Multidimensional analysis of diffusion MRI to classify prostate cancer at 68Ga-PSMA-11 PET-MR

Background:

1. Prostate cancer is the most common cancer in men worldwide. Initial screening and diagnosis relies on. Initial screening and diagnosis relies on the digital rectal examination, serum prostate-specific antigen (PSA) testing, and transrectal ultrasonography (US)-guided biopsies.
2. Significance of grading: Depending on cancer stage and grade, treatment may involve observation, surgery (prostatectomy), radiation therapy (external beam or brachytherapy), hormonal therapy, chemotherapy, or a combination of these.
3. At present, the imaging modality to choice for the detection of prostate cancer is multi-parametric magnetic resonance imaging. Diffusion MRI (ADC\IVIM\DKI\FROC) are able to improve the diagnostic performance.
4. Pitfalls of using traditional imaging method.

MR imaging, CT and bone scanning have limited accuracy in depicting retroperitoneal small lymph node metastases that do not trigger size criteria at CT and MR imaging and small-volume bone metastases.

1. Molecular imaging has great potential to improve prostate cancer staging. Prostate-specific membrane antigen (PSMA) is a membrane glycoprotein that is overexpressed on prostate cancer cells.
2. PSMA-11 PET/MR hybrid imaging enables the simultaneous correlation of PET and MR quantitative metrics such as standardized uptake value (SUV) and apparent diffusion coefficient (ADC) as both studies are co-registered.
3. The aim of this study is to determine the relationship between SUVmax and parameters derived from different diffusion model and differentiate patients with intermediate-risk or high-risk cancer.

Method:

**PCA (diffusion modal, normalized data)->PCA validation->spearman correlation table (parameters v.s. SUVmax) ->Contour plot (PC1 V.S SUV, PC2 V.S. SUV) ->Predictive ROC, Gleason score (prognosis)**

1. Patients: 50 patients. Patients were included in the study if they presented for initial evaluation of histologically proven prostate cancer prior to any treatment. PSA>4ng/ml, Gleason score (GS) = [5,10]. Scan time: 60-70 minutes after injection. [Add: PI-RADS≥4]
2. Preparation of 68Ga-PSMA-11
3. PSMA PET/MR protocol.

T1\T2 FSE highres\T2 FSE fs\FROC

1. PSMA PET/CT protocol (option)
2. Image analysis. PET images were reviewed in correlation with MR imaging images for identification of focal 68Ga-PSMA-11 uptake within the prostate. SUVmax were recorded. The MR images (multiparametric, including DW imaging) were analyzed preoperatively, blinded to the PET/MR imaging results by radiologists specializing in body MR imaging.

ROI: Cancer lesion size was evaluated on the axial, sagittal and coronal FROC sequence planes and was reported on the largest single dimension. Then the maximal spherical ROI was manually drawn on the selected plane and parameters were calculated. The spherical ROI was copied and applied onto the PET images and lesion SUV max was determined.

ROI: Figure 1

1. Statistical Analysis:

(1) Bland-Altman Plot, PET/CT SUVmax V.S. PET-MR SUVmax (option)

(2) Multidimensional analytical workflow. (Figure 2)

Data normalization.

PCA analysis was performed in SPSS. To assess the relationship between the different MRI measures, we used a NL-PCA in the general workflow. NL-PCA is suitable for a set of variables including mixed measurement levels (nominal, ordinal, and numeric).

To determine the stability of the NL-PCA, we performed…

(3) Spearman Correlation:

SUVmax V.S. parameters derived from diffusion MRI model (e.g. MK, MD, f, D, Dstar, ADC) and Gleason score V.S. all the parameters

(4) ROC/AUC to find the best parameter to predict the Gleason score (prognosis)

(5) Levels of validity.

Result:

1. Bland-Altman plot (option, Figure 3)
2. MRI measures will group as coherent multivariate principal component (PC) ensembles, and that distinct PCs and individual variable will significantly correlated with SUV max and Gleason score

[Spearman correlation with SUV max, Table1; Spearman correlation with Gleason score, Table2]

1. Distinct PCs and individual variable will show discriminant validity for predicting Gleason Score (Prognosis) (Figure 4)

Discussion:

1. We have investigated the feasibility of using a set of novel diffusion parameters in PSMA PET-MR to differentiate intermediate- and high-risk prostate cancer.
2. Why we choose PET-MR? Better than CT, MR, and PET/CT. Previous studies have proved that (1) PET/MR SUVmax and ADC are able to differentiate intra-prostatic cancer and normal prostatic tissue in naïve prostate cancer patients. (2) PSMA PET-MR imaging could differentiate intermediate- or high-risk prostate cancer, which provides valuable diagnostic information and may inform the need for and extend of pelvic node dissection.

Why we use multi-parametric diffusion model

1. ADC has been applied to assess prostate cancer, including evaluating the aggressiveness of prostate cancer. However, ADC values varied within the same Gleason Score groups, and there was considerable overlap among the groups in the present study, which compromising the specificity and diagnostic accuracy.
2. The sub-optimal performance of ADC for tumor grading originates, at least in part, from the use of a Gaussian diffusion model (i.e. mono-exponential) which assumes a homogeneous diffusion process in tumor despite overwhelming evidence of tumor heterogeneity. In the presence of heterogeneity, biexponential model, like IVIM and other non-Gaussian diffusion models, including DKI and FROC, can be more effective in charactering the complex diffusion process.
3. As we know, ADC is a quantitative biomarker for tissue cellularity. However, in addition to the cellularity, microvasculature can also be a significant component in an image voxel, which will affect the prognosis of prostate cancer.
4. Microstructures: DKI+FROC

The diffusion kurtosis mode, generalizes the monoexponential Gaussian model to the non-Gaussian regime. As a single diffusion coefficient is no longer sufficient to describe diffusion process in a complex and heterogeneous tissue, FROC diffusion model could be used to provide new parameter.

Water molecules can produce a variable spatial displacement in each move. This spatial heterogeneity is a direct reflection of the underlying tissue structural complexity.

1. Why PC1 is better than PC2 (or PC2 is better than PC1): weights of parameters and why these parameters are important.
2. If PC is better than other parameter: None is dispensable

If not: Highlight that parameter: e.g. β is better than others. Smaller β value exhibit a larger degree of intra-voxel heterogeneity. Previously study showed that β had weak correlation with D or μ.

1. Limitation: retrospective studies. Small sample size. An extension of the FROC model to capturing temporal heterogeneity, as demonstrated recently (CTRW), suggests new opportunities to further improve the performance.