

VBM Analysis Of Quantitative Relaxometry Maps In Amyloid Positive And Negative Cases As A Potential Biomarker For Amyloid Deposition



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Using Synthetic MRI to measure brain tissue properties (T1, T2, R1, R2,PD), we found that these values change with amyloid levels in Alzheimer's disease, especially in moderate-to-severe cases. Later a comparison of these maps from Amyloid negative(FTD) and amyloid positive cohort (Alzheimer’s) against a healthy control cohort was done.

INTRODUCTION

Alzheimer’s Disease (AD) and Frontotemporal Dementia (FTD) are characterized by distinct patterns of protein deposition (amyloid and tau versus only tau deposition) with clinical presentations that challenges early diagnosis. While quantitative MRI relaxometry is well established in cardiac imaging of amyloid deposition, its application to neurodegeneration disease remains unexplored. Synthetic MRI offers a non-invasive approach to generate quantitative relaxometry maps (T1, T2, R1, R2, PD) simultaneously. This study investigates whether neurodegeneration specific protein deposition causes signature changes on derived relaxometry maps.

METHODS

We are using Amyloid PET to identify AD from FTD cohorts based on their PET behaviour of Amyloid positive and Amyloid Negative respectively .VBM analysis of their quantitive maps is done The derived quantitative maps were T1 T2 R1 R2 and PD .Healthy controls were enrolled only for MRI and not PET study and were used to generate normative reference range for quantitive maps. Multi-dynamic multi-echo (MDME)/QRAP master sequences for Synthetic MRI were acquired using a simultaneous PET/MRI protocol on a Siemens Biograph mMR 3T scanner in age matched cohorts (AD n=15, FTD n=9) and PET only acquisition in HC (n=15). Synthetic MRI software (syngo.MR XA 20A, Siemens Healthineers) automatically processed MDME/QRAP master data to generate calibrated absolute maps: T1, T2, PD, R1, R2 along with volumetric

segmentation (total intracranial volume, grey matter volume, white matter volume, CSF volume). The output were 2D maps and using in house developed solution we did VBM analysis on these maps.

Predefined regions of interest (ROIs) were the Centiloid mask (bilateral frontal lobe, anterior cingulate cortex (ACC), parietal cortex, posterior cingulate cortex (PCC), striatum, and lateral temporal lobe). It was analyzed against the cerebellum as an internal reference for normalizing the values. Values of AD, FTD, and HC were used for analysis. This method was adapted from the Centiloid scoring method of amyloid PET, used to scale the severity of amyloid deposition.

Mean and standard deviation for normative ranges for T1, T2, PD, R1, and R2 were derived from the normalized ratio for individual AD and FTD patients and its statistically significance were evaluated.

RESULTS

For a head-to-head comparison, we followed the methodology adopted for centiloid values in Amyloid PET in terms of centiloid mask used and normalization with cerebellum to obtain the values of relaxivity

In the 24 patients we studied, Amyloid Negative cases on PET and clinical cognitive impairment (FTD) were 9 and Amyloid positive (AD) were 15).Normalized values were generated for the maps by (Cerebral cortex/Whole cerebellum) ratio correlation graphs were performed using normalized relaxivity values against Centiloid values.

Objective 1:Correlation of severity scores and relaxivity measures

When normalized maps of **amyloid-positive** cases were correlated with Centiloid values, we found a pattern of increase in T1 and T2 values and decrease in R1 and R2 values ,with centiloid scales above 60.Centiloid scale values below 60 and above 100 did not reflect these changes likely because of low amyloid load that does not cause significant relaxometry changes and in advanced cases, due to loss of neuronal tissue respectively (Figure 1B,1D,1F,1H).

When normalized maps of **amyloid-negative** cases were correlated with Centiloid values, we found an increase in T2 and a decrease in R2 values, unlike in amyloid-positive cases (Figure 1A,1C,1E,1G). We need to assess the significance of these changes by correlating them with Tau-PET, as Centiloid showed a negative value relative to the control group, which may indicate non-amyloid protein deposition.

Objective 2 : Healthy control database versus per patient measures of relaxivity maps.

We calculated the mean and corresponding standard deviation (mean ± SD) from the normalized relaxometry maps from healthy control database.(Table 1)

In the **amyloid positive** patients a significant increase in the T2 and T1 and a decrease in R1(Blue- Table 1)with increasing Centiloid values was noted. Alongside PD changes were unique to this group

In the **amyloid negative**, patients a significant increase in T2 was noted,(Green - Table 1). Alongside an increase in T1 and a decrease in R1, R2 was also noted with decreasing centiloid values.

Limitations : Lack of Amyloid PET images in healthy control

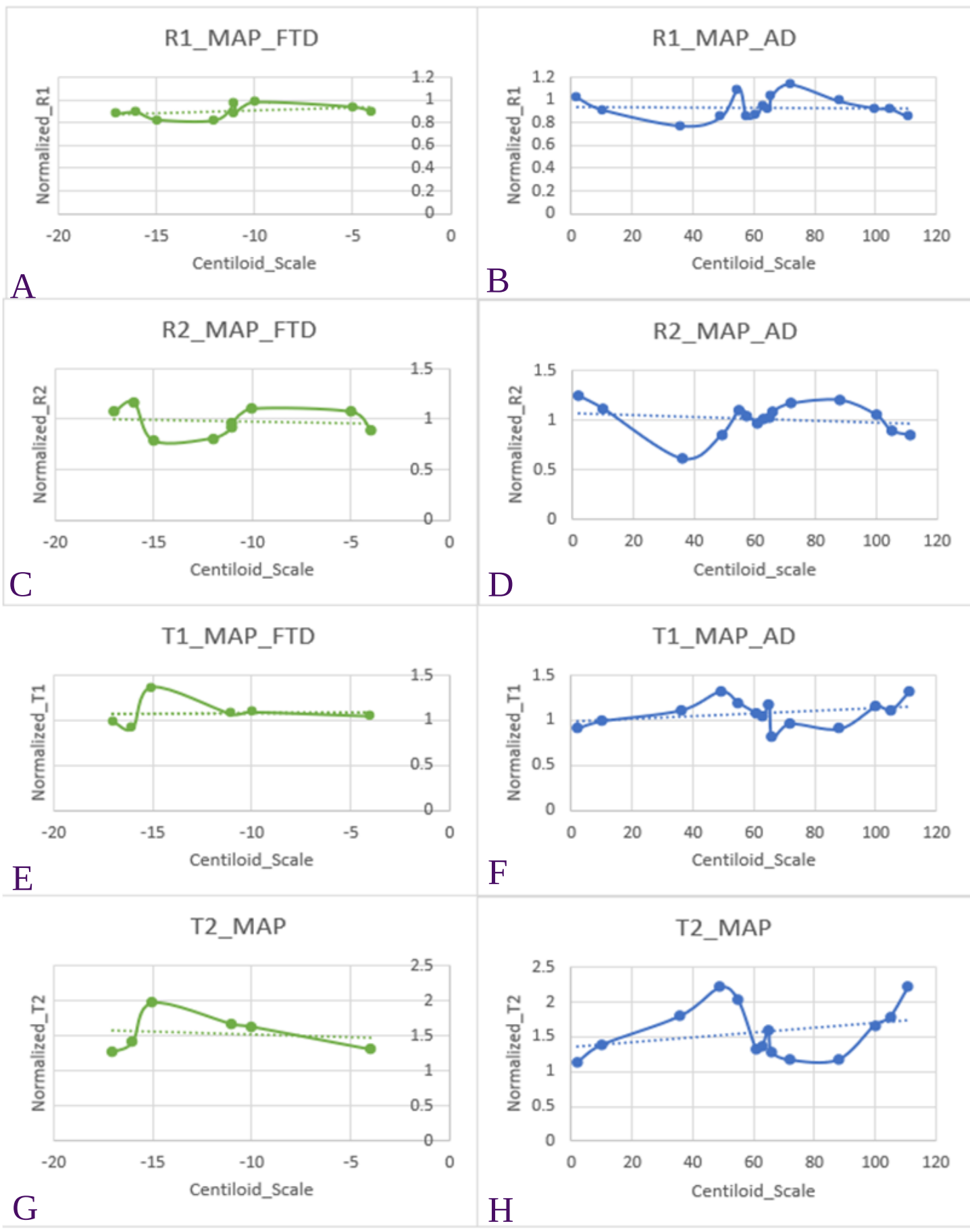


Figure 1: Normalized R1, R2, and T1 ,T2 relaxometry values plotted against amyloid burden (Centiloid scale) showing distinct relaxometry trends between amyloid-negative (FTD:green : A,C,E,G) and amyloid-positive (AD: blue: B,D,F,H) groups.

FTD	Centiloid	SD_PD	SD_R1	SD_R2	SD_T1	SD_T2
S_001	-17	-0.84859	-1.58878	0.511776	-0.62427	-0.6051
S_002	-16	-1.80558	-1.40728	1.415263	-1.41379	0.546943
S_003	-15	0.939186	-2.33947	-2.41643	3.310404	5.075903
S_004	-12		-2.40731	-2.13375		
S_005	-11	-0.20823	-0.24397	-1.09882	0.203898	2.636655
S_006	-11	1.754173	-1.46555	-0.5902		
S_007	-10	0.119713	-0.11939	0.770082	0.441865	2.324395
S_008	-5	0.047649	-0.72454	0.471948		
S_009	-4	-0.86464	-1.32215	-1.34527	-0.02281	-0.28062
AD	Centiloid	SD_PD	SD_R1	SD_R2	SD_T1	SD_T2
S_010	2	-1.24702	0.462928	2.12294	-1.39102	-1.64776
S_011	10	0.009253	-1.05212	0.851087	-0.57166	0.324915
S_012	36	0.721688	-3.13972	-4.14185	0.670631	3.671316
S_013	49	0.413716	-2.07587	-1.78543	2.80913	6.92231
S_014	55		1.657708	0.793506	1.525143	5.521867
S_015	57.5	-0.60537	-1.95007	0.149854		
S_016	61	0.888173	-1.71396	-0.54741	0.315328	-0.21892
S_017	63	0.531963	-0.43164	-0.09967	-0.03435	0.159236
S_018	65	0.40995	-0.91466	0.054908	1.191215	2.034816
S_019	66	-3.94664	0.785768	0.591053	-2.37802	-0.44436
S_020	72	0.306453	2.165463	1.37341	-0.88027	-1.40281
S_021	88	-2.31404	0.026832	1.719583	-1.46043	-1.38861
S_022	100	-0.10857	-0.8937	0.250043	1.068705	2.572976
S_023	105	1.819561	-1.02183	-1.31164	0.675453	3.47858
S_024	111	0.413716	-2.07587	-1.78543	2.80913	6.92231

Table 1:Subject-level normalized relaxometry values (SD_PD, SD_R1, SD_R2, SD_T1, SD_T2) for FTD and AD cases ranked by Centiloid score.

CONCLUSION

Synthetic MRI maps may have a potential in neurodegenerative proteinopathy especially amyloid and taupathy. Future directions include prion diseases and syn-nucleiopathy and also whether spatial mapping of these depositions can be done similar to amyloid PET.

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