Abstract #360 | Oral or Poster presentation

Contrast agent-free diffusion weighted-MRI and T1/2 mapping for therapy response monitoring in murine pancreatic ductal adenocarcinoma (PDAC)

Simon Baller[1], Irina Heid[1], Geoffrey J. Topping[2], Katja Steiger[3,4], Anna-Maria Schmidmüller[1], Felix Harder[1], Franz Schilling[2], Rickmer Braren[1,5]

[1] *Technical University of Munich, Klinikum rechts der Isar, Institute of Diagnostic and Interventional Radiology, Munich, Germany*
[2] *Technical University of Munich, Klinikum rechts der Isar, Department of Nuclear Medicine, Munich, Germany*
[3] *Technical University of Munich, Klinikum rechts der Isar, Institute of Pathology, Munich, Germany*
[4] *Technical University of Munich, Klinikum rechts der Isar, Comparative Experimental Pathology (CEP), Munich, Germany*
[5] *German Cancer Consortium (DKTK) Partner Site Munich, Munich, Germany*

Introduction

Pancreatic ductal adenocarcinoma is one of deadliest cancers worldwide[1]. Non-invasive (semi)-quantitative MRI methods such as diffusion weighted imaging (DWI) or T1 and T2 mapping are important diagnostic tools for characterization of tissue composition and require no exogenous contrast agent application[2,3]. This work aims to investigate the use of the ADC, T1 and T2 values in a preclinical trial of endogenous murine PDAC treated with the standard therapy protocol Gemcitabine(GEM)/Abraxane.

Methods

Tumor Model: 6 *Ptft1a*$^{wt/cre}$;*KRAS*$^{wt/G12D}$;*p53*$^{fl/fl}$ mice, endogenous PDAC tumors.
Chemotherapy: Mice received 100 µg/g GEM intraperitoneally and 30 µg/g Abraxane intravenously (n=3), or vehicle (n=3), on day 0 (post scan) and day 2.
Imaging System: Small animal preclinical 7T MRI (Bruker/Agilent).
Imaging:
-T2w RARE anatomical images;
-DWI ADC maps (10 slices, 10 repetitions, 14 min, 0.35x0.35x1.75mm^3);
-Inversion-recovery RARE T1 maps (1 slice, 5 min, 0.58x0.58x3.5 mm^3);
-Multi-slice multi-echo T2 maps (10 slices, 5 min, 0.35x0.35x1.75 mm^3);
Analysis: ADC, T1, and T2 maps were fit in MatLab and analysed in ITK-Snap (29 3D regions of interest (ROI) in ADC-Maps, 26 3D ROIs in T2-Maps and 8 2D ROIs in T1-Map). Statistical analysis was performed in GraphPad PRISM 7.0.

Results/Discussion

We established free-breathing abdominal multiparametric MRI comprising T1 and T2 mapping and DWI in a murine endogenous PDAC model (Fig. 1). Visually identified distinct tumor nodules revealed heterogeneous distribution of values in all analyzed modalities, which resembles the clinical situation.

Chemotherapy caused significant changes in all parameters at day 3 in the treatment group, in contrast to the vehicle group (mean values: $ADC_{G/A\ day0}$= 1.63±0.09 *10^{-3}mm^2/s; $ADC_{G/A\ day3}$=1.69±0.08*10^{-3}mm^2/s; $ADC_{veh\ day0}$= 1.56±0.14*10^{-3}mm^2/s; $ADC_{veh\ day3}$=1.51±0.09*10^{-3}mm^2/s; $T2_{G/A\ day0}$=71±4ms; $T2_{G/A\ day3}$=64±5ms; $T2_{veh\ day0}$=65±6ms; $T2_{veh\ day3}$=67±4ms; $T1_{G/A\ day0}$=2.3±0.2s; $T1_{G/A\ day3}$=2.0±0.1s; $T1_{veh\ day0}$=2.3±0.2s; $T1_{veh\ day3}$=2.2±0.2s, Fig. 2). These findings suggest that DWI and T1/T2 mapping may be useful for therapy response monitoring in PDAC. Histopathology of corresponding tumor regions will be investigated using HE-/Movat-staining[3].

Conclusions

We established a multiparametric quantitative MRI protocol without the need for exogenous contrast agent injection for therapy response monitoring in a clinically relevant preclinical PDAC model. Comparative analyses of regionally matched MRI-derived parameter values and histopathology will be applied and correlated with distinct molecular subtypes.

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Disclosure

I or one of my co-authors have **no financial interest** or **relationship** to disclose regarding the subject matter of this presentation.

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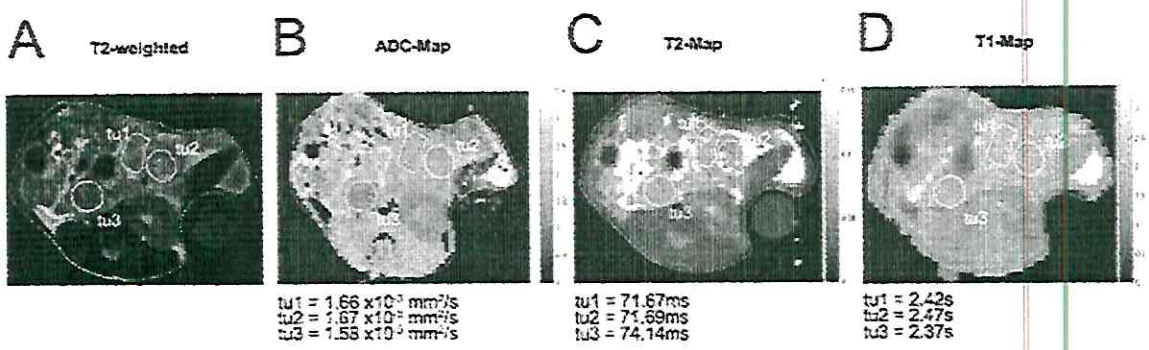

Figure 1: Multiparametric MRI consisting of T1, T2, and ADC mapping in murine endogenous PDAC.
A) Axial T2-weighted anatomical image of 3 different tumors. **B)** Monoexponential plus constant offset model fitted ADC-Map (10 b-values: 211-1519 s/mm^2) **C)** T2-Map fit with a monoexponential plus constant model, 10 echo times up to 160 ms **D)** T2-Map fit with a monoexponential plus constant model, 10 inversion times up to 3.76s

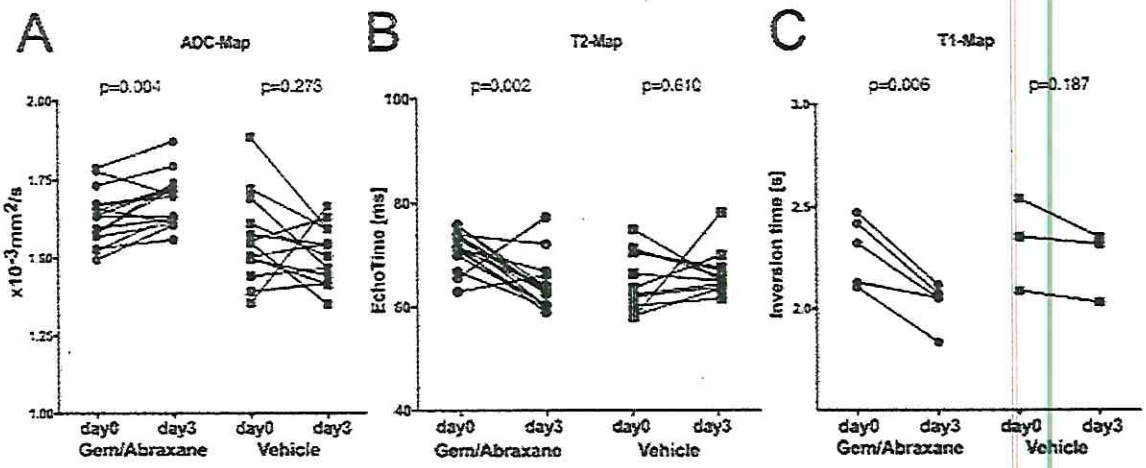

Figure 2 Therapy response monitoring with quantitative MRI parameters.
A) Mean ADC values. **B)** Mean T2 echo times. **C)** Mean T1 inversion times.