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Imaging breakthroughs in dementia: Pioneering 3D T1-weighted MPRAGE vs. routine spin echo with a focus on Alzheimer's disease

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ABSTRACT

Background. Dementia, a spectrum of neurocognitive disorders, leads to progressive cognitive and functional decline, primarily affecting memory and executive functions. Among the most common causes is Alzheimer's disease (AD), which accounts for 60-80% of dementia cases. Neuroimaging, particularly Magnetic Resonance Imaging (MRI), plays a critical role in diagnosing dementia, helping differentiate between various subtypes such as Alzheimer's disease, vascular dementia (VaD), frontotemporal dementia (FTD), and Lewy body dementia (LBD). This study explores the utility of 3D T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) and conventional spin echo sequences in distinguishing dementia subtypes, with a focus on Alzheimer's disease.

Methods. This cross-sectional study included 40 elderly subjects diagnosed with cognitive impairment or dementia. Participants were assessed using 3D T1 MPRAGE sequences to calculate Medial Temporal Lobe Atrophy (MTA) indices and Entorhinal Cortex and Related Areas (ERICA) scores, alongside conventional spin echo sequences. MRI served as the primary imaging modality to differentiate between Alzheimer's disease, vascular dementia, and other dementia subtypes. Statistical analyses included descriptive statistics, inferential tests, and Receiver Operating Characteristic (ROC) curves to evaluate diagnostic accuracy.

Results. The average MTA score for Alzheimer's disease was 3.33, significantly higher than that for vascular dementia (2.73), frontotemporal dementia (2.33), and Lewy body dementia (0.6). The mean ERICA score for Alzheimer's disease was 3.0, higher than FTD (0.83), VaD (0.55), and LBD (0.0). Lewy body dementia exhibited significantly larger hippocampal volumes than other dementia subtypes. The ROC curve for MTA in predicting Alzheimer's disease yielded an area under the curve (AUC) of 0.833, with a sensitivity of 98.7% and an overall diagnostic accuracy of 80%. The ERICA score achieved an AUC of 1.0, demonstrating perfect diagnostic accuracy for Alzheimer's disease.

Conclusion. The study underscores the superior diagnostic accuracy of 3D T1 MPRAGE in calculating MTA and ERICA scores, enhancing early detection and differentiation of Alzheimer's disease from other dementia subtypes. The integration of these advanced imaging techniques provides a powerful diagnostic tool, ensuring more reliable and early diagnosis in clinical practice. This research highlights the potential of 3D T1 MPRAGE in revolutionizing dementia diagnostics, paving the way for improved patient outcomes.

Keywords: Parkinson's disease, Alzheimer's disease, ERICA score, MTA score, 3D T1 MPRAGE, Lewy body dementia, vascular dementia, frontotemporal dementia

INTRODUCTION

Dementia refers to a diverse spectrum of neurocognitive disorders characterized by a progressive decline in cognitive and functional capacities, often arising from various underlying etiologies, including Alzheimer's disease. Rather than constituting a single clinical entity, dementia encompasses a broad range of neurodegenerative processes that induce pathological changes in the brain. These changes

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lead to significant impairments in higher-order cognitive functions, particularly memory, executive function, and problem-solving skills, to the extent that they interfere with daily activities and independent living. Additionally, dementia is frequently associated with behavioral changes, emotional disturbances, and altered social interactions [1,2]. Alzheimer's disease accounts for 60-80% of dementia cases, while mixed dementia is defined by the co-occurrence of neuropathological features from multiple dementia subtypes. Globally, an estimated 55 million individuals are affected by dementia, with over 60% residing in low- and middle-income countries [3]. Neuroimaging plays a crucial role in the diagnostic evaluation of patients with suspected dementia. Techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are indispensable for excluding reversible causes of cognitive decline, including brain tumors, subdural hematomas, and normal pressure hydrocephalus. In recent years, neuroimaging has become increasingly essential in the diagnostic criteria for various neurodegenerative conditions associated with dementia [4,5].

The objective of this study was to evaluate the role of 3D T1 MPRAGE (3D T1-weighted Magnetization Prepared Rapid Gradient Echo) in the calculation of the MTA index, ERICA score, and the application of conventional spin echo sequences for differentiating vascular dementia, Alzheimer's disease, and other dementias, including Parkinson's plus syndrome. The primary aim was to assess the efficacy of 3D T1 MPRAGE in quantifying the MTA (Medial Temporal Lobe Atrophy) index and its diagnostic utility in distinguishing vascular dementia, Alzheimer's disease, and other neurodegenerative dementias, including Parkinson's disease. Secondary objectives included determining the value of 3D T1 MPRAGE in conjunction with the ERICA (Entorhinal Cortex and Related Areas) score for assessing the entorhinal cortex and related areas in the early detection and differentiation of Alzheimer's disease and other dementia syndromes. Additionally, the study aimed to evaluate the diagnostic performance and potential utility of conventional spin echo sequences, including T2-weighted imaging and FLAIR (Fluid-Attenuated Inversion Recovery), in identifying and quantifying vascular pathology, and in differentiating vascular dementia from other dementia subtypes.

MATERIALS & METHODS

Materials

This descriptive cross-sectional study was conducted over an 18-month period at the Department of Radiology, Saveetha Medical College, Chennai. A total of 40 patients diagnosed with dementia or cognitive impairment were enrolled based on specific inclusion criteria. Patients included were elderly individuals of both genders diagnosed with Alzheimer's disease, vascular dementia, or other dementia types, such as Parkinson's Plus Syndrome. Patients with contraindications to MRI, including metallic implants or claustrophobia, were excluded from the study.

Methods

The study aimed to evaluate the role of 3D T1 MPRAGE in calculating MTA and ERICA scores and its utility in differentiating between Alzheimer's disease, vascular dementia, and other types of dementia, including Parkinson's Plus Syndrome. MRI was employed as the primary imaging modality. Conventional spin echo sequences were used alongside 3D T1 MPRAGE for anatomical orientation and volumetric measurements. Data were acquired using a standardized MRI protocol, and images were analyzed for hippocampal atrophy and entorhinal cortical thinning to calculate MTA and ERICA scores. Comparison of T1 weighted imaging and 3 D MPRAGE /T1 TFE sequence is shown in Figure 1.

Statistical analysis

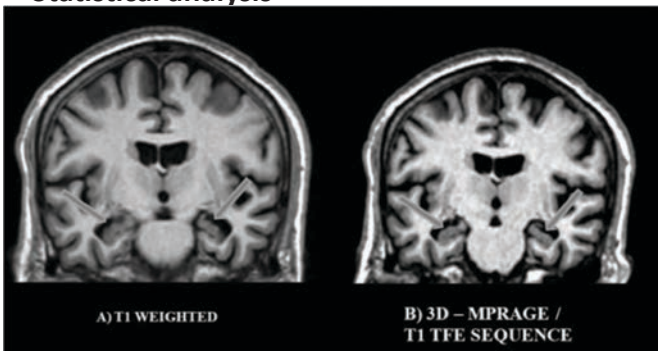

FIGURE 1. T1 weighted AND 3 -MPRAGE/T1 TFE sequence (MPRAGE)The magnetization-prepared rapid gradient echo, (TFE) turbo field echo

Descriptive and inferential statistical analyses were conducted. Mean, standard deviation, median, and mode were used to summarize continuous variables, while categorical data were represented using frequencies and proportions. The diagnostic accuracy of MTA and ERICA scores was evaluated using ROC curves. A significance level of $p < 0.05$ was applied. Data analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Version 24.0, Armonk, NY).

RESULTS

The mean age (years) was 65.68 (± 7.27) ranging from 52 to 79 years. Among the subjects, 20 (50%) were less than or equal to 65 years, and 20 (50%)

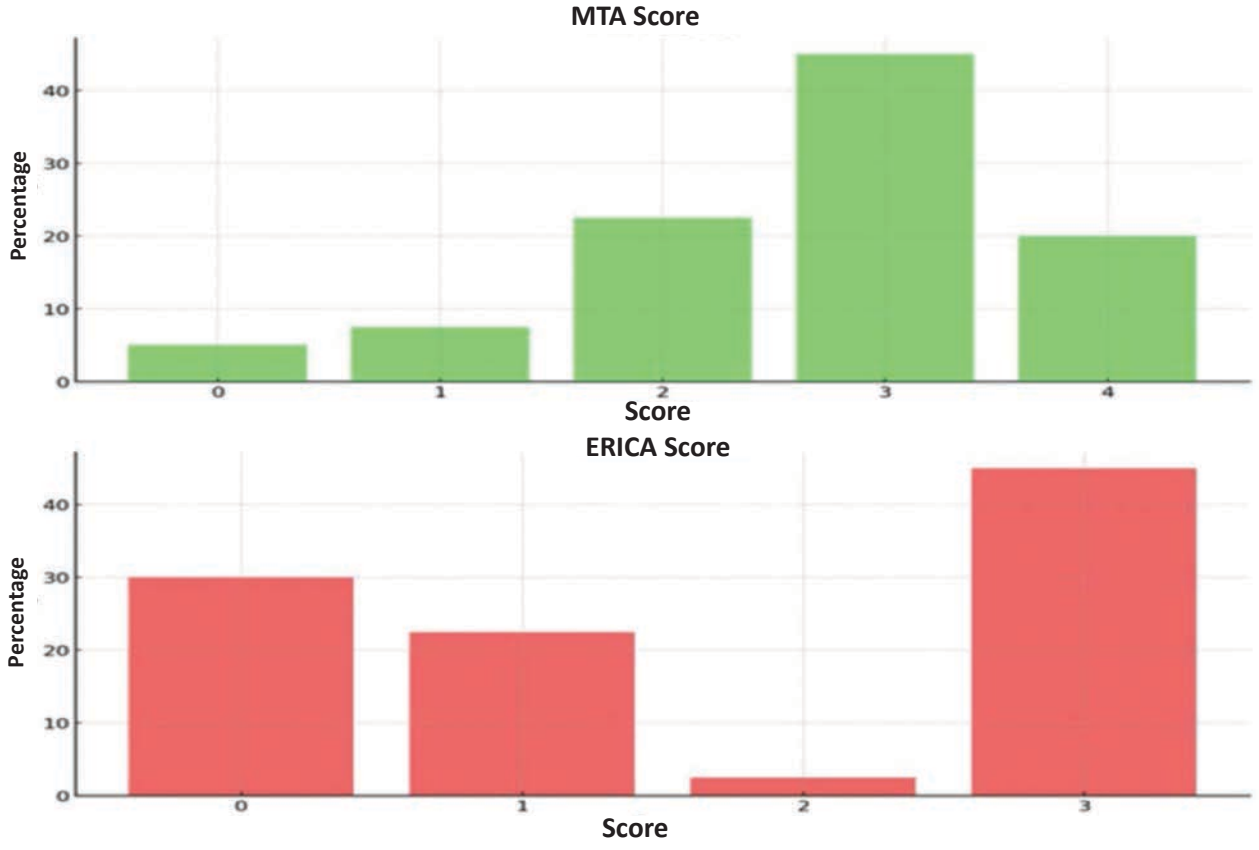

FIGURE 2. Visual comparison of the scoring systems used to assess cognitive impairment and atrophy in dementia patients

were more than 65 years. Among the subjects, 20 (50%) were males and 20 (50%) were females. Among the subjects, 18 (45%) had Alzheimer's dementia, 11 (27.5%) had VaD (Vascular Dementia), 6 (15%) had FTD (Fronto Temporal Lobe Dementia) and 5 (12.5%) had LBD (Lewy Body Dementia). Among the subjects, 8 (20%) had MTA score 4, 18 (45%) had score 3, 9 (22.5%) had score 2, 3 (7.5%) had score 1, and 2 (5%) had score 0. Among the subjects, 18 (45%) had ETA score 3, 1 (2.5%) had score 2, 9 (22.5%) had score 1, and 12 (30%) had score 0. Visual comparison of the scoring systems is represented in Figure 2.

MTA Score: Shows the distribution of Medial Temporal Atrophy (MTA) scores among participants, ranging from 0 to 4, with higher scores indicating greater atrophy. The percentage of participants in each score category (0, 1, 2, 3, 4) is displayed.

ERICA Score: Depicts the distribution of Entorhinal Cortical Atrophy (ERICA) scores among participants, ranging from 0 to 3, with higher scores indicating more severe atrophy. The percentage of participants in each score category (0, 1, 2, 3) is displayed.

The mean MTA score for individuals with Alzheimer's disease was 3.33, significantly higher than the average score for those with vascular dementia (VaD), which was 2.73. Frontotemporal dementia (FTD) had an intermediate score of 2.33, while Lewy body dementia (LBD) presented the lowest average score of 0.6. These differences across diagnostic groups were statistically significant, with a p-value of less than 0.05, as indicated in Table 1.

Similarly, the average ERICA score for Alzheimer's disease was 3.00, exceeding the scores for FTD, VaD, and LBD, which were 0.83, 0.55, and 0.00, respectively. These intergroup differences were statistically significant ($p < 0.05$), as outlined in Table 2.

Hippocampal volume measurements revealed

TABLE 1. MTA score with diagnosis

Diagnosis	MTA Score			ANOVA P-Value
	N	Mean	S.D.	
AD	18	3.33	0.49	0.001
VaD	11	2.73	0.79	
FTD	6	2.33	0.52	
LBD	5	0.60	0.55	
Post Hoc-Test	**N**	**Mean Diff**	**S.D.**	**P-Value**
AD vs. VaD	29	0.61	0.23	0.011
AD vs. FTD	24	1.00	0.28	0.001
AD vs. LBD	23	2.73	0.30	0.001
VaD vs. FTD	16	0.39	0.30	0.200
VaD vs. LBD	16	2.13	0.32	0.001
FTD vs. LBD	11	1.73	0.36	0.001

Medial Temporal lobe Atrophy (MTA), Alzheimer's Disease (AD), Vascular Dementia (VaD), Fronto Temporal Dementia (FTD), Lewy Body Dementia (LBD)

TABLE 2. ERICA score with diagnosis

Diagnosis	ERICA Score			ANOVA P-Value
	N	Mean	S.D.	
AD	18	3.00	0.00	0.001
VaD	11	0.55	0.52	
FTD	6	0.83	0.75	
LBD	5	0.00	0.00	
Post Hoc-Test	**N**	**Mean Diff**	**S.D.**	**P-Value**
AD vs. VaD	29	2.45	0.15	0.001
AD vs. FTD	24	2.17	0.19	0.001
AD vs. LBD	23	3.00	0.20	0.001
VaD vs. FTD	16	0.29	0.20	0.158
VaD vs. LBD	16	0.55	0.21	0.014
FTD vs. LBD	11	1.73	0.36	0.001

Entorhinal Cortical Atrophy (ERICA), Alzheimer's Disease (AD), Vascular Dementia (VaD), Fronto Temporal Dementia (FTD), Lewy Body Dementia (LBD)

TABLE 3. The mean and standard deviation of hippocampal volume in the right, left and the total volume

Diagnosis	RT HP Volume Mean (cmÂ³)	RT HP Volume Std Dev (cmÂ³)	LT HP Volume Mean (cmÂ³)	LT HP Volume Volume Std Dev (cmÂ³)	Total HP Volume Mean (cmÂ³)	Total HP Volume Std Dev (cmÂ³)
AD	1.9	0.14	1.89	0.14	3.84	0.29
VaD	2.28	0.11	2.31	0.12	4.59	0.2
FTD	1.95	0.16	1.85	0.1	3.82	0.24
LBD	2.52	0.08	2.68	0.08	5.18	0.13

Right (RT), Left (LT), Hippocampus (HP), Alzheimer's Disease (AD), Vascular Dementia (VaD), Fronto Temporal Dementia (FTD), Lewy Body Dementia (LBD)

that the mean right hippocampal volume was 2.09 cm³ (±0.26), with a range from 1.6 to 2.6 cm³, while the mean left hippocampal volume was 2.1 cm³ (±0.32), ranging from 1.7 to 2.8 cm³. The mean total hippocampal volume was 4.21 cm³ (±0.55), spanning from 3.4 to 5.3 cm³. Individuals with LBD exhibited the largest right hippocampal volume at 2.52 cm³, surpassing those with VaD (2.28 cm³), FTD (1.95 cm³), and Alzheimer's disease (1.9 cm³). These differences were statistically significant ($p < 0.05$). Similarly, the left hippocampal volume in LBD patients was 2.68 cm³, greater than that in VaD (2.31 cm³), Alzheimer's disease (1.89 cm³), and FTD (1.85 cm³) patients, with statistically significant differences ($p < 0.05$). The total hippocampal volume was also largest in LBD patients at 5.18 cm³, compared to VaD (4.59 cm³), Alzheimer's disease (3.84 cm³), and FTD (3.82 cm³). These differences were statistically significant ($p < 0.05$), as shown in Table 3 and Figure 3.

The area under the curve (AUC) for the MTA score in predicting Alzheimer's dementia was 0.833 (95% CI: 0.705-0.961), with a threshold score of 2.5 providing a sensitivity of 98.7%, a specificity of 63.64%, a positive predictive value of 69.23%, a negative predictive value of 86%, and an overall diagnostic accuracy of 80%. The AUC for the ERICA score was 1.0, denoting perfect predictive ability for Alzheimer's disease, with a threshold of 2.5 yielding a sensitivity of 98%, a specificity of 94%, a positive predictive value of 97.4%, a negative predictive value of 84%, and a diagnostic accuracy of 92%. For predicting VaD, the AUC for total hippocampal volume was 0.809 (95% CI: 0.67-0.948). A cutoff value of

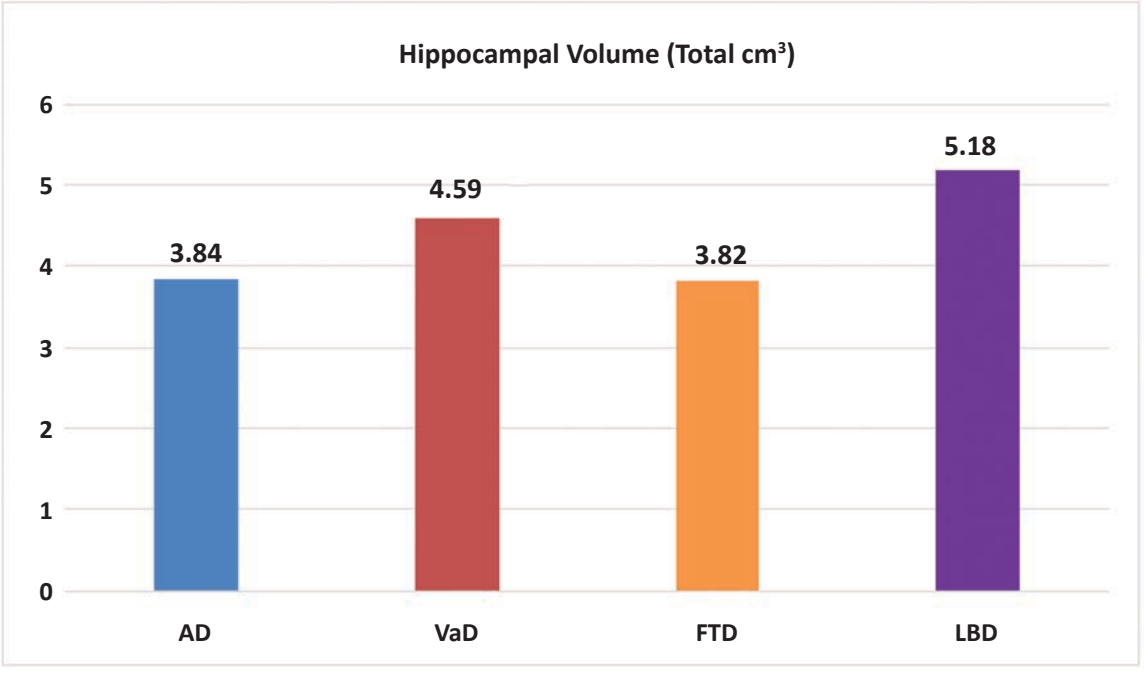

FIGURE 3. Hippocampal volume (total cm³)
Alzheimer's Disease (AD), Vascular Dementia (VaD), Fronto Temporal Dementia (FTD), Lewy Body Dementia (LBD)

4.25 cm³ was associated with a sensitivity of 90.91%, a specificity of 79.31%, a positive predictive value of 62.5%, a negative predictive value of 95.83%, and a diagnostic accuracy of 82.5%, as detailed in Table 4.

TABLE 4. ROC of MTA score, ERICA score, hippocampal volume for predicting Alzheimer's dementia

Test result variable	Area under curve	95% confidence interval	P value
MTA Score	0.833	0.705 - 0.961	0.001
ERICA Score	1.000	1.000 - 1.000	0.001
Hippocampal Volume (Total cm³)	0.809	0.670 - 0.948	0.003

Medial Temporal lobe Atrophy (MTA), EntoRhInal Cortical Atrophy (ERICA)

DISCUSSION

The study aimed to assess the efficacy of 3D T1 MPRAGE sequences in calculating the medial temporal atrophy (MTA) index and the ERICA score, alongside conventional spin-echo sequences, for differentiating Alzheimer's disease from other forms of dementia, including Parkinson's plus syndromes. The mean age of the participants was 65.68 years (±7.27), ranging from 52 to 79 years. Among the cohort, 20 individuals (50%) were aged 65 years or younger, and 20 (50%) were older than 65 years. Gender distribution was equal, with 20 males (50%) and 20 females (50%). Diagnostically, 18 participants (45%) were classified with Alzheimer's dementia, 11 (27.5%) with vascular dementia (VaD), 6 (15%) with frontotemporal dementia (FTD), and 5 (12.5%) with Lewy body dementia (LBD).

A 2015 epidemiological study conducted in China reported a weighted prevalence of dementia in individuals aged 60 and above as 4.22% (95% CI: 2.27-6.17%), with a higher prevalence observed in women and a marked increase with advancing age [6]. Wei et al. [7] investigated the application of new visual rating scale cut-offs for MRI-based assessment of Alzheimer's dementia in a Chinese population. For age groups 50-64, 65-74, and 75-84 years, MTA cut-offs demonstrated sensitivities and specificities of >1.0 (92.3% and 68.4%), ≥1.5 (90.4% and 85.2%), and ≥2.0 (70.8% and 82.3%), respectively. Further, Enkrich et al. [8] revealed that patients diagnosed with Alzheimer's dementia exhibited significantly higher scores on both the MTA scale (mean: 2.13) and the ERICA scale (mean: 2.05) compared to individuals with subjective cognitive decline (SCD). An ERICA score of 2 or above demonstrated superior diagnostic accuracy (91%) over the MTA score (74%), with sensitivity rates of 83% versus 57%, and specificity of 98% versus 92%, in distinguishing Alzheimer's-related dementia from SCD.

Ferreira LK et al. [9] demonstrated that subjects with AD have significantly increased ERICA scores (mean: 1.92) and MTA scores (mean: 1.7) in both hemispheres compared to sub-groups without "dementia". MTA exhibits higher specificity, while ERICA demonstrates stronger sensitivity in the "dementia" for Alzheimer's disease and MCI (Mild Cognitive Impairment) groups, both surpassing a 70% threshold. The accuracy rates for ERICA and MTA scores in the control-normal cognitive group were 56.6% and 70%, respectively. In the MCI group, the accuracy rates were 53.8% for ERICA and 59.6% for MTA. In the AD group, the accuracy rates were 67% for ERICA and 41% for MTA. Vijayakumar et al, [10] demonstrated that the average total volume of the hippocampus in individuals with AD was 3.916 (± 0.3) cm³, in healthy subjects was 5.202 (±0.76) cm3, and in those with vascular "dementia" was 4.660 (±0.22) cm³.

A significant reduction in hippocampal volume and ratio was observed in individuals with vascular dementia (11%), Alzheimer's disease (25%), mixed dementia (21%), and normal pressure hydrocephalus (5%) compared to the control group. Additionally, left hippocampal atrophy was noted, exhibiting asymmetry. The severity of dementia was inversely correlated with hippocampal volume, with greater atrophy associated with increased cognitive decline.

Du et al. [11] reported that individuals with subcortical ischemic vascular disease (SIVD) experienced a 21.7% reduction in entorhinal cortex (ERC) volume and an 18.2% reduction in hippocampal volume compared to cognitively healthy individuals. Conversely, patients with SIVD showed a 24.4% increase in ERC volume and an 11.1% increase in hippocampal volume compared to those with Alzheimer's disease.

Hippocampal atrophy is widely regarded as a key indicator of Alzheimer's disease. As demonstrated by Pini et al. [12], hippocampal volume loss in Alzheimer's patients is markedly greater than in those with other types of dementia, especially in the early stages of the disease. This observation is consistent with our findings, where we noted significantly reduced hippocampal volumes in individuals with Alzheimer's compared to those with vascular or Lewy body dementia. The pronounced atrophy seen in Alzheimer's patients underscores the diagnostic value of hippocampal volume as a critical biomarker, aiding clinicians in distinguishing Alzheimer's from other dementia subtypes with greater accuracy.

The medial temporal atrophy (MTA) score has proven invaluable in differentiating Alzheimer's from other forms of dementia. Scheltens et al. [13] identified MTA scoring as one of the most reliable visual markers for Alzheimer's pathology. In our study, the elevated MTA scores among the Alzheimer's cohort reaffirm the utility of MPRAGE imaging in detecting subtle structural alterations in the medial temporal lobe, characteristic of AD. This finding

is further supported by other studies, which validate the MTA score's effectiveness in differentiating Alzheimer's from other dementias, such as vascular dementia and Lewy body dementia.

The ERICA score has high sensitivity in detecting early Alzheimer's disease, particularly through its focus on entorhinal cortex atrophy. Our results align with these findings, as patients with Alzheimer's in our study exhibited significantly higher ERICA scores compared to those with vascular or frontotemporal dementia. Given that the entorhinal cortex is one of the first regions impacted by Alzheimer's pathology, the ERICA score's ability to identify early atrophy in this area renders it an invaluable tool for early diagnosis. This capacity to detect early-stage alterations offers clinicians a vital opportunity for timely intervention and more precise differentiation from other dementia subtypes.

This multimodal approach offers a more nuanced understanding of brain structure, illuminating the regions most affected by Alzheimer's pathology. Our findings support this assertion, with both MTA and ERICA scores being highest in the Alzheimer's group. The combined use of these scores enhances diagnostic precision, particularly when distinguishing Alzheimer's from other conditions like Lewy body dementia, which typically spares the hippocampus and thus exhibits much lower scores on these scales.

The utility of 3D T1 MPRAGE in distinguishing Alzheimer's from vascular dementia and other neurodegenerative conditions is particularly noteworthy. As advancements in neuroimaging techniques continue to evolve, the integration of artificial intelligence (AI) in clinical settings holds significant promise for enhancing diagnostic accuracy and accelerating medical breakthroughs. Chopra et al. [14] highlighted how AI can revolutionize clinical trials and diagnostics by optimizing data analysis and improving predictive models, which can be particularly beneficial in distinguishing between various dementia subtypes based on neuroimaging findings. Our study echoes the finding that vascular dementia patients show lower MTA and ERICA scores compared to those with Alzheimer's. The ability of 3D T1 MPRAGE to discern these subtle differences enhances its value as a tool for differential diagnosis in clinical practice, offering greater specificity in identifying the underlying type of dementia.

The key learning points are:

1. **Role of advanced imaging techniques in dementia diagnosis:**
   - The study highlights the superior diagnostic capabilities of 3D T1-weighted MPRAGE sequences compared to conventional spin-echo MRI for identifying and differentiating Alzheimer's disease from other dementia subtypes.
   - The importance of advanced imaging in quantifying Medial Temporal Lobe Atrophy (MTA) and Entorhinal Cortex and Related Areas (ERICA) scores as critical biomarkers for Alzheimer's diagnosis.
2. **Significance of MTA and ERICA scores:**
   - MTA scores provide high sensitivity and specificity for detecting structural changes characteristic of Alzheimer's, aiding in distinguishing it from other dementias such as vascular dementia and Lewy body dementia.
   - ERICA scores demonstrate exceptional diagnostic accuracy for early Alzheimer's detection by focusing on entorhinal cortex atrophy, a hallmark of the disease.
3. **Hippocampal volume as a biomarker:**
   - The study supports the value of measuring hippocampal volume to differentiate Alzheimer's from other dementia subtypes, emphasizing that hippocampal atrophy is more pronounced in Alzheimer's disease.
   - Quantitative hippocampal assessment can help distinguish Lewy body dementia and vascular dementia, which present distinct volumetric patterns.
4. **Clinical implications and utility of 3D T1 MPRAGE:**
   - The use of 3D T1 MPRAGE enables clinicians to detect early structural changes, enhancing early diagnosis and intervention potential.
   - This technique may improve patient outcomes through more targeted and timely treatment strategies.
5. **Comparative advantages over conventional imaging:**
   - The study establishes that conventional spin-echo sequences have limitations in identifying specific atrophic changes, underscoring the added precision and diagnostic clarity of 3D T1 MPRAGE.
6. **Integration of multimodal imaging approaches:**
   - Combining MTA and ERICA scores, alongside advanced imaging protocols, offers a comprehensive approach to dementia diagnostics, leading to better differentiation between Alzheimer's and other conditions.
   - This integrative approach can guide more personalized and accurate clinical decision-making.

7. **Future directions and AI integration potential:**
   - o There is potential for incorporating artificial intelligence to further enhance diagnostic precision and differentiate dementia subtypes through advanced neuroimaging analysis, as highlighted in the discussion.

CONCLUSION

This study underscores the superior efficacy of 3D T1 MPRAGE in calculating the Medial Temporal Lobe Atrophy (MTA) index, demonstrating its distinct ability to differentiate Alzheimer's disease from other dementia subtypes, including Parkinson's plus syndromes. By providing excellent anatomical detail, it enables precise visualization and volumetric assessment of critical regions such as the hippocampus and medial temporal lobe, areas frequently affected early in Alzheimer's. 3D MPRAGE's superior gray-white matter contrast aids in identifying cortical thinning and structural changes, enhancing differentiation from other dementias, such as vascular or frontotemporal forms. Its ability to track disease progression with reproducible imaging across follow-ups makes it valuable for monitoring neurodegeneration. It facilitates early detection and quantitative assessments like hippocampal volume measurement and ERICA scores. The application of 3D T1 MPRAGE enables a more accurate and reliable assessment of MTA, surpassing conventional imaging sequences in precision. Moreover, the integration of the ERICA score with this advanced imaging modality provides a powerful diagnostic tool for the early detection of Alzheimer's disease, offering improved consistency and reproducibility in clinical practice. Thus, the combined use of 3D T1 MPRAGE and the ERICA score markedly enhances the early and accurate diagnosis of Alzheimer's disease, positioning it as a valuable asset in the clinical evaluation of dementia.

Authors' contributions:
Conceptualization, Vinoth Pandian ,Karthik Krishna Ramakrishnan, and Sharmeela S; methodology, Karthik Krishna Ramakrishnan ,and Sharmeela S; validation, Karthik Krishna Ramakrishnan, Sharmeela S and Vinoth Pandian, Nivashini G.R; formal analysis , Sharmeela S, Vinoth Pandian, Nivashini G.R investigation, Sharmeela S and Nivashini G.R ; resources, Karthik Krishna Ramakrishnan.; data curation, Sharmeela S and Vinoth Pandian.; writing—original draft preparation, Vinoth Pandian ,Sharmeela S., Nivashini G.R; writing—review and editing, Sharmeela S. Vinoth Pandian, Nivashini G.R; visualization, Sharmeela S and. Nivashini G.R; supervision, Karthik Krishna Ramakrishnan and Vinoth Pandian.; project administration, Karthik Krishna Ramakrishnan, Arunthathy Thangarajah; All authors have read and agreed to the published version of the manuscript.
All the authors contributed equally to this article.

Competing interests:
The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Informed consent:
I undersign and certificate that I have obtained the written consent of the identified persons or their legal guardians for the presentation of the cases within the present scientific paper.

Human and animal rights:
"Consent was obtained or waived by all participants in this study. Saveetha Medical College and Hospital Institutional Ethics Committee issued approval 080/06/2023/IEC/SMCH.The research conducted complied with the ethical standards in accordance with Helsinki Declaration (of 1975, revised in 2013), as well as national regulations in the field."
All authors have confirmed that this study did not involve animal subjects or tissue.

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Data availability:
Data sharing does not apply to this article as no new data were created or analyzed in this study.

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