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Reliability of MRICloud automatic segmentation for measuring brain ventricular volumes in Parkinson's disease patients

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Abstract

Background Parkinson's disease is the second most common neurodegenerative disease. In Parkinson's disease, enlargement of the ventricles is expected, and when the normal anatomical shape of the ventricles is distorted, automatic segmentation methods may not be able to make accurate measurements. Therefore, it is important to evaluate the reliability of automatic segmentation methods. Our aim in this study is to obtain volumetric measurements of brain ventricles in Parkinson's disease patients with MRICloud and compare these with the manual method in relation to healthy controls.

Methods 40 idiopathic Parkinson's disease patients and 44 healthy controls were included in our study retrospectively. Brain ventricle volumes of both groups were measured using MRICloud and manual segmentation method. The volumes of both groups were compared. The reliability of MRICloud was evaluated by comparing it with manual segmentation, which is considered the gold standard.

Results We found statistically significant volumetric differences in several regions, such as the atrial part of the right lateral ventricle ($p = .030$), the atrial part of the left lateral ventricle ($p = .030$), and the occipital horn of the right lateral ventricle ($p = .030$) between the PD and control groups. In the PD group, the intraclass correlation coefficients (ICC) value is 0.936, 0.837, 0.642, and 0.853 for the right lateral ventricle, left lateral ventricle, 3rd ventricle, and 4th ventricle, respectively. In the control group, the ICC value is. 999, 0.998, 0.912, and 0.815 for the right lateral ventricle, left lateral ventricle, 3rd ventricle, and 4th ventricle, respectively.

Conclusions Our findings suggest that MRICloud is a good method for detecting the volumes of normal and pathological brain ventricles, except for the 3rd ventricle. In addition to clinical criteria, we think MRICloud is a reliable and useful method to help diagnose Parkinson's disease and track the progression of the disease.

Keywords MRICloud, Brain ventricles, Parkinson's disease, Automatic segmentation

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Introduction

Brain ventricles are cerebrospinal fluid-filled cavities consisting of two lateral ventricles, the 3rd ventricle, and the 4th ventricle. These spaces are connected through foramina. The lateral ventricles consist of 5 parts: frontal (anterior) horn, occipital (posterior) horn, temporal (inferior) horn, atrium, and body. These parts are adjacent to important structures such as the hippocampus, thalamus, basal nuclei, and corpus callosum [1].

Ventricular enlargement is an important structural biomarker and may occur in normal aging [2] or in many neurodegenerative diseases, such as Alzheimer's Disease [3], Parkinson's Disease (PD) [4]. Ventricular enlargement can be assessed directly and objectively by measuring its volume [5].

Multiple methods are used in MRI clinical studies to assess brain volume. They can be divided into manual, semi-automatic, and fully automatic [6]. These methods have advantages and disadvantages compared to each other. Manual segmentation is a very time-consuming, tedious task that often involves longer procedures, and the results are highly dependent on human expertise [7]. Automatic segmentation methods save time and effort because they process medical images quickly and accurately, especially in large sample groups [8]. However, in case the normal anatomical shape of the ventricles is distorted and they expand irregularly, accurate measurements may not be made with automatic segmentation methods [9]. Pathological ventricles, which are especially common in elderly people, are not included in some automatic segmentation methods [10].

Enlargement of the brain ventricles is expected in PD, which is the second most common neurodegenerative disease after Alzheimer's disease [11]. Also, changes in ventricular volume can be evaluated to distinguish PD from other Parkinsonian syndromes [12]. In the literature, brain ventricles in PD have been evaluated with many different segmentation methods. To our knowledge, there is no study using MRICloud to evaluate the brain ventricles in PD.

Our aim in this study is to obtain volumetric measurements of brain ventricles in PD patients with MRICloud and to evaluate its reliability by comparing it with the manual segmentation method in relation to healthy controls.

Materials and methods

This study was approved by the Clinical Research Ethics Committee of the affiliated university, per the Declaration of Helsinki (KAEK-647).

Subjects

Adult individuals who underwent MRI were analyzed retrospectively using the PACS system (Picture Archiving and Communication System). 40 idiopathic PD patients (12 women and 28 men) and 44 age-matched healthy controls (28 women and 16 men) were included in this study. PD patients' mean age was 64.38 ± 11.46 years, with the age range 50–82 years. Duration of disease was 65.2 ± 67.15 months. Healthy controls' mean age was 60.48 ± 7.30 years, with an age range of 50–78 years. The PD and control groups were matched in terms of age ($p = .064$) but not in terms of sex ($p = .002$).

All patients in the hospital archive who met the United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria for idiopathic Parkinson's disease were retrospectively screened. MRIs of these patients were assessed, and all patients with available T1-MPRAGE sequences were included in the study. Patients with secondary Parkinsonism and other accompanying neurodegenerative diseases (Alzheimer's disease, Wilson's disease, etc.), and patients with MRI images affected by artifacts, were excluded from the study. Clinical diagnoses were made by an experienced neurologist at XX University, Faculty of Medicine, Department of Neurology. The control group consisted of individuals whose brain ventricles were within normal limits and who did not have dementia, alcoholism, and chronic drug use.

A priori power analysis was performed using G*Power 3.1.9.7, indicating that a minimum of 28 patients was required to achieve 80% statistical power at a 5% significance level, assuming a moderate-to-high effect size. As this study was retrospective in nature, all eligible patients identified through the hospital archive were included to maximize statistical power and data representativeness.

MRI data acquisition

Magnetic resonance images were performed by a 3T whole-body system (Spectra; Siemens-Healthcare, Germany). The MRI examination protocol had a 3D T1 Magnetization Prepared- RApid Gradient Echo (MPRAGE) sequence (Repetition time/echo time, 1900/2.41; matrix, 256 189; field of view, 270 mm; slice thickness, 1 mm with no gap; flip angle, 9°; number of axial slices, 176; acquisition time, 3 min 48 s) through the whole brain.

Automated segmentation of brain ventricles

MRICloud software (www.MRICloud.org) was used to perform volumetric analysis of brain ventricles in both PD and control groups. MRICloud is a cloud-based automatic segmentation method that performs whole-brain segmentation from T1-MPRAGE images. One of its biggest advantages is that atlases specific to different ages can be selected.

MRICloud is a publicly available web-based, free service for multi-contrast imaging segmentation and quantification, providing a high-throughput neuroinformatics platform for automated brain MRI segmentation and

analytical tools for quantification through distributed remote computing and Web-based user interfaces [13]. It is developed by researchers from Johns Hopkins University [14].

MRICloud uses multi-atlas label-fusion (MALF) algorithms for normalization and registration. There are two major components in the algorithms: the first is image registration, and the second is the multi-atlas label fusion process. In the registration step, atlases are transformed to the target image using Large Deformation Diffeomorphic Metric Mapping (LDDMM) [15].

All MRIs are bias-corrected and linearly aligned to the JHU-MNI atlas space according to MRICloud. First, the atlases are linearly aligned using Large Deformation Diffeomorphic Metric Mapping (LDDMM) warped to the subject image, and then the multiatlas fusion algorithmis applied [16]. Please read [17, 18] for more information.

After the scanning, DICOM images were downloaded from the PACS system. Header and image files were created from DICOM images via DTIStudio. Header and image files were uploaded to MRICloud by selecting Segmentation, T1-MultiAtlas under the BrainGPS section. Then, image orientation and atlas were selected. The atlas used for the processing of our data was the Adult50-90yrs_293Labels_31atlases_V11B. Volumetric analysis was performed automatically by MRICloud software, and the results were downloaded under the "my jobs status" section on the web page. Ventricular volumes were corrected to total intracranial volume to avoid differences in head sizes.

MRICloud software was used in our study due to its advantages, such as ease of use, the ability to run large cohorts in a short time, and the ability to select different atlases according to the age of the sample.

MRICloud software has been used successfully in many studies [13, 19]. However, to the best of our knowledge, our study is the first to use MRICloud for ventricle segmentation in Parkinson's disease.

Manual segmentation of brain ventricles

We used the ImageJ program (version 1.54 g, https://imagej.net/ij/download.html) for manual segmentation. DICOM files converted to 16-bit images. Each ventricle was selected as a region of interest (ROI), respectively. Slices were aligned along the anterior commissure-posterior commissure (AC-PC) line and the interhemispheric fissure using ITKSnap before manual marking. Images containing ventricles were opened with ImageJ. Due to contrast differences, the ventricular areas were easily distinguished from adjacent areas. ROIs in each slice were delineated with the freehand tool. The borders of the 3rd ventricle were determined as follows: Anterior commissure and optic chiasm anteriorly, posterior commissure and rostrum corpus callosum posteriorly, corpus mammillare inferiorly, fornix superiorly, and thalamus laterally. The borders of the 4th ventricle were determined as the brainstem anteriorly, the cerebellum posteriorly, and laterally. The borders of the lateral ventricles, the corpus callosum, septum pellucidum, and interventricular foramen medially, the frontal cortex anteriorly, and the occipital cortex posteriorly were determined. Manual segmentations were performed according to previous studies [20]. Then, the area for each ROI was calculated. The areas for all slices were summed and multiplied by the slice thickness of 1 mm to calculate the volumes. For manual segmentation, 10 subjects were randomly selected for each group. Simple random sampling was used to provide a statistically significant validation subset while preserving the demographic and clinical characteristics of the overall study population. Two researchers, blinded to groups and performed manual segmentation on each subject in each slice. The means of the volumes measured by two researchers were calculated and compared with the volumes obtained with MRICloud. For inter-rater reliability, the single-measure intraclass correlation coefficient (ICC) values indicated excellent reliability for the left and right lateral ventricles (left = 0.969; right = 0.970), good reliability for the third ventricle (0.871), and moderate reliability for the fourth ventricle (0.681). The average-measure ICC values demonstrated excellent reliability for the left and right lateral ventricles (left = 0.984; right = 0.985) and the third ventricle (0.931), and good reliability for the fourth ventricle (0.811).

Post hoc power analyses were performed using G*Power 3.1.9.7. Based on the observed effect sizes, the achieved statistical power for each ventricular segment exceeded 95% across all measurements, indicating sufficient power to detect the observed effects.

Statistical analysis

Statistical analysis was performed using IBM SPSS ver. 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). The Shapiro-Wilk test was used to check whether the data conformed to a normal distribution. The Mann-Whitney U test was used to evaluate the differences between groups. To control for potential sex-related neuroanatomical differences, group comparisons of ventricular volumes were performed using analysis of covariance (ANCOVA), with sex included as a covariate, following normalization to intracranial volume. Multiple comparisons were corrected using false discovery rate (FDR). FDR correction was performed using the Benjamini–Hochberg procedure. Adjusted p-values were computed as p×m/i and corrected for monotonicity. A value of $p < .05$ was considered statistically significant.

To compare the mean differences of volume measurements obtained from MRICloud and manual

Table 1 The mean volumes and standard deviations of the brain ventricles of PD and control groups (mm^3)

	PD Group ($n=40$) (Mean ± Sd)		Control Group ($n=44$) (Mean ± Sd)	
	Right	Left	Right	Left
LV_Frontal	7203.8 ± 3454	6367.2 ± 2959.2	5552.6 ± 2534.2	4953.5 ± 2233
LV_Body	5454.1 ± 3037.8	5497.4 ± 2943.5	3957.3 ± 2146.2	4008.3 ± 1778.7
LV_Atrium	3478.4 ± 1954.4	3004.2 ± 1506.7	2500 ± 1383.5	2083.7 ± 983.6
LV_Occipital	284 ± 159.3	292.1 ± 191.9	196.3 ± 101.8	201.1 ± 86.3
LV_Temporal	1546 ± 853.2	1499.2 ± 751.1	1173.8 ± 538.1	1243.7 ± 466.7
LV	17966.3 ± 8887.9	16659.9 ± 7655.5	13380.1 ± 6246.1	12490.2 ± 5071.9
3rd Ventricle	2654.4 ± 686.5		2252.1 ± 522.3	
4th Ventricle	2276.7 ± 383.5		2305.5 ± 624.8	
Total Ventricle	39557.4 ± 16875.1		30427.9 ± 11861.4	

LV lateral ventricle, *PD* parkinson's disease, *Sd* standard deviation

Table 2 Comparison of brain ventricle volumes of PD and control groups (mm^3)

	F (Group)		*p* (uncorrected)		FDR-q		partial η^2	
	Right	Left	Right	Left	Right	Left	Right	Left
LV_Frontal	2.110	1,508	0.150	0,223	0.150	0.279	0.025	0,018
LV_Body	3.246	2.195	0.075	0.142	0.125	0.237	0.039	0.026
LV_Atrium	6.744	7.920	**0.011**	**0.006**	**0.030**	**0.030**	0.077	0.089
LV_Occipital	6.544	2.713	**0.012**	0.103	**0.030**	0.237	0.075	0.032
LV_Temporal	2.435	0.514	0.123	0.475	0.150	0.475	0.029	0.006
LV	4.083	3.404	**0.047**	0.069	0.115	0.115	0.048	0.040
3rd Ventricle	5.148		**0.026**		0.115		0.060	
4th Ventricle	0.031		0.860		0.860		0.000	
Total Ventricle	1.937		0.168		0.210		0.023	

P–values were adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure following ANCOVA, with sex included as a covariate. *LV* Lateral Ventricle

segmentation, a paired t-test was used with a significance level of α = 0.05 and a 95% confidence interval. Normality was assessed using the Shapiro-Wilk test on paired differences, and multiple test corrections were applied using the False Detection Rate (FDR) correction using the Benjamini-Hochberg method approach to ensure statistical robustness.

The ICC, a two-way mixed-model, absolute agreement, and Cronbach's α were used to test the inter-method reliability between MRICloud and manual segmentation. The ICC value was interpreted as ICC < 0.50 poor, 0.50 < ICC < 0.75 moderate, 0.75 < ICC < 0.90 good, and 0.90 < ICC excellent reliability [21].

Results

A total of 40 patients and 44 age-matched healthy controls were included in this retrospective study. The mean ages of the PD and control groups were 64.38 ± 11.46 and 60.48 ± 7.30 years, respectively. There was no statistically significant difference between the two groups according to age distribution ($p > .05$).

We investigated the differences in brain ventricles between the PD and control groups. MRICloud software was used to perform volumetric analysis. The mean volumes and standard deviations of the brain ventricles of both the PD and control groups are presented in Table 1. The mean volumes of the brain ventricles were larger in the PD group than in the control group. Only the mean volume of the 4th ventricle was slightly larger in the control group.

We found statistically significant volumetric differences in several regions, such as the atrial part of right lateral ventricle ($p = .011$), the atrial part of left lateral ventricle ($p = .006$), the occipital horn of right lateral ventricle ($p = .012$), right lateral ventricle ($p = .047$), and 3rd ventricle ($p = .026$) between the PD and control groups. After false discovery rate (FDR) correction, only the atrial part of the right lateral ventricle ($p = .030$), the atrial part of the left lateral ventricle ($p = .030$), and the occipital horn of the right lateral ventricle ($p = .030$) remained statistically significant. Table 2 shows a comparison of brain ventricular volumes between the PD and control groups.

Brain ventricle volumes obtained by MRICloud and manual segmentation for all groups were compared with the paired t-test, and it was seen that there was no statistical difference between the methods ($p > .05$). A comparison of the means and standard deviations of brain ventricle volumes obtained by MRICloud and manual segmentation is shown in Fig. 1. The mean volumes, standard deviations, p-values of the paired t-test, and ICC values for each brain ventricle section are presented in Table 3.

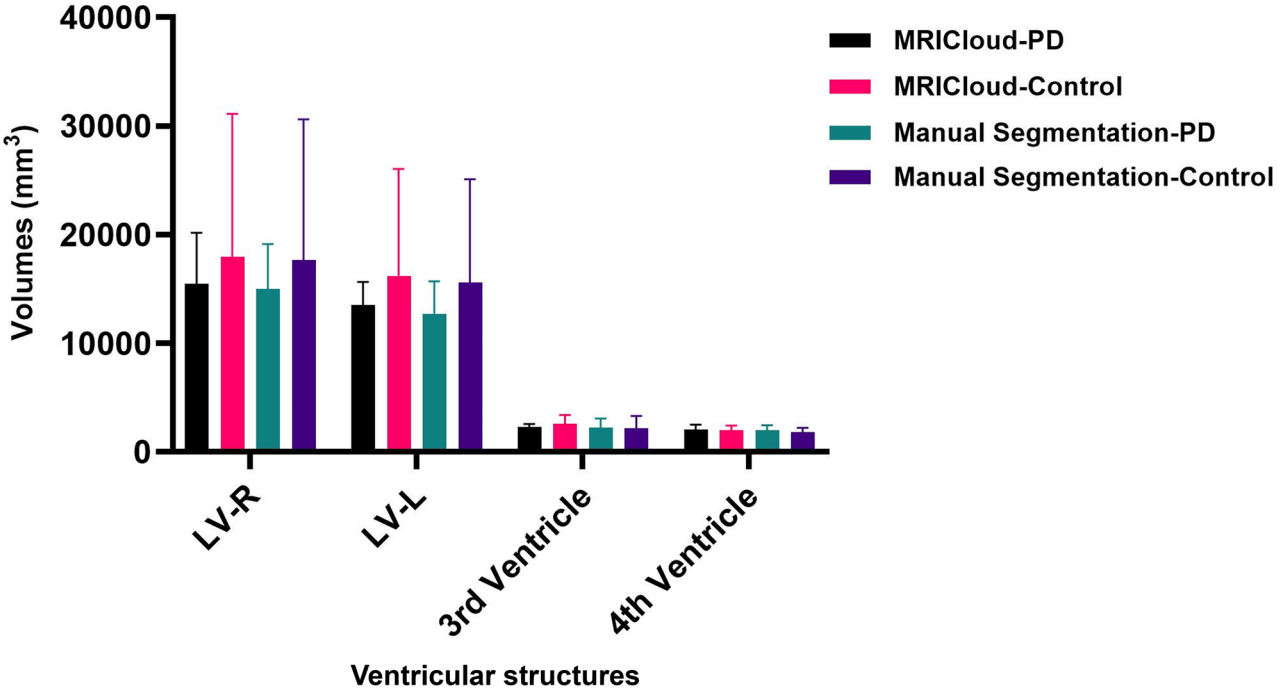


Fig. 1 Comparison of ventricular volumes between PD patients and controls obtained using MRICloud and manual segmentation methods. Volumes of the right lateral ventricle (LV-R), left lateral ventricle (LV-L), third ventricle, and fourth ventricle are shown. Bars represent mean ventricular volume (mm^3), and error bars indicate standard deviation

Table 3 Comparison and correlation of MRICloud and manual segmentation

	PD Group (Mean ± Sd)					Control Group (Mean ± Sd)				
	MRICloud	Manual Segmentation	*p*	FDR *p*	ICC %95 CI	MRICloud	Manual Segmentation	*p*	FDR *p*	ICC %95 CI
LV_Right	15489.6 ± 4696.9	15021.8 ± 4135.9	0.679	0.825	0.936	17949.8 ± 13173.9	17677.2 ± 12947.7	0.511	0.511	0.999
LV_Left	13,537 ± 2114.7	12726.2 ± 3005.1	0.409	0.825	0.837	16214.8 ± 9843.7	15608.2 ± 9486.1	0.110	0.220	0.998
3rd Ventricle	2325.6 ± 244.4	2256.8 ± 819.7	0.825	0.825	0.642	2620 ± 789.6	2191.4 ± 1140.1	0.091	0.220	0.912
4th Ventricle	2083 ± 447.9	1985.40 ± 477.5	0.564	0.825	0.853	2031.2 ± 399	1851.2 ± 372.2	0.232	0.309	0.815

P–values derived from paired t–tests were corrected using the Benjamini–Hochberg procedure (FDR p). *FDR* False Discovery Rate, *ICC* Intraclass Correlation, *CI* Confidence Interval, *Sd* Standard Deviation, *LV* Lateral Ventricle, *PD* Parkinson's Disease

In the PD group, the ICC value is 0.936, 0.837, 0.642, and 0.853 for the right lateral ventricle, left lateral ventricle, 3rd ventricle, and 4th ventricle, respectively. In the control group, the ICC value is. 999, 0.998, 0.912, and 0.815 for the right lateral ventricle, left lateral ventricle, 3rd ventricle, and 4th ventricle, respectively. In the PD group, the right lateral ventricle showed excellent reliability, the left lateral ventricle and the 4th ventricle showed good reliability, and the 3rd ventricle showed moderate reliability. In the control group, all ventricles except the 4th ventricle showed excellent reliability. The 4th ventricle showed good reliability.

In terms of inter-rater reliability, the single-measure ICC values indicated excellent reliability for the left and right lateral ventricles (left = 0.969; right = 0.970), good reliability for the third ventricle (0.871), and moderate reliability for the fourth ventricle (0.681). The average-measure ICC values demonstrated excellent reliability for the left and right lateral ventricles (left = 0.984; right = 0.985) and the third ventricle (0.931), and good reliability for the fourth ventricle (0.811).

Discussion

This study aimed to evaluate the reliability of the MRICloud by comparing the brain ventricle volumes of PD patients and healthy controls. To our knowledge, this is the first study to measure brain ventricular volumes in PD with MRICloud. The PD group showed enlargement in the atrial parts of both lateral ventricles and the occipital horn of the right lateral ventricle compared to the control group. ICC showed strong and excellent

reliability except for the 3rd ventricle when comparing manual segmentation with MRICloud.

Functional and structural brain imaging plays an important role in clinics and research. MRI-based brain imaging is frequently used in the diagnosis and follow-up of many diseases [22]. Analysis of these images provides objective data to understand the nature of the disease and evaluate its progression [23].

Various manual, semi-automatic, and automatic software are used for MRI-based global and regional volume measurements [24]. When different methods and techniques are used to measure an anatomical structure, results are expected to vary due to procedural differences in each method. However, these changes are not expected to be statistically significant [25]. MRICloud has been used for volume measurement in various diseases. It has been compared with the manual segmentation method, which is the current gold standard [7], in a limited number of studies.

Acer et al. [26] compared only the lateral ventricle volumes obtained with MRICloud, ALVIN, and volBrain software in healthy subjects with manual segmentation. They reported that MRICloud is the best tool for automatic segmentation of lateral ventricles based on the Dice index, ICC, and concordance correlation coefficient agreement. Similarly, in our study, there was no significant difference between the ventricular volume measurements obtained from MRICloud and the manual segmentation method in the healthy control group, and ICC showed excellent reliability for the lateral ventricles.

Segmentation algorithms are generally developed using young, healthy individuals. There are a limited number of large studies conducted with elderly healthy elderly populations. Therefore, it may be difficult to determine the boundaries of brain tissue in individuals with significant atrophy [27]. In our study, no significant difference was observed between the ventricular volumes measured by MRICloud and manual segmentation in the PD group, where the elderly population is especially affected, and pathological ventricles are expected to be seen. The ICC has shown excellent reliability for the right lateral ventricle, good reliability for the left lateral ventricle and 4th ventricle, and moderate reliability for the 3rd ventricle. Excellent and good ICC values support the reliability of MRICloud in estimating the volumes of normal and pathological brain ventricles.

Various diseases affect the volume and morphology of the ventricles. Segmentation of the ventricular system is important for understanding pathological changes in the morphology and volume of the ventricles [5]. In PD, dilation occurs in the brain ventricles as a result of atrophy in gray matter structures such as the basal ganglia, hippocampus, and thalamus [28]. Camicioli et al. stated that the increase in ventricular volume in PD may be associated with the decline of motor functions and that ventricular enlargement may be a reliable marker for global brain degeneration [11].

In PD patients with normal cognition, cortical morphology may appear intact or slightly atrophic. When combined with cognitive impairment, the atrophic change can be severe [29]. Morphologic changes in brain ventricles have been reported in PD when cognitively normal patients are compared with those with mild cognitive impairment (MCI) [4, 30] or dementia [11]. Among these studies, the number of studies that segmented all ventricles is very limited.

Dalaker et al. compared the ventricular volumes of PD patients with normal cognition, PD patients with MCI, and healthy controls using the automatic segmentation method Freesurfer, and found that the 4th ventricle, 3rd ventricle, and the inferior horn of the left lateral ventricle were significantly enlarged in the PD group with MCI [30]. Apostolova et al. performed only lateral ventricle segmentation with the semi-automatic segmentation method and associated the frontal, temporal, and occipital horns of both lateral ventricles with MCI [31]. Mak et al. stated that the total ventricular volume measured by an automatic segmentation method, VIENA, was significantly increased in the PD group with MCI compared to PD without MCI and healthy controls [4].

Nahir et al. compared the lateral ventricle volumes of 54 PD patients and 26 healthy controls with BrainSuite software, an automatic segmentation method. They reported that the average right and left lateral ventricle volumes of PD patients were higher, but they could not find a statistically significant difference [32]. Kocaman et al. compared the brain ventricle volumes of 21 idiopathic PD patients and 20 healthy controls with MRIStudio, an atlas-based automatic segmentation method, and found a statistically significant difference only in the occipital part of the left lateral ventricle. However, the sample size in their studies is small [33].

When we compared the ventricular volumes of the idiopathic PD and control groups obtained with MRICloud, we found a statistically significant difference between the atrial parts of both lateral ventricles and the occipital horn of the right lateral ventricle.

The different results found in the literature between studies performing ventricle segmentation in PD may be due to the following reasons: (1) Different sample sizes, (2) Patients at different disease stages, (3) Lateralization of PD relative to the onset of symptoms, and (4) the poor reliability of different methods in segmenting pathological ventricles.

Disease-related clinical factors, including symptom laterality, motor severity, and cognitive status, are likely to influence ventricular morphology in Parkinson's disease. Longer disease duration and higher motor severity can

lead to ventricular enlargement secondary to progressive and widespread neurodegeneration [4, 11]. Furthermore, asymmetric disease involvement can lead to differential effects on individual ventricular segments rather than global enlargement [28]. Additionally, ventricular enlargement has been reported to be more pronounced in patients experiencing cognitive decline due to Parkinson's disease [30, 31].

However, the primary aim of this study was methodological rather than clinical. Specifically, this study was designed as a retrospective validation of automatic ventricular segmentation against manual measurements to assess the robustness and consistency of segmentation techniques across a heterogeneous range of ventricular morphologies. The findings from the comparison of PD and control groups should not be interpreted as evidence that ventricular enlargement is a clinical biomarker.

Detailed clinical stratification, such as Hoehn and Yahr stage, UPDRS scores, disease laterality, or medication status, could not be consistently obtained for each patient from archived records. Although these variables were not included in the analysis, since both techniques were applied to the same imaging dataset, it is unlikely that their potential confounding effects systematically influenced the comparison between manual and automatic methods. Therefore, the methodological findings regarding measurement agreement and reliability remain valid within the studied population.

Automatic segmentation methods are frequently preferred nowadays as they save time, are effective, and can obtain objective data. Automatic segmentation methods provide a great advantage over manual segmentation in diagnosing and monitoring diseases, especially in studies with large populations.

In our study, we compared the ventricular volume measurements of PD patients and healthy controls, and we think that MRICloud is a good method for detecting morphological changes between healthy subjects and patients.

This study has several limitations that need to be mentioned. First, the groups were not distributed homogeneously in terms of sex. To prevent head differences that may arise from sex differences, we proportioned the measured volumes to the total intracranial volume and used sex as a covariate for analysis. Second, the retrospective design restricted access to comprehensive clinical data, including Hoehn and Yahr stage, UPDRS motor scores, disease laterality, and medication status. As these factors are known to influence neuroanatomical changes in Parkinson's disease, their absence limits the ability to interpret ventricular measurements in relation to clinical severity. Third, cognitive status was not assessed, and patients could not be stratified into cognitively normal PD, PD with mild cognitive impairment, or Parkinson's disease dementia. Given the well-established association between ventricular enlargement and cognitive impairment in Parkinson's disease, this represents a significant limitation. Future prospective studies incorporating detailed motor, cognitive, and treatment-related variables are warranted to evaluate the clinical relevance of ventricular measurements obtained using automated segmentation techniques.

In conclusion, we compared volumetric measurements of brain ventricles obtained with MRICloud and the manual segmentation method to evaluate the reliability of the MRICloud method. The ICC showed excellent reliability for both lateral ventricles and the 3rd ventricle, and good reliability for the 4th ventricle in the control group. The ICC showed excellent reliability for the right lateral ventricle, good reliability for the left lateral ventricle and 4th ventricle, and moderate reliability for the 3rd ventricle in the PD group. Our findings suggest that MRICloud may be useful for the assessment of ventricular volumes, but its reliability is dependent on the ventricle, especially in pathological anatomy.

PD is a disease that remains asymptomatic for a long time. It takes a long time until the patient shows symptoms, resulting in a lot of neuron loss during this period. In addition to established clinical criteria, MRICloud may provide complementary information; however, its reliability is ventricle-dependent, particularly in pathological anatomy, and it should not be considered a standalone tool for PD diagnosis or tracking progression.

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Author contributions
Author Contributions: NO: Conception, Design, Data Collection and/or Processing, Analysis, Literature Review, Writing, Critical Review, ZNK: Design, Data Collection and/or Processing, NA: Conception, Design, SSO: Supervision, Data Collection and/or Processing, US: Analysis, Data Collection and/or Processing, LBS: Conception, Supervision, Fundings, Critical Review. All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Clinical Research Ethics Committee of the Akdeniz University (Ethics committee approval: KAEK-647).

Informed consent
Standard clinical informed consent was obtained at the time of the scan. Informed consent for this specific study was not applicable, given the retrospective nature of this research.

Competing interests
The authors declare no competing interests.

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