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Original Contribution

Inter-scanner variability in Hounsfield unit measured by CT of the brain and effect on gray-to-white matter ratio

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ABSTRACT

Purpose: The density ratio of gray matter (GM) to white matter (WM) on brain computed tomography (CT) (gray-to-white matter ratio, GWR) helps predict the prognosis of comatose patients after cardiac arrest. However, Hounsfield units (HU) are not an absolute value and can change based on imaging parameters and CT scanners. We compared the density of brain GM and WM and the GWR by using images scanned with different types of CT machines.
Method: 102 patients with normal readings who were scanned using three types of CT scanners were included in the study. HU were measured at the basal ganglia level by two observers with circular regions of interest.
Result: The difference in GM was 0.98–10.30 HU and WM was 1.05–7.55 HU. The mean value of measured HU and GWR were different for each CT group. The ANOVA test showed significant difference all variables. The post hoc test for GWR, which was used to compare the differences between each scanner, was statistically significant. Interclass correlation coefficients of measured GM and WM between the two observers were very high (Cronbach's $\alpha = 0.995$ and 0.990, respectively) and GWR was showed good confidence level (0.798).
Conclusion: In this study, the HU values of GM and WM in the normal adult brain differed up to 23% among scanners. Unfortunately, the GWR may not compensate for the HU difference between GM and WM occurring between scanners. Therefore, rather than applying consistent GWR cut-offs, the protocol or manufacturer differences between imaging scanners should be considered.

1. Introduction

Predicting the prognosis of a comatose patient after cardiac arrest is important for reducing patient suffering and for economic and psychological costs. Since the 1970s, studies have analyzed the pupillary light response, the level of neuron-specific enolase (NSE), somatosensory evoked potential (SSEP), amplitude integrated electroencephalography (aEEG), and the gray matter (GM) to white matter (WM) ratio (GWR) [1]. Among these factors, GWR is a predictor used to confirm brain damage in patients following cardiac arrest and has been widely utilized [2-11]. As a result of these studies, the American Heart Association (AHA) guideline of 2015 reported a normal GWR of 1.3 and that a low GWR in patients who have not received target temperature management (TTM) can predict a poor neurologic outcome [1].

Brain damage in a comatose patient after cardiac arrest is directly related to neurologic outcome. In the initial step of damage, brain swelling or edema occurs, and the reduction of GM and WM differentiation appears specifically [12-18]. We can measure GM and WM using Hounsfield units (HU) through computed tomography (CT). However, recent research has reported that other types of CT scanners showed greater variability [10]. Inter-imager variability of analog to digital converter (ADC) measurements for human brain magnetic resonance imaging (MRI) has been proven [19]. Additionally, radiologists have demonstrated that it is important to consider the imaging scanner's protocol or machine variability in these studies [20]. Therefore, there is contradiction in applying a standard measurement of the GWR by different CT scanners in predicting the prognosis of comatose patients uniformly. Based on existing research, there are no reports on the differences in CT scanners and how they affect the GWR. Therefore, we measured the HU of CT images of normal adults taken by three different types of CT instruments and analyzed the difference between GM and WM, as well as the effect of inter-scanner variability on the GWR.

2. Method

2.1. Patients selection

Since 2008, we have used three types of CT scanners (A - Somatom Definition Flash; Siemens Healthcare, Germany, B - Lightspeed VCT; GE Healthcare, UK, and C - Discovery CT750 HD; GE Healthcare, UK). The parameters of each CT were the same in voltage and thickness but

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Table 1
Acquisition parameters for each CT scanner.

Scanner	Manufacturer	Channel	Current (mA)	Voltage (kV)	Slice thickness (mm)
Somatom Definition	Siemens	128	270[a]	100	5
Lightspeed VCT	GE	64	240	120	5
Discovery CT750 HD	GE	256	200	120	5

[a] Tube current was controlled automatically.

different in current (Table 1). Patients were randomly selected. We selected 102 patients in total, with three equal groups of 34 patients. Each of these 3 groups represented individuals who had received their brain CT from one of the three unique CT machines that were investigated. There were 34 individuals recruited into the study for each of the three CT scanners investigated. The selected patients were examined for headaches, simple trauma, and medical examination (Table 2). The images were read as normal finding by radiologists, and the researchers reviewed the images once again to ensure that they were normal. Age and gender were assigned uniformly for each CT group. This study was reviewed and approved by the ethics committee of our hospital (SC17RESI0084).

2.2. Density measurements of GM and WM

The images were only measured in non-contrast brain CT. Two investigators, who are board certified in emergency medicine (8 yr and 2 yr), were trained by the radiologist and measured each patient's image. The age, sex, history, and reason for CT were blinded to the investigator. Basal ganglia (BG) level axial images of the brain CT were selected for color mapping. The color-mapping method is useful for HU and is expressed in color to allow the observer to distinguish between GM and WM to identify the anatomy. Thereafter, the caudate nucleus (CN) site, putamen (PU), corpus callosum (CC) and the anterior site of the posterior internal capsule (PIC) are divided into three sections (Fig. 1). In each section, by using the region of interest (ROI), HU measures the highest region in the GM (CN, PU) and the lowest region in the WM (PIC, CC). The ROI measures the range of the circle (0.1 cm^2), and both sides are measured in the same way. The average of six measurements in each site (CN, PU, PIC, CC) was defined as the HU of the site, respectively. The measurements of the two observers were blinded to each other.

Table 2
Baseline characteristics of the patients and reason for CT for patients in each group

	A (n = 34)	B (n = 34)	C (n = 34)	p
Age, years, mean ± SD	51.6 ± 14.6	50.7 ± 14.6	51.6 ± 15.8	0.964
Male, N (%)	15 (44.1)	18 (52.9)	16 (47.1)	0.760
Underlying disease, N (%)				
Hypertension	9 (26.5)	7 (20.6)	12 (35.3)	0.392
Diabetes	5 (14.7)	1 (2.9%)	2 (5.9)	0.171
CAD	2 (5.9)	1 (2.9)	0 (0)	0.357
Liver disease	1 (2.9)	1 (2.9)	4 (11.8)	0.203
Pulmonary disease	1 (2.9)	1 (2.9)	0 (0)	0.600
Reason for CT, N (%)				
Headache	24 (70.6)	18 (52.9)	16 (47.1)	0.125
Simple trauma	8 (23.5)	11 (32.4)	11 (32.4)	0.654
Medical examination	2 (5.9)	5 (14.7)	7 (20.6)	0.207

Patients with previous stroke history or congenital abnormality were not selected. None of the selected patients had renal disease.
A; Somatom Definition, B; Lightspeed VCT, C; Discovery CT750 HD.
SD; standard deviation, CAD; coronary artery disease, CT; computed tomography.

2.3. Statistical analysis

The mean of the HU values measured by two observers was used for statistical analysis. We tested distributions of continuous variables (measured HU and GWR) with Sapiro-Wilk test. All variables showed normal distribution according to the normality test. The one-way ANOVA and Tukey's test were used for analysis between three groups. As a result of the analysis, a p value of <0.05 was considered statistically significant. Interclass correlation coefficients (ICCs) were used to analyze agreement between the two observers. Statistical analysis was performed using SPSS (IBM SPSS Statistics ver. 18.0 for Windows).

3. Results

The mean value of measured HU and GWR were different for each CT group. The ANOVA test showed significant difference (Table 3). The GM attenuation (average of CN and PU) and WM attenuation (average of PIC and CC) were significant different. Specifically, box plot comparison showed that the differences between the scanner A group and B and C groups were substantial (Fig. 2). There was an obvious difference between scanners among the various manufacturers. The box plot comparison of GWR showed a clear difference (Fig. 3).

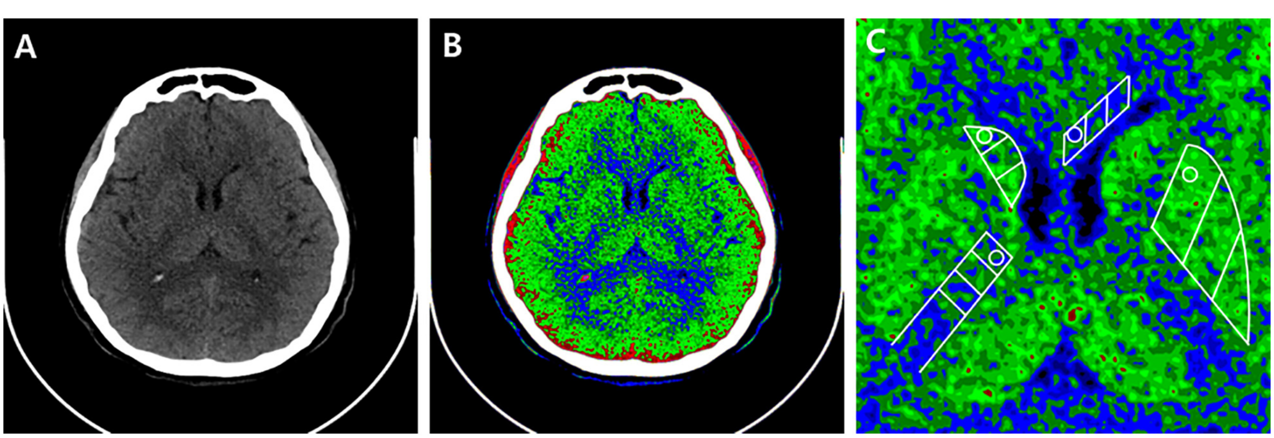

Fig. 1. Brain CT image of Basal ganglia level. A-original image B-color mapping image C-density measurement using ROI (0.1 cm^2).

Table 3
Comparison of GM, WM, GWR by imager group.

Imager	A (Somatom) (N = 34)	B (Light speed) (N = 34)	C (Discovery) (N = 34)	p-Value[a]
CN	43.49 ± 0.96	32.79 ± 0.91	34.00 ± 1.14	<0.001
PU	43.50 ± 0.77	33.60 ± 0.70	34.35 ± 0.90	<0.001
PIC	33.02 ± 0.72	25.21 ± 0.64	26.25 ± 0.85	<0.001
CC	33.20 ± 1.05	24.90 ± 0.80	25.96 ± 1.19	<0.001
GM[b]	43.50 ± 0.80	33.20 ± 0.74	34.18 ± 0.97	<0.001
WM[b]	32.61 ± 0.75	25.06 ± 0.60	26.11 ± 0.93	<0.001
CN/PIC	1.317 ± 0.028	1.301 ± 0.036	1.296 ± 0.040	0.038
PU/PIC	1.317 ± 0.023	1.333 ± 0.033	1.309 ± 0.036	0.007
CN/CC	1.351 ± 0.292	1.317 ± 0.035	1.311 ± 0.040	<0.001
PU/CC	1.352 ± 0.034	1.350 ± 0.038	1.325 ± 0.043	0.007
BG-GWR	1.334 ± 0.017	1.325 ± 0.025	1.310 ± 0.030	<0.001

CN/PIC; CN to PIC ratio, PU/PIC; PU to PIC ratio, CN/CC; CN to CC ratio, PU/CC PU to CC ratio, BG-GWR; GM to WM ratio.
[a] Statistical significances were tested by ANOVA test.
[b] GM: average of CN and PU; WM: average of PIC and CC.

The Tukey's test, which was used to compare the differences between each scanner, was statistically significant (Fig. 4). A and C groups differed in all ratio values except for PU/PIC (CN/PIC; p-value 0.036, CN/CC; p-value < 0.001, PU/CC; p-value 0.013, BG-GWR; p-value < 0.001). There was a significant difference between A and B group only in CN/CC, B and C group in PU/PIC and BG-GWR (CN/CC; p-value < 0.001, PU/PIC; p-value 0.005, BG-GWR; p-value 0.032).

The ICCs test was used to determine the inter-rater reliability between the two observers; Cronbach's α showed a high confidence level of GM and WM (0.995 and 0.990) and ICCs value of the BG-GWR was good (0.798).

4. Discussion

This study was designed to investigate the differences in results that can occur when using with different scanner. Because the HU values are different when the CT scanner is different, it would not be possible to set a fixed reference. Previously, there have been many studies on GWR, but no studies have considered this difference. As the results of this study, the difference between the manufacturers as we thought showed a clear difference in attenuation and we concluded that the GWR could not fully compensate for these differences.

By using recent research on extracorporeal membrane oxygenation, in a commentary on the analysis by Lee et al. of the GWR of patients with successful cardiac arrest resuscitation, Chen commented on several considerations [6, 20]. One comment was that the HU value can change due to variations in CT scanners and imaging parameters.

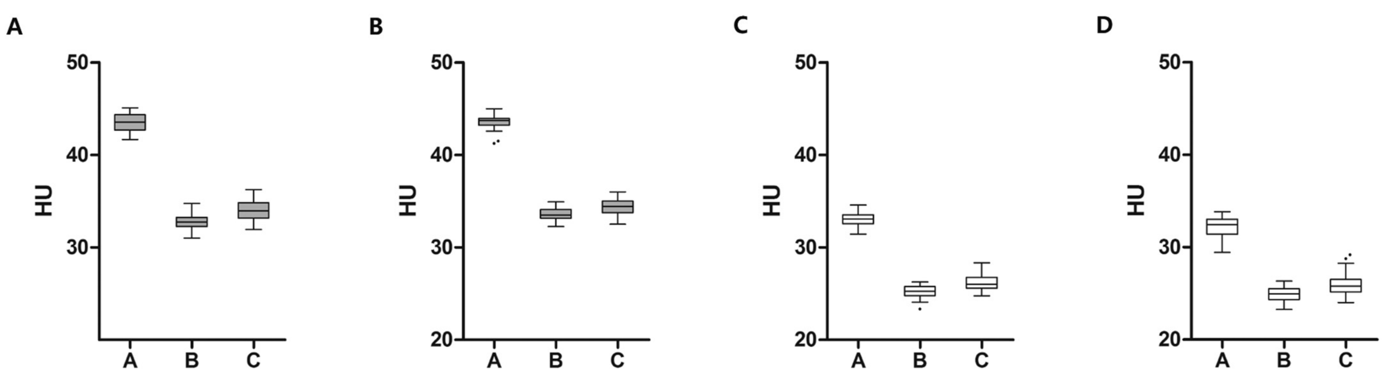

Fig. 2. Box-plot showing the comparison of GM and WM between each CT group. A: Caudate neucleus; B: Putamen; C: Posterior internal capsule; D: corpus callosum (gray box-GM, white box-WM).

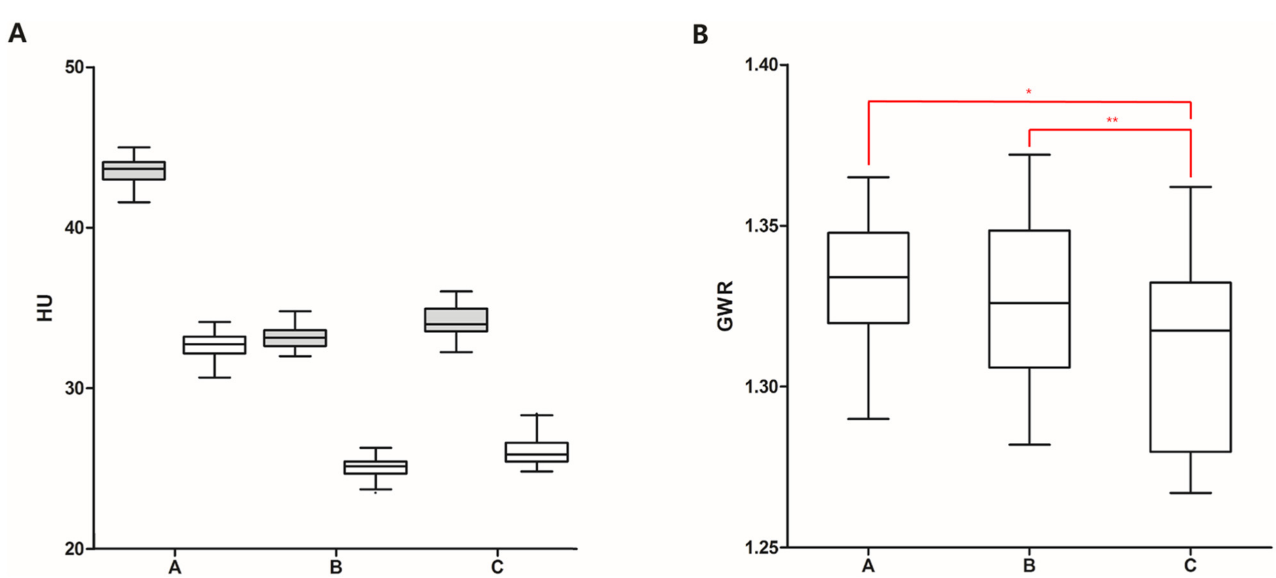

Fig. 3. Box-plot showing the comparison of GWR between each CT group. A: average of GM (CN, PU) and WM (PIC, CC) (gray box-GM, white box-WM); B: box plot of GWR. * Significant difference between imager groups based on Tukey test (A vs. C, p-value < 0.001) ** Significant difference between imager groups based on Tukey test (B vs. C, p-value < 0.032).

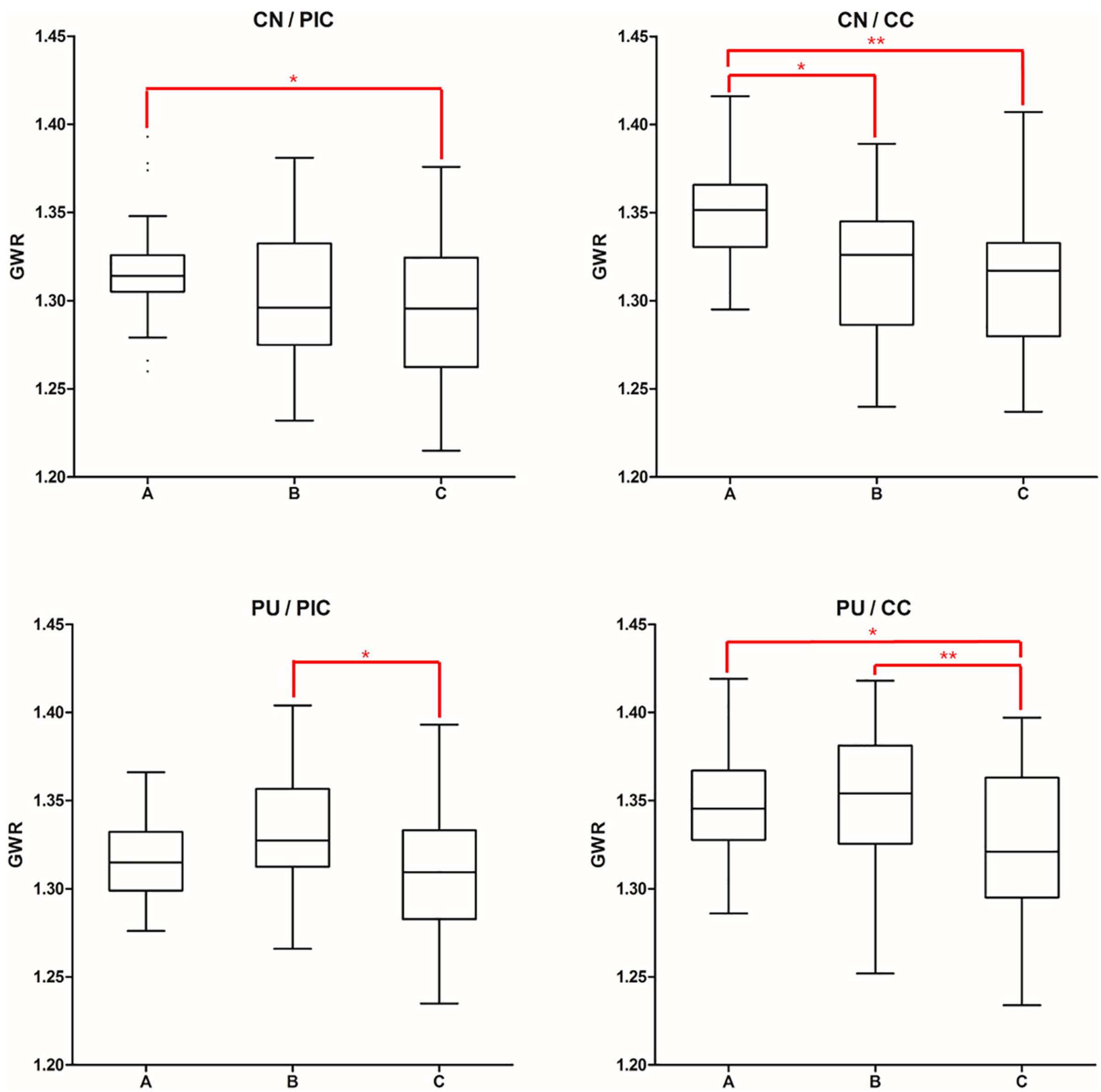

Fig. 4. Box-plot showing the comparison of GWR on each site and post hoc test. * Significant difference between imager groups based on Tukey test.

Specifically, the attenuation coefficient of the CT scanner is dependent on X-ray tube voltage (kVp); therefore, a significant change can appear in different kVps [21]. In a recent study, Gentsch et al. devised a simplified method for measuring the GWR in 111 post-cardiac arrest patients and reported a neurological outcome [10]. In the study, the authors mentioned that the three types of CT scanners used resulted in variability. Other studies have used multi-center studies or two or more scanners but have not analyzed the effects of imaging parameters [5, 8]. Our findings show that measured HU in GM and WM differ by up to 23% between CT scanners. In addition, GWR showed significant differences in the ANOVA test, and Tukey's post hoc test showed a significant difference in the CT group of A or B and C. The results of our study differ from those of the control group (normal patients) in the study by Torbey et al. (the GWR of the control group in the BG = 1.45) [3]. Therefore, future studies on the GWR should consider CT scanner variability and imaging parameters.

Many previous studies using HU of GM and WM as an indicator have emphasized their significance. It is important to minimize the variability of the method and perform a comparison analysis for accuracy. There were various types of measurement methods but the most commonly used was measuring a circle with a width of 0.1 cm^2 GM (putamen, caudate nucleus, medial cortex of the frontoparietal area, and medial cortex of the frontoparietal area) and WM (posterior internal capsule, corpus callosum and frontoparietal area). Torbey et al. analyzed the GWR of a post-cardiac arrest and comatose patient for the first time [3]. They reported that death could be predicted at a GWR (CN/PIC) <1.18 measured at the BG level. Choi et al. used a method similar to that of the previous study, but only anterior halves of the posterior internal capsule were measured [11]. This is because there are focal low-attenuating lesions in 60% of normal patients which are ill defined, bilaterally symmetrical, and approximately 5 mm in diameter in the posterior half of the posterior internal capsule [22]. Therefore, our study also conducted measurements using this method.

The analysis was based on ROI, which is the value of the measured site that represents the total value of the area. However, ROI value changes in value by measuring slightly beside the area. To overcome the limitation, a color-mapping method was devised. In fact, the CN and PIC are not homogeneous, as shown in the color-mapped image in Fig. 1. Therefore, measuring the ROI in a single area is not appropriate. The values of three sections in each region were measured, and the total of six left and right values were measured where the average value was measured as a representative value. ICC analysis of the two observers was performed to evaluate the reproducibility of the measurement method designed. All three scanner groups showed above excellent agreement. However, the ICC of the GWR is lower than measured value because it is estimated the agreement of the calculated results.

Our research has some limitations. First, the quality of data collection was limited because of the retrospective design of the study. The current set ups for three types of CT scanners were not the same. Second, the current study did not use a CT scanner only for the same patient at the same time. In fact, various factors can affect the GWR. According to Chen et al., aging and timing can also affect the GWR [20]. However, these types of studies using CT should always consider radiation hazards. Therefore, ethic problems may occur if humans or animals are subjects. Third, the research subjects were restricted to normal adults. The significance of the GWR is an early prognostic parameter for the outcome of post-cardiac arrest patients. Therefore, an investigation of comatose patients who have survived cardiac arrest will be required in future studies.

5. Conclusion

Our study confirmed different measured HU values and GWR in normal adult brain CT image in different CT scanners. Especially, GWR may not fully compensate for differences in measured values between scanners. Therefore, to apply the GWR to prediction prognosis of a comatose patient after cardiac arrest, it will be important to consider the differences in protocols and manufacturers among imaging.

Conflicts of interest

The authors have no competing interests to declare.

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