Effectiveness of low-tube current for reducing radiation dose in cerebral CT perfusion

Type
Research paper

Keywords
CT perfusion, image quality, radiation dose, Low-tube current, Iodine delivery rate

Abstract

Introduction
Objective: This study aims to investigate the reduction of radiation dose in cerebral CT perfusion by lower low-tube current.

Material and methods
Two hundred patients, who underwent cerebral non-contrast computed tomography (CT) and CT perfusion, were randomized into four groups according to tube current and contrast media (CM) concentration: group A (60 mAs, 320 mgI/ml), group B (60 mAs, 370 mgI/ml), group C (100 mAs, 320 mgI/ml), and group D (100 mAs, 370 mgI/ml). Among these four groups, the CT dose index (CTDvol), dose length product (DLP) and effective dose (ED) was calculated. The quantitative image comparison included maximum enhancement, noise, signal-to-noise ratio (SNR), cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT) from five regions of interests (ROIs).

Results
Ranging from 100 mAs to 60 mAs, groups A and B achieved 40% lower CTDIvol, DLP and ED, when compared with groups C and D. Both the maximum enhancement and noise of all ROIs were higher in groups A and B, when compared to groups C and D (P<0.05). The CBV values were higher in groups B and D, when compared to groups A and C (P<0.05). The image quality (IQ) of each group of perfusion maps met the requirements for imaging diagnosis.

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The reduction in tube current from 100 mAs to 60 mAs for cerebral CT perfusion led to a 40% reduction in radiation dose without sacrificing image quality.
Effectiveness of low-tube current for reducing radiation dose in cerebral CT perfusion

Running title: Low-tube current for CT

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Abstract

**Objective:** This study aims to investigate the reduction of radiation dose in cerebral CT perfusion by lower low-tube current. **Methods:** Two hundred patients, who underwent cerebral non-contrast computed tomography (CT) and CT perfusion, were randomized into four groups according to tube current and contrast media (CM) concentration: group A (60 mAs, 320 mgI/ml), group B (60 mAs, 370 mgI/ml), group C (100 mAs, 320 mgI/ml), and group D (100 mAs, 370 mgI/ml). Among these four groups, the CT dose index (CTDIvol), dose length product (DLP) and effective dose (ED) was calculated. The quantitative image comparison included maximum enhancement, noise, signal-to-noise ratio (SNR), cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT) from five regions of interests (ROIs). **Results:** Ranging from 100 mAs to 60 mAs, groups A and B achieved 40% lower CTDIvol, DLP and ED, when compared with groups C and D. Both the maximum enhancement and noise of all ROIs were higher in groups A and B, when compared to groups C and D ($P<0.05$). The CBV values were higher in groups B and D, when compared to groups A and C ($P<0.05$). The image quality (IQ) of each group of perfusion maps met the requirements for imaging diagnosis. **Conclusion:** The reduction in tube current from 100 mAs to 60 mAs for cerebral CT perfusion led to a 40% reduction in radiation dose without sacrificing image quality. **Keyword:** CT perfusion; Low-tube current; Radiation dose; Image quality; Iodine delivery rate
Introduction

Cerebral computed tomography perfusion (CTP) is a widely used and highly accurate imaging method for detecting ischemic lesions in acute stroke. CTP can distinguish the infarct core from penumbra brain tissues, and aid in the decision to use thrombolytic therapy [1-3]. However, the high radiation dose (RD) accompanying CTP remains a major concern for this technique [4]. Reducing the risk of radiation exposure has always been the goal of imaging studies. In modern computed tomography (CT), low tube voltage scanning has been commonly used as a strategy for dose reduction. Iodine attenuation is higher at low kilovolt peak (kVp). Therefore, the signal-to-noise ratio (SNR) can be kept constant with reduced radiation exposure. The greatest potential of a low kVp for reducing exposure is mainly limited to high iodine-enhancing examinations, such as CT angiography or arterial phase imaging [5].

An alternative approach for reducing the RD in CT is to reduce the tube current, since this current is linear with RD. However, as the tube current decreases, the image noise would inevitably increase, potentially jeopardizing the correct diagnosis. Therefore, it is important to determine whether the increased signal from the higher attenuation of iodine under lower tube current conditions could compensate for the increased noise in low-dose CTP scans, and thereby maintain image quality (IQ).

At present, iodinated contrast media (CM) at different concentrations are commercially available for daily CT vascular examinations. The clinical goal of CM administration and CT scan timing is to achieve a diagnostically adequate contrast enhancement in a target organ at the lowest radiation exposure (the shortest scan duration) and injected iodine mass (iodine load) acceptable for a given patient’s cardiovascular and renal function [6]. Previous studies have demonstrated that arterial enhancement is directly affected by the iodine delivery rate (IDR). Even with modern CT and the
assistance of iterative reconstruction, increasing the IDR favors higher quality images [7].

Therefore, the present study was conducted to investigate the feasibility of maintaining the image quality of CTP and further reducing the RD by lower mAs in an already low kVp setting, using different concentrations of CM, and a fixed IDR and iodine load.

Materials and Methods

The prospective study was approved by the ethics committee of a local institutional review board. An informed consent was obtained from all patients.

Study population

A total of 200 consecutive patients, who underwent non-contrast CT and CTP between June 2016 and September 2017, were prospectively enrolled. Inclusion criteria: (1) patients suspected with acute ischemic stroke (AIS) and referred for non-contrast CT and CTP; (2) patients who were at least 18 years old. Exclusion criteria: (1) patients with non-contrast CT showing cerebral hemorrhage; (2) patients who suffered from a disease and cannot undergo a contrast-enhanced CT examination (such as thyrotoxicosis, severe renal insufficiency, allergies or severe congestive heart failure [III-IV], etc.); (3) patients with insufficient peripheral vein conditions that do not allow for the injection of a CM at the protocol flow rate; (4) patients with a body mass index (BMI) greater than 28 [8,9]; (5) patients with a CTP showing cerebral ischemia or infarction occurring in the bilateral cerebral hemispheres; (6) patients accompanied by a disease that significantly affects the cerebral blood flow pattern (such as aneurysms, arteriovenous malformations, dural arteriovenous fistulas, etc.); (7) patients with significant motion artifacts during the CTP scan, resulting in the inability to perform an image analysis.
CTP acquisition and dataset reconstruction

All examinations were performed on a 256-slice multi-detector CT scanner (Philips Brilliance iCT; Philips Healthcare, Cleveland, OH, USA). The CTP protocol was as follows: FOV, 20 cm; matrix, 512 × 512; scan range, 8 cm from the sella floor to the high vertex. The CTP scan was initiated at five seconds after the CM bolus, and a total of 40 scans were acquired with a fixed temporal resolution of 1.5 seconds in both the arterial and venous phases, resulting in an overall scan duration of 60 seconds.

Patients were randomly assigned into four groups, according to different tube currents and CMs with different iodine concentrations. There were 50 patients in each group. In groups A and B, the CTP scan was performed with a low tube current of 60 mAs to reduce the RD. Patients in groups C and D were scanned with a conventional tube current of 100 mAs. Ioversol of 320 mgI/ml (Hengrui Pharmaceuticals, Jiangsu, China) was used for groups A and C, while iopamidol of 370 mgI/ml (Braccosine pharmaceuticals, Shanghai, China) was used for groups B and D. The CM was injected through the right cubital vein with the same IDR, total iodine load and injection time for each group, followed by a 30-ml saline flush at the same flow rate used for the CM injection. The grouping method and injection parameters are listed in Table 1.

Image post-processing

The CTP source images were automatically reconstructed into a 5-mm thick CTP source image using iterative reconstruction technology. The iDose4 level3 was chosen for all groups to reduce the image noise and compensate for the decreased SNR of the reconstructed image due to the RD reduction. Then, the source images were post-processed using the Philips workstation's Brain perfusion software, employing a deconvolution algorithm to obtain perfusion parameter maps of the cerebral blood
volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT). The software automatically selects the arterial input function from the anterior cerebral artery and selects the venous output function in the superior sagittal sinus.

**Measurement of radiation exposure**

The volume CT dose index (CTDIvol, unit in mGy) and dose length product (DLP, unit in mGy×cm) were extracted from the individual patient protocol record. The effective dose (ED, unit in millisieverts) was estimated by multiplying DLP by a region-specific conversion coefficient of 0.0023 mSv/(mGy×cm) [10].

**Quantitative image analysis**

In order to analyze the IQ of the CTP source images, SNRs from five regions of interest (ROIs), which were selected at the basal ganglia level placed at the non-ischemic hemisphere of the temporal maximum intensity projection (tMIP), were calculated. The SNR was calculated using the following equation: SNR = mean of the maximum enhancement / noise (standard deviation). These five ROIs were in the frontal white matter, head of the caudate nucleus, lentiform nucleus, thalamus, and occipital white matter. The tMIP was derived from the CTP source images, which displays the maximum tissue enhancement in Hounsfield units for each pixel based on the time-attenuation curve (TAC). The mean of the maximum enhancement and noise from all pixels were measured within each ROI. The mean of each perfusion parameter was measured for the CBV, CBF and MTT maps, respectively, and the five ROIs were consistent with the tMIP. The methods used to achieve the quantitative parameters are presented in Figure 1.

**Qualitative image analysis**
The qualitative perfusion image analysis was independently performed by two radiologists with 12 and five years of experience in neurovascular imaging. The overall diagnostic image quality for the perfusion maps were rated using a 5-point scale for each patient (1 = unacceptable/non-diagnostic; 2 = poor, diagnostic confidence significantly reduced; 3 = moderate, but sufficient for diagnosis; 4 = good; 5 = excellent) [11]. Before the start of the assessment, the readers were instructed on the criteria for image grading, and together, they assessed 10 test cases that were not included in the study.

**Statistical analysis**

The software program SPSS 17.0 (IBM, Chicago, USA) was used to conduct the statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD). Discontinuous variables were expressed in percentage (%). For multiple comparisons, each value was compared by one-way ANOVA after the Dunnett’s test, with each datum conforming to the normal distribution, while non-normally distributed continuous data were compared using non-parametric tests. The counting data were tested by chi-square test. The comparison of age, body mass index and various RD parameters was analyzed by one-way ANOVA. The analysis of variance of factorial design was used to evaluate the statistical differences between the main effects of RD and CM iodine concentrations, and the interaction of these two factors for the mean of maximum enhancement, noise, SNR, and each perfusion parameter (CBV, CBF and MTT) among the four groups. The Kruskal-Wallis test was used to compare the statistical differences between the qualitative assessment results in each group, and kappa analysis was used to evaluate the consistency between the two radiologists. A Kappa value higher than 0.75 was regarded as consistent, a value within 0.40-0.75 was regarded as fair, and a value of <0.40 was regarded as poor. $P<0.05$ was considered statistically significant.
Results

Patient demographics

A total of 290 patients underwent non-contrast CT and CTP for eligibility in the trial. Among these patients, 90 patients were excluded, while the remaining 200 patients (132 males and 68 females; age range: 49-81 years old, mean age: 62.5 years old) were included in the final analysis. The eligibility of these patients is summarized in Figure 2. The detailed characteristics of the patient population are presented in Table 1. There was no significant difference in age, gender and body mass index among the four groups ($P>0.05$).

Radiation dose

The RD represented by CTDIvol, DLP and ED in groups A and B were 40% lower, when compared to groups C and D (96 mGy, 768 mGy/cm and 1.77 mSv vs. 160 mGy, 1,280 mGy/cm and 2.94 mSv). The dose parameters are summarized in Table 1.

Quantitative image analysis

There was no significant difference in SNR among all groups. The main effects of the RD and CM iodine concentrations, and the interactions were not statistically significant, in terms of the differences in SNR values in all ROIs for each group. The maximum enhancement of all ROIs on the tMIP images in groups A and B were higher than those in groups C and D, demonstrating a significant RD main effect ($P<0.01$, for all ROIs). The image noise of all ROIs were lower in groups A and B, when compared to groups C and D, demonstrating a significant RD main effect ($P<0.01$, for ROI1 and ROI5; $P<0.05$, for ROI2, ROI3 and ROI4). In the frontal white matter only, the maximum enhancement and noise in groups A and C with low iodine concentrations of CM were
significantly higher than those in groups B and D, demonstrating the significant main effect of CM iodine concentration ($P<0.05$). The interaction of RD and CM iodine concentrations exhibited no statistical differences, in terms of maximum enhancement and noise among all ROIs in the four groups.

In comparing the perfusion parameters, the CBV values for all ROIs in groups B and D with high iodine concentrations were significantly higher than those in groups A and C, demonstrating the significant effect of CM iodine concentration ($P<0.05$). The CBF values in the caudate nucleus head (ROI2) in groups A and B were higher than the values in groups C and D, showing a significant RD effect ($P<0.05$). No other ROI exhibited such an effect. Furthermore, the main effects of the RD and CM iodine concentrations, and the interactions were not statistically significant, in terms of the differences in MTT values in all ROIs from each group. The detailed results for maximum enhancement, SNR, CBV, CBF and MTT for the five ROIs in the four groups are summarized in Tables 2-5.

**Qualitative image analysis**

There were no statistical differences in the qualitative image evaluation among the four groups for any of the perfusion image sets, demonstrating that the IQ from each group of perfusion maps met the requirements for imaging diagnosis. In terms of the consistency analysis, the Kappa values for the CBV in groups B and C were fair (0.742 and 0.746, respectively), while for groups A and D, these values, as well as the CBF and MTT in each group, were all consistent (Kappa value: 0.753-0.811). The results of the IQ assessment undertaken by the two radiologists for each group are presented in Figures 3-4.
Discussion

To the best of our knowledge, the present study is the first to use a factorial design analysis to explore the effects of the simultaneous reduction of tube current and CM iodine concentration on the IQ of CTP source images and perfusion maps [12,13]. Previously, a set of studies have shown that the IQ of CTP significantly decreased when the tube current dropped to 50 mAs or lower [14,15]. Therefore, the lower tube current was reduced to 60 mAs in the present study to ensure an acceptable image quality. König et al. [16] compared the IQ of the CTP obtained with an iodine concentration of 300 mg I/ml and 400 mg I/ml, and the same injection rates between groups. The results revealed that higher IDR resulted in a significantly higher maximum enhancement, and a higher iodine concentration was beneficial for increasing the contrast between the gray and white matter in the perfusion images. However, when the same IDR and total iodine load was fixed among the groups, the contrast enhancement of different concentrations of CM tended to be consistent in the angiographies [17,18], while evidence showing such effects on the perfusion imaging datasets is rare. In the present study, two CMs with different iodine concentrations (320 mgI/ml vs. 370 mgI/ml) were selected to determine the potential effects of CM concentrations on CTPs with a constant IDR and under low-tube current scanning. These results revealed that higher concentrations led to higher CBV values in the perfusion maps.

In the present study, both maximum enhancement and noise increased on the tMIP image in groups A and B, and these exhibited a significant RD main effect, while the SNR was not significantly affected by the changes in RD. Previous studies have also revealed that a decrease in the X-ray penetration ability caused by reduced RD can significantly increase the maximum enhancement in the CTP source image [14,15,19,20]. The reason for the increase in maximum enhancement in these cases was that the tube
current was lower, while it remains unclear whether the other conditions were constant. The most likely cause is that when the tube current dropped to a certain extent, the Philips scanner automatically adjusted the KV-spectrum to ensure that the IQ of the original image would be acceptable.

Since the present study used a constant IDR when injecting the CM, theoretically, the contrast concentration in brain tissues should not be significantly different. Therefore, the difference in CM iodine concentration has no significant main effect on the tMIP images. In the present study, the SNR was not significantly affected by the changes in RD, indicating that the decrease in RD causes an increase in image noise, and increases the maximum enhancement. Therefore, the SNR is kept relatively stable. This also confirms the feasibility of further reducing RD, while maintaining a diagnostically acceptable image quality.

It is noteworthy that based on the findings from the perfusion parameters, although the IDR was adjusted to be the same, a higher CM concentration led to a significantly higher CBV value. However, there was no significant difference in the results for CBF and MTT. This may be due to the fact that the CBV value was calculated as the area under the time attenuation curves in a parenchymal region, divided by the arterial area under the TAC. Regardless of the fixed IDR used, there is still a significant difference in the morphology of TAC for the first pass of CM with different iodine concentrations [5, 21]. When AIS occurs, the CBV becomes a key parameter that distinguishes between the cerebral infarction core and ischemic penumbra [22-24]. Therefore, it is still prudent to use a CM with low iodine concentration in the CTP. Furthermore, in the case of the same IDR, compared with the low iodine concentration, the use of a CM with high iodine concentration can reduce the rate of bolus injection. This would be beneficial for patient comfort, and reduce the risk of extravasation [25-27].
There were several limitations in the present study. First, merely the image quality for different combinations of tube current and CM iodine concentration on the CTP in normal brain tissue was evaluated. Hence, the ischemic and infarcted tissue remains unknown, and should be further researched. Second, the present study shows that the alteration in CM iodine concentration changes the CBV in normal brain tissue, and the apparent decrease in CBV is a vital parameter for identifying cerebral ischemia and infarction. Therefore, further research is needed to assess the impact of different combinations of RD and CM concentration on CTP, image quality, and even the diagnosis for ischemic and infarcted brain tissues. Third, the present study was only single-center trial, and the sample size was limited. Fourth, the present study only investigated patients with acute ischemic stroke, and there was insufficient data on patients with other diseases. The value of CT perfusion by lower low-tube current on different disease remains unknown, and should be further researched in the future.

**Conclusion**

The reduction in tube current from 100 mAs to 60 mAs for cerebral CT perfusion leads to a 40% reduction in radiation dose without sacrificing image quality.
References:

1. Tan J, Aysenne A, Singh V. Thrombolysis in real time: Demonstration of revascularization with intravenous thrombolysis therapy in the CT scanner. J Neuroimaging 2017;27:50-8.

2. Tsogkas I, Knauth M, Schregel K, et al. Added value of CT perfusion compared to CT angiography in predicting clinical outcomes of stroke patients treated with mechanical thrombectomy. Eur Radiol 2016;26:4213-9.

3. Vanninen R, Putaala J, Bode M, Nyman M, Pekkola J, Manninen H. Imaging of an acute stroke patient when planning therapy for arterial thrombosis. Duodecim 2016;132:1973-82.

4. Hoang JK, Wang C, Frush DP, et al. Estimation of radiation exposure for brain perfusion CT: standard protocol compared with deviations in protocol. AJR Am J Roentgenol 2013;201:W730-4.

5. Aschoff AJ, Catalano C, Kirchin MA, Krix M, Albrecht T. Low radiation dose in computed tomography: the role of iodine. Br J Radiol 2017;90:20170079

6. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology 2010;256:32-61.

7. Raman SP, Johnson PT, Deshmukh S. CT dose reduction applications: available tools on the latest generation of CT scanners. J Am Coll Radiol 2013;10:37-41.
8. Zhou BF; Cooperative Meta-Analysis Group of the Working Group on Obesity in China. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults--study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci 2002;15:83-96.

9. Li XY, Jiang Y, Hu N, et al. Prevalence and characteristic of overweight and obesity among adults in China, 2010. Chin J Prev Med. 2012; 46(8):683-686

10. Menzel H, Schibilla H, Teunen D. European Guidelines on Quality Criteria for Computed Tomography. Luxembourg: Official Publication of the European Communities. 2006; 32-33.

11. Weinman JP, Mirsky DM, Jensen AM, Stence NV. Dual energy head CT to maintain image quality while reducing dose in pediatric patients. Clin Imaging. 2019;55:83-88.

12. May MS, Wiesmueller M, Heiss R, et al. Comparison of dual- and single-source dual-energy CT in head and neck imaging. Eur Radiol. 2019 ;29(8):4207-4214.

13. Wang T, Gong Y, Shi Y, Hua R, Zhang Q. Feasibility of dual-low scheme combined with iterative reconstruction technique in acute cerebral infarction volume CT whole brain perfusion imaging. Exp Ther Med. 2017; 14(1):163-168.
14. Othman AE, Brockmann C, Yang Z, et al. Effects of radiation dose reduction in volume perfusion CT imaging of acute ischemic stroke. Eur Radiol, 2015; 25(12):3415-3422.

15. Murphy A, So A, Lee TY, et al. Low dose CT perfusion in acute ischemic stroke. Neuroradiology. 2014; 56(12):1055-1062.

16. König M, Bültmann E, Bode-Schnurbus L, et al. Image quality in CT perfusion imaging of the brain. The role of iodine concentration. Eur Radiol. 2007 Jan; 17(1):39-47.

17. Paparo F, Garello I, Bacigalupo L, et al. CT of the abdomen: degree and quality of enhancement obtained with two concentrations of the same iodinated contrast medium with fixed iodine delivery rate and total iodine load. Eur J Radiol. 2014; 83(11):1995-2000.

18. Kok M, Mihl C, Seehofnerová A, et al. Automated tube voltage selection for radiation dose reduction in CT angiography using different contrast medium concentrations and a constant iodine delivery rate. AJR Am J Roentgenol. 2015; 205(6):1332-1338.

19. Niesten JM, van der Schaaf IC, Riordan AJ, et al. Radiation dose reduction in cerebral CT perfusion imaging using iterative reconstruction. Eur Radiol. 2014; 24:484-493
20. Li ZL, Li H, Zhang K, et al. Improvement of image quality and radiation dose of CT perfusion of the brain by means of low-tube voltage (70 KV). Eur Radiol. 2014; 24(8):1906-13.

21. Corcuera-Solano I, McLellan AM, Doshi AH, Pawha PS, Tanenbaum LN. Whole-brain adaptive 70-kVp perfusion imaging with variable and extended sampling improves quality and consistency while reducing dose. AJNR Am J Neuroradiol. 2014; 35(11):2045-2051.

22. Bae K T. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology. 2010; 256:32-61

23. Haranhalli N, Mbabuike N, Grewal SS, et al. Topographic correlation of infarct area on CT perfusion with functional outcome in acute ischemic stroke. J Neurosurg. 2019 Jan 11:1-9.

24. Leigh R, Knutsson L, Zhou J, van Zijl PC. Imaging the physiological evolution of the ischemic penumbra in acute ischemic stroke. J Cereb Blood Flow Metab. 2018;38(9):1500-1516.

25. Cortijo E, Calleja AI, García-Bermejo P, et al. Relative cerebral blood volume as a marker of durable tissue-at risk viability in hyperacute ischemic stroke. Stroke. 2014; 45:113-118.
26. Clement O, Webb JA. Acute adverse reactions to contrast media: mechanisms and prevention. In: Contrast media. Safety issues and ESUR guidelines. Thomsen HS, Webb JA, eds. 3rd edn. Berlin, Germany: Springer; 2014.

27. Newhouse JH, Kho D, Rao QA, Starren J. Frequency of serum creatinine changes in the absence of iodinated contrast material: implications for studies of contrast nephrotoxicity. AJR Am J Roentgenol 2008; 191(2):376–82.

28. Hofmann MH. Contrast agent application and protocols. In: Multislice CT. Reiser MF, Becker CR, Nikolaou K, Glazer G, eds. 3rd edn. Berlin, Germany: Springer; 2009.
Figure legends

**Figure 1** Five ROIs in the non-ischemic hemisphere at the basal ganglia level of the tMIP were selected in the frontal white matter (ROI 1), the head of the caudate nucleus (ROI 2), the lent form nucleus (ROI 3), the thalamus (ROI 4), and the occipital white matter (ROI 5). The mean of the maximum enhancement and standard deviation (a) were measured within the ROI. The five ROIs were applied to the perfusion parameter maps at the same level, and the mean CBV (b), CBF (c) and MTT (d) were measured.

**Figure 2** Trial screening and randomization

**Figure 3** The CT images with different low-tubes.

**Figure 4** Comparison of the perfusion map IQ scores assessed by the two radiologists among the four groups. CBV (a), CBF (b) and MTT (c) were from radiologist 1, while CBV (d), CBF (e) and MTT (f) were from radiologist 2. There were no significant differences in IQ scores between the two radiologists.
Table 1: Patient demographic data and dose parameters for CTP in the four groups

| Parameter                  | Group A (n=50) | Group B (n=50) | Group C (n=50) | Group D (n=50) | P value |
|----------------------------|----------------|----------------|----------------|----------------|---------|
| Age (years)                | 63.06±7.80     | 61.44±5.94     | 63.70±7.69     | 62.70±7.44     | 0.463   |
| Sex (male/female)          | 35/15          | 31/19          | 34/16          | 32/18          | 0.828   |
| BMI (kg/m²)                | 24.29±1.82     | 24.26±1.98     | 24.43±1.95     | 24.85±1.49     | 0.347   |
| Cerebral CTP               |                |                |                |                |         |
| Tube voltage (KVp)         | 80             | 80             | 80             | 80             | -       |
| Tube current (mAs)         | 60             | 60             | 100            | 100            | -       |
| Radiation dose             |                |                |                |                |         |
| CTDIvol (mGy)              | 96             | 96             | 160            | 160            | -       |
| DLP (mGycm)                | 768            | 768            | 1280           | 1280           | -       |
| Effective dose (mSv)       | 1.77           | 1.77           | 2.94           | 2.94           | -       |
| Contrast medium injection  |                |                |                |                |         |
| CM concentration (mgI/ mL) | 320            | 370            | 320            | 370            | -       |
| CM volume (mL)             | 50             | 43             | 50             | 43             | -       |
| Flow rate (mL/s)           | 5.0            | 4.3            | 5.0            | 4.3            | -       |
| DR (gI/s)                  | 1.6            | 1.59           | 1.6            | 1.59           | -       |
| Total iodine load (g)      | 16             | 15.9           | 16             | 15.9           | -       |
| Injection time (s)         | 10             | 10             | 10             | 10             | -       |
Table 2: The comparison of maximum enhancement and noise in the four groups

| Groups | ROI 1       | ROI 2       | ROI 3       | ROI 4       | ROI 5       |
|--------|-------------|-------------|-------------|-------------|-------------|
| Group A| 41.16±3.74  | 55.96±3.25  | 56.78±4.00  | 55.72±2.90  | 41.33±3.28  |
| Group B| 40.69±3.10  | 55.59±3.36  | 58.76±5.00  | 55.99±4.42  | 42.47±4.12  |
| Group C| 39.24±2.77  | 53.10±3.08  | 55.06±3.15  | 53.00±3.06  | 38.67±2.81  |
| Group D| 37.98±2.54  | 52.84±3.15  | 54.87±3.14  | 53.86±3.38  | 38.72±3.13  |

| P value | | | | | |
|---------| | | | | |
| Dose*Contrast | 0.365 | 0.900 | 0.051 | 0.545 | 0.255 |
| Dose    | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| Contrast| <0.05 | 0.486 | 0.105 | 0.252 | 0.215 |

| Noise  | | | | | |
|--------| | | | | |
| Group A| 4.46±1.06 | 5.37±0.98 | 5.57±1.19 | 5.67±1.16 | 4.29±0.62 |
| Group B| 4.12±0.73 | 5.48±1.09 | 5.74±1.52 | 5.72±1.15 | 4.45±1.01 |
| Group C| 3.78±0.91 | 5.09±1.24 | 5.26±1.21 | 5.06±1.14 | 3.89±0.96 |
| Group D| 3.50±0.72 | 5.03±1.10 | 5.35±1.00 | 5.35±1.08 | 3.95±0.95 |

| P value | | | | | |
|---------| | | | | |
| Dose*Contrast | 0.781 | 0.595 | 0.830 | 0.445 | 0.707 |
| Dose    | <0.01 | <0.05 | <0.05 | <0.05 | <0.01 |
| Contrast| <0.05 | 0.871 | 0.446 | 0.279 | 0.386 |
Table 3: The comparison of SNR in the four groups

| Groups  | ROI 1     | ROI 2     | ROI 3     | ROI 4     | ROI 5     |
|---------|-----------|-----------|-----------|-----------|-----------|
| Group A | 9.93±1.51 | 10.76±2.00| 10.59±2.01| 10.19±1.97| 9.87±1.14 |
| Group B | 10.15±1.61| 10.53±2.12| 10.75±2.22| 10.10±1.82| 9.97±1.66 |
| Group C | 10.56±2.28| 11.02±2.52| 10.99±2.43| 10.95±2.23| 10.50±2.44|
| Group D | 10.38±1.52| 10.97±2.24| 10.55±1.84| 10.44±2.01| 10.23±1.93|

*P* value

|                  | Dose*Contrast | Dose  | Contrast |
|------------------|---------------|-------|----------|
| Dose*Contrast    | 0.426         | 0.772 | 0.321    |
| Dose             | 0.085         | 0.276 | 0.733    |
| Contrast         | 0.926         | 0.660 | 0.652    |

0.467 0.468 0.299 0.746
Table 4: The comparison of CBV and CBF in the four groups

| Groups     | ROI 1        | ROI 2        | ROI 3        | ROI 4        | ROI 5        |
|------------|--------------|--------------|--------------|--------------|--------------|
| **CBV**    |              |              |              |              |              |
| Group A    | 1.79±0.44    | 3.72±0.71    | 3.94±0.88    | 3.93±0.82    | 1.86±0.38    |
| Group B    | 2.00±0.44    | 3.80±0.47    | 4.40±0.90    | 4.20±0.77    | 1.90±0.35    |
| Group C    | 1.92±0.44    | 3.53±0.61    | 4.28±0.85    | 4.08±0.76    | 1.68±0.30    |
| Group D    | 1.96±0.40    | 3.84±0.59    | 4.38±0.75    | 4.28±0.76    | 1.92±0.42    |
| **P value**|              |              |              |              |              |
| Dose*Contrast | 0.153      | 0.180        | 0.134        | 0.799        | 0.056        |
| Dose       | 0.412        | 0.391        | 0.178        | 0.305        | 0.138        |
| Contrast   | <0.05        | <0.05        | <0.05        | <0.05        | <0.01        |
| **CBF**    |              |              |              |              |              |
| Group A    | 18.89±5.1    | 52.29±14.62  | 51.52±16.08  | 45.47±10.50  | 17.27±4.92   |
| Group B    | 19.58±3.91   | 52.43±11.36  | 56.78±12.16  | 49.70±9.81   | 18.36±3.65   |
| Group C    | 19.06±3.15   | 49.61±9.08   | 55.43±14.50  | 48.05±10.42  | 16.63±3.53   |
| Group D    | 18.57±4.15   | 48.30±9.58   | 53.31±11.64  | 47.84±10.96  | 16.82±3.57   |
| **P value**|              |              |              |              |              |
| Dose*Contrast | 0.312      | 0.652        | 0.059        | 0.134        | 0.418        |
| Dose       | 0.472        | <0.05        | 0.910        | 0.807        | 0.053        |
| Contrast   | 0.862        | 0.715        | 0.420        | 0.174        | 0.254        |
Table 5: The comparison of MTT in the four groups

| Groups | ROI 1     | ROI 2     | ROI 3     | ROI 4     | ROI 5     |
|--------|-----------|-----------|-----------|-----------|-----------|
| Group A| 7.24±1.88 | 4.66±0.73 | 4.81±0.89 | 5.57±1.00 | 8.08±2.40 |
| Group B| 6.95±1.23 | 4.87±0.83 | 4.81±0.75 | 5.33±0.79 | 7.62±1.21 |
| Group C| 6.57±1.37 | 4.67±0.72 | 4.91±0.88 | 5.33±0.86 | 7.50±1.11 |
| Group D| 6.86±1.19 | 4.92±1.05 | 5.09±0.86 | 5.51±1.28 | 7.63±1.31 |

*P value*

|          | Dose*Contrast | Dose | Contrast | Dose | Contrast |
|----------|---------------|------|----------|------|----------|
|          | 0.151         | 0.064| 0.988    | 0.904| 0.056    | 0.436    | 0.137    | 0.835    | 0.477    | 0.194    | 0.204    |
290 patients were assessed for eligibility

- 44 were excluded
  - 2 Thyrotoxicosis
  - 3 Renal insufficiencies
  - 7 Allergies
  - 1 Severe congestive heart failure
  - 5 Cerebral hemorrhages on non-contrast CT
  - 6 Insufficient peripheral vein conditions
  - 20 BMD < 28

246 patients underwent randomization

- 61 were examined by 60mAs tube current and 320mg/mL CM
  - 11 were excluded
    - 9 Cerebral ischemia or infarction occurred in bilateral cerebral hemispheres
    - 1 Accompanied by aneurysms
    - 1 Obvious motion artifacts

- 60 were examined by 60mAs tube current and 370mg/mL CM
  - 10 were excluded
    - 7 Cerebral ischemia or infarction occurred in bilateral cerebral hemispheres
    - 3 Obvious motion artifacts

- 62 were examined by 100mAs tube current and 320mg/mL CM
  - 12 were excluded
    - 10 Cerebral ischemia or infarction occurred in bilateral cerebral hemispheres
    - 1 Accompanied by arteriovenous malformations

- 63 were examined by 100mAs tube current and 370mg/mL CM
  - 13 were excluded
    - 12 Cerebral ischemia or infarction occurred in bilateral cerebral hemispheres
    - 1 Accompanied by aneurysms

- 50 were included in group A
- 50 were included in group B
- 50 were included in group C
- 50 were included in group D
