Quantitative Analysis of Multi-parametric FLT-PET/MRI in Evaluating Early Treatment Response in Renal Cell Carcinoma

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TARGET AUDIENCE: This research is intended to reach radiologists and oncologists who incorporate multi-modal imaging protocols when assessing early or functional response to cancer treatment.

PURPOSE: Tyrosine kinase inhibitors are a newly developed cytostatic drug treatment for renal cell carcinoma (RCC). Current assessment of chemotherapy treatment relies on changes in overall tumor morphology using RECIST[1], but these changes appear months into the treatment regime. Computer extracted feature analysis in conjunction with PET and MRI may be able to more accurately identify subtle changes in the tumor microenvironment as a result of treatment compared to evaluating gross changes in tumor size alone. Further, the quantitative combination of these multi-parametric (MP)–PET/MRI parameters may allow for improved evaluation of treatment response. We present a quantitative voxel-by-voxel image analysis framework to enable evaluation of early response in RCC to tyrosine kinase inhibitor treatment, using computerized tools to bring PET and MRI protocols into alignment and then constructing a weighted MP-PET/MRI signature for early treatment response.

Parameters	T2W	DWI	PET
Sequence	TSE	DwiSE	WB FLT
Matrix Size	480 x 480	192 x 192	144 x 144
Slice Thickness (mm)	5	5	4
Acquisition Parameters	TR/TE = 1590/80 ms	b-value = 0	Duration = 180000 ms

METHODS: For a single RCC patient, three distinct sets of integrated PET/MRI acquisitions were obtained. Two sets (test/re-test, Day 01/Day 02) were acquired one week prior to cytostatic drug treatment and one set was acquired three weeks into treatment (Day 22). Each acquisition set was acquired using the Ingenuity TF PET/MR (Philips, Cleveland, OH) and consisted of one T2-weighted (T2W) MRI, Diffusion Weighted Imaging (DWI) MRI, and PET protocol (see Table). [18F] labeled fluorothymidine was used as the PET radiotracer, due to promise in imaging cell proliferation[2]. ADC maps were calculated based on DWI MRI. A total of 30 first-order statistical, gray level, gradient, and Haralick texture feature maps were extracted from T2W MRI to capture structural homogeneity and heterogeneity characteristics[3]. The steps within our framework consisted of: (i) Expert annotations made on the test T2W MRI of RCC and normal functioning tissue regions. (ii) 3D deformable co-registration between corresponding protocols across time points, in order to enable per-voxel comparisons between pre- and post-treatment acquisitions. (iii) Ranking of T2W MRI features in terms of ability to specifically identify treatment response in RCC regions, (iv) Quantitative MP-PET/MRI feature extraction within the annotated regions, including SUV (f_{SUV}, from PET), ADC (f_{ADC}), and top-ranked T2W MRI texture feature Sum Average (f_{SUVAV}) intensity values. Absolute percent difference maps between test/re-test (D1/D2) and test/treatment (D1/D22) were calculated for each MP-PET/MRI parameter on a per-voxel basis using $D_P = norm\left(\left|\%\Delta\left(f_P^{R,D22}, f_P^{R,D1}\right)\right| - \left|\%\Delta\left(f_P^{R,D2}, f_P^{R,D1}\right)\right|\right), R \in \{RCC, Normal\ Tissue\}, P \in \{SUV, ADC, SUMAV\}$ to yield a weighted difference map $\overline{D} = \sum a_P * D_P$. A cost function was used to determine each of the weights (a_P).

RESULTS: Treatment change was evaluated on a per-voxel basis within the RCC region and compared against any change seen in the normal tissue. SUV (D_{SUV}) was identified with the highest weight while ADC and Sum Average yielded an equal but much lower weight. Individually, each parameter difference map showed markedly higher changes in the RCC region compared to normal tissue. The weighted MP-PET/MRI map identified outer right region of the RCC as demonstrating highest change.

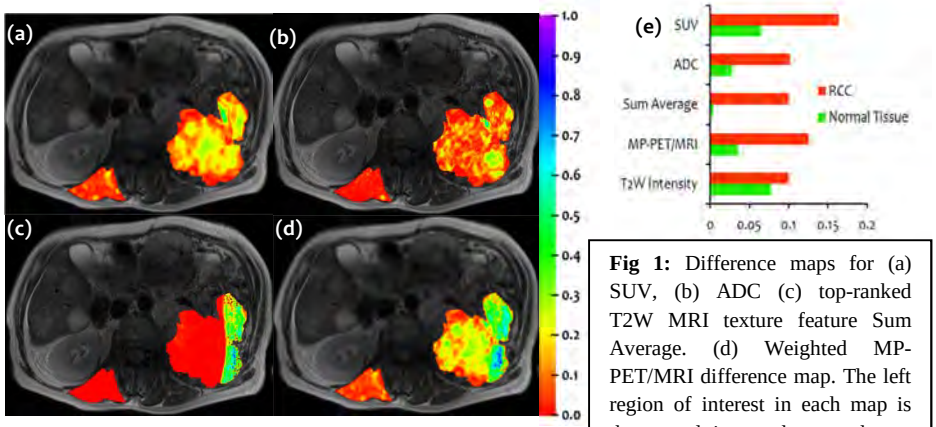

Fig 1: Difference maps for (a) SUV, (b) ADC (c) top-ranked T2W MRI texture feature Sum Average. (d) Weighted MP-PET/MRI difference map. The left region of interest in each map is the normal tissue, where no change is expected. The right region is RCC, where change due to treatment is expected. (e) Bar plots quantitatively comparing the change seen in RCC versus normal tissue. The integrated MP-PET/MRI map demonstrates the highest specificity to treatment-related change compared to individual parameters.

DISCUSSION: Each parameter difference map uniquely identified treatment change based on the type of information captured. The weighted combination of MP-PET/MRI parameters appeared more informative as well as sensitive and specific compared to the individual parameters.

CONCLUSION: We have presented the preliminary results for a framework to quantitatively analyze MP-PET/MRI parameters in early treatment response evaluation of RCC, which enables creation of a combined MP-PET/MRI difference map to better visualize treatment-related changes

REFERENCES: [1] Therasse P. et al, J Natl Cancer Inst, 2000 v2.3:205-16. [2] Chen W. et al, J Nucl Med, 2005, v46.6:945-52. [3] Viswanath et al, J Mag Res Img, 2012.