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Comparison of 1.5 T and 3 T MRI hippocampus texture features in the assessment of Alzheimer's disease

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ABSTRACT

Objective: Many studies evaluated how the Magnetic Resonance Imaging (MRI) field strength affects the effectiveness to detect neurodegenerative changes of Alzheimer's disease (AD), derived from atrophy or thickness. To the best of our knowledge, no study evaluated before how tissue texture changes are affected. In this research, hippocampus texture features extracted from 1.5 T and 3 T MRI are evaluated how are affected by the magnetic field strength.

Methods: MR imaging data from 14 Normal Controls (NC), 14 with Mild Cognitive Impairment (MCI), 11 MCI converters (MCIc) and 10 CE subjects scanned at 1.5 T and 3 T were included. Haralick's texture features were extracted from the hippocampus, along with hippocampal and amygdala volumes and cortical thickness. One-way ANOVA, paired-samples and Wilcoxon signed t-tests were used to evaluate if there were significant differences between the features.

Results: 3 T texture features were significantly different for NC vs AD, NC vs MCI and MCI vs AD, whereas, 1.5 T for MCI vs AD only. Amygdala and hippocampal volumes, showed significant differences for NC vs AD for both MRI strengths, whereas cortical thickness for MCI vs MCIc for the 3 T. Paired sample t-test and Wilcoxon signed-rank test revealed significant differences for Angular Second Moment (ASM), contrast, correlation, variance, sum variance and entropy, the amygdala volume and cortical thickness. Between NC vs MCI, 3 T texture revealed higher Area Under Curve (AUC).

Conclusion: 3 T texture revealed significant differences for more features compared to 1.5 T, whereas, atrophy and thickness had similar results.

Significance: 3 T texture changes provide earlier diagnosis compared to 1.5 T volume or texture changes.

1. Introduction

Despite continued advances in exploring the nature of the Alzheimer's Disease (AD), there are still many unresolved issues regarding the pathophysiology of this highly heterogeneous disease in terms of diagnosis and disease follow-up. Other clinical syndromes (atypical AD forms) might cause similar symptoms, making necessary the identification of disease related biomarkers in patient selection and treatment response. According to World Health Organization (WHO) the number of people living with dementia worldwide is currently estimated at 47 million and is projected to increase to 75 million by 2030. The disease

diagnosis still remains probable and only post-mortem material will reveal deposits of amyloid- β ($A\beta$) plaque deposition and tau protein (Neurofibrillary Tangles - NFTs) in the brain tissue [1]. Thus, the diagnosis is based on clinical and neuropsychological tests, such as the Mini Mental State examination (MMSE) [2] or Clinical Dementia Rating (CDR) [3]. However, these tests will detect the disease after structural changes within the brain will occur [4].

Structural Magnetic Resonance Imaging (MRI) is being used to image subtle anatomic changes within the brain and evaluate the disease *in vivo*. Several MRI analysis methods such as volumetry, thickness, Voxel Based Morphometry (VBM) have been used to quantify and identify AD

related biomarkers. MRI is widely used to detect brain structural changes caused from neurodegeneration and its importance in the assessment of AD was underlined by its inclusion in the new diagnostic criteria [5]. Hippocampal atrophy is one of the most valid and used biomarker in the evaluation and prediction of AD [6–8]. Furthermore, amygdala atrophy was comparable to hippocampal atrophy [9] and patterns of loss of cortical thickness from MRI have been also reported in early phase of AD [10]. For a review on quantitative MRI brain studies in the assessment of AD, the reader is referred to [11].

Theoretically, increasing the magnetic field strength from 1.5 T to 3 T, roughly doubles the signal-to-noise ratio (SNR), and provides a higher contrast to noise ratio (CNR), per unit scan time, to better differentiate gray/white matter and other tissues. Therefore, the boundaries between gray and white matter are better seen in 3 T images and as a result the delineation is easier. However, the higher magnetic field of 3 T comes with a cost of increased level of artifacts [12] which might affect the features extracted from the images. Furthermore, with stronger fields, the magnetic field inhomogeneity increases as well due to susceptibility increase in spatial variations [13]. Currently, most MRI studies are conducted at 1.5 T [14–17]; however, some studies investigated a stronger magnetic field, such as from 3 T as tabulated in Table 1, investigating whether 3 T MRI strength fields can provide better atrophy detection compared to 1.5 T [18–22]. Overall, 1.5 T and 3 T scans did not significantly differ in their power to detect neurodegeneration from atrophy.

In the assessment of AD most of the structural MR imaging studies have been using biomarkers that are derived from larger scale tissue changes such as atrophy. On the other hand, texture analysis, evaluates the statistical properties of the image quantitatively, therefore, texture based biomarkers might be able to detect smaller scale changes of neurodegeneration. Texture analysis in the assessment of AD was previously investigated in both classification and prediction modelling of

Table 1
Volumetric studies comparing 1.5 T and 3 T MRI features in the assessment of AD

Main Author	Region of Interest	Data Type	Subjects	Description
Briellmann et al., 2001, [18]	Hippocampus	Volume	NC	Control hippocampal volume measurements obtained at 1.5 T and at 3 T were not different.
Chow et al., 2015, [19]	Hippocampus	Volume	NC, MCI, AD	3 T images, with their higher contrast and higher signal-to-noise ratio, may enhance the topographic localization of atrophy.
Ho et al., 2010 [20]	Whole brain	Volume	AD, MCI	1.5 T and 3 T scans did not significantly differ in their power to detect neurodegenerative changes.
Macconald et al., 2014, [21]	Hippocampus	Volume	NC, AD	Hippocampal volume and atrophy rates discriminated well between controls and AD subjects, and there was no evidence of a difference in predictive ability between 1.5 T and 3 T.
Lötjönen et al., 2011, [22]	Hippocampus	Volume	NC, MCI, AD	When comparing hippocampus volume extracted from 1.5 T and 3 T images, the absolute value of their difference was low (equal to 3.2 %).

Abbreviations: NCnormal controls; MCI mild cognitive impairment; ADAlzheimer’s disease; TTesla.

AD with very encouraging results [23,24], where it was seen that texture achieved higher Area Under Curve (AUC) compare to volume.

The main objective of this study was to evaluate if smaller scale tissue changes in AD derived from texture are more easily detectable in 3 T which could lead to an earlier diagnosis. Specifically, texture features were extracted from the hippocampus of normal controls (NC), mild cognitive impairment (MCI) and AD subjects in order to evaluate how well each magnetic field strength detects textural differences between these groups. To the best of our knowledge, this is the first study that compared texture features extracted from 1.5 T and 3 T images for the hippocampus. However, for comparison, we included larger scale changes as well, such as volumetric features derived from hippocampus and amygdala, plus, cortical thickness which also represents a well-known AD biomarker [9,25–27]. In this study, it is hypothesized that through texture features, stronger magnetic fields could provide better differentiation between the aforementioned groups.

2. Materials and methods

2.1. The alzheimer’s disease neuroimaging initiative

For the preparation of this article data were obtained from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (<http://adni.loni.usc.edu/>). The ADNI was launched in 2003 as a public-private partnership, led by principal investigator Michael W. Weiner, MD. The primary goal of ADNI was to test whether serial MRI, positron emission tomography (PET), other biological markers and clinical and neuropsychological assessment can be combined to measure the progression of MCI and early AD.

2.2. Subjects

Baseline scans of a total of 49 subjects were included in the study (14 NC, 14 MCI, 11 MCIC and 10 CE subjects) who underwent both 1.5 T and 3 T MR imaging. Inclusion criteria for NC were: MMSE scores between 24 and 30; CDR of zero; absence of depression, MCI and dementia. Inclusion criteria for MCI were: MMSE scores between 24 and 30; CDR of 0.5; objective memory loss, measured by education adjusted scores on Wechsler Memory Scale Logical Memory II [28], absence of significant levels of impairment in other cognitive domains; absence of dementia. Inclusion criteria for AD were: MMSE scores between 20 and 26; CDR of 0.5 or 1.0; NINCDS/ADRDA criteria for probable AD [5], [29]. Detailed description of inclusion/exclusion criteria can be found in the ADNI protocol (adni.loni.usc.edu/methods/documents/). Subject baseline demographics are summarized in Table 2.

2.3. MRI data

All the subjects had a standardized protocol on both 1.5 T and 3 T MRI units from 3 MR imaging vendors (GE Healthcare, Milwaukee, Wisconsin; Philips Healthcare, Best, the Netherlands; or Siemens, Erlangen, Germany) with a standardized protocol developed to evaluate 3D T1-weighted sequences for morphometric analyses. T1-weighted

Table 2
Demographics data

Variables at Baseline	NC (n = 14)	MCI (n = 14)	MCIC (11)	AD (n = 10)	p value
Sex (M/F)	4/10	10/4	8/3	3/7	.030
Age (mean ± SD)	74.9 (5.2)	71.8 (8.1)	74.4 (6.6)	75.0 (7.5)	.588
MMSE Score (mean ± SD)	29 (1.1)	27 (1.4)	26 (1.4)	23 (2.2)	.000

Abbreviations: NC: normal controls; MCI: mild cognitive impairment; MCIC: MCI converters; AD: Alzheimer’s disease; MMSE: mini mental state examination; SD: standard deviation.

volumetric 3D sagittal magnetization prepared rapid gradient-echo (MPRAGE) baseline scans collected for each subject. The 1.5 T and 3 T scanning protocols used a 3D sagittal volumetric sequence. The typical 1.5 T acquisition parameters were TR =2400 ms, minimum full TE, TI = 1000 ms, flip angle = 8°, FOV =24 cm, with a 256 × 256 × 170 acquisition matrix in the x-, y-, and z-dimensions, yielding a voxel size of 1.25 × 1.25 × 1.2 mm³. For 3 T scans, the typical parameters were a TR =2300 ms, minimum full TE, TI =900 ms, flip angle = 8°, FOV =26 cm, with a 256 × 256 × 170 acquisition matrix in the x-, y-, and z-dimensions, yielding a voxel size of 1.0 × 1.0 × 1.2 mm³.

FreeSurfer v6.0 software, Martinos Center for Biomedical Imaging, Harvard-MIT, Boston USA [30] was used for the segmentation and volumetric representations of the subcortical brain regions were used in this study (the hippocampus and the amygdala) and the surface-based estimation of cortical thickness through the calculation of the shortest distance between gray and white matter. Default parameters were used and bilateral ROIs were joined. FreeSurfer is based on Surface-based Analysis (SBA) and derives morphometric measures from geometric models of the cortical surface. It uses a probabilistic atlas derived from a manually labeled training set of expert measurements and automatically performs subcortical and cortical segmentation of the brain. The FreeSurfer pipeline, conforms the MRI scans to an isotropic voxel size of 1 mm³, and their intensity was normalized using the automated N3 algorithm [31], followed by skull stripping and neck removal. Details of these have been previously discussed in detail [30], [32].

Hippocampal texture features were calculated using KNIME Analytics platform [33]. The following Haralick texture features [34] were computed: Angular Second Moment (ASM), Contrast, Correlation, Variance, Sum Average, Sum Variance and Entropy. Their average was calculated in four directions (0°, 45°, 90°, 135°) with the distance between adjacent pixels set to 1.

2.4. Statistical analysis

Baseline score differences for cognitive tests, volume, thickness and texture were examined between the 4 groups through one-way ANOVA and statistical significance was $p < .05$. One-way ANOVA with post hoc Bonferroni correction was also used to examine the between-group differences. Then a paired-samples *t*-test was used for normally distributed data for a direct comparison between 1.5 T versus 3 T texture, volume and thickness measures. In the cases where the assumption of normality as assessed by Shapiro-Wilk's test was not met, a Wilcoxon signed-rank test was used. Furthermore, through a logistic regression model receiving operating characteristic (ROC) curves, we determined the performance of both systems and their ability to distinguish NC from

MCI subjects.

Statistical analysis was performed with IBM SPSS Statistics Version 24 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.)

3. Results

3.1. Baseline demographics for baseline measures

Baseline demographics including gender, age and MMSE scores are tabulated in Table 2. As expected, the NC subjects had the highest MMSE score compared to the other groups. Furthermore, there were significant differences for sex and MMSE score variables but not for age.

3.2. Summary statistics for texture, volume and thickness features

In Table 3, features extracted from 1.5 T showed no statistical significant differences among the groups, except for hippocampal entropy ($p = 0.035$), and hippocampal and amygdala volumes, ($p = 0.004$ and $p = .006$ respectively). On the other hand, features extracted from 3 T images, revealed statistical significant differences among all groups for all texture features including hippocampal and amygdala volumes. Cortical thickness was also statistically significant between the groups for both 1.5T and 3T, $p = .031$ and $p = .015$ respectively.

3.3. Between-group comparisons

A one-way ANOVA with post hoc Bonferroni correction was conducted on baseline scans to determine if there were significant texture characteristics differences between the four groups. Subjects were classified into four groups NC vs AD, NC vs MCI and MCI vs AD. Texture features were extracted from the hippocampus and data were normally distributed, as assessed by Shapiro-Wilk's test ($p > .05$) and statistical significance was defined as $p < .05$. There were no outliers in the data, as assessed by boxplot inspection, and all data are presented as mean ± standard deviation (SD).

As seen in Table 4, 1.5 T hippocampal texture features, showed significant difference for entropy only in the MCI vs AD group. Furthermore, hippocampal and amygdala volume showed significant differences between NC vs AD group.

On the other hand, 3 T hippocampal texture features, revealed significant differences in more cases. Specifically, for NC vs AD group, all texture features (except correlation) showed significant differences. Furthermore, significant differences were also seen for NC vs MCI and MCI vs AD. Similarly to 1.5 T, volumetric measures of hippocampus and

Table 3
Texture, volumetric and thickness features for the NC, MCI, MCIc and AD groups for 1.5 T and 3 T MRI systems

Features	Mean (SD)									
	NC		MCI		MCIc		AD		p value	
	1.5 T	3 T	1.5 T	3 T	1.5 T	3 T	1.5 T	3 T	1.5 T	3 T
Hippocampal Texture features										
ASM	.102 (.035)	.070 (.021)	.105 (.043)	.095 (.037)	.105 (.023)	.102 (.024)	.121 (.032)	.112 (.033)	.616	.009
Contrast	166 (20.0)	150 (14.9)	169 (15.0)	173 (9.9)	179 (19.8)	180 (14.0)	180 (19.5)	177 (17.8)	.209	.000
Correlation	.54 (.07)	.46 (.09)	.52 (.083)	.47 (.10)	.54 (.043)	.54 (.03)	.53 (.055)	.54 (.022)	.805	.024
Variance	190 (33.3)	154 (21.6)	184 (25.5)	172 (30.5)	204 (10.3)	189 (22.8)	201 (9.0)	205 (9.1)	.181	.000
Sum Average	41 (4.2)	43 (3.1)	39 (5.3)	41 (5.3)	39 (2.5)	38 (2.3)	38 (4.3)	37 (4.2)	.487	.010
Sum Variance	593 (123)	463 (84)	567 (100)	517 (120)	619 (64)	584 (73)	622 (32)	638 (29)	.466	.000
Entropy	3.7 (.21)	3.9 (.16)	3.7 (.08)	3.7 (.18)	3.7 (.14)	3.7 (.24)	3.5 (.17)	3.6 (.14)	.035	.009
Volumetric Features (mm ³)										
Hippocampus	3685 (380)	3709 (365)	3388 (598)	3299 (557)	3041 (344)	3217 (684)	3038 (463)	3148 (421)	.004	.040
Amygdala	1461 (163)	1625 (189)	1298 (243)	1364 (288)	1292 (235)	1392 (304)	1113 (146)	1227 (341)	.006	.009
Thickness (mm)										
Cortex	2.32 (.056)	2.34 (.030)	2.31 (.068)	2.34 (.073)	2.24 (.12)	2.28 (.076)	2.24 (.07)	2.29 (.064)	.031	.015

Abbreviations: SD: standard deviation; NC: normal controls; MCI: mild cognitive impairment; MCIc: MCI converter; AD: Alzheimer's disease; MMSE: mini mental state examination; ASM: Angular second moment.

Table 4
Hippocampal texture, volume and thickness differences at 1.5 T and 3 T MRI systems

	Mean Difference (SE)							
	NC vs AD		NC vs MCI		MCI vs MCIC		MCI vs AD	
	1.5 T	3 T	1.5 T	3 T	1.5 T	3 T	1.5 T	3 T
Texture features								
ASM	-.018 (.01)	-.0420 (.01)*	-.002 (.01)	-.023 (.01)	.000 (.01)	-.008 (.01)	.016 (.01)	-.018 (.01)
Contrast	-13.40 (7.7)	-26.84 (5.9)*	-2.93 (7.0)	-22.73 (5.5)*	-9.07 (7.5)	-6.71 (5.9)	-10.45 (7.7)	-4.10 (5.8)
Correlation	-.007 (.02)	-.076 (.03)	-.020 (.02)	-.003 (.03)	-.024 (.02)	-.069 (.03)	-.013 (.03)	-.073 (.03)
Variance	-11.3 (10.7)	-50.9 (10.4)*	-5.7 (9.1)	-17.6 (8.9)	-19.8 (10.0)	-17.5 (9.5)	-17.1 (10.7)	-33.3 (10.4)*
Sum Average	-2.78 (1.7)	-5.18 (1.6)*	-1.16 (1.6)	-1.80 (1.5)	-3.52 (1.7)	-2.68 (1.6)	-1.61 (1.8)	-3.38 (1.66)
Sum Variance	-28.9 (41.6)	-174.5 (39.5)*	-25.9 (35.4)	-54.3 (33.7)	-51.6 (37.8)	-66.9 (36.0)	-54.9 (41.6)	-120.1 (39.5)*
Entropy	-.135 (.06)	-.274 (.01)*	-.080 (.06)	-.192 (.07)	-.080 (.07)	-.026 (.07)	-.21 (.07)*	-.082 (.080)
Volumetric Features (mm ³)								
Hippocampus	-646 (193)*	-561 (214)*	-296 (176)	-410 (195)	-347 (200)	-81 (208)	-350 (193)	-150 (214)
Amygdala	-347 (92)*	-398 (115)*	-162 (79)	-261 (105)	-6.0 (83)	-28 (112)	-184 (91)	-136 (115)
Thickness measures (mm)								
Cortex	-.082 (.03)	-.052 (.02)	-.007 (.032)	-.003 (.024)	-0.70 (.034)	.069 (.025)*	-.070 (.034)	-.056 (.026)

Abbreviations: SE: Standard error; ASM: Angular Second Moment; NC: Normal controls; MCI: Mild cognitive impairment; MCIC: MCI converter; AD: Alzheimer's disease.

amygdala showed significant differences between NC vs AD group only, whereas, cortical thickness between MCI vs MCIC subjects for the 3 T.

3.4. Between systems comparison (1.5 T, 3 T)

A paired-samples *t*-test was used to determine whether there was a statistically significant mean difference between the two magnetic fields for both hippocampal texture, volumes and thickness. Data inspection, revealed no extreme outliers, thus, all data were kept in the analysis.

Hippocampal ASM, contrast and sum average, hippocampal and amygdala volume and cortical thickness met the assumption of normality, as assessed by Shapiro-Wilk's test ($p > .05$), therefore, the paired-samples *t*-test was used. Statistically significant differences between the two systems were seen for hippocampal ASM, amygdala volume and cortical thickness (Table 5). Within diagnostic groups, significant texture differences from paired-samples *t*-test ($p < .05$) were seen in the NC group for hippocampal ASM ($t = 3.440, p = .004$), contrast ($t = 2.284, p = .041$) and amygdala volume ($t = 3.873, p = .002$). There were no significant differences within the MCI or AD groups.

Four of the hippocampal texture features (corelation, variance, sum

Table 5
Hippocampal Paired-Sample *t*-test for normally distributed texture, volume and thickness features between 1.5 T and 3 T MRI systems

1.5 T - 3 T	Paired Differences				
	Mean (SD)	95 % CI	t	df	Sig.
Texture features					
ASM	.015 (.029)	.007 - .024	3.730	47	.001
Contrast	3.98 (20.75)	-2.17 - 10.15	1.303	45	.199
Sum Average	.93 (4.14)	-2.13 - .270	1.559	47	.126
Volume measures (mm ³)					
Hippocampus	10.8 (188)	-44.4 - 66.1	.396	46	.695
Amygdala	112.5 (171)	61.5 - 163.5	4.47	46	.000
Thickness Measures (mm)					
Cortex	.031 (.076)	.009 - .053	2.862	47	.006

Abbreviations: SD: Standard deviation; CI: Confidence Interval; ASM: Angular Second Moment.

variance and entropy) violated the assumption of normality, as assessed by Shapiro-Wilk's test ($p < .05$), therefore, the Wilcoxon signed-rank test was used. As seen in Table 6, there were statistically significant median difference for all four texture features. Within diagnostic groups, statistically significant differences ($p < .05$) were seen for NC group in all four-texture features: corelation ($z = 2.354, p = 0.019$), variance ($z = 2.542, p = 0.011$), sum variance ($z = 2.542, p = 0.011$) and entropy ($z = 2.551, p = 0.011$). In the MCI group only correlation showed statistically significant difference ($z = 2.040, p = 0.041$), whereas in the AD group, there was statistically significant difference for variance ($z = 2.366, p = .018$) and sum variance ($z = 2.028, p = 0.043$).

3.5. Classification modelling

Furthermore, we compared the classification power between the two systems for NC and MCI subjects. We chose this comparison, as MCI subjects do not fulfil the criteria for dementia, as their cognitive function is comparable to NC subjects and we wanted to explore if through 3 T images their differentiation would be more pronounced. Specifically, we calculated a binary logistic regression model for each individual texture, volume and cortical thickness variable and by using ROC curves, we determined their AUC (Table 7). The combination model included raw MRI biomarker scores as well as age and gender as covariates.

Overall, features extracted from both 1.5 T and 3 T systems were statistically significant for the classification of this group. However, in all cases higher AUC values were seen from features extracted from 3 T

Table 6
Hippocampal Wilcoxon signed-rank test for not-normally distributed texture features between 1.5 T and 3 T MRI systems

Features	Medians (Inter Quartile range - IQR)		z	p value
	1.5 T MRI	3 T MRI		
Texture features				
Corelation	.550 (.090)	.526 (.103)	2.98	.003
Variance	201 (23.4)	185 (57.3)	2.27	.023
Sum Variance	622 (113.6)	574 (.207.5)	2.15	.031
Entropy	3.70 (.273)	3.66 (.304)	2.45	.014

Table 7

Classification of NC from MCI subjects through textural, volumetric and thickness features extracted from 1.5 T and 3 T MRI systems

Texture Features	1.5 T		3 T		<i>p</i> value	
	AUC	95 % CI	AUC	95 % CI	1.5 T	3 T
Texture features						
ASM	0.806	0.629 - 0.983	0.837	0.691 - 0.982	0.006	0.002
Contrast	0.816	0.652 - 0.981	0.941	0.848 - 1.000	0.004	0.000
Correlation	0.806	0.631 - 0.981	0.816	0.645 - 0.987	0.006	0.004
Variance	0.811	0.638 - 0.985	0.827	0.671 - 0.982	0.005	0.003
Sum Average	0.796	0.621 - 0.970	0.827	0.668 - 0.985	0.008	0.003
Sum Variance	0.816	0.645 - 0.987	0.827	0.673 - 0.980	0.004	0.003
Entropy	0.839	0.683 - 0.996	0.824	0.663 - 0.985	0.004	0.003
Volume measures (mm ³)						
Hippocampus	0.867	0.721 - 1.0	0.893	0.764 - 1.0	0.001	0.000
Amygdala	0.907	0.778 - 1.0	0.918	0.813 - 1.0	0.000	0.000
Thickness measures (mm ²)						
Cortex	0.824	0.658 - 0.990	0.802	0.622 - 0.982	0.004	0.008

Abbreviations: AUC: area under curve; CI: confidence interval; ASM: Angular Second Moment, ICV: Intracranial Volume.

and ranged between 0.816–0.941 compared to 1.5 T ranges (0.796–0.907).

4. Discussion

The main objective of this study was to evaluate whether a higher magnetic field, such as from a 3 T MRI, could capture more significant differences on MCI and AD subjects from a 1.5 T MRI. Specifically, smaller scale changes derived from hippocampal texture, and larger scale changes derived from hippocampal and amygdala volume and cortical thickness were extracted from both 1.5 T and 3 T systems and their values between NC, MCI and AD subjects were compared.

As seen in Table 4, texture features extracted from 3 T, revealed statistically significant differences among the groups in more cases compared to 1.5 T which showed statistically significant difference only for entropy in MCI vs AD group. Similar findings were also reported in the study by Macdonald et al., [21] where it was also documented that the 3 T system was able to detect more changes that were not apparent at the 1.5 T system. This finding can be attributed to the fact that due to the higher SNR of the 3 T images, degenerative changes are more easily detectable [19]. Furthermore, both systems had the same results regarding volumetric measures, revealing statistically significant results for NC vs AD group only, for both hippocampus and amygdala. It seems that both hippocampal and amygdala atrophy magnitude is comparable and this was also seen in another study [9]. In general, it seems that both magnetic strengths do not significantly differ in their power to detect atrophy changes and this finding is consistent with the study by Ho et al., 2010 [35].

The finding of capturing more statistically significant changes with texture compared to volume, suggests that texture changes occur earlier than atrophy and they can be captured from structural MRI. This finding is also supported by a recent study by Lee et al., [23] and Sørensen et al., [24], where it was found that MRI hippocampal texture features predicted progression to AD earlier than hippocampal volume. Probably, this explains the fact that no volumetric changes were seen for the groups where MCI subjects were included as their neurodegeneration is not as advanced as in AD subjects; however, their neurodegenerative changes were captured by texture features.

In the between systems comparison, the paired-samples *t*-test and

Wilcoxon signed-rank test (Table 5 and Table 6) revealed statistically significant differences between 1.5 T and 3 T, in five of the seven texture features, whereas hippocampal volume did not. No hippocampal volume differences between 1.5 T and 3 T were also reported by Macdonald et al., [21], for both automated and manual hippocampal segmentations. Similar hippocampal atrophy patterns between the 1.5 T and 3 T MRI systems were also reported by Chow et al., [19]. Amygdala volume and cortical thickness also revealed statistically significant differences between the two magnetic strengths.

Higher AUC values were seen from the features extracted from the 3 T system in the classification of NC from MCI subjects. We investigated specifically this group, as is of great importance to detect accurately MCI subjects instead of AD subjects, in order to provide them with the appropriate cure before converting to AD. Similar to other studies [19], [21], the discriminative ability was similar between the two systems, although, AUCs in 3 T were also higher.

In this study, Haralick features generated from the Gray Level Co-occurrence Matrix (GLCM) to determine the group differences were computed. Haralick texture features were also used in both Positron Emission Tomography (PET) [36] and structural MRI [14], [15] [37], studies. One of the first studies that used Haralick features was the study by Freeborough and Fox, 1998 [15] where it was found that MRI texture features could aid in the diagnosis and tracking of the Alzheimers disease. Haralick features were also used in the recent study by Luk., et al., (2018) [14] MRI were texture features were extracted from the whole brain and their AUCs ranged between 0.722 – 0.866 in the discrimination between NC and AD subjects. Furthermore, the study by Gao et al., 2018 [37] showed that the addition of texture features effectively improved the classification of AD and the prediction of MCI conversion to AD. However, texture is not a frequently used method compared to others such as volumetry, perhaps, due to its difficulty in understanding its concept and terms.

One major limitation of this study is the small sample size. Furthermore, we had access only to 1.5 T and 3 T data. Nowadays, MRI systems with higher magnetic fields are also available such as 7 T and perhaps they could reveal more statistically significant differences between texture characteristics and superior possibilities for detecting between-group differences. However, higher magnetic fields are more susceptible to chemical shift artifacts, and this could be also an area of research on how this artifact affect quantitative imaging compared to 1.5 T. Perhaps, another limitation could be the fact that the ADNI 3 T protocol was designed in such way in order the tissue contrast would match the 1.5 T scans [38]. This could affect the comparison between the two systems or even the effectiveness of the 3 T system. Future studies could include longitudinal analysis between the two systems and evaluate if 3 T systems could capture more changes with time.

5. Conclusions

In this study structural MRI features were extracted from both 1.5 T and 3 T images of NC, MCI and AD subjects. In general, the texture features extracted from 3 T revealed statistically significant differences for more features compared to 1.5 T, whereas for the larger scale changes such as volume and cortical thickness the two systems appear to have similar results. These findings, suggest that 3 T images, seem to enhance brain neurodegeneration as captured by texture analysis, perhaps due to higher CNR and SNR provided by stronger magnetic fields. The added value in the literature from this study is the fact that through texture features extracted from a 3 T MRI, it is possible to detect even more changes in texture features compared to texture features extracted from a 1.5 T, which could lead to an even earlier diagnosis.

*The mean difference is significant at the 0.05 level

CRedit authorship contribution statement

Stephanos Leandrou: Conceptualization, Investigation,

Methodology. **Stephanie Constanti:** Data curation. **Constantinos S. Pattichis:** Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- [1] H. Braak, E. Braak, Frequency of stages of Alzheimer-related lesions in different age categories, *Neurobiol. Aging* 18 (no. 4) (1997) 351–357.
- [2] M.F. Folstein, S.E. Folstein, P.R. McHugh, Mini-mental state. A practical method for grading the cognitive state of patients for the clinician, *J Psychiatr Res* 12 (no. 3) (1975) 189–198.
- [3] J.C. Morris, The Clinical Dementia Rating (CDR): current version and scoring rules, *Neurology* 43 (no. 11) (1993) 2412–2414.
- [4] H. Braak, E. Braak, Neuropathological staging of Alzheimer-related changes, *Acta Neuropathol.* 82 (no. 4) (1991) 239–259.
- [5] B. Dubois, et al., Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria, *Lancet Neurol.* 6 (no. 8) (2007) 734–746, [https://doi.org/10.1016/S1474-4422\(07\)70178-3](https://doi.org/10.1016/S1474-4422(07)70178-3).
- [6] L. Ferrarini, G.B. Frisoni, M. Pievani, J.H.C. Reiber, R. Ganzola, J. Milles, Morphological hippocampal markers for automated detection of Alzheimer's disease and mild cognitive impairment converters in magnetic resonance images, *J. Alzheimers Dis.* 17 (no. 3) (2009) 643–659, <https://doi.org/10.3233/JAD-2009-1082.0>.
- [7] C.R. Jack, Alzheimer disease: new concepts on its neurobiology and the clinical role imaging will play, *Radiology* 263 (no. 2) (2012) 344–361, <https://doi.org/10.1148/radiol.12110433>.
- [8] C.R. Jack, et al., Magnetic resonance imaging in alzheimer's disease neuroimaging initiative 2, *Alzheimers Dement.* 11 (no. 7) (2015) 740–756, <https://doi.org/10.1016/j.jalz.2015.05.002>.
- [9] S.P. Poulin, R. Dautoff, J.C. Morris, L.F. Barrett, B.C. Dickerson, Amygdala atrophy is prominent in early Alzheimer's disease and relates to symptom severity, *Psychiatry Res.* 194 (no. 1) (2011) 7–13, <https://doi.org/10.1016/j.psychres.2011.06.014>.
- [10] G.A. Marshall, et al., Regional cortical thinning and cerebrospinal biomarkers predict worsening daily functioning across the Alzheimer's disease spectrum, *J. Alzheimers Dis.* 41 (no. 3) (2014) 719–728, <https://doi.org/10.3233/JAD-132768>.
- [11] S. Leandrou, S. Petroudi, P.A. Kyriacou, C.C. Reyes-Aldasoro, C.S. Pattichis, Quantitative MRI brain studies in mild cognitive impairment and alzheimer's

- [12] M.A. Bernstein, J. Huston, H.A. Ward, Imaging artifacts at 3.0T, *J. Magn. Reson. Imaging* 24 (no. 4) (2006) 735–746, <https://doi.org/10.1002/jmri.20698>.
- [13] J.F. Schenck, The role of magnetic susceptibility in magnetic resonance imaging: MRI magnetic compatibility of the first and second kinds, *Med. Phys.* 23 (no. 6) (1996) 815–850, <https://doi.org/10.1118/1.597854>.
- [14] C.C. Luk, et al., Alzheimer's disease: 3-Dimensional MRI texture for prediction of conversion from mild cognitive impairment, *Alzheimers Dement. Amst. (Amst)* 10 (2018) 755–763, <https://doi.org/10.1016/j.dadm.2018.09.002>.
- [15] P.A. Freeborough, N.C. Fox, MR image texture analysis applied to the diagnosis and tracking of Alzheimer's disease, *IEEE Trans. Med. Imaging* 17 (no. 3) (1998) 475–479, <https://doi.org/10.1109/42.712137>.
- [16] S.G. Costafreda, et al., Automated hippocampal shape analysis predicts the onset of dementia in mild cognitive impairment, *NeuroImage* 56 (no. 1) (2011) 212–219, <https://doi.org/10.1016/j.neuroimage.2011.01.050>.
- [17] R. Cuingnet, et al., Automatic classification of patients with Alzheimer's disease from structural MRI: a comparison of ten methods using the ADNI database, *NeuroImage* 56 (no. 2) (2011) 766–781, <https://doi.org/10.1016/j.neuroimage.2010.06.013>.
- [18] R.S. Briellmann, A. Syngienotis, G.D. Jackson, Comparison of hippocampal volumetry at 1.5 tesla and at 3 tesla, *Epilepsia* 42 (no. 8) (2001) 1021–1024, <https://doi.org/10.1046/j.1528-1157.2001.0420081021.x>.
- [19] N. Chow, et al., Comparing 3T and 1.5T MRI for mapping hippocampal atrophy in the alzheimer's disease neuroimaging initiative, *AJNR Am. J. Neuroradiol.* 36 (no. 4) (2015) 653–660, <https://doi.org/10.3174/ajnr.A4228>.
- [20] A.J. Ho, et al., Comparing 3 T and 1.5 T MRI for tracking Alzheimer's disease progression with tensor-based morphometry, *Hum. Brain Mapp.* 31 (no. 4) (2010) 499–514, <https://doi.org/10.1002/hbm.20882>.
- [21] K.E. Macdonald, et al., Automated template-based hippocampal segmentations from MRI: the effects of 1.5T or 3T field strength on accuracy, *Neuroinform* 12 (no. 3) (2014) 405–412, <https://doi.org/10.1007/s12021-013-9217-y>.
- [22] J. Lötjönen, et al., Fast and robust extraction of hippocampus from MR images for diagnostics of Alzheimer's disease, *NeuroImage* 56 (no. 1) (2011) 185–196, <https://doi.org/10.1016/j.neuroimage.2011.01.062>.
- [23] S. Lee, H. Lee, K.W. Kim, Alzheimer's Disease Neuroimaging Initiative, Magnetic resonance imaging texture predicts progression to dementia due to Alzheimer disease earlier than hippocampal volume, *J. Psychiatry Neurosci.* 45 (no. 1) (2020) 7–14, <https://doi.org/10.1503/jpn.180171>.
- [24] L. Sørensen, et al., Early detection of Alzheimer's disease using MRI hippocampal texture, *Hum. Brain Mapp.* (2015), <https://doi.org/10.1002/hbm.23091>.
- [25] E. Busovaca, et al., Is the Alzheimer's disease cortical thickness signature a biological marker for memory? *Brain Imaging Behav.* 10 (no. 2) (2016) 517–523, <https://doi.org/10.1007/s11682-015-9413-5>.
- [26] B.C. Dickerson, et al., Alzheimer-signature MRI biomarker predicts AD dementia in cognitively normal adults, *Neurology* 76 (no. 16) (2011) 1395–1402, <https://doi.org/10.1212/WNL.0b013e3182166e96>.
- [27] O. Querbes, et al., Early diagnosis of Alzheimer's disease using cortical thickness: impact of cognitive reserve, *Brain* 132 (no. 8) (2009) 2036–2047, <https://doi.org/10.1093/brain/awp105>.
- [28] R.W. Elwood, The wechsler memory scale—revised: psychometric characteristics and clinical application, *Neuropsychol. Rev.* 2 (no. 2) (1991) 179–201, <https://doi.org/10.1007/BF01109053>.
- [29] G. McKhann, D. Drachman, M. Folstein, R. Katzman, D. Price, E.M. Stadlan, Clinical diagnosis of alzheimer's disease report of the NINCDS-ADRDA work group* under the auspices of department of health and human services task force on alzheimer's disease, *Neurology* 34 (no. 7) (1984) 939, <https://doi.org/10.1212/WNL.34.7.939>.
- [30] B. Fischl, et al., Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain, *Neuron* 33 (no. 3) (2002) 341–355.
- [31] J.G. Sled, A.P. Zijdenbos, A.C. Evans, A nonparametric method for automatic correction of intensity nonuniformity in MRI data, *IEEE Trans. Med. Imaging* 17 (no. 1) (1998) 87–97, <https://doi.org/10.1109/42.668698>.
- [32] B. Fischl, et al., Automatically Parcellating the Human Cerebral Cortex, *Cereb. Cortex* 14 (no. 1) (2004) 11–22, <https://doi.org/10.1093/cercor/bhg087>.
- [33] M.R. Berthold, et al., KNIME: the konstantz information miner, in *data analysis, Mach. Learn. Appl.* (2008) 319–326.
- [34] R.M. Haralick, K. Shanmugam, I. Dinstein, Textural features for image classification, *IEEE Trans. Syst. Man Cybernetics SMC-3* (6) (1973) 610–621, <https://doi.org/10.1109/TSMC.1973.4309314>.
- [35] A.J. Ho, et al., Comparing 3 t and 1.5 t MRI for tracking alzheimer's disease progression with tensor-based morphometry, *Hum. Brain Mapp.* 31 (no. 4) (2010) 499–514, <https://doi.org/10.1002/hbm.20882>.
- [36] D.L. Campbell, H. Kang, S. Shokouhi, Application of Haralick texture features in brain [18F]-florbetapir positron emission tomography without reference region normalization, *Clin. Interv. Aging* 12 (2017) 2077–2086, <https://doi.org/10.2147/ CIA.S143307>.
- [37] N. Gao, et al., Contourlet-based hippocampal magnetic resonance imaging texture features for multivariate classification and prediction of Alzheimer's disease, *Metab. Brain Dis.* 33 (no. 6) (2018) 1899–1909, <https://doi.org/10.1007/s11011-018-0296-1>.
- [38] A.J. Ho, et al., Comparing 3 t and 1.5 t MRI for tracking alzheimer's disease progression with tensor-based morphometry, *Hum. Brain Mapp.* 31 (no. 4) (2010) 499–514, <https://doi.org/10.1002/hbm.20882>.