POSTER SESSION 4: Diagnostic

P4.1

The value of CT texture analysis for evaluating response to neoadjuvant chemotherapy for colorectal liver metastases

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Objective: To explore whether the computed tomography (CT) histogram analysis of baseline CT portal images before treatment can help predict the response of patients with colorectal liver metastases (CRLM).
Materials and Methods: Thirty-four patients (A total of 132 lesions) diagnosed with CRLM were retrospective enrolled and underwent contrast-enhanced CT before and after neoadjuvant chemotherapy (FOFOX, FOLFIRI or CapeOX). All patients underwent pre-treatment CT baseline scan within four weeks for primary tumor assessment and a second CT scan in 2 to 3 month for response evaluation. Histogram analysis of CT portal images of patients with CRLM and response is mainly assessed using Response Evaluation Criteria In Solid Tumors (RECIST Version 1.1). The texture parameters of the metastatic tumor were analyzed statistically to find the differences in baseline CT histogram parameters between the two groups before and after treatment. The ROC curves were depicted to characterize each parameter value for evaluating the treatment outcome. The optimal cut-off values (obtained according to the maximal Youden index = sensitivity + specificity-1), the corresponding sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy could be calculated. ROIs (regions of interest) were manually drawn on the largest cross-sectional area of the primary lesions by two radiologists in consensus.
Results: 21 responding and 13 non-responding patients were evaluated. The value of mean, variance, skewness and percentile (10th， 50th, 90th , 99th) in patients with respond were much lower than that in non-respond ($p < 0.05$). The kurtosis and 1st percentile values between two groups exhibited no significant difference (p=0.769, p=0.06, respectively). The optimal cutoff value for the accurate identification of patients with respond was 167 for 90th percentile (74.42% sensitivity, 91.3% specificity, 66.67% PPV, 66.67% NPV, 81.82% accuracy, and 0.854 AUC, respectively).
Conclusion: The computed tomography (CT) histogram analysis of baseline CT portal images before treatment can help predict the response of patients with colorectal liver metastases.

P4.2

Differential diagnosis of pulmonary metastasis from non-metastasis in patients with colorectal cancer by histogram parameters based on CT

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Objective: To determine whether whole-lesion histogram parameters of pulmonary nodules based on computed tomography (CT) images can distinguish between lung metastasis and non-metastasis in patients with colorectal cancer (CRC).
Methods: We analyzed the chest CT images of 276 CRC patients with pulmonary lesions between January 2010 and October 2016. Patients were divided into two groups: metastasis group which was confirmed by pathology and non-metastasis group which was confirmed by follow-up and tissue samples. Whole-tumor volumetric texture analysis was performed on CT images by semi-automatically contouring a region of interest around the tumor outline for each slice by using proprietary software. Histogram parameters including kurtosis, skewness, mean, volume, sphere value and standard deviation were derived from the pixel distribution histogram by software algorithm. Multivariate logistic regression analysis was performed to build a discriminating model with histogram parameters to investigate the differentiating factors of LM from NM. Receiver operating characteristic curve analysis were generated to evaluate its discriminating performance.
Results: Of 276 nodules, pathologic analysis confirmed 141 LMs, 15 NMs and follow-up confirmed 30 LMs, 90 NMs.Multivariate analysis revealed that kurtosis and sphere value were significantly higher (0.73 versus -0.79, OR=0.77, P<.0001; 1.59 versus 0.65, OR=15.17, P<.0001, respectively) while skewness was significantly lower (-1.03 versus 0.13, OR=0.25, P<.0001) in LM compared to NM. Area under the ROC curves (AUC), to discriminate between LM and NM, were significantly higher for sphere value (AUC=0.87, 95% CI 0.82–0.90), skewness (AUC=0.85, 95% CI 0.80–0.89) and kurtosis (AUC=0.67, 95% CI 0.61–0.72) compared to all other parameters. With median attenuation, the standard deviation, volume, kurtosis, skewness and sphere value, the logistic regression model showed excellent accuracy in the differentiation of LM from NM (AUC=0.92, 95% CI 0.88–0.94, 88.9% sensitivity, 81.9% specificity).
Conclusion: In patients with CRC, higher kurtosis, sphere value and lower skewness are significant differentiators of LM from NM, and LM can be accurately differentiated from NM by using CT histogram analysis.

P4.3

Development of Novel Sodium Fluoride-PET Response Criteria for Solid tumors (NAFCIST) in Osteosarcoma: From RECIST to NAFCIST

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Purpose: The development of osteosarcoma therapeutics has been challenging, in part because of the lack of appropriate criteria to evaluate responses. We developed a novel criteria in clinical trial of radium-223 dichloride (223RaCl2) for response assessment in osteosarcoma- NAFCIST.
Experimental Design: Patients received 1-6 cycles of 223RaCl2, and cumulative doses varied from 6.84 MBq to 57.81 MBq. Molecular imaging with technetium (Tc)-99m phosphonate scintigraphy, fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) or sodium fluoride-18(Na18F)PET was used to characterize the disease. Correlation of biomarkers and survival was analyzed with NAFCIST measure from Na18F-PET.
Results: Of the 18 patients, 17 had bone lesions visible in at least one of the imaging studies. In 4/7 patients with multiple skeletal lesions (>5), FDG-PET and NaF-PET studies could be compared. The skeletal tumor locations varied in our patient population: [Cranium =2, extremities =7, pelvis =10, spine =12, and thorax= 9]. The 18F-FDG-PET and Na18F-PET studies could be compared in all four patients who had multiple lung lesions (>5). Overall RECIST response was seen in one patient, but four patients experienced mixed responses better defined by Na18F-PET. Changes in NAFCIST were correlated with changes in bone alkaline phosphatase levels(r = 0.54), and negatively with cumulative dose of 223RaCl2. (r = -0.53). NAFCIST correlated with survival (p value 0.037), versus PERCIST did not (p-value 0.19).
Conclusions: Our results indicate that Na18F-PET should be used in osteosarcoma staging. NAFCIST may be a promising criteria for high-risk osteosarcoma response evaluation, and correlates with survival. Further validation studies are needed.

P4.4

The Clinical Impact of New AJCC Stage for Treated Pancreatic Ductal Adenocarcinoma

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Background: The new AJCC stage (8th edition) for pancreatic ductal adenocarcinoma (PDAC) stratifies the patients by tumor size [pT1, ≤2 cm (pT1a, ≤0.5 cm; pT1b, >0.5 cm and 2 cm and ≤4 cm, and pT3, >4 cm] and the number of positive lymph nodes (N0, no regional nodal metastasis; N1, 1-3 positive nodes; ≥4 positive nodes). However the prognosis of this new T stage system has not been validated in patients who received neoadjuvant therapy and pancreaticoduodenectomy (PD).
Materials and methods: Our study population consists of 398 patients (176 females and 222 males; median age: 64.1 years) who received neoadjuvant therapy and underwent PD for PDAC at our institution from 1999-2012. All PD specimens were processed using a standardized pathologic evaluation system. The T and N stages were correlated with clinicopathologic parameters and survival using SPSS Statistics.
Results: There were 9 ypT0 (pathologic complete response with no residual carcinoma, 2.3%), 152 ypT1 (38.2%: 16 ypT1a [4%], 14 ypT1b [3.5%], and 122 ypT1c [30.7%]), 203 ypT2 (51%), and 34 ypT3 (8.5%) patients. The ypN0, ypN1 and ypN2 disease was present in 183 (46.0%), 142 (35.7%) and 73 (16.3%) patients respectively. Both the new ypT stage and ypN stage correlated significantly with disease-free survival (DFS) and overall survival (OS). The new T stage correlated with nodal metastasis ($p<0.001$) and tumor regression grade ($p0.05$). In multivariate analysis, new ypN stage was a significant predictor for both DFS ($p<0.001$) or OS ($p<0.001$)
Conclusions: Our study shows that the new ypT stage and ypN stage are significant prognostic factors in patients who received neoadjuvant therapy and PD. Our study suggests that tumor size cutoff for T2 should be 1.0 cm for patients with PDAC who received neoadjuvant therapy.

P4.5

The preliminary study of 18F-FES PET in predicting metastatic breast cancer patients receiving fulvestrant with docetaxel

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Purpose: We aimed to evaluate the efficacy of combining fulvestrant with docetaxel in hormone-receptor positive and HER2-negative metastatic breast cancer, and the clinical prediction value of 18F-FES PET/CT.
Methods: Twenty-two patients with pathology confirmed ER/PR+, HER2- metastatic breast cancer were prospectively enrolled and randomly divided into two groups (T: docetaxel, n=8 and TF: docetaxel+fulvestrant, n=14). Among them, six patients in group TF and 9 patients in group T underwent both 18F-FES and 18F-FDG PET/CT before and after two cycles of treatment.
Results: The median PFS was numerically longer in TF group than that in T group (12.3 vs. 9.9 months). The percentage of patients without disease progression after 12 months was 62.5% in the combination arm compared with 21.4% in the single-agent docetaxel arm (P=0.08). According to 18F-FES PET/CT scans, SUVmax of all metastatic lesions decreased in group TF after 2 cycle of treatment. However, 6/9 patients in group T had at least one lesion with higher post-treatment SUVmax (P=0.028). In group TF, the patients with PFS>12 months had significant greater SUVmax changes of 18F-FES than those with PFS12 months: 91.0±12.0 versus PFS<12 months: 20.7±16.2; t=-4.64, P=0.01). In addition, the SUVmax changes of 18F-FES showed good agreement with PFS (correlation coefficient=0.946, P=0.004), which reflected its potential to predict prognosis.
Conclusions: Our preliminary study showed that the addition of fulvestrant to docetaxel might improve PFS in metastatic breast cancer patients. 18F-FES PET/CT, as a noninvasive method, could be utilized to predict its prognosis.

P4.6

Quantification of PI3K p110a, PTEN, and AKT I and II in colorectal cancer cell lysate and tissue samples using immuno-MALDI (iMALDI)

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Colorectal cancer is one of the most common cancers in both incidence and cancer-related deaths (PMID:28248415). The PI3K/AKT/mTOR pathway is commonly upregulated in colorectal cancer and is the target of many anti-cancer therapies (PMID:25591826), but current patient stratification methods for targeted therapy are based mostly on genomic data and are often unsatisfactory. The goal of this project was to develop immuno-MALDI (iMALDI) mass spectrometry (MS) assays to quantify the expression and phosphorylation levels of proteins in the PI3K/AKT/mTOR pathway.
iMALDI combines antibody enrichment with MALDI-MS detection (PMID: 21136662). After enzymatic digestion of the sample, analyte-specific endogenous peptides (END) and their stable-isotope labeled (SIS) analogues are enriched using antibodies immobilized on magnetic beads. The beads are magnetically separated from the sample, washed, and spotted on a MALDI target. Matrix is added and the target peptides are analyzed. Protein quantification is based on the END: SIS ratio. Quantification of phosphorylation level is achieved by splitting the sample into two aliquots, and treating one with phosphatase (PMID:20524616). The amount of phosphorylated END originally in the sample is determined from the resulting increase in the amount of unphosphorylated END.
Unique tryptic peptides containing the cancer-related phosphorylation sites in PI3K p110α, PTEN, and AKT I and II were selected, confirmed experimentally, and used to raise polyclonal antibodies. Quantification of AKT I and II expression and phosphorylation levels were achieved in various cancer cell lines, as well as in flash-frozen and formalin-fixed tumour tissue samples, using 10 µg cell lysate. Endogenous PI3K p110α and PTEN were detected in 25 µg MDA-MB-231 breast cancer cell lysate. The next steps of this project include combining the PI3K p110 α, PTEN, and AKT assays into a single multiplexed assay, as well as adding additional protein targets from the PI3K/PI3K/mTOR pathway. After the method has been fully validated, it will be automated and used for the analysis of colorectal cancer xenograft mice and patient samples. Combined with genomic data, these levels can be used to build a predictive model for a patient's response to targeted therapy.