Prospective Evaluation of Serial Quantitative MR Imaging of Patients with Brain Cancer on a 0.35T MR-linac

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INTRODUCTION

Quantitative MRI (qMRI) has shown significant promise for defining tumor margins, assessing invasion, and quantifying tumor changes after treatment. By implementing qMRI on a 0.35T MR-linac, acquisition of serial images during the course of radiation therapy (RT) has become possible.

AIM

The aim of this work is to evaluate the feasibility of using onboard qMRI to detect changes within the tumor and brain tissue during the course of radiation treatment.

METHODS

- A multi-echo gradient echo MR method (STAGE: Strategically Acquired Gradient Echo[1], TR: 40ms, TE: 5, 20.63, 34.14 ms, FA: 10°, 50°) was optimized at 0.35T to generate T1, R2* and proton density (PD) brain maps in 10 minutes
- Ten patients with Glioblastoma were consented to an Institutional Review Board approved prospective trial
- Imaging was performed at simulation (Sim), weekly during RT, and 3 months post RT (Follow-up)
- All STAGE qMRI maps of each patient were rigidly registered to images acquired at RT Simulation using SPM 12 (The Wellcome Trust Centre for NeuroImaging, University College London, UK)
- As the normal control region, clinical target volume (CTV) was flipped with respect to the brain midline while maintaining a separation margin between the normal region and CTV
- White Matter (WM) and Gray Matter (GM) masks of the SIM T1W image were created using FSL (FMRIB Software Library, FMRIB, Oxford, UK) to assess normal qMRI values within the normal regions
- To assess qMRI stability, coefficient of variation (CV) was calculated within the WM, GM across time points in all three maps
- Temporal changes of qMRI map voxels within the clinical target volume receiving 60 Gy (CTV 60) were evaluated for response assessment

RESULTS

- Figure 1 shows T1, R2* and PD maps between the time of simulation (Sim), last week of treatment (End-Tx) and 3 Month Follow-up (FwUp) for one patient (Patient 3). Borders of the normal region and CTV 60 are highlighted in Sim T1 map
- qMRI maps in Figure 1 show increase of T1 and PD values, and decrease of R2* values for this patient, as well as overall increase of the size of the abnormal region across time
- T1 values in the normal WM across all patients were generally lower than in the CTV 60 region and also had lower temporal variability (Figure 2)
- Mean T1 values in the sub-cortical WM of the normal region ranged from 351ms to 405ms (384.50 ± 15.70ms) across all patients which is comparable to previously reported T1 values at 0.35T[2]
- CV of the T1, R2* and PD within the course of treatment was lower than the full course of study (Table 1)
- On average, R2* values showed higher variation within the WM, GM and CTV 60 across all timepoints (Table 1)
- CV of T1 values in the normal WM across all time points and all patients was 1.28 ± 0.56% (range: 0.73% - 2.49%) and were lower than these values within the CTV 60 (5.15 ± 4.81%, range: 1.44% - 16.03%)
- The highest increase of T1 values within the CTV 60 with respect to the time of simulation was 62.67% at follow-up (Patient 3). The R2* and PD values within this period decreased by 39.07% and increased by 16.07% respectively. This patient passed away ~1 year after end of treatment.

Table 1. Coefficient of Variation (CV) of the T1, R2 and PD maps within the normal white matter (WM), normal gray matter (GM) and region receiving 60 Gy CTV (CTV 60) from time of simulation to follow up (Full) and only within the duration of RT (RT). All values are in % and Mean ± StdDev and (Min-Max) across all patients are presented.*

CV	T1	R2*	Proton Density
WM (Full)	1.28 ± 0.56 (0.73-2.49)	1.38 ± 0.26 (0.92-1.72)	1.12 ± 0.36 (0.61-1.82)
GM (Full)	1.59 ± 0.55 (1.01-2.78)	2.36 ± 0.45 (1.34-3.01)	1.34 ± 0.40 (0.66-1.93)
CTV 60 (Full)	5.15 ± 4.81 (1.44-16.03)	6.22 ± 4.59 (1.70-13.89)	2.44 ± 1.18 (1.40-4.84)
WM (RT)	1.26 ± 0.67 (0.55-2.72)	1.17 ± 0.37 (0.60-1.94)	1.04 ± 0.41 (0.54 –2.02)
GM (RT)	1.46 ± 0.34 (1.03-2.24)	1.94 ± 0.41 (1.48 -2.48)	1.20 ± 0.42 (0.69-1.80)
CTV 60 (RT)	2.54 ± 2.60 (0.92-10.24)	3.88 ± 2.25 (1.37-11.93)	1.81 ± 0.94 (0.78-4.06)

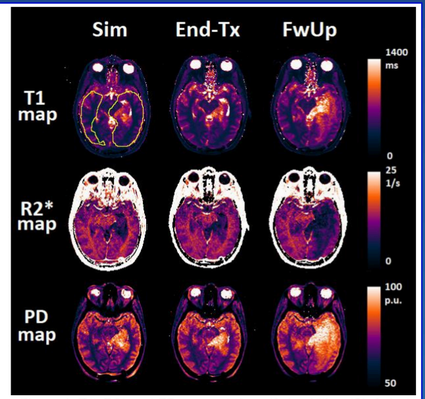

Figure 1. T1, R2 and PD maps at time of simulation (Sim), last week of treatment (End-Tx) and 3 Month Follow-up (FwUp) for Patient 3. Borders of the normal region and CTV 60 are highlighted in Sim T1 map.*

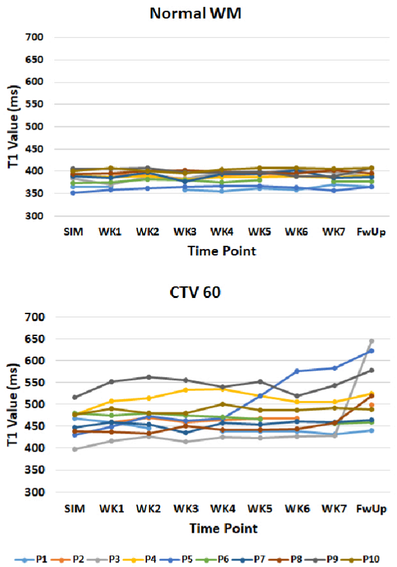

Figure 2. T1 values within the normal white matter (WM) and defined clinical target volume receiving 60 Gy of dose (CTV 60) for 10 patients with GBM across nine timepoints

CONCLUSIONS

- STAGE qMRI maps acquired on a 0.35T MR-linac were stable in normal brain tissue
- Changes within the CTV were substantial yet patient-specific
- Previous studies have shown variations within the T1 values of healthy brain at different ages [3] which can explain the range of values within the normal WM regions in our patient cohort.
- Future work will correlate long term survival data to variations in qMRI maps within the CTVs to highlight potential imaging biomarkers.

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