Can CEST be used as an aging biomarker?

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INTRODUCTION: As global life expectancy rises, there is a growing interest on recognizing the importance of aging and identifying biomarkers for its characterization, especially the detection of accelerated aging. A previous study found significative difference in CEST amide and rNOE pools between younger (age 24.6 ± 1.4) and older (age 58.1 ± 6.1) groups at 7T [1]. To examine the potential of CEST contrast as an age biomarker further, we exploratively analyzed the age-related variations in four CEST pools among 30 glioma patients, separately analyzing tumor and healthy tissues.

METHODS: 43 glioma patients (18 to 76 years) were scanned using a 7T scanner (Terra, Siemens, 32ch Rx, and 1ch Tx head coil) with the primary goal of presurgical tumor characterization. For each subject, FLAIR, MPRAGE and CEST images were acquired. The CEST acquisition consisted of a 3D snapshot GRE CEST at nominal B_1 levels of 0.72 μT and 1.00 μT [2]. CEST contrast was quantified by 5-pool Lorentzian fitting (water, guanidine, amide, NOE, and MT) performed on normalized, denoised, and B0-/B1-corrected Z-spectra, as described before [1]. The white matter (WM), grey matter (GM), deep grey matter (DGM) and tumor tissue were segmented from the FLAIR and MPRAGE maps using an in-house developed segmentation algorithm [3,4]. Only subjects with a tumor volume of less than 25% of the WM+GM volume were considered for analysis to ensure correct segmentation. Additionally, subjects were excluded if $\Delta B_0 > 0.2$ ppm, B_1 deviated by more than 50% from the nominal value or if strong artifacts were observed.

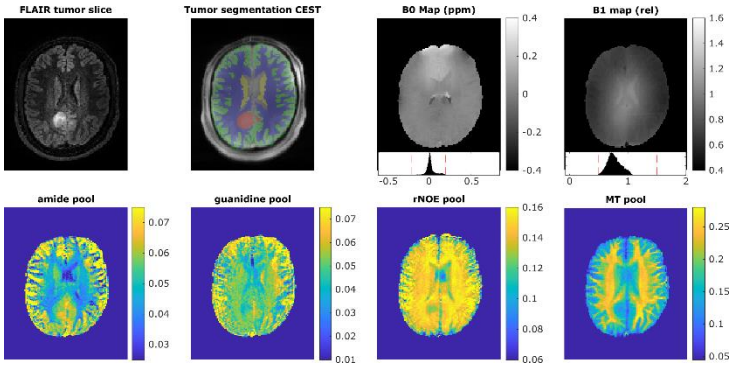

Figure 1: Representative subject included in the analysis. Female, age 21, with astrocytoma, WHO grade 2, slice 10, volume 1,56%.

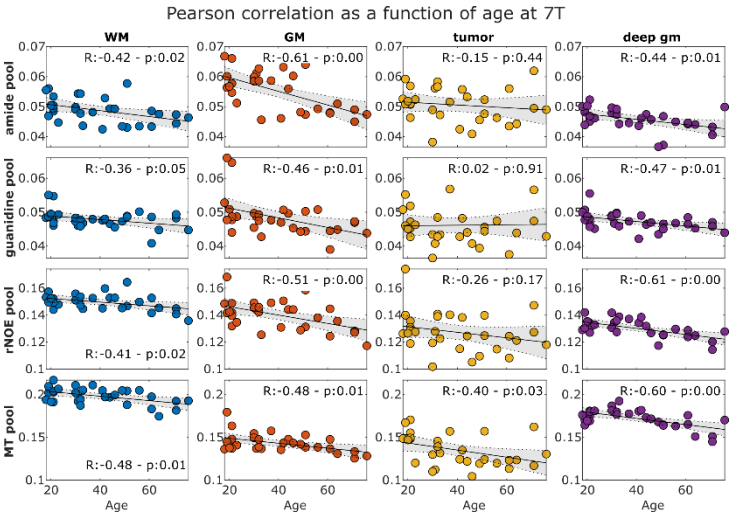

Figure 2: Pearson correlation coefficients (R) and p-values for each CEST pool as a function of age.

RESULTS: 13 subjects were excluded from age analysis according to the exclusion criteria detailed above, the remaining 30 were analyzed. A representative included case is shown in Figure 1. Significant age dependence was observed in every pool in GM, WM and DGM but not in tumor. Age correlation was always negative and stronger in the GM and DGM tissues.

DISCUSSION: The proposed multipool CEST experiment allowed the observation of age-related changes in CEST pools. Age dependence in Amide and rNOE was significant as previously reported, although with lower correlation than in the previous study [1]. In our approach, also CEST pools like guanidine showed an age dependence. The tumorous areas do not show an age trend, implying the independence of this pathology regarding age in the context of CEST imaging. Improved pipelines such as PICAE can be employed to potentially reduce the influence of B1 imperfections and diminish the number of excluded subjects [5]. Moreover, analyses in dedicated cohorts are warranted.

CONCLUSION: The CEST multi-pool evaluation of this work confirmed previous age dependence of rNOE and Amide groups, but also detected effects in Guanidine and MT. Future research will focus on age-related CEST changes to distinguish normal from pathological aging.

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