Optimizing Fractional Intensity Threshold for FSL-Brain Extraction Tool (BET) and Comparing with FreeSurfer on 3D T1W MR Images

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ABSTRACT

Objective: To find out the optimal Brain Extraction Tool (BET) parameter (fractional intensity threshold) for measuring the brain volume compared with the standard manual method in our institute and to compare with those of automated FreeSurfer software

Methods: This retrospective study was performed in 10 healthy adult subjects with data of 3D-T1W on 3T MR machine. The manual gold standard brain volume measurements were done by two independent readers. The automated segmentations using BET with varied parameters and FreeSurfer software were also performed. Then, the two automated methods were compared with the manual tracing to make the optimal parameter by seeking for the highest intraclass correlation coefficient (ICC) using SPSS software.

Results: The fractional intensity threshold for whole brain volume measurement of 0.1- 0.6 showed high ICC with the manual gold standard (ranging from 0.639 to 0.748). The best value was 0.1, showing highest ICC of 0.748 ($p < 0.006$) with confidence interval of 95% equal to (0.242; 0.932). There were no optimal parameters for right and left hippocampus volume measurement by BET due to very low ICC between BET and the reader (ICC ranging from 0.017 to 0.139 and from 0.012 to 0.110, for the right and left hippocampus volume, respectively). The ICC values of the automated FreeSurfer method with the manual tracing were also very low (0.063, 0.068, and 0.063 for right, left and bilateral hippocampi respectively).

Conclusion: The optimal BET parameter (fractional intensity threshold) for automated brain volume measurement in our institute is 0.1 similar to the suggested value by prior study with high agreement (ICC=0.748) to the manual method.

Keywords: Fractional intensity threshold; MRI; BET; FreeSurfer (Siriraj Med J 2018;70: 391-396)

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with disruption of neuronal function and gradual deterioration in cognition, function and behavior.[1] It is the most common cause of dementia in the elderly[1,2] and characterized by deposition of neurofibrillary tangles and amyloid plaques.[2,3] However, it is clinically diagnosed by progressive memory loss affecting activities of daily living.[4] The presence of medial temporal lobe atrophy is considered to associate with Alzheimer's disease. As a result, the measurement of medial temporal lobe or hippocampus has been accepted to be useful in detection of the disease.[5]

A manual segmentation is generally accepted as the gold standard measurement of brain volume for atrophic changes. However, it is not practical due to being

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time-consuming. Fortunately, automated techniques have been developed to replace the conventional method. FreeSurfer is a set of powerful automated software tools for reconstruction of the brain's cortical surface from structural MRI data, including volumetric segmentation of visible brain structures, especially the hippocampus.[6] The white and grey matter is segmented by integrating information of image intensity, location and spatial relationships between subcortical structures.[7] The automated Brain Extraction Tool (BET) refers to the separation of brain and non-brain tissue technique, and is provided as part of the FSL software. The program is fast and easy to use.[8,9,10] The automated BET measurement values vary depending on the parameter called "fractional intensity threshold", ranging from 0 to 1. There was a prior study about the optimal value showing that the BET parameter of 0.1 was the best for all acquisition protocols after removing the neck slices.[11] However, due to different settings in our institute, the best value may be not the same. Therefore, the purpose of this study was to find out the optimal fractional intensity threshold used to measure the Thai brain volumes compared with the standard manual method and to compare between the two automated methods.

MATERIALS AND METHODS

Subjects

The study was part of the Siriraj Thai language paradigm for functional imaging which is approved by the Siriraj Institutional Review Board (Si 423/2011). The data for this retrospective study were retrieved from the database of the project with official permission. The subjects were excluded if they have gross brain abnormalities. Finally, a total of 10 Thai healthy volunteers (5 men and 5 women) were enrolled in this study. The mean age for all subjects was 25.5 years (ranging from 22 to 36 years). The mean ages for male and female subjects were 25 years (ranging from 23 to 29 years) and 26 years (ranging from 22 to 36 years), respectively.

Image acquisition

The examinations were performed by 3.0 T MRI scanner (Achieva, Philips Medical Systems, Best, NL) in whole brain T1-weighted axial 3D Turbo fast field echo (3D TFE) (voxel size = 1x1x1 mm , repetition time (TR) = 7.7 msec, echo time (TE) = 3.6 msec, flip angles = 8^o, TFE factor = 144, FOV = 230x290 mm, matrix = 232x288, slice thickness = 1 mm, NSA = 1).

Manual segmentations

The manual segmentations were performed by one reader, a resident in diagnostic radiology, using AW VolumeShare 2 software. The whole brain tracing was made by drawing along the outer surface of the dura using the lowest point of the medulla oblongata as the most inferior point (outlined by border of the foramen magnum). The signal threshold was visually adjusted to exclude low signal of the CSF in the ventricle and subarachnoid space whereas preserving brain parenchyma was aware. The ventricular system, the cavernous sinus, the optic nerves, the optic tracts, the optic chiasm and the pituitary gland were excluded. Then the volume of whole brain was calculated.

The hippocampal tracing was made by drawing along the outer surface of the bilateral hippocampi in coronal plane. The anterior aspect of the hippocampus was limited by tracing from the body part and only amygdala was seen on the images. The posterior aspect was limited at the last image before the visualized crus of the fornix. Only the hippocampal proper was selected and separated from the parahippocampal gyrus by an imaginary line perpendicular to the border between subiculum and entorhinal cortex.

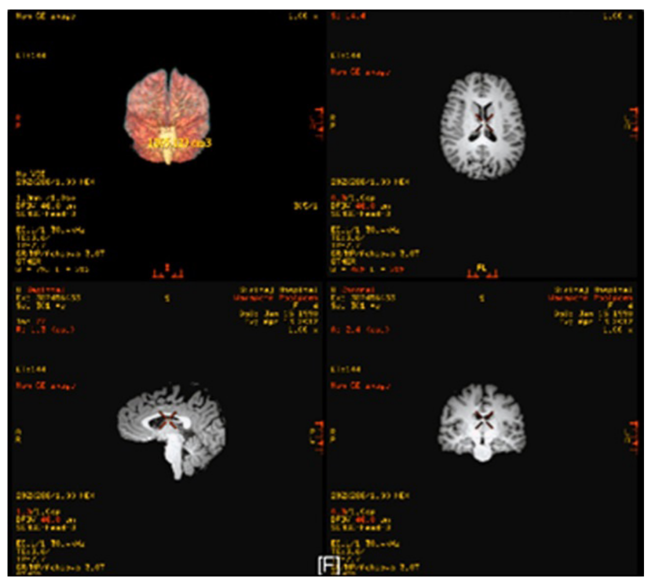

Fig 1. Manual segmentation for whole brain volume.

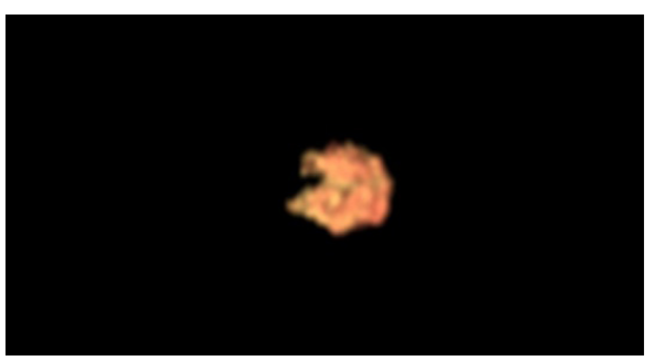

Fig 2. Manual segmentation of hippocampal volume.

Automated segmentations

The automated segmentations were performed using FSL-Brain Extraction Tool (BET) and FreeSurfer 5.0 software. The BET parameter (fractional intensity threshold) was used in different values, ranging from 0 to 1. Then, the brain volumes measured by BET at various parameters and FreeSurfer were compared with those of the manual segmentations by the reader to seek for the highest intraclass correlation coefficient (ICC) computed by SPSS software (Mahidol University license).[12,13]

RESULTS

The measurement of whole brain volume was shown in Table 1. The whole brain volumes measured by the reader ranged from 1,071.53 to 1,370.37 cm^3 ($\bar{x}$ =1,191.45 cm^3, *SD* =100.73).

The whole brain volume measurement by BET with different fractional intensity threshold and ICC of brain volume measurement between BET and the reader's manual segmentations was shown in Table 2.

According to the results in Table 2, the fractional intensity threshold between 0.1 to 0.6 showed high agreement to the manual gold standard range of the reader with the value of ICC ranging from 0.639 to 0.748. The optimal value was 0.1, indicating the highest ICC of 0.748 ($p < 0.006$) with confidence interval of 95% equal to (0.242; 0.932).

The result of measurement of the right and left hippocampus volumes by BET with different fractional intensity threshold values; and the ICC values between BET and the reader were shown in Table 3 and Table 4, respectively.

For the right hippocampus volume measurement, the fractional intensity threshold between 0 to 1 showed the low agreement with the manual gold standard (ICC ranging from 0.017 to 0.139). Similar to the left hippocampus volume measurement, the fractional intensity threshold between 0 to 1 showed the low agreement with the manual gold standard (ICC ranging from 0.012 to 0.110).

The hippocampal volume measurement by FreeSurfer software and the ICC values between FreeSufer and the reader manual tracing were shown in Table 5.

The ICC values of hippocampus volume measured by FreeSurfer and the reader show very low agreement with the manual gold standard at ICC = 0.063 (Right hippocampus) and 0.068 (Left hippocampus), respectively.

TABLE 1. The manual measurement of whole brain volume

Subjects/ Whole brain volume (cm^3)	Reader
1	1,098.80
2	1,081.33
3	1,370.37
4	1,205.12
5	1,134.70
6	1,298.24
7	1,071.53
8	1,287.47
9	1,188.34
10	1,178.60
Mean	1,191.45
Standard Deviation	100.73

TABLE 2. Whole brain volume (cm³) measured by BET at various parameters and ICC of measured volumes between BET and the reader.

Subjects/ **WB volumes	0*	0.1*	0.2*	0.3*	0.4*	0.5*	0.6*	0.7*	0.8*	0.9*	1*
1	3,169.31	1,080.51	1,070.05	1,059.11	1,053.04	1,042.87	1,030.80	1,023.06	771.29	470.00	261.57
2	2,973.92	1,013.21	1,000.55	986.77	972.50	968.01	942.88	905.77	638.17	382.56	184.13
3	3,050.44	1,312.47	1,288.89	1,270.90	1,266.69	1,262.18	1,239.85	1,166.60	715.22	467.63	277.24
4	3,297.36	1,156.56	1,135.46	1,127.00	1,108.60	1,106.54	1,111.22	1,059.41	805.77	482.54	257.42
5	1,163.12	1,169.06	1,145.61	1,134.41	1,125.75	1,122.19	1,102.81	1,036.94	752.65	418.99	230.81
6	3,061.31	1,342.73	1,315.32	1,301.61	1,292.64	1,276.98	1,275.95	1,229.25	886.09	518.02	263.08
7	3,773.39	1,260.64	1,229.79	1,193.35	1,177.77	1,165.84	1,143.98	1,117.45	869.67	559.56	322.86
8	2,916.10	1,269.01	1,220.82	1,210.47	1,197.34	1,195.34	1,175.30	1,138.99	847.91	507.36	282.39
9	2,617.09	1,175.65	1,160.65	1,153.97	1,143.20	1,141.14	1,142.32	1,083.18	765.53	446.45	237.20
10	1,298.75	1,145.57	1,099.89	1,084.09	1,079.84	1,066.68	1,049.33	1,030.00	740.76	430.36	226.83
***Reader	0.002	0.748	0.719	0.719	0.697	0.683	0.639	0.438	0.017	0.005	0.002

*BET Parameter (Fractional Intensity Threshold), **WB volumes: whole brain volumes in cm³
***ICC of measured whole brain volumes using BET at various parameters and reader's measured volumes.

TABLE 3. Right hippocampus volume (cm³) measured by BET at various parameters and ICC of measured volumes between BET and the reader.

Subjects/ ***RH volumes (cm³)	0*	0.1*	0.2*	0.3*	0.4*	0.5*	0.6*	0.7*	0.8*	0.9*	1*
1	3.600	4.613	4.956	5.096	4.646	4.735	4.847	4.765	4.952	0.928	**N/A
2	1.620	4.067	3.802	4.073	4.007	3.976	0.129	3.997	0.361	**N/A	1.202
3	3.982	0.744	4.772	5.09	5.112	5.08	4.366	4.134	4.403	3.773	**N/A
4	1.125	4.901	4.967	4.95	4.844	4.943	4.956	4.784	4.598	4.567	0.793
5	**N/A	5.562	4.792	4.535	4.716	2.691	4.531	4.762	1.201	4.102	0.908
6	5.763	3.846	5.842	7.769	**N/A	5.723	5.684	10.291	5.65	5.444	5.484
7	9.609	5.416	5.558	1.248	5.43	5.383	5.396	5.359	5.466	5.408	0.308
8	7.375	5.437	1.138	1.199	0.633	**N/A	**N/A	1.131	5.42	0.575	0.937
9	4.938	4.987	4.979	5.017	4.94	5.019	5.023	4.935	3.911	4.867	4.935
10	2.916	1.197	4.842	4.751	6.543	4.761	4.693	4.987	3.133	1.197	2.934
****Reader	0.139	0.034	0.028	0.017	0.029	0.021	0.126	0.080	0.126	0.095	0.073

*BET Parameter (Fractional Intensity Threshold), **N/A: data not available, ***RH volumes: right hippocampus volumes,****ICC of measured right hippocampus volumes using BET at various parameters and reader's measured volumes.

TABLE 4. Left hippocampus volume (cm³) measured by BET at various parameters and ICC of measured volumes between BET and the reader.

Subjects/ ***LH volumes (cm³)	0*	0.1*	0.2*	0.3*	0.4*	0.5*	0.6*	0.7*	0.8*	0.9*	1*
1.	3.938	4.358	4.354	4.473	4.394	4.366	4.366	4.457	4.166	0.841	**N/A
2.	2.419	4.329	4.265	4.325	4.379	4.310	0.154	4.294	0.286	1.433	1.106
3.	1.663	0.735	5.556	5.396	5.348	5.456	5.316	5.345	5.230	4.640	**N/A
4.	0.955	4.835	4.830	4.877	4.877	4.872	4.852	4.910	4.792	4.607	0.416
5.	**N/A	2.478	4.098	4.027	4.034	1.029	3.857	4.026	1.105	3.151	0.589
6.	5.467	2.652	5.587	11.691	8.426	5.598	5.592	11.156	5.113	5.071	5.027
7.	8.945	4.734	4.774	1.240	4.894	4.906	4.747	4.876	4.697	4.633	0.190
8.	3.343	5.250	1.050	1.052	1.125	8.863	8.207	0.722	5.060	0.689	1.201
9.	4.837	4.982	4.957	4.956	4.973	4.971	4.949	4.932	2.490	4.883	4.768
10.	4.800	1.161	4.776	4.781	6.618	4.809	4.716	4.741	2.027	1.152	1.130
****Reader	0.110	0.080	0.014	0.029	0.022	0.012	0.087	0.035	0.105	0.019	0.089

*BET Parameter (Fractional Intensity Threshold), **N/A: data not available, ***LH volumes: left hippocampus volumes, ****ICC of measured left hippocampus volumes using BET at various parameters and reader's measured volumes.

TABLE 5. Hippocampal volumes (cm³) measured by FreeSurfer and the reader with ICC values.

Subjects/ volume (cm³)	FreeSurfer: Right hippocampus	Reader 2: Right hippocampus	FreeSurfer: Left hippocampus	Reader 2: Left hippocampus	FreeSurfer: Bilateral hippocampi	Reader 2: Bilateral hippocampi
1	4.040	2.529	3.866	2.795	7.906	5.324
2	3.991	2.101	3.754	2.171	7.745	4.272
3	4.697	2.698	4.492	2.690	9.189	5.388
4	4.092	2.263	3.453	2.259	7.545	4.522
5	4.719	2.960	4.084	2.874	8.803	5.834
6	5.029	3.311	4.723	3.064	9.752	6.375
7	4.286	2.929	4.052	2.820	8.338	5.749
8	5.185	2.803	4.832	2.855	10.017	5.658
9	4.498	2.306	4.397	2.585	8.895	4.891
10	4.119	2.404	4.056	2.713	8.175	5.117
*Reader	0.063		0.068		0.063	

*ICC of measured hippocampus volumes using FreeSurfer and reader's measured volumes.

DISCUSSION

This study was initiated to adjust the optimal BET parameter called "fractional intensity threshold" which affects the estimated brain volumes[8] and to compare the two automated methods. According to the previous study about the optimal BET parameter of automated brain volume measurement in patients with multiple sclerosis, the best value for all MRI sequences after removing the neck slices was 0.1.[14] However, the study included patients who performed both 1.5 T and 3.0 T MRI studies.[14] This variety might affect the study result.[15] This study was done in the healthy adults who performed the same MRI scanner (3.0 T MRI scanner). Thereby, such variation was eliminated.

The optimal fractional intensity threshold for whole brain volume measurement in this study was 0.1 which is similar to the suggested value in the previous study.[15] However, this study could not seek optimal values for automatic hippocampus volume extraction using BET and Freesurfer since the agreements with the manual goal standard were very low. FreeSurfer was superior to BET in terms of no need to adjust parameters, although the result from this study show limited use of both BET and FreeSurfer for measuring hippocampal volume.

This exploratory study implied that in different situations, research with automated segmentation needs to be adjusted and validated with an acceptable gold standard before clinical implementation. The study also showed low agreements of the measurement implying inappropriateness for clinical practice. Further study for the solution is needed with a larger sample size and more readers. This study was limited by the small sample size and the validity of the manual gold standard measurement which depended on operators' skills, experiences and knowledge. Furthermore, it was done in only healthy subjects. The application of the study to patients with brain abnormalities especially atrophy, such as Alzheimer's disease may be questionable.

CONCLUSION

The optimal BET parameter (fractional intensity threshold) for automated whole brain volume measurement in our institute is 0.1 with high ICC value. Adjusted threshold with manual segmentation should be performed and absolute value from BET was not appropriate to use in clinical practice unless an appropriate solution is found.

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