images, according to EORCT criteria, 7 patients had PR, 1 SD and 4 had PD. NACT understaged 4 patients because PET-CT scan found new lesions in 2/4, PD for metabolic progression (>25% increase of SUV_{max}) in lymph node disease in another one and PR instead of CR in the last one. In 2 cases in which CT scan showed SD, PET-CT scan showed PR. 33.3% of patients underwent surgical intervention after NACT.
Progressive disease or stable disease according to PET-CT (new tumour manifestations or increasing SUV) was well correlated with an unfavourable outcome.
Conclusions: FDG-PET is suitable to assess response to NACT in patients with stage IIIA NSCLC accurately. ^{18}FDG-PET-CT may be helpful in improving restaging after NACT since it allows a reliable assessment of residual tumour viability and it can find new lesions.

2107 POSTER

Diagnostic Performance of Selective Positron Emission Tomography for Lung Cancer Computed Tomography Screening: a Meta-Analysis

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Background: The effective lung cancer screening modality has not been established yet. Positron Emission Tomography (PET) has proven to be helpful in lung cancer for staging and evaluation and might be potentially used as a successful screening modality. The objective of our study is to estimate the diagnostic performance of selective PET for lung cancer computed tomography screening via a meta-analysis of a subgroup analysis from a systematic review.
Material and Methods: A systematic review is performed by reviewing primary studies focusing on PET screening for lung cancer using the following keywords "(lung cancer) AND (positron emission tomography) AND ((screen) OR (screening))" in Pubmed® on Nov 30th, 2010. The preliminary results will be partly presented in ISPOR 16th annual international meeting. Studies reported evidence of lung cancer computed tomography (CT) screening programs with selective PET were further identified as a subgroup analysis and were separately reported in the present study. Methodological quality was assessed using the modified criteria recommended by the Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests used in a previous study. A random effect model was used to calculate the pooled diagnostic performance of selective PET screening.
Results: Among the identified studies (n = 2733), three studies were included in this meta-analysis. In total, 207 participants received PET in the prevalent screening, accounting for 2.5−3% of individual trial participants. The quality assessment was viewed as acceptable (> = 75% of maximal score in each trial). The estimated pooled sensitivity and specificity with 95% confidence interval was 86% (76−93%) and 92% (85−96%) respectively in the prevalent screen.
Conclusions: PET can be used as a selective modality in combination with CT for screening lung cancer in high risk population, with a high diagnostic performance.

2108 POSTER

Combination of 99mTc-MIBI Scintigraphy, Fine Needle Aspiration and Ultrasound in the Preoperative Assessment of Patients With Hypofunctioning Solitary Thyroid Nodules (HSTN)

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Purpose: To evaluate diagnostic accuracy of 99mTc-MIBI scintigraphy in multimodality evaluation of patients with hypofunctioning solitary thyroid nodules.
Materials and Methods: 73 patients 19−65 y.o. with HSTN on the 99mTc-pertechnetate scan were included in this retrospective analysis. Planar thyroid imaging in anterior, semi-lateral and lateral projections was performed 15−30 and 120 min after intravenous injection of 370–540 MBq 99mTc-sestaMIBI. All acquisitions were done on rectangular dual-head gamma camera equipped with low-energy, high-resolution, parallel-hole collimators. Images with focal and scattered patchy uptake of 99mTc-MIBI were scored as abnormal and suspicious for thyroid malignancy. Obligatory examinations included ultrasound thyroid examination (US) and US guided percutaneous aspiration biopsy (PAB) from nodules. All 73 patients were operated and have histological verification of disease.
Results: Scintigraphy revealed abnormal accumulation of 99mTc-MIBI in “cold” thyroid nodules in 61 of 73 evaluated patients. According to histological verification after surgery 55 cases were true positive, 8 − true negative, 4 − false negative and 6 − false positive. It must be mentioned that 4 of 6 patients with false positive results had follicular adenoma which must be also operated. Sensitivity (Sen), Specificity (Sp) and Accuracy (Ac) of scintigraphy with 99mTc-MIBI was as follows 93%, 57% and 80%.
PAB was non-diagnostic in 5 cases. All 5 patients had abnormality on 99mTc-MIBI scintigraphy and cancer on histology. PAB was false positive in another 2 cases. Finally, Sen, Sp and Ac of PAB was 91%, 85% and 90%. US examinations were true positive in 55, true negative − in 9, false negative − in 4 and false positive − in 5 cases with Sen (93%), Sp (64%), Ac (88%).
Combination of 99mTc-MIBI scintigraphy and PAB was significantly more accurate (Sen 97%, Sp 96% and Ac 93%) than PAB and US separately or in combination.
Conclusion: In patients with HSTN scintigraphy with 99m-MIBI characterized by high sensitivity but its combination with PAB offers the best diagnostic accuracy.

2109 POSTER

Combination of Functional and Anatomic Imaging in Diagnosis of Axillary Lymph Node Metastases (LNMs) in Patients With Breast Cancer (BC)

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Purpose: To evaluate different imaging strategies for diagnosis of axillary LNMs in patients with primary BC.
Material and Methods: Ninety nine consecutive patients with primary BC were examined during period from 13.10.2008 to 27.04.2010. Functional imaging by scintigraphy (AxSc) with 99mTc-MIBI was performed in static and tomography modes 15 min after i/v injection. Focal areas of tracer accumulation in axial region were considered as sings of LNMs. Ultrasound (US) examination of axillary region was performed on 7.5 kH scanner. Nodes with diameter more than 1 cm were considered abnormal.
All patients were operated with axial LN dissection and subsequent histological evaluation.
Results: Scintigraphic signs of LNMs revealed in 40 patients: 23 − true positive, 17 − false positive. Among 58 women with normal AxSc results 8 had LNMs and 40 − uninvolved nodes. Sensitivity (Sen), Specificity (Sp) and Accuracy (Ac) of AxSc were as follows: 74%, 75% and 74%.
Sonography diagnosed LNMs in 44 women: 30 were metastatic on histology while other 14 − uninvolved. On the contrary, 8 of 47 US normal sized nodes were metastatic on histology. US had following values when used for diagnosis of axillary LNMs: Sen − 79%, Sp − 77%, Ac − 77%.
When LNMs were diagnosed as the combination of concordantly abnormal US and AxSc examinations Sp reached 96%, Sen dropped down to 52% and Ac − 79%. Another model was based on the assumption that LNMs must be diagnosed in all patients with abnormal US or AxSc examinations. According to this strategy Sen reached 87%, Sp − 68% and Ac − 78%.
Conclusions: 1. We found comparative accuracy of US and AxSc in diagnosis of axillary LNMs in patients with primary BC. 2. Combination of both modalities can significantly improve sensitivity (87%) or specificity (96%) of final conclusion which is determined by established diagnostic strategy and criteria’s that are used for BC diagnosis.

2110 POSTER

Human Adipose Tissue Derived Mesenchymal Stem Cells as Vehicles for Cell-based Glioma Therapy; a Model Based on Non-invasive Bioluminescence Imaging

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Background: Lately adipose tissue mesenchymal stem cells (hAMSCs) have emerged as cellular vehicles for therapy of solid tumours, due

to their ease of isolation and manipulation, and wound/tumour homing capacity. HAMSCs have been successfully used in suicide gene therapy, employing the prodrug activating system based on Herpes simplex virus type I thymidine kinase (HSV-TK)/ganciclovir (GCV). In the current study we demonstrate an effective model of glioblastoma therapy based on the use of genetically modified hAMSCs and *in vivo* monitoring of tumour and therapeutic cells.
Methods: Bioluminescence imaging (BLI) of cells expressing different luciferases allows the simultaneous monitoring of different cell populations, cell distribution, proliferation or differentiation. We stably transduced hAMSCs for expression of *Renilla* luciferase, HSV-TK and red fluorescent protein, generating RLuc-R-TK-AMSC and U87MG human malignant glioma cells for expression of *Firefly* luciferase and green fluorescent protein, generating Pluc-G-U87 cells. SCID mice were stereotactically implanted in the brain with Pluc-G-U87 and RLuc-R-TK-AMSC cells and subjected to GCV treatment. Tumour response was monitored in vivo by bioluminiscence imaging. Therapeutic cell differentiation was assessed by labeling the above *Renilla* luciferase expressing hAMSCs with a *Firefly* luciferase reporter regulated by the CD31, endothelial specific, promoter and *in vivo* monitorization.
Results: Continuous monitoring of tumour size by BLI showed that hAMSCs/GCV treatment resulted in a significant reduction (99.9% vs. control) of tumour cell number. In addition, the combination of BLI and confocal microscopy analysis of therapeutic cells suggests that efficient tumour eradication results from hAMSCs homing to tumour vessels, where they differentiate to endothelial cells, intensifying their cytotoxic effect by destroying tumour vasculature and negating nutrient supply.
Conclusion: We propose that genetically modified hAMSCs can be useful vehicles in clinical applications to deliver localized therapy to glioma surgical borders after tumour resection.

Oral Presentations (Mon, 26 Sep, 14:45−16:15)
Oncotechnology

2150 ORAL

Diffuse Reflectance Spectroscopy as an Optical Guidance Tool for Breast Biopsies

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Background: During diffuse reflectance spectroscopy (DRS), tissue is illuminated by a broadband white light. Subsequent alterations in the light spectrum occur due to scattering and absorption. Specific quantitative biochemical and morphological information from the examined tissue can be derived from spectral changes and provide information on cellular metabolic rate, vascularity, intra-vascular oxygenation and alterations in tissue morphology. Thus, DRS allows specific differentiation between tissues by differences on molecular and morphological level and has the potential to be incorporated into optical tools for cancer diagnosis and therapy. We hypothesize that an individualised approach in breast tissue analysis will improve discrimination accuracy for a DRS optical biopsy guidance tool.
Methods: DRS was performed on excised normal and malignant breast tissue from 24 female breast cancer patients. Tissue samples from macroscopic normal adipose tissue, glandular tissue, Ductal Carcinoma in situ (DCIS) and invasive carcinoma were included in the optical analysis. Optical spectra were collected over a wavelength range from 500 to 1600 nm. Model based data analysis was performed on the collected tissue spectra from all patients collectively and each patient individually. Results were compared to histology analysis.
Results: A total of 555 spectra were collected from 115 tissue locations in the mastectomy specimen. Six patients were diagnosed with DCIS, 16 patients had an invasive carcinoma and 2 patients had both DCIS and an invasive carcinoma. The classification accuracy of the data from all patients divided into two groups (*normal breast tissue* and *malignant tissue*) was achieved with a sensitivity and specificity of respectively 90% and 95%. The overall classification accuracy was 93%.
Classification of the data was also performed for each patient individually. Individualised approach yielded a 100% discrimination accuracy between normal and malignant breast tissue for 20 of the 24 patients.
Conclusion: DRS is able to discriminate malignant breast tissue from normal breast tissue with high accuracy. A 93% discriminative accuracy in an overall analysis was further enhanced to 100% for most of the included patients in an individual analysis. These results support further validation of this method during *in-vivo* studies, and eventually the application of DRS in minimal invasive tools (biopsy needles). A feasibility study in the clinical setting has been initiated.

2151 ORAL

Tissue Composition Estimated With an Interventional Fiber Optic Probe During Liver Tissue Resection

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Background: In the field of surgical and interventional oncology, it is of major importance to know where to excise tumorous tissue and to exactly assess its margins. A new development renders tissue characterization of tissue possible through the use of fiber optic probes and optical spectroscopy. These spectroscopic measurements are translated into clinically relevant physiological parameters and can be used to discriminate tumours from healthy tissue.
Material and Methods: Optical measurements were collected with a custom-made optical probe that comprises an optical fiber connected to a light source and two other fibers connected to detectors that resolve light from 500 to 1600 nm. The measured signals correspond to diffuse reflectance spectra from which the various physiological and morphological parameters of interest are derived by fitting an analytical model to the measurements. In total, 14 samples that underwent partial liver hepatectomy were measured and 230 spectra were collected at the tumour sites and 212 spectra at the normal tissue surrounding the tumour. From the tissue optical properties derived from the fitting model, biological concentrations are derived such as blood, water, lipid and bile volume fractions as well as morphological parameters such as the scattering of light in tissue correlated to tissue density. Kruskal-Wallis statistical test is applied to the data to investigate which tissue parameters demonstrate significance difference between tumours and healthy tissue ($P < 0.01$).
Results: Medians and corresponding standard deviations were computed for the parameters derived from the measurements acquired within the 14 samples of each tissue category. After application of the Kruskal-Wallis statistical test, the bile and water volume fractions as well as the reduced scattering amplitude showed significant differences as summarized in the table.

	Healthy liver (14 samples)	Tumours (14 samples)	*P*-value
Bile (%)	5.5±2.3	1.0±1.1	0.00005
Water (%)	76±4	93±17	0.005
Scattering amplitude (cm^{-1})	17±3	10±3	0.00001

Conclusions: Diffuse optical spectroscopy enables discrimination between metastatic tumours and healthy liver tissue based on the bile and water volume fractions as well as the reduced scattering amplitude. Hence, optical sensing at the tip of a probe has an interesting potential for tumour margin assessment during liver resection.

2152 ORAL

Feasibility of Boosting Local Dose to Tumour Endothelial Cells Using Vascular-targeted Bismuth Nanoparticles During Radiotherapy

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Background: The use of coated bismuth nanoparticles (BiNs) and their bioconjugates has recently been shown for enhanced *in vivo* imaging of the vasculature in mice, with high x-ray contrast mainly due to photo-electric absorption. In this study the dosimetric potential of exploiting this photo-electric effect to significantly boost local dose to tumour endothelial cells (ECs) during radiotherapy is examined.
Methods: A tumour vascular endothelial cell (EC) is modeled as a slab of 2 μm (thickness) × 10 μm (length) × 10 μm (width). Analytic calculations based on the electron energy loss formula of Cole were carried out to estimate the dose enhancement from photoelectrons to the EC from BiNs attached to the exterior surface of the EC. The endothelial dose enhancement factor (EDEF), representing the ratio of the dose to the EC with and without nanoparticles was calculated for different nanoparticle concentrations. The investigated concentration range considers the non-uniform distribution of nanoparticles, with significantly higher local concentration expected near the EC. Five radiotherapy sources