VP, and the results warrant further in vivo evaluation of this novel agent.

No. 1229

BIOMARKERS OF TUMOR CELL PROLIFERATION: EFFECT OF PLOIDY, RECRUITMENT, AND TAMOXIFEN TREATMENT ON SIGMA-2 RECEPTOR DENSITY IN BREAST TUMOR CELLS. R.H. Mach, K. Sten, I Al-Nabulsi, S.R. Childers, and K.T. Wheeler Wake Forest University School of Medicine, Winston-Salem, NC 27157.

Recently, our group reported that sigma-2 receptors may be a suitable biomarker for assessing the proliferative status in breast tumors using noninvasive imaging techniques such as PET and SPECT (Cancer Res 57: 156; 1997). This conclusion was based on the observation that mouse mammary adenocarcinoma cells, line 66, downregulated their sigma-2 receptors during the transition from the proliferative (P) to the quiescent (Q) state. The goals of the current study were to determine: 1) if the recruitment of 66Q cells back to 66P cells is characterized by an upregulation of sigma-2 receptors; 2) if the expression of sigma-2 receptors is a function of the ploidy of the cells; and, 3) if this differential density in sigma-2 receptors as a function of proliferative status is observed in human tumor cell lines.

Both 66Q (diploid) and 67Q (aneuploid) cells were trypsinized and reseeded to promote exponential growth (e.g., a transition from the Q to the P state). This transition from the 66Q to 66P and 67Q to 67P state resulted in a significant increase in the sigma-2 receptor density on a receptors/cell basis. Further incubation of the 66P and 67P cells caused a reentry into the quiescent state that resulted in a downregulation of sigma-2 receptors with kinetics similar to that previously reported (Cancer Res 57: 156; 1997). These data suggest that the higher density of sigma-2 receptors in P versus Q cells is independent of the ploidy of the cells, and that the density of sigma-2 receptors is directly proportional to the proliferative status of the tumor cells.

A second set of experiments was conducted in order to explore if the above observations occur in cultured human breast tumor cells. Human breast adenocarcinoma cells (MCF-7 cells) were initially grown in cell culture for 3 days and then treated for additional 3 or 6 days with 1 nM tamoxifen, which stops cell proliferation. The density of sigma-2 receptors was then measured in both the treated and untreated controls on days 6 and 9. The results of this experiment showed that MCF-7 cells which were treated from day 3 to day 6 or day 9 with 1 nM tamixofen had no increase in cell number over that measured on day 3, and their sigma-2 receptor density was reduced by a factor of ~2 from that measured in untreated day 6 or day 9 MCF-7 cells. These data suggest that the density of sigma-2 receptors in human breast tumor cells is proportional to their proliferative status, and that PET and SPECT radiotracers possessing a high affinity and selectivity for sigma-2 receptors may provide information about the proliferative status of breast tumors using noninvasive imaging procedures. Supported by a grant from Mallinckrodt, Inc.

The following abstract was accepted for poster presentation to the Oncology Diagnosis: FDG abstract category and presented at the 45th Annual Meeting of the Society of Nuclear Medicine in Toronto, Ontario, Canada. Due to production complications, this abstract was not included in the May Abstract Book Supplement toThe Journal of Nuclear Medicine. Please disregard the abstract currently listed on page 251P, No. 1106, in the May Abstract Book Supplement and refer to the abstract below. We apologize for any confusion.

SNM Scientific Program Committee

No. 1106

THE IMPORTANCE OF GLUCOSE TRANSPORT ON FDG ACCUMULATION BY NEOPLASMS IN VIVO: A COMPARTMENT ANALYSIS. **S. Nakamura, N. Sadato, T. Tsuchida, N. Takahashi, H. Kumada, H. Uematsu, K. Sugimoto, A. Waki, K. Yamamoto, N. Hayashi, Y. Yonekura and Y. Ishii. Biomedical Imaging Research Center and Department of Radiology, Fukui Medical University, Fukui, Japan.**

Both glucose transport and hexokinase activity are thought to be related to high F-18 fluorodeoxyglucose (FDG) uptake in neoplasms, but their contribution level is not known. To determine which is the predominant factor for FDG uptake in tumors in vivo, dynamic FDG-PET and compartment analysis were performed. Six patients with lung cancer underwent dynamic FDG-PET for 60 min after i.v. injection with 370 MBq of FDG, with time-frame of 4 x 30 sec, 8 x 60 sec, and 5 x 10 min. Plasma time-activity curves were estimated from a ROI in the left atrium. Seven patients with head and neck cancer underwent dynamic FDG-PET with the same time frame, with plasma time-activity curves measured by intermittent arterial samplings. Using 3 compartment 3 parameter model (on the assumption $k_4 = 0$), K_1, k_2, k_3 and net influx constant ($K_i = K_1k_3/(k_2+k_3)$) were calculated. Results: FDG uptake measured by standardized uptake value (SUV) showed significant correlation with K_1 ($r = 0.979$, $p < 0.0001$, t test) across 13 tumors, confirming the feasibility of the parameter estimation. SUV showed positive correlation with both K_1 ($y = 0.030 x - 0.001$, $p = 0.0178$, t test) and k_3 ($y = 0.013 x + 0.025$, $p = 0.0053$, t test), with steeper slope of K_1 than k_3. There was no significant group difference in K_i, SUV, K_1 or k_2, but k_3 in head and neck cancer was significantly smaller than that in lung cancer (Table) and showed a positive correlation with SUV ($y = 0.010 x + 0.013$, $p = 0.017$, t test).

	lung (n = 7)	head and neck (n = 6)	p (t test)
K_1	0.186 ± 0.168	0.118 ± 0.049	0.3616
k_2	0.809 ± 0.732	0.331 ± 0.183	0.1499
k_3	0.123 ± 0.045	0.056 ± 0.021	0.0068
K_i	0.025 ± 0.015	0.018 ± 0.008	0.3258
SUV	5.889 ± 3.272	4.305 ± 1.829	0.3166

These results suggest that FDG accumulation of in vivo neoplasms is governed by both glucose transport and hexokinase activity, and that k_3 is affected by the origin of the neoplasms.