from Group1 (for all $p < 0.001$). Group 2 did not differ from Group 3 ($p = 0.61$). Both BRCA1 ($n = 49$) and BRCA2 ($n = 51$) mutation carriers from the combined Group 2 and 3 ($n = 100$) demonstrated higher serum TK1 activity than healthy women from Group 1 (for all $p < 0.001$). There was no difference in TK1 activity between BRCA1 and BRCA2 mutation carriers ($p = 0.57$). Higher TK1 activity was found in BC patients with BRCA1/2 mutation from Group 5, compared to those without the mutation from Group 4 ($p = 0.002$). The area under the TK1 ROC curve ($\pm$ standard error) in the model considering Group 1 vs. combined Group 2 and 3 was 0.73 ± 0.03. The optimal cut-off value corresponded to 30 Du/L of TK1 activity and supplied a sensitivity of 63.3% and specificity of 77.5% for identifying BRCA1/2 mutation carriers.
Conclusions: BRCA1/2 mutation carriage is significantly associated with elevated serum TK1 activity both in healthy women and in patients with breast cancer.

1463 POSTER

CA19-9 in Combination With Abdominal CT Scan for Diagnosis of Mass-forming Intrahepatic Cholangiocarcinoma

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Background: Cholangiocarcinoma (CCA) is one of the most important cancer in Thailand. The diagnosis of CCA with pathology is widely accepted. Unfortunately, tissue diagnosis of mass-forming intrahepatic cholangiocarcinoma is difficult to perform according to tumour site, risk of procedure and accessibility. The aims of this study are assessing the diagnostic utility of CA19-9 for mass-forming cholangiocarcinoma in combination with CT scan of the liver.
Methods: The medical records of patients with the diagnosis of cholangiocarcinoma (CCA) and hepatocellular carcinoma (HCC) during January 2005 to December 2009 were reviewed. Each case was checked for pathology and CT scan report performed at Maharaj Nakorn Chiang Mai Hospital and excluded each case with either report from other hospitals. Demographic data, clinical manifestation, laboratory results including CA19-9 and CT scan of the liver were carefully examined in order to established the diagnostic utility in mass-forming CCA without pathological diagnosis.
Results: 79 CCA patients and 66 HCC patients were included in CA19-9 cut off levels analysis. 31 CCA patients and 44 HCC patients were included in CT scan characteristics evaluation and scoring according to Chiang Mai CT score for CCA. Chaing Mai CT score for CCA consists of 3 features which are thin/thick rim enhancement at periphery on arterial phase, capsular retraction and dilated bile duct peripheral to tumour giving score 1, 4, and 2 respectively. The specificity of CA19-9 value 500 U/mL in diagnosing CCA was 95.5% with sensitivity 50.6%, PPV 91.8% and likelihood ratio of positive(LR+) 11.24. The CT score greater than 2 demonstrates PPV of more than 90% in diagnosis of CCA. The CA19-9 level of 140 U/mL in combination with CT score 2 demonstrated LR+ as high as 57.09.
Conclusion: CA19-9 level combined with Chiang Mai CT score for CCA are good diagnostic tool for diagnosis of mass-forming cholangiocarcinoma with high specificity, high positive predictive value and high likelihood ratio of positive.

1464 POSTER

Comparison of HER-2 and Hormone Receptor (HR) Status Between Primary Breast Cancer and Corresponding Distant Metastatic Sites With Double Check Assessment

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Background: Although the vast majority of breast cancer carcinoma maintains the same biological features at relapse, recent studies suggested that some lesions may have a change in HER2 and HR status during tumour progression. As such, it may be advisable to biopsy metastatic disease for optimal treatment planning.
Aim: To compare HER2 and HR status of metastatic breast cancer with those of the original tumour with simultaneously double check assessment to reduce analytical procedures errors.
Methods: From 2008 to 2010, 118 patients with biopsy proven relapses were identified. HER-2 analysis was performed in both primary and metastasis material. Results were interpreted as hercepTest® guideline's. Discordant cases were evaluated by fluorescence *in situ* hybridization (FISH) too. ER and PR were also screened by IHC analyses.
Results: 118 primary breast cancer tumours and their corresponding distant metastasis were analyzed. Among paired primary/metastatic tumours, we found 13 discordant cases, 8 in ER or PR, 4 in HER 2 showed discordance by IHQ and FISH and1 case in both parameters.
Results are summarized in Table 1.

Table 1: Discordant cases with double check assessment

Primary tumour	ER	PR	HER2	Metastatic site	ER	PR	HER2
1	+	+	0	cervical node	+	−	0
2	+	+	0	Pleura	+	−	0
3	+	+	0	Lung	+	−	0
4	+	+	0	Pleura	−	−	0
5	+	+	0	Ovary	−	+	0
6	+	+	0	peritoneum	−	−	0
7	+	−	0	Bone	+	+	0
8	+	+	0	Skin	−	−	0
9	−	−	1+	Supraclavicular node	−	−	2+
10	+	+	1+	Supraclavicular node	+	+	3+
11	+	+	2+	Liver	+	+	0
12	+	−	0	Liver	−	−	3+
13	+	−	3+	Bone	−	−	0

Conclusions: 13/118 (11%) of relapsed tumours had changes in HER2 or ER or PR status. with double check evaluation The tendency showed a lost in HR and a gain in HER 2 positivity This study suggests that biopsies of relapsed/metastatic breast cancers should be performed, in concordance with largest series recommendations previously published.

Oral Presentations (Mon, 26 Sep, 14:45−16:25)
Radiotherapy

2000 ORAL

Prognostic Value of Metabolic Response Assessed by 18F-FDG PET During Radiotherapy for Cervix and Head and Neck Carcinoma

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Background: Sequential FDG-PET/CT performed during the course of radiotherapy has been poorly explored and may be an early surrogate of patient outcome. The aim of this study was to analyze metabolic changes during radiotherapy at 40 Gy and its prognostic impact in cervix and head and neck cancer (HNC) patients (pts).
Materials and Methods: This prospective study included 2 populations:
a. HNC: 22 pts. Stages were: II (23%), III (27%) and IV (50%). Primitive tumour sites were: 11 oropharynx, 5 hypopharynx, 1 cavum and 6 larynx. Treatment was: external beam radiation therapy (EBRT) (70 Gy) with concurrent cetuximab.
b. Cervical cancer: 35 pts. FIGO stages were: IB2: 4, IIA: 5, IIB: 11, IIIA: 2, IIIB: 1, IV: 2. Treatment was: EBRT (46 Gy) with concurrent chemotherapy (Cisplatinum), followed by brachytherapy $\pm$ Surgery.

All pts were evaluated by FDG PET: before treatment (PET1), during EBRT at 40 Gy (PET2), and after the end of RT (PET3). Following FDG-PET parameters were analyzed: maximal standardized uptake value (SUVmax) and metabolic tumour volume (MTV). MTV was segmented: by fixed threshold of all voxels >2.5 of SUV for HNC and by a threshold of 40% of SUVmax for cervix cancer. The predictive values of these parameters (as continuous variable or with cut-off values defined by ROC analysis) were searched (Cox model and log rank) for disease free survival (DFS).
Results: Median follow-up was 15 months (3−31) in HNC and 17 months (3−36) in cervix cancer. The 2-year DFS rates were: 53% and 72%, for HNC and cervix cancer, respectively.
– **At PET1**: no metabolic parameter was significant on DFS.
– **At PET2**: SUVmax and MTV were correlated with DFS in univariate analysis ($p < 0.05$) for cervix and HNC. SUVmax >8 for HNC decreased DFS (RR = 3.1, 95% CI: 0.9–10.5, $p = 0.05$). SUVmax >6.3 for cervix cancer (mean value of SUVmax at PET 2) decreased DFS ($p = 0.01$).

– **At PET3**: Both SUVmax and MTV decreased DFS ($p = 0.003$ and $p = 0.004$ respectively) in HNC. For cervix cancer, only MTV was correlated with DFS.

Conclusion: 18F-FDG PET at 40 Gy seems to be a prognostic factor of DFS in HNC and cervix cancer, potentially being used to intensify treatment for bad responders.

2001 ORAL

Nanoscale Radiotherapy − NBTXR3 Hafnium Oxide Nanoparticles as Promising Cancer Therapy

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Background: There is considerable interest in approaches that could improve the therapeutic window of radiotherapy, which represents a crucial modality of treatment in oncology. We present the rationale for designing NBTXR3 nanoparticles activated by radiotherapy and validate the concept. We performed the Monte Carlo calculations for the first time based on the "local model" simulation that showed a dose enhancement of radiation to tumour cells of approximately nine-fold. NBTXR3 was shown to deposit high energy when the ionizing radiation source is "on" and to have chemically inert behavior in cellular and subcellular systems demonstrated by very good systemic tolerance, thus decreasing potential health hazards.

Material and Methods: We used conventional methods, implemented in different ways, to explore interactions of high Z matter and ionizing radiation with biological systems. In addition, microtomography was performed to explore the nanoparticle volume occupancy inside the tumour and its persistence overtime in mouse tumour models. The antitumour activity of NBTXR3 and tolerance were evaluated in Ewing tumour (A673) and fibrosarcoma (HT1080) using high energy source.

Results and Conclusion: We created and developed NBTXR3 nanoparticles with a crystalline hafnium oxide core which provide high electron density structure and inert behavior in biological media. NBTXR3 nanoparticles' characteristics, size, charge and shape, allow for efficient interaction with biological entities, cell membrane binding and cellular uptake. The nanoparticles were shown to form clusters at the subcellular level in tumour models. Of most importance, we show NBTXR3 intratumour bioavailability with dispersion of nanoparticles in the three dimensions and persistence within the tumour structure, supporting the use of NBTXR3 as effective antitumour therapeutic agent. Antitumour activity of NBTXR3 showed marked advantage in terms of survival, tumour specific growth delay and local control in A673 and HT1080 human tumour models. Changing radiotherapy benefit-risk ratio is challenging. These data are supportive for the first clinical development of hafnium oxide nanoparticles, with an on/off mode of action through successive fractions of radiation therapy using current equipment available in hospitals.

2002 ORAL

4D List Mode PET/CT in Free Breathing Stereotactic Radiotherapy

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Background: Target movement is still a major problem in high precision radiotherapy like stereotactic body radiotherapy (SBRT). Techniques like gating or tracking can solve this problem but often require invasive intervention or prolonged application time, 4 D CT pictured only few breathing phases, which could be a problem especially for patients with poor lung function.

4D list mode-capable PET/CT allows valid detection of target motion and reduction of planning target volume (PTV) up to 35% compared to planning based on CT in maximal inspiration and exspiration.

The aim of this study was evaluation of this new method particularly with regard to feasibility, local tumour control rate, and toxicity.

Material and Methods: 140 patients with 167 lesions were enrolled. They suffered from primary or secondary thoracal or abdominal cancer. Planning procedure included free breathing contrast enhanced PET/CT with list mode-based reconstruction. For liver lesions, accuracy was improved by additional MRI with different contrast enhanced phases. Planning target volume (PTV) contained gross tumour volume (GTV), 2 mm set-up margin and safety margins based on list mode detected motion. All patients underwent SBRT with prescribed radiation dose to the 65% enclosing isodose. Normally, 3 x 12.5 Gy were delivered. Tumours close to lung hilus, stomach, or small bowel received 7.0 Gy in 5 fractions. All patients received prophylactic antiemetic medication one hour before starting SBRT. In case of radiotherapy close to the stomach, patients got proton pump inhibitors for three months starting with first SBRT.

Clinical history, laboratory findings, early and late toxicity scores, PET/CT, and MRI in cases of liver lesions were gathered at the 6-week follow-up visit and then at 3-month, 6-month, 9-month, and 12-month follow-ups.

Results: All lesions were visible in PET and movement was detected by list mode PET/CT in all cases. The patients tolerated planning procedure and SBRT very well. No early or late toxicity $\geqslant$ grade 2 (CTCAE v.3.0) was reported.

1/167 lesions showed an in field relapse, local control is 98.5% (2 to 23 months observation time, mean 7.9).

Conclusion: Good tumour control rate and low toxicity demonstrate excellent applicability of 4D list mode-based target delineation in free breathing high precision radiotherapy.

2003 ORAL

Perfusion and Permeability Study in High Grade Glioma Patients: Implications on Outcome and Importance of Steroids Uptake Before Radiotherapy

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Background: High grade gliomas (HGG) represent the most frequent group of primary malignant brain neoplasm. Conventional imaging evaluation is not a direct measurement of tumour aggressiveness. Evaluation of microvascular characteristics as Perfusion and Permeability could be more appropriate.

Material and Methods: At Institut Gustave Roussy, since January 2008 and up to December 2010, all patients diagnosed with HGG and residual disease 1 week before Radiotherapy (RT) were evaluated with perfusion and permeability magnetic resonance imaging, and treated either to Stupp protocol (60 Gy in 30 fractions plus concomitant temozolomide (TMZ) 75 mg/m^2, then adjuvant TMZ, 150–200 mg/m^2) for grade IV or RT alone in grade III gliomas (with TMZ after failure). Disease free survival (DFS) was estimated using the Kaplan–Meier method; comparison between groups was performed using the log-rank test. Multivariate analysis was performed by Cox model. Chi-square tests were used to analyze the relationship between variables of interest.

Results: Median follow up was of 15 months and 79 patients were studied. Median age was 60 years (range: 17−82), there were 15 grade III and 64 grade IV gliomas (81%). A total of 49 patients was under steroids (64%) just before RT. There were 42 patients with tumours presenting detectable permeability (53%) and median relative cerebral blood volume estimate (r-CBV) was 4 (range: 1.7 to 8.3). Median DFS was 9 months. There was no difference between the high perfusion (r-CBV > 4) and the low perfusion group (r-CBV $\leqslant$ 4) with a HR of 0.78. Patients with detectable permeability had a worse DFS when compared to "no permeability" group (respectively 22% vs. 38% at 1 yr, with a HR of 1.32), but without statistical significance ($p = 0.3$). There was no correlation between permeability and perfusion ($p = 0.85$). Patients under steroids had a worst DFS ($p = 0.04$) and this item was not correlated to bulk of residual tumour. Multivariate analysis confirmed this result ($p = 0.03$).

Conclusions: Patients under steroids before RT presented a worse prognosis. In our series, no correlation was shown between perfusion and permeability in HGG with residual disease, and higher values of rCBV had no impact on outcome. High permeability could be still interesting to study in the future as a possible independent prognostic marker, even if no definitive assumption could be made because of the limited number of patients studied.

2004 ORAL

Rosiglitazone(RGZ) Attenuates Pulmonary Fibrosis and Radiation-induced Intestinal Damage

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Background: Rosiglitazone (RGZ) is a peroxisome proliferator activated receptor (PPAR) gamma agonist with anti-inflammatory, anti-fibrotic