OP160

Partial Volume Correction of Amyvid and FDG PET data using the discrete iterative Yang technique

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Introduction: Partial volume effects can severely compromise both visual and quantitative PET, particularly in the populations referred for dementia PET imaging. Atrophy and cortical thinning can lead to apparent reductions in tracer uptake that are purely an effect of anatomical features, which compromises the ability of the PET study to accurately map underlying physiological processes. To overcome these issues, partial volume correction (PVC) techniques can be applied. In this study we introduce the "discrete iterative Yang" (diY) technique, and look at the improvement in tracer uptake in a cohort of Amyloid and FDG PET studies. Methods: A mix of twenty-two patients and age-matched controls were involved in this study. All subjects had Amyvid PET, FDG PET, and a recent T1 weighted MR study. T1 data were co-registered to FDG PET and 18F-Amyvid data before being segmented and parcellated into volumes using the Niftyseg algorithm [1]. PET data were then up-sampled to the MR voxel size before PVC was applied using the diY technique. In essence the technique involves the PET image being represented as a piecewise constant image, which is convolved with the system point spread function. The ratio of the original and convolved images is used as correction factors that are applied to the PET image. The regional mean values are estimated iteratively. After a few iterations of this process, the PET image can be considered to be partial volume corrected. Once the correction had been applied, the visual and quantitative changes to the PET distributions were assessed pre and post correction. Results: Of the 22 subjects, 13 had a scan negative for amyloid deposits. After PVC, global grey-matter SUVr in these subjects decreased by an average of 12.2% (95%CI: 8.7-15.7) due to a reduction of spill-in from non-specific white matter uptake. In Amyloid positive patients, SUVr increased by 26.7% (95%CI: 22.17-31.26%) by reducing spill-out from cortical grey matter. Similarly in control FDG studies SUVr in cortical grey matter increased by 26.3% (95%CI: 25.22-27.41) after the application of the PVC. Visually there was better contrast between grey and white matter areas on Amyloid PET, and FDG PET with abnormalities better differentiated with diY PVC applied. Conclusions: Partial volume correction using diY improves quantitative accuracy, and offers better differentiation between normal and abnormal studies.

Reference: [1] Cardoso MJ et al 2012. Geodesic Information Flows in Med. Image Comput. Comput Assist. Interv. : MICCAI 2012;7511:262-270 2012.

OP161

Prognostic and predictive values of initial 18FDG PET features using random forest classifier: Application to patients after chemo-radiotherapy for oesophageal cancer

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Aim: Many features can be extracted from 18FDG PET images to describe cancer. We propose a machine learning technique based on a Random Forest (RF) classifier to select features having a prognostic or predictive value among a large amount of different characteristics.Materials and methods: 65 features are extracted from medical records (age, stage ⋯) and PET images: classical features (SUV, Metabolically Tumor Volume (MTV) ⋯), 1st order features (skewness, entropy ⋯) and texture parameters from texture matrices: Gray Level Cooccurrence Matrix (GLCM), Gray Level Zone Length Matrix (GLZLM) and Gray Level Difference Matrix (GLDM). Patient classification is performed using RF algorithm with 2000 decision trees, firstly without any Feature Selection (FS), and secondly with a FS. The selection is performed in 2 steps. First, a correlation analysis is done using the Spearman method to keep uncorrelated features. They are compared two by two and are considered as correlated if the Spearman coefficient (sp) verified $|sp| \geq 0.8$ and $p < 0.05$. Next, the RF algorithm is applied on the remaining features to find the most relevant features using the importance index. The RF classifier has been applied to a database of 66 patients with an oesophageal cancer treated by radio-chemotherapy (CRT). The classification accuracy has been evaluated using the Out-Of-Bag (OOB) error.Results: When the RF classifier is applied to the 65 initial features, OOB error reaches 33.3% and 25.8% for prognostic and predictive studies respectively. The FS strategy improves the classification accuracy, to reach an OOB error of 22.7% and 22.7% respectively. The Spearman analysis revealed that none of the clinical data are correlated with PET characteristics, neither for correlation (GLCM), Cluster Shade (CS, GLCM) Busyness (GLDM) and Zone Percentage (ZP, GLZLM). Twelve groups of correlated features can be created leading to 31/65 features selected. The best 3 prognostic features are MTV, correlation (GLCM) and the Nutritional Risk Index (NRI), whereas the best 3 predictive features are MTV, ZP and correlation (GLCM).Conclusion: ML technique, such as random forest classifier, is an interesting tool to find the

most relevant among a large amount of features, to classify patients. A FS is mandatory to improve the classification accuracy. In case of oesophageal cancer, MTV and texture parameters appear as relevant feature and improve predictions.

OP162

Biomathematical modeling approach to predict clinical SUVR in amyloid PET imaging towards efficient radioligand discovery and development

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Aim: Purpose of the study is to develop a new methodology to predict clinical SUVR of amyloid PET radioligands by extending biomathematical modeling, which was previously proposed by Guo et al. [1]. Methods: 6 amyloid radioligands, [11C]PIB, [11C]BF-227, [11C]AZD2184, [18F]FACT, [18F]Flobetapir and [18F]AZD4694 were explored in this study. For each tracers, time-activity curves (TACs) were generated using one-tissue compartment model with arterial plasma input function and calculated kinetic parameters (K1, k2 and BPND). By biomathematical modeling simulation, K1, k2 and BPND values were derived using lipophilicity (logP), apparent volume (Vx), free fraction in plasma (fP), free fraction in tissue (fND), dissociation constant (KD) and density of Amyloid β (Bavail) [1]. Lipophilicity was using ClogP (chemoffice ver. 2012, Hulinks Inc.), moriguchi logP, MlogP (dproperties, Affinity Science corp.). Vx was also computed using dproperties. Both fP and fND were calculated by relational expressions among logP, fND and fP. Regression lines of logP vs. fND and fND vs. fP. were derived from three publications, Guo et al. [1], Summerfield et al. [2] and Wan et al.[3]. KD was obteined from publications. Bavail was fixed at 3nM for healthy control (HC) and 50nM for severe Alzheimer Disease (AD) patient. Predicted SUVRs of HC and AD were then obtained by dividing the summed TACs of the target region over that of the reference region. The predicted SUVRs of HC and AD for each tracer were then compared with previously reported in vivo SUVRs of HC and AD groups respectively. The correlations between predicted and reported SUVRs were compared for 6 combinations of logP and regression line (ClogP-Guo, ClogP-Summerfield, ClogP-Wan, MlogP-Guo, MlogP-summerfield and MlogP-Wan). Results: Good correlations between predicted SUVR(y) and in vivo SUVR(x) were observed in the case of MlogP-Summerfield ($y = 1.05 x + 0.04$, $r2 = 0.70$) and MlogP-Wan ($y = 2.67 x - 1.42$, $r2 = 0.70$). On the other hand, poor correlation was observed in case of ClogP-Guo ($y=0.59x+0.36$, $r2=0.38$). Conclusion:Proposed methodologies (MlogP-Summerfield and MlogP-Wan) were able to predict SUVR with good correlation against in vivo SUVRs for 6 amyloid tracers, showing potential to be applied to other amyloid radioligands. Reference: [1] J Nucl Med. 2009, 50(10):1715-23. [2] J Pharmacol Exp Ther, 2006; 316:1282-90 [3] J. Med. Chem. 2007, 50:4606-15

OP163

Correlation of SUV and tumor to blood standard uptake ratio (SUR) with the metabolic uptake rate derived from quantitative dual time point measurements.

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Aim: Determination of tumor SUV is widely used for quantitative assessment of tumor metabolism in FDG-PET. However, the SUV approach has several well known limitations compromising its ability to act as a surrogate parameter of glucose consumption. Recently, we have shown that SUR overcomes most of these limitations as long as FDG kinetics in the target structure can be considered irreversible [1,2]. Excellent linear correlation of SUR and Km from Patlak analysis was found using dynamic imaging of liver metastases. However, due to the perfectly standardized uptake period used for SUR determination and the comparatively short uptake period these results are not directly applicable to clinical whole body examinations, in which the uptake periods often vary considerably. Therefore, the aim of this work was to investigate the correlation of SUR and Km in clinical whole body scans, where Km was approximated by Ks derived from dual time point (DTP) measurements [3]. Methods: DTP FDG-PET/CT was performed in 76 consecutive patients with histologically proven NSCLC. In the PET images the primary tumor was delineated with an adaptive threshold method. For determination of the blood SUV the aorta was delineated manually in the attenuation CT. The aorta ROI was transferred to the PET image. Blood SUV was computed as the mean value of the aorta ROI. SUR values were computed as ratio of tumor SUV and blood SUV. SUR values were scan-time-corrected to 60 min p.i. as described in [2]. Metabolic uptake rate Ks was computed similar to the procedure in [3]. The correlation of SUV and SUR with Ks was investigated. Results: There was highly significant correlation of SUR and Ks (R^2=0.9). However, the correlation coefficient appeared somewhat lower than previous results obtained from dynamic imaging and standardized uptake times (R^2=0.96 [1]). As expected, SUV showed