Initial observations from multimodal imaging assessment of rectal tumors with dynamic contrast enhanced and diffusion weighted magnetic resonance imaging, perfusion computed tomography and positron emission tomography.

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INTRODUCTION: Despite the advances in screening, imaging and treatment, overall 5-year survival in patients with rectal cancer still remains below 50% [1], indicating a need for progress to improve outcomes. Previous studies have shown the capability of single modality imaging with dynamic contrast enhanced magnetic resonance (DCE-MR) [2], diffusion weighted magnetic resonance (DW-MR) [3], perfusion computed tomography (pCT) [4], or 2-[(18)F]fluoro-2-deoxyglucose positron emission tomography (FDG-PET) [5] to monitor the response to neoadjuvant chemoradiation therapy or to predict therapy outcome in locally advanced rectal tumors. To the best of our knowledge however, no previous study has formally evaluated the combination of these functional imaging techniques for the assessment of rectal tumors. The aims of our study were to compare the findings of DCE-MR, DW-MR, pCT and FDG-PET in monitoring neoadjuvant chemoradiation therapy and predicting therapy outcome in locally advanced rectal tumors.

METHODS AND MATERIALS: The study was approved by our institutional ethics committee, and written informed consent was obtained from all participants before entry into study. From March 2009 to September 2009, patients with locally advanced non-mucinous rectal adenocarcinoma (T3 or higher, or N1-2, as staged by MRI) were prospectively enrolled in the study and underwent a multimodality imaging assessment, including DCE-MR, DW-MR, pCT and FDG-PET, before and after neoadjuvant chemoradiation therapy.

MR exams were performed on a 1.5T scanner (Avanto, Siemens Medical Systems, Erlangen, Germany). DCE-MR used a dynamic T1-weighted sequence performed at 5s intervals for 8 minutes after intravenous injection (0.2mL/kg, 3.5mL/sec) of contrast agent (Magnevist; Schering, Berlin, Germany), followed by a 20mL saline flush. Diffusion-weighted echo-planar images were acquired at 5 b-values (0, 50, 250, 500, 900s/mm^2). CTp exams were performed with a 16-slice CT scanner (LightSpeed 16; GE Healthcare, Milwaukee, USA) with dynamic CT scans acquired over 2 minutes after intravenous injection of 40mL of nonionic iodinated contrast material (Ultravist; Schering, Berlin, Germany), followed by 40mL of saline solution. The FDG-PET/CT studies were performed with a PET/CT system (Discovery ST, GE Medical System, Milwaukee, USA). Sixty minutes after the administration of 5 MBq of FDG in fasting state PET images were acquired in 3D mode, matrix 256x256.

Data was analyzed with dedicated software (MRIWorkbench, Institute of Cancer Research, Sutton, England) for DCE-MR; in house software for DW-MR; manufacturer provided software for pCT (CT Perfusion 3, GE Healthcare, Milwaukee, USA), and PET images were analyzed with a dedicated software Advantage 4.4 (GE Medical System, Milwaukee, USA) through the measurement of the volumetric maximal standardized uptake value ($SUV_{Vol\text{-}max}$). A radiologist defined separate ROIs for each modality that were applied to the functional maps to extract regional values of the following quantitative parameters: Ktrans, Kep, Ve and IAUC60 (for DCE-MR); apparent diffusion coefficient (ADC) for DW-MR; blood flow (BF), blood volume (BV), mean transit time (MTT) and permeability-surface area product (PS) for pCT; and standardized uptake value (SUV) for FDG-PET. According to the pathologic stage of the surgical specimen, patients were divided in 3 response groups: complete response; local down-staging; and no local down-staging or an increase in local tumor stage. In anticipation of a future ANOVA analysis of the data in a larger study population, we have calculated the correlations between individual quantitative parameters inclusive of all groups, as well as performed t-tests on the differences between the complete response group and the non-response group for the various quantitative parameters.

RESULTS: 6 patients have been enrolled to date (4M, 2F; mean age 55.1 years, age range 42-74 years). Preliminary analysis of this small group shows correlation between Kep and PS (R=0.93) and a trend to correlation between Ktrans and PS (R= 0.47), whereas negative correlations are seen between Ktrans and SUV (R=-0.78), and between Ve and SUV (R=-0.86). ADC showed a negative trend to correlation only with SUV (R=0.504). A significant treatment-related change in ADC (1111±99 vs 1484 ± 40s/mm^2) was seen in the two subjects with post-treatment assessment.

Of the two patients that have completed neoadjuvant chemoradiation therapy to date, one had local downstaging, and showed decreases in Ktrans, BF, BV, PS, SUV and an increase in Kep, Ve, MTT and ADC, whilst the other had no local downstaging, and showed stable values of Kep and BF, decreases in Ktrans, Ve, PS and SUV, and increases in BV, MTT and ADC. This latter patient, who had no local down staging, had lower baseline Ktrans, Ve, BF, BV and SUV, when compared to the other patient.

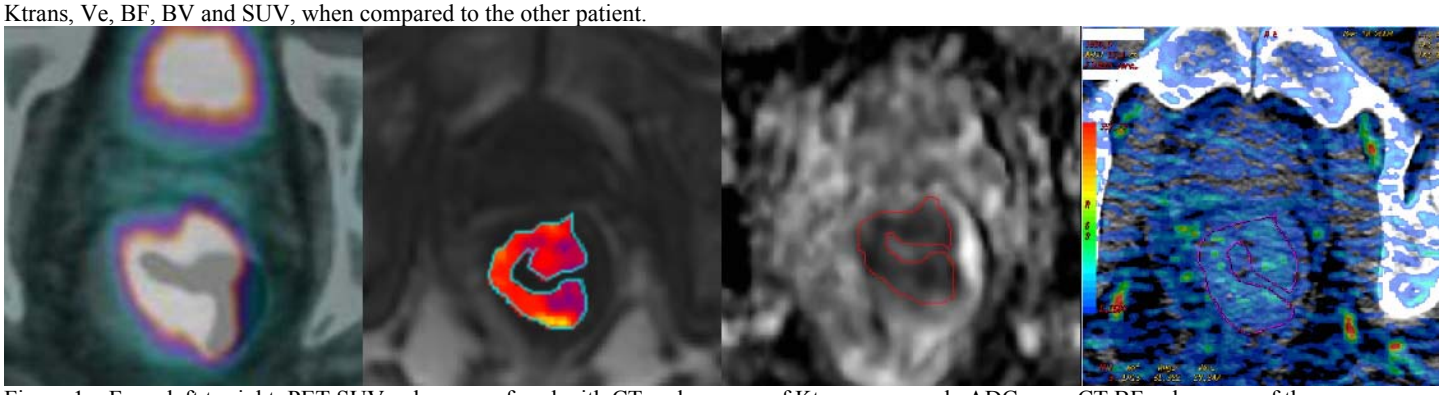

Figure 1 – From left to right: PET SUV colourmap fused with CT, colour map of Ktrans, greyscale ADC map, CT BF colourmap of the same patient prior to undergoing neoadjuvant chemoradiation therapy.

CONCLUSIONS: Our preliminary results suggest that there is a correlation between quantitative parameters Kep and PS, estimates of capillary permeability on DCE-MR and pCT respectively, whilst the DCE-MR derived values of Ve and Ktrans correlate negatively with SUV. ADC showed a trend to negative correlation only with SUV prior to treatment, but on the data available showed a clear change in response to treatment.

References:[1] Tepper JE et al. J Clin Oncol 2002;20: (7)1744–1750 [2] George ML et al. Br J Surg. 2001 Dec;88(12):1628-36. [3] Kim SH et al. Radiology. 2009 Oct;253(1):116-25. [4] Bellomi M et al. Radiology. 2007 Aug;244(2):486-93. [5] Denecke T et al. Eur Radiol. 2005 Aug;15(8):1658-66. Epub 2005 Apr 2.