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ORIGINAL ARTICLE – OPEN ACCESS

A Comparison of Automated Segmentation and Manual Tracing of Magnetic Resonance Imaging to Quantify Lateral Ventricle Volumes

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ABSTRACT

Objective: Ventricular volume measurements have been proposed as a useful biomarker for several neurological diseases. The goal of this study was to compare the performance of 3 fully-automated tools, volBrain (http://volbrain.upv.es), ALVIN (Automatic Lateral Ventricle Delineation) (https://sites.google.com/site/mrilateralventricle/), and MRICloud (http://mri-cloud.org), with expert hand tracing to quantify lateral ventricle (LV) volume using magnetic resonance images.

Materials and Methods: The sample comprised 24 healthy subjects (age: 25.1±5.7 years, all male). Volumes derived from each automated measurement were compared to hand tracing results performed by 2 specialists to assess the percent volume difference using the intraclass correlation coefficient (ICC), concordance correlation coefficient (CCC), Dice index value, and Bland-Altman analysis.

Results: The ICC agreement of the Manual_1 and Manual_2 was very good (0.979), and there was no statistically significant difference (p>0.001). The volume difference of all methods was similar. The CCC with MRICloud and ALVIN was higher than that of volBrain. Bland-Altman plots indicated that the 3 automated methods demonstrated acceptable agreement.

Conclusion: Compared with hand tracing, the LV volumes generated by MRICloud were more accurate than those of volBrain and ALVIN. LV volume values can provide valuable data related to the volumetric dependencies of the anatomical structures in various clinical conditions that can now be easily obtained using automated tools.

Keywords: ALVIN, lateral ventricle, manual tracing, MRICloud, volBrain

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INTRODUCTION

The 2 largest ventricles of the brain, the lateral ventricles (LVs), are located in each hemisphere of the brain. They are ependymal cavities that contain cerebrospinal fluid (CSF), which plays a significant role in the function of the brain. The LV volume in a healthy subject has been reported to be 5–7 cm^3 on the left and 5–8 cm^3 on the right side (1). LV enlargement is associated with a loss in brain parenchyma volume, which frequently results in magnetic resonance imaging (MRI) volumetry findings of decreased brain volume, reduced global cortical thickness and increased volume in the LVs and subarachnoid spaces (2). Increased LV volume has been reported in diseases with atrophy of the brain (3, 4). Therefore, MRI measurements are increasingly being considered a potentially useful diagnostic measure in many neurological diseases, such as caudate and basal ganglia volume in schizophrenia, amygdala volume in dementia, and the hippocampal and LV volume in Alzheimer's disease (5, 6). Knowledge of volumetric changes in brain structures may also facilitate the prediction of disease progression in various neurodegenerative diseases.

Several studies have examined manual tracing methods, automatic, and semi-automatic methods to evaluate brain and LV volume (3, 4, 7). The manual tracing method is commonly performed using 3-dimensional (3D) MRI on each slice of the series. Manual tracing is the gold standard for segmentation in volumetric research studies, but slice-by-slice assessment is the most time-consuming method (5, 8).

To the best of our knowledge, there are no LV volume studies in the literature that have compared the manual method with volBrain (http://volbrain.upv.es), ALVIN (Automatic Lateral Ventricle Delineation) (https://sites.google.com/site/mrilateralventricle/), and MRICloud (http://mricloud.org), which are automated methods. The aim of this research was to determine LV volumes using the manual method and compare the results with those obtained using automated tools and to obtain information about the reliability of the various methods.

MATERIALS and METHODS

Participants

The MRI data were obtained from a project in Erciyes University Scientific Research Projects Coordination Unit (grant no: TIR-2017-5045). The MRI was performed at the Erciyes University Gevher Nesibe Hospital

Department of Radiology. The images of 24 healthy subjects (age: 25.1±5.7 years, all male) were used to compare manual and automated segmentation of the LV.

Ethics Approval

The Erciyes University Ethics Committee granted approval for this study. All of the participants provided written informed consent.

MRI Protocol

A 1.5T Siemens area scanner with a 32-channel head coil (Siemens Healthineers GmbH, Erlangen, Germany) was used to obtain T1-weighted 3D magnetization-prepared rapid gradient echo (MPRAGE) sequence images: sagittal, repetition time (TR)/echo time (TE)/flip angle=1900 ms/2.7 ms/20°, TI:1100, Field-of-view (FOV)=25 cm, 1 mm slice thickness, 192 slices, matrix=256×256, voxel size=1×1×1 mm^3. The data were converted into analysis format using the MRIcron software (http://www.sph.sc. MriCloud edu/comd/rorden). The converted data were uploaded to the volBrain, ALVIN, and MRICloud platforms.

Manual Tracing

Manual tracing is considered the gold standard for volumetric quantification of regional brain structures (5, 8). Brain imaging specialists (BK, EAY) performed manual tracing of the LV, frontal horn, temporal horn, occipital horn, and the body, or central part using a previously reported technique (9).

Manual tracing of the LV was performed using ImageJ software (https://imagej.nih.gov/ij/) in native space and orientation on contiguous axial slices, beginning from the most superior and proceeding to the most inferior slice. The ImageJ has been widely used in published studies. Manual tracing of a sample subject with 50 representative axial slices of the LV is provided in Figure 1. LV segmentation took 15–20 minutes per patient. All corrections were made manually using ITK-SNAP software (http://www.itksnap.org) and a standard LV segmentation protocol.

Automated Segmentation

VolBrain

VolBrain is an open-access platform that provides a fully automatic pipeline for volumetric brain analysis that is able to quickly provide accurate volumetric information of different brain structures (10, 11). VolBrain uses a patch-based segmentation method (12).

Conventional, 3D, T1-weighted images from the volBrain library were used to perform automated subcortical structure segmentation was performed. The volumes and label maps were provided within 3 minutes (Fig. 2).

ALVIN

ALVIN was used with SPM8 software (https://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Unified segmentation produces images of gray matter, white matter, and CSF from MRI data, but does not segment subcortical structures. ALVIN applies a binary mask to spatially normalized CSF-segmented images produced using unified segmentation. As the segmented images already demarcate the main boundaries of the LVs, the purpose of the mask is to exclude CSF present outside the LVs, such as in the third ventricle, superior cistern, or sulcal CSF (3, 13) (Fig. 3).

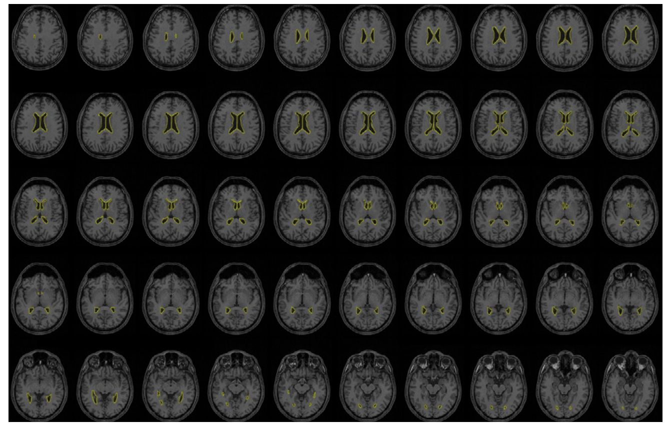

Figure 1. Lateral ventricle segmentation in axial slice magnetic resonance images determined using ImageJ

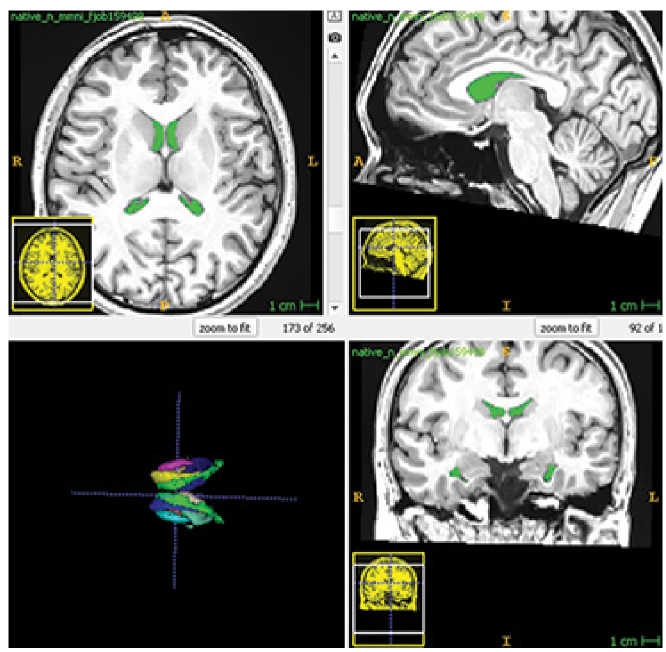

Figure 2. Green areas indicate axial, sagittal, 3D, and coronal lateral ventricle images derived using volBrain

A: Axial; I: Inferior; L: Left; P: Posterior; R: Right

MRICloud

MRICloud is a fully-automated cloud service for brain segmentation of MPRAGE images based on the Multiple-Atlas Likelihood Fusion algorithm, Johns Hopkins University multi-atlas inventories of 286 defined structures, and Ontology Level Control technology (14). The adult_286labels_ 11atlases_V5L atlas was used for the current data (Fig. 4).

The mean time needed to calculate LV volume using MRICloud, volBrain, and ALVIN was 2 hours, 5 minutes, and 3 minutes, respectively. However, volBrain, MRICloud and ALVIN are very different systems. VolBrain and MRICloud are a web-based automated system for volumetric measurement, whereas ALVIN uses MATLAB (MathWorks, Inc., Natick, MA, USA) SPM software. ALVIN provides LV volume, but volBrain also provides measurements of the volume in the thalamus, hippocampus, cerebellum and other brain structures.

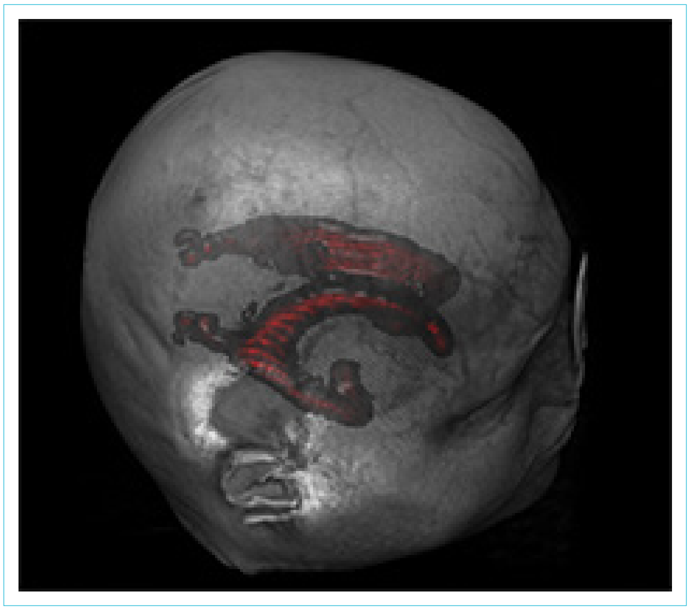

Figure 3. **3D view of the lateral ventricle using ALVIN**

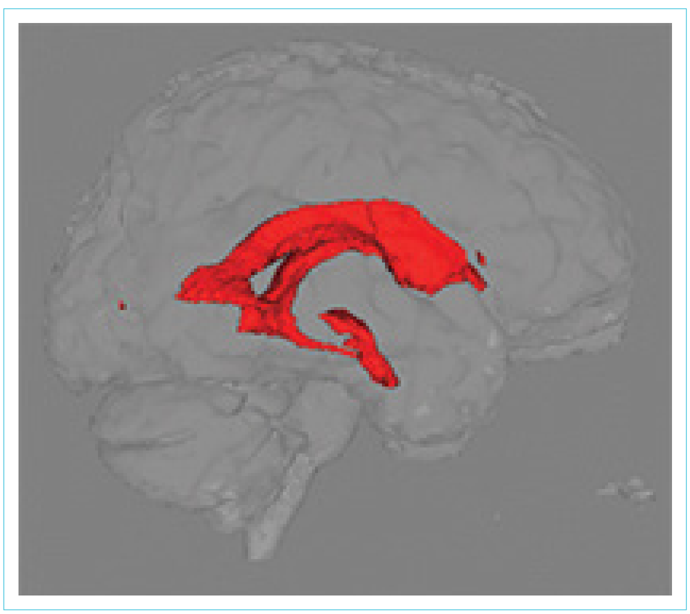

Figure 4. **3D view of the lateral ventricle obtained with MRICloud**

Analysis of Volume Difference

Eq (1) was the equation used to compare the difference in volume of the studied techniques against the gold standard, manual tracing. P1 is the volume of a structure obtained using one automated method and P2 is the gold standard. Calculations were made for each subject and compared. A positive volume difference demonstrates overestimation relative to the manually obtained volume, a negative indicates underestimation, and those approaching 0% show convergence of the volumes obtained from other techniques and the gold standard.

Eq (1) D (P1, P2)=[V(P1) - V(P2)] / V(P2) * 100%

The Dice similarity index was applied to evaluate the reproducibility of manual segmentation and the spatial overlap accuracy of the automated segmentation. The index calculations were performed using software developed in-house with the MATLAB platform (version 2012a) (Eq 2).

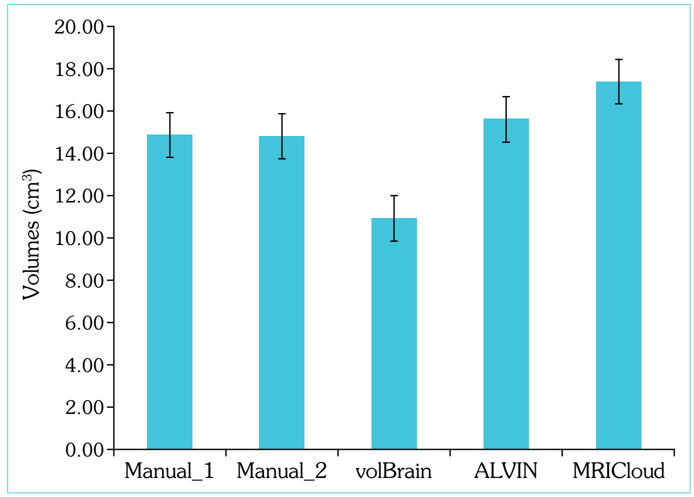

Figure 5. **The volumes of the lateral ventricle using 5 result**

Eq (2) $Dice = 2\frac{V(A \cap B)}{V(A) + V(B)}$

V(A) and V(B) are the volumes of structures in subject A and B, respectively. It is assumed that A and B are binary segmentations. According to the Dice index value, 0 represents no spatial match, and 1 represents an excellent consistency or overlap between the 2 selected volumes (15).

The agreement between automated methods and manual tracing was measured using Bland-Altman plot analysis.

Statistical Analysis

Passing-Bablok regression analysis was used to compare methods. Constant and proportional errors were assessed based on the confidence intervals of the estimated regression coefficients. A constant error was considered to be present if the confidence interval of the constant excluded 0, and a proportional error was considered to be present if the confidence interval of the slope excluded 1. The results were defined as poor if the intraclass correlation coefficient (ICC) was <0.6, satisfactory at 0.6< ICC <0.8, good at 0.8< ICC <0.9, and excellent with an ICC >0.9. The ICC and concordance correlation coefficient (CCC) were calculated with 95% confidence intervals. TURCOSA software (Turcosa Analytics Ltd. Co., Kayseri, Turkey, www.turcosa.com.tr) was used to perform the analysis. A p value of <5% was considered statistically significant.

RESULTS

The mean volume of the LV obtained using the Manual _1, Manual_2, volBrain, ALVIN, and MRICloud methods was 14.86±6.18, 14.80±6.26, 10.93±5.26, 15.61±6.18 and 17.39±6.29 cm^3, respectively (Fig. 5, Table 1). There was no statistically significant difference between Manual _1 and Manual_2 (p>0.001).

Table 1. Comparison of automated techniques and manual tracing to determine volumes of lateral ventricle

Technique	Structure volume (cm³)	% volume difference±SD	
		Comparison with manual_1	Comparison with manual_2
Manual_1	14.86±6.18	–	2.6±14.4
Manual_2	14.80±6.26	-1.0±11.8	–
volBrain	10.93±5.26	7.8±28.9	10.1±30.4
ALVIN	15.61±6.18	-28.1±14.8	-27.6±10.4
MRICloud	17.39±6.29	19.3±17.1	21.3±17.1

Structure volumes were expressed as mean±SD. SD: Standard deviation

The Percentage Volume Difference Between the Manual and Automated Techniques

The volume estimates of the LV obtained using each technique are presented in Table 1. All of the automated technique estimates were (-28.1 to 19.3%) compared with Manual_1 estimates and (-27.6 to 21.3%) compared with Manual_2 estimates (Table 1).

The Dice similarity index was calculated for the ALVIN, MRICloud, and volBrain, and the 2 manual measurements. The Dice values for Manual_1 vs. MRICloud were greater than those of ALVIN and volBrain (Table 2).

Comparison of Correlations Between the Manual and Automated Techniques

Good agreement was observed with average ICC agreement values >0.9, indicating that consistent and reliable volume measurements were feasible.

The Passing-Bablok regression analysis results indicated that there was no statistically constant error or proportional error in a comparison of the Manual_1 (gold standard) and the ALVIN method. The ALVIN method can be said to provide a similar measurement to that of the Manual_1 method. There was no statistically constant error or proportional error between the Manual_1 and the MRICloud method. It can be said that the MRICloud method makes similar measurements to the Manual_1 method (ICC: 0.965, CCC: 0.858). There was a statistically constant error between the Manual_1 and the volBrain method and no proportional error. The volBrain method can be said to make similar measurements to the Manual_1 method (Table 3).

There was both a statistically constant error and a proportional error between the Manual_2 (gold standard) and the ALVIN method. The ALVIN method did not perform similar measurements to the Manual_2 method. There was no statistically constant error between the Manual_2 and the volBrain method, while there was a proportional error. The volBrain method can be said to provide similar measurements to the Manual_2 method (ICC: 0.977, CCC: 0.774). There was a statistically constant error between the Manual_2 and the MRICloud methods and no proportional error. It can be said that the MRICloud method makes a similar measurement to the Manual_2 method (ICC: 0.978, CCC: 0.879) (Table 3).

Table 2. Dice index comparison of ALVIN, MRICloud, and volBrain automated segmentation methods with 2 manual measurements

Methods	Dice value
Manual_1 vs. ALVIN	0.81
Manual_1 vs. MRICloud	0.92
Manual_1 vs. volBrain	0.88
Manual_2 vs. ALVIN	0.80
Manual_1 vs. MRICloud	0.89
Manual_1 vs. volBrain	0.85

Data reported as mean values

The Manual_1 method can be said to provide similar measurements to the Manual_2 method. The ICC agreement of the Manual_1 and Manual_2 methods was very good (0.979) with a statistically significant difference ($p<0.001$). The CCC results indicated that moderate agreement (0.959) with a precision of 0.959 was achieved. Examination of the adaptation coefficients reveals how well the methods agree with each other. The MRICloud method had the highest ICC value, or greatest agreement with the manual methods (gold standard) (Table 3).

Analysis of Bland-Altman Plots

The volume estimations for the LV were examined separately for each method. Compared to Manual_1 and Manual_2 estimates, the range estimate for the LV was MRICloud: (-7.0 to 2.0) and (-6.2 to 1.0), ALVIN: (-7.7 to 6.2) and (-7.6 to 6.0), and volBrain: (-0.6 to 8.4) and (0.5 to 7.3). Bland-Altman plots of the similarities of the automated measurements and the Manual_1 and Manual_2 gold standard measurements are provided in Figure 6.

DISCUSSION

Enlargement of the LVs is one of the most consistent findings in both schizophrenia and bipolar disorder. Ventricular volume increase is also a key sign of progression in Alzheimer's disease and mild cognitive impairment (13). In the present study, the performance of the 3 automated segmentation methods was assessed against manual segmentation data. Our findings indicated that the automated segmentation volumes of the LVs demonstrated correlation with manually traced volumes. We found that the automated methods demonstrated good agreement between them (ICC: 0.911–0.979) and compared with the gold standard (CCC: 0.739–879) ($p<0.001$). The MRICloud method CCC was superior to that of the ALVIN and volBrain methods.

Several software options are available for automatic or semi-automatic segmentation of brain structures (16) and to analyze structural properties of the human brain using MRI, such as FSL (Functional Magnetic Resonance Imaging of the Brain Analysis Group, Oxford University, Oxford, UK) (17), AFNI (Analysis of Functional NeuroImages; National Institute of Mental Health Scientific and Statistical Computing Core, Bethesda, MD, USA) (18), BrainVoyager (Brain Innovation BV, Maastricht, Netherlands) (19), FreeSurfer (Laboratory for Computational Neuroimaging, Athinoula A. Martinos Center for Biomedical

Table 3. Comparison and agreement statistics of manual and automated techniques

Parameter estimates	Passing-Bablok regression		Agreement statistics	
	β0	***β1***	**ICC**	**CCC**
Manual_1-Manual_2				
Coefficient			0.979	0.959
95% CI			0.951/0.991	0.907/0.982
Interpretation			Very good agreement	Moderate agreement
p			<0.001	0.959
Manual 1-ALVIN				
Coefficient	-0.371	0.946	0.911	0.830
95% CI	-3.476/2.856	0.742/1.141	0.794/0.962	0.649/0.922
Interpretation	No constant error	No proportional error	Very good agreement	Poor agreement
p			<0.001	0.837
Manual 1-volBrain				
Coefficient	3.942	1.011	0.958	0.739
95% CI	2.071/5.336	0.839/1.194	0.904/0.982	0.571/0.848
Interpretation	Constant error	No proportional error	Very good agreement	Poor agreement
p			<0.001	0.932
Manual 1-MRICloud				
Coefficient	1.226	1.133	0.965	0.858
95% CI	-1.277/3.364	0.943/1.292	0.919/0.985	0.728/0.929
Interpretation	No constant error	No proportional error	Very good agreement	Poor agreement
p			<0.001	0.933
Manual 2-ALVIN				
Coefficient	-2.725	1.121	0.915	0.836
95% CI	-3.940/-1.471	1.043/1.203	0.804/0.963	0.661/0.925
Interpretation	Constant error	Proportional error	Very good agreement	Poor agreement
p			<0.001	0.844
Manual 2-volBrain				
Coefficient	1.697	1.220	0.977	0.774
95% CI	0.956/2.509	1.150/1.295	0.947/0.990	0.634/0.865
Interpretation	No constant error	Proportional error	Very good agreement	Poor agreement
p			<0.001	0.970
Manual 2-MRICloud				
Coefficient	-3.612	1.087	0.978	0.879
95% CI	-5.101/-1.931	0.973/1.183	0.950/0.991	0.772/0.938
Interpretation	Constant error	No proportional error	Very good agreement	Poor agreement
p			<0.001	0.957

β0: Constant; β1: Regression coefficient; CCC: Concordance correlation coefficient; CI: Confidence interval; ICC: Intra-class correlation coefficient

Imaging, Charlestown, MA, USA) (20, 21), MRI Studio (Johns Hopkins Medical Institute Laboratory of Brain Anatomical MRI, Baltimore, MD, USA) (7) and SPM (20, 22). Several automated methods have been used to calculate LV volume (13, 23–26). Automated techniques have advantages and disadvantages. A fully automated method is reliable (16). In addition, results can be obtained quickly and easily, which may be particularly useful in clinical trials of treatments for neurological disorders (27). Furthermore, most of the automated techniques are freely available to perform more specific volume measurements. However, some structures are small, and the intensity of spatial relations is non-uniform and non-contrasted (16).

Despite the availability of several sophisticated automated and semi-automated segmentation methods, there have been relatively few published comparisons of automated segmentation and hand tracing to determine LV volume (4, 13, 23–25, 28).

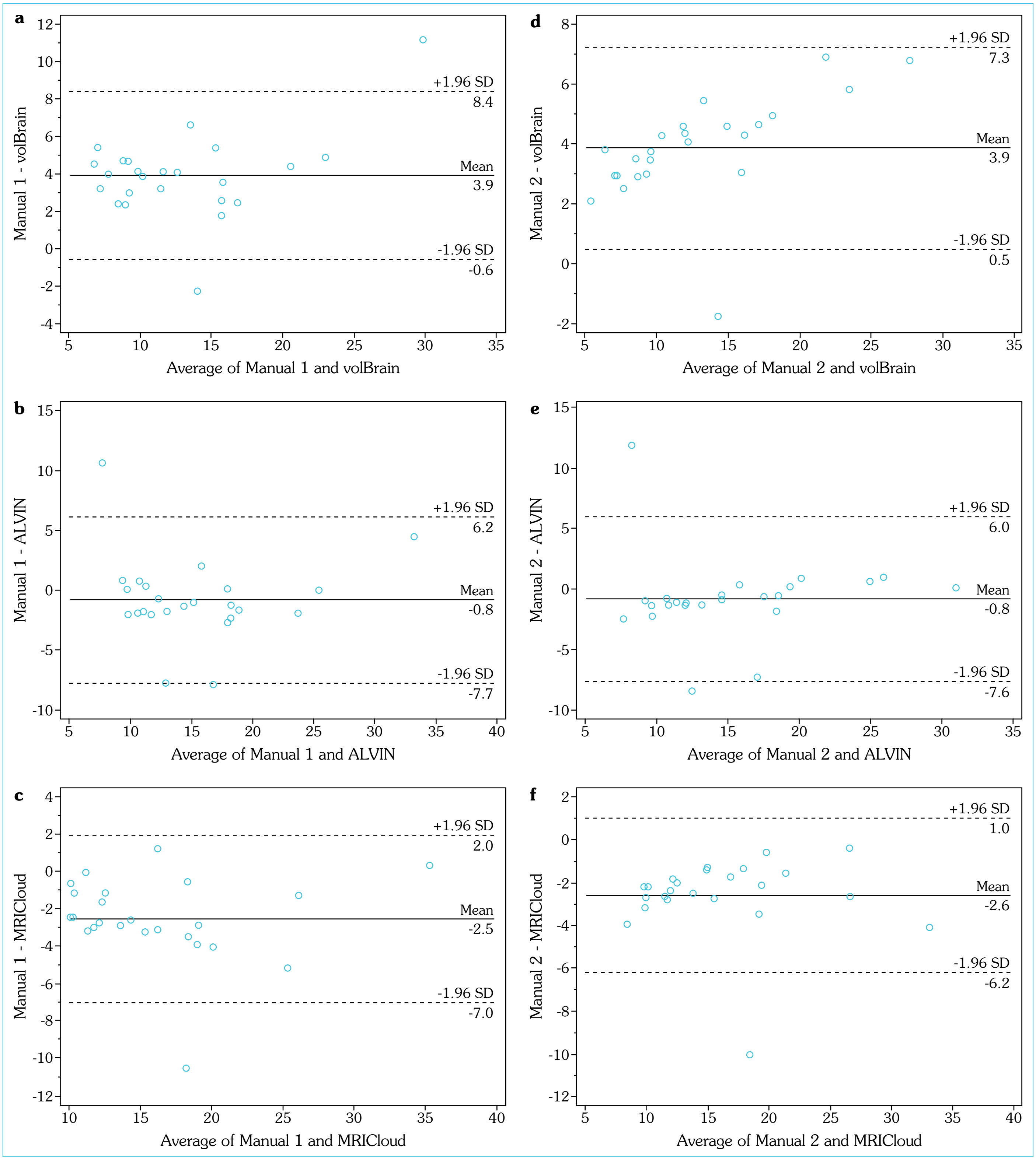

Figure 6. Lateral ventricle Bland-Altman plots of Manual_1 method and (a) volBrain, (b) ALVIN, (c) MRICloud. Bland-Altman plots of Manual_2 method and (d) volBrain, (e) ALVIN, (f) MRICloud. The mean is represented by the continuous line while the lower (-1.96×SD) and upper limits (+1.96×SD) of the agreement are represented by dashed lines

Bhalla and Mahmood (25) and Guenette et al. (23) used FreeSurfer, Wang et al. (24) used volBrain, Kempton et al. (13) used MEASURE, a PC-based software based on the Cavalieri principle (Johns Hopkins University laboratory), ALVIN, FSL FIRST (FMRIB's Integrated Registration and Segmentation Tool; Functional Magnetic Resonance Imaging of the Brain Analysis Group, Oxford University, Oxford, UK) and FreeSurfer, Kocaman et al. (4) used MRI Studio, and Rezende et al. (28) used MRICloud to measure LV volume.

Increasing the efficiency, objectivity, and reliability of automated segmentation techniques is important to quantification of the LVs. Quantitative MRI studies have revealed differences in the volume of the LV in several diseases and conditions. LV volumes have been reported to be increased with normal aging and neurological disorders, such as Alzheimer's disease, dementia, schizophrenia, and bipolar disorder (29). Bartos et al. (30) found that the most atrophied structures were the hippocampus and the amygdala, while the cornu inferior of both LVs, the other ventricles, and the choroid plexus were enlarged.

Differences in LV volume in various neurological disorders have been examined (3, 4, 13). Ertekin et al. (3) studied patients with Alzheimer's disease and a control group, and recorded LV volume measurements of 11.8 cm^3 using ALVIN and 12.3 cm^3 using ImageJ in the patient group. The agreement between the measurements of the 2 techniques was very good. The ICC and CCC demonstrated excellent agreement between the automated and manual methods. In the study performed by Kocaman et al. (4), the LV volume was 29.06±11.18 cm^3 using MRI Studio and 27.42±12.27 cm^3 using ImageJ in patients with Parkinson's disease, which also showed very good agreement (ICC 0.978). Kempton et al. (13) measured the LV volumes of young adults using ALVIN, FSL-FIRST, and FreeSurfer as well as MEASURE. The volumes recorded were: 13.32±8.0 cm^3, 20.17±8.11cm^3, 15.0±3.0 cm^3, and 15.2±7.74 cm^3, respectively. When the automated and manual methods were compared, the ICC demonstrated very good agreement.

Studies in the literature, with the exception of that conducted by Ertekin et al. (3), have reported that LV volumes measured using automated methods were higher than those volumes measured manually.

We observed good agreement with average ICC agreement values >0.9, indicating consistent and reliable volume measurements. We found that MRICloud produced the highest CCC value.

Limitations of this study include the fact that all of the participants in the sample were male. Future studies that expand the current approach to a larger sample size using both sexes would be valuable.

CONCLUSION

Automated methods are simple, rapid (except MRICloud), and reproducible methods to determine LV volume with an excellent ICC correlation in comparison with the manual tracing method. We concluded that MRICloud was the best tool, and is generally preferrable to ALVIN and volBrain for automated segmentation of the LV, based on the Dice index, ICC, and CCC agreement. Automated brain volume calculation can be a valuable, rapid radiological tool to diagnose or monitor disease status in the central nervous system. Additional research with a larger sample size and the use of multiple raters to minimize bias and increase statistical confidence will provide additional useful data.

Ethics Committee Approval: The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 21.02.2014, number: 2014/122).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – NA; Design – NA, SBG; Supervision – NA, SBG; Resource – LD, ATI; Materials – LD, ATI; Data Collection and/or Processing – LD, ATI, NA; Analysis and/or Interpretation – BK, BOK, EAY, Fİ; Literature Search – NA, BK, BOK, EAY; Writing – NA, BK, Fİ; Critical Reviews – NA, BK, BOK, EAY, Fİ, SBG, LD, ATI.

Conflict of Interest: The authors have no conflict of interest to declare.

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