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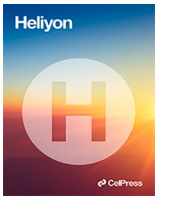

Research article

A retrospective study of non-equidistant interstitial brain CT perfusion scanning and prediction of time to peak

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ABSTRACT

Background: Exploring the limits of CT cranial perfusion scan acquisition intervals and predicting time to peak.

Methods: A retrospective analysis was conducted on 45 patients with suspected stroke who underwent brain CTP scans. Different sampling intervals were set based on the TDC. The patients were divided into four groups: Group 1 underwent continuous scanning with a uniform interval of 1.5 s; Group 2 had a uniform interval of 3 s; Group 3 had a 1.5-s interval between arterial and venous peak vertices with 1 point retained before and after the peak for 1.5 s and with a remaining acquisition interval of 4.5 s; and Group 4 had a uniform interval of 4.5 s. Statistical analysis was performed on the perfusion parameters of each group. Additionally, in 286 patients who underwent head and neck CTA examinations, the peak time of contrast medium was recorded, and the peak time was predicted based on factors such as age, height, weight, heart rate, systolic blood pressure, diastolic blood pressure, triglycerides, and total cholesterol. The results compared with Group 1 and Group 2, as well as Group 1 and Group 3, the P values of CBF, CBV, MTT, and Tmax in the left and right cerebral hemispheres of healthy subjects and in the infarct and noninfarct areas of patients were all >0.05. A comparison between Group 1 and Group 4 showed that right cerebral hemisphere CBF and CBV, left cerebral hemisphere CBF, CBV, and Tmax, infarct area CBV and Tmax, and noninfarct area CBF, CBV, and MTT had P values > 0.05, while other groups all had P values < 0.05. Bland–Altman analysis showed that the perfusion parameters in Group 1 were consistent with those in Group 2, and those in Group 1 were consistent with those in Group 3. The radiation doses in the second and third groups were lower, and the dose in the third group was lower than that in the second group.

Conclusion: Continuous acquisition between the peak points of the arterial and venous phases, with 1 point reserved before and after the peak and a 4.5-s interval for the rest, represents the maximum time interval for CTP scanning and can effectively reduce the radiation dose. The formula Tmax (s) = 0.290 × height (cm) − 0.226 × heart rate (times/min) + 0.216 × age (years) − 1.901 × triglycerides (mmol/L) − 0.061 × systolic blood pressure (mmHg) − 7.216 ($R2 = 0.449$, $F = 17.905$, $P < 0.01$) was established for predicting time to peak enhancement.

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1. Introduction

Stroke has gradually become one of the most threatening diseases to human health, ranking first among the causes of death in China and being the leading cause of disability in adults. Time is a critical factor in the treatment of acute ischemic stroke. Early detection and treatment within 3 h or 4.5 h, and at the latest within 6 h, can significantly reduce the mortality and disability caused by stroke. CT perfusion (CTP) has been established as an easy-to-operate noninvasive diagnostic method [1]. It can provide both morphological and functional imaging data, and it can be used to quickly diagnose superacute stroke (local microvascular compensation dilation with only changes in cerebral blood flow velocity or simultaneous changes in cerebral blood flow and local microvascular compensation dilation), determine the ischemic penumbra and infarction area, evaluate the severity of cerebral tissue ischemic lesions, and assess the treatment efficacy of ischemic injury. Although CTP is very mature in imaging technology, the X-ray radiation from a 40 s CTP scan is equivalent to a year's radiation exposure in the natural environment due to its high radiation dose. The average dose level during whole-brain CTP/CT angiography (CTA) data acquisition was 6.8 mSv [2], twice that of natural background radiation sources; in comparison, the natural background radiation exposure is approximately 2.4 mSv per year [3]. In addition, cumulative radiation doses to patients can increase health risks and can cause problems such as skin irritation, hair loss, cataract formation, and even cancer [4]. However, due to the limitations of its imaging principle, the sampling frequency cannot be too low. In this study, the accuracy of the perfusion results was ensured, and the radiation dose was significantly reduced by adjusting the sampling frequency in different time periods individually.

2. Materials and methods

This study collected data from 45 cranial perfusion examinations and 286 patients with suspected cerebrovascular disease who underwent head and neck CTA examination from October 2021 to September 2022 in our hospital. The cranial perfusion examination data inclusion criteria: Patients with clinical symptoms of suspected stroke within 6 h were subjected to head CTP scan in the Imaging Department of our hospital. The exclusion criteria were patients with severe motion artifacts, poor contrast agent development, cerebrovascular malformation, moyamoya disease, and craniotomy during the CTP scan. In each group, there were 45 participants, of which 29 were male and 16 were female, with an age range of 54–73 years old. Among them, there were 27 patients with acute ischemic stroke (16 males and 11 females) and 18 patients without acute ischemic stroke (10 males and 8 females). Each group had several ROIs, including 2 in the semioval center, 6 in the basal ganglia, and 2 in the circle of Willis.

A total of 286 patients underwent head and neck CTA examinations, including 156 males and 130 females. The age of the patients ranged from 24 to 76 years, with an average age of 52 years. Patient information, including age, height, weight, heart rate, systolic blood pressure, diastolic blood pressure, triglycerides, and total cholesterol, was recorded prior to the scan. The patient data are presented in Table 1.

2.1. CTP scan protocol

CTP imaging was performed on a third-generation Siemens dual-source CT scanner using continuous dynamic scanning and rocking bed technology. The detector collimation width was 128 mm × 0.6 mm, and the gantry rotation time was 250 ms/rotation. The scan pitch was 1.2, and the tube voltage was 70 kV with a tube current of 120 mA. A double-barrel high-pressure injector was used to inject 40 mL of nonionic contrast agent iodinated propofol (370 mgI/100 mL) at a rate of 4.0 mL/s into the right antecubital vein, followed by 20 mL of saline at the same rate. Scanning was performed 8 s after injection and lasted for 37.5 s, with a sampling interval of 1.5 s, resulting in 25 sets of images. The reconstruction interval was 1.0 mm, and the layer thickness was 1.5 mm using Deconvolution (DC) Mathematical Model, Joint Iterative Reconstruction (IR) - Iterative Reconstruction Technique for Raw Data (Sinogram Affirmed Iterative Reconstruction, SAFIRE).

A Test-Bolus technique was employed prior to the formal CTA scan to determine the Scan Delay Time (SDT). A volume of 20 mL of iodinated contrast agent was administered, followed by an additional 20 mL of saline at a rate of 4 mL/s. After an 8-s delay following the contrast injection, multiple repeated scans were conducted at the level of the bifurcation of the common carotid artery in the neck. Each scan lasted 1 s with a 1-s interval between scans. The scan was halted when the peak CT attenuation value of the right carotid artery at this level was reached and when the CT attenuation value began to decrease. Circular regions of interest (ROIs) were selected within the right carotid artery on the obtained images. The center of the ROI was aligned as closely as possible with the center of the

Table 1
Conditions of patients undergoing CTA scanning.

Individual factors	Mean ± Standard Deviation	Scope
Age (years)	50.10 ± 11.06	24–70
Heigh (cm)	164.05 ± 8.39	137.0–186.0
Weight (kg)	69.96 ± 12.68	45.0–101.0
Heart Rate (times/min)	69.67 ± 10.73	41.0–103.0
Systolic Blood Pressure (mmHg)	141.44 ± 24.00	98.0–208.0
Diastolic Blood Pressure (mmHg)	89.99 ± 17.67	55.0–188.0
Triglycerides (mmol/L)	1.79 ± 1.10	0.57–5.65
Total cholesterol (mmol/L)	4.03 ± 1.21	0.77–6.80

vessel and encompassed 2/3 of the vascular cross-section, avoiding vessel walls and any adjacent plaques. Subsequently, a time-density curve (TDC) was generated for the ROIs. The traction maximization (Tmax) value on the curve was added to 4 s to determine the SDT for that specific patient. The preinjection scan parameters were set at 120 kV and 40 mA, with a slice thickness of 0.5 mm. Finally, the Tmax value for the patient was recorded. The test-bolus monitoring level and the generated TDC for the ROIs are depicted in Fig. 1a and b.

2.2. Parameter measurement and processing

The CT perfusion data were processed using Siemens Healthineers Syngo. via software. A deconvolution algorithm was applied to all images for motion correction to reduce artifacts. Automated bone removal was employed to eliminate signals from bones, air, sulci, and ventricles. The middle cerebral artery was selected as the arterial input function, and the signals from the sinuses were used as the venous output function. ROIs were manually placed to obtain pseudocolor maps of blood volume (CBV), blood flow (CBF), mean transit time (MTT), Tmax, and TDC.

The data from all four groups were postprocessed for perfusion on the workstation using a sampling method to eliminate the original images. The four groups were subjected to different sampling interval treatments, with each group including all 45 patients. The first group consisted of images with a 1.5 s interval, serving as the control group or original images (Fig. 2-A). The second group comprised images with a uniform interval of 3 s, with sampling points removed at intervals, scanning at intervals of 3 s each time, i.e., 0 s, 3 s, 6 s, …, until the end of the scan (Fig. 2-B). The third group, based on the arterial and venous TDC, retained the peaks of both arterial and venous phases. One continuous sampling point was retained before and after each peak, and the remaining curve was sampled at intervals of 4.5 s. For instance, if the arterial peak was at 15.5 s and the venous peak was at 20 s, sampling within the range of 14 s–21.5 s used the same interval as the control Group 1.5 s, while the rest of the intervals were set at 4.5 s (Fig. 2-C). The fourth group consisted of images with uniform intervals of 4.5 s, scanning at intervals of 4.5 s each time, i.e., 0 s, 4.5 s, 9 s … until the end of the scan (Fig. 2-D). ROIs were placed at three levels: the center of the semioval center (Fig. 3-A,D), the basal ganglia (Fig. 3-B,E), and the Wills circle (Fig. 3-C,F). The number of ROIs in each group was as follows: 2 in the semioval center area, 6 in the basal ganglia area, and 2 in the arterial ring area. Patients with stroke, including the ischemic area with an area within the range of 0.60–0.65 cm^2, were included. The ROI error for each subject was within ± 0.02 cm^2. An equal number of ROIs were placed in the left and right ventricles, avoiding the edges of blood vessels, brain sulci, ventricles, and brain parenchyma (Fig. 3). To ensure the same ROI positions for the four groups of data, a reference grid was manually placed on the screen to ensure that the positions, sizes, and planes of the ROIs were the same for the same subject in all four groups.

2.3. Radiation dose

The CT dose index (CTDI) and dose-length product (DLP) of the scanned subjects were automatically generated and recorded. The effective dose (ED) was calculated using the formula ED = DLP × k [conversion factor, k = 0.0021 mSv/(mGy·cm)]. Dividing the above radiation dose parameters by the number of samples yielded the corresponding values for a single sample, which were then multiplied by the adjusted number of samples to obtain the radiation dose for the four groups.

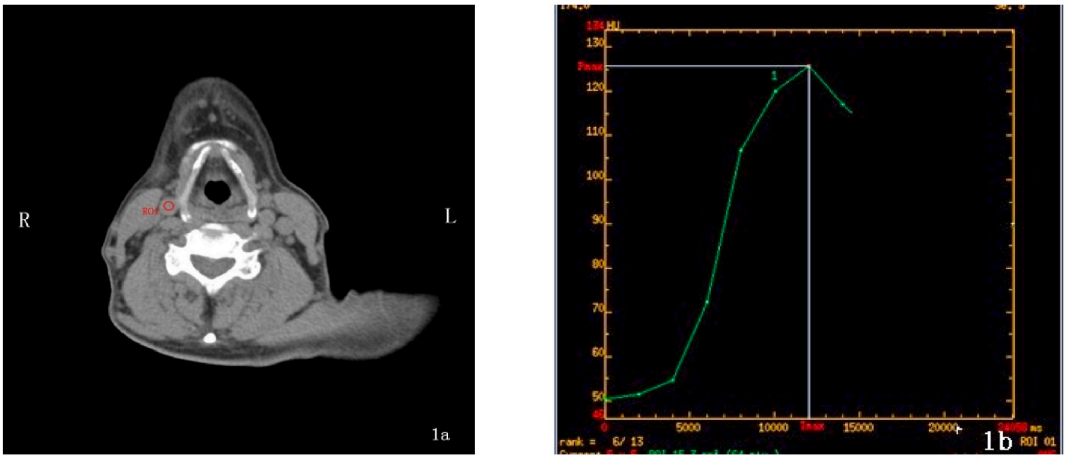

Fig. 1. a shows the bifurcation level of the common carotid artery monitored by Test-Bolus, and the red circular ROI is the monitoring area. Fig. 1b shows the TDC generated by the postprocessing software for the ROI of a patient's monitoring region. The injection scheme is a continuous injection of 370 mgI/mL iopromide at a speed of 4 mL/s, and the TDC shows a Tmax of 20 s. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

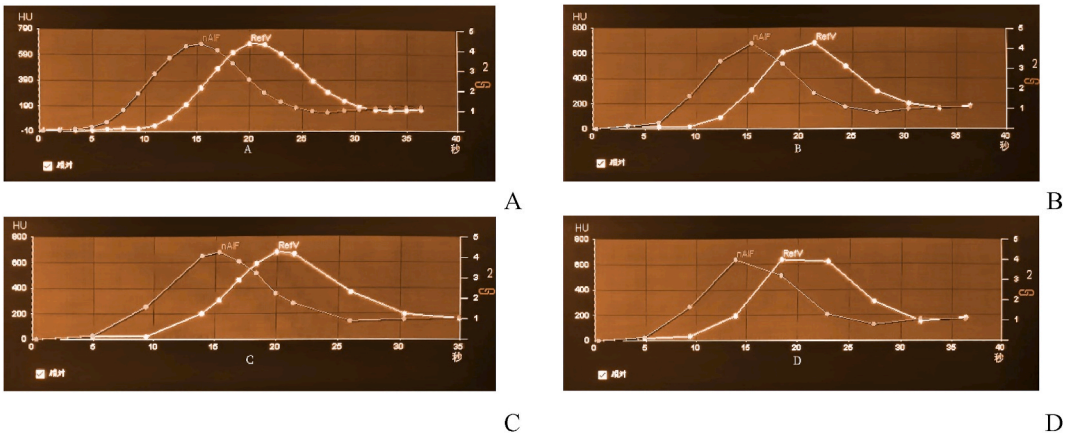

Fig. 2. A:Continuous scanning at intervals of 1.5 s. B: Uniformly spaced scanning every 3 s. Scanning at intervals of 3 s each time. C: Collection interval of 1.5 s between dynamic and static peak vertices, and retention of one continuous sampling point before and after the dynamic and static peak values, with a collection interval of 4.5 s for the rest. D: Scanning at uniform intervals of 4.5 s. Scanning at intervals of 4.5 s each time.

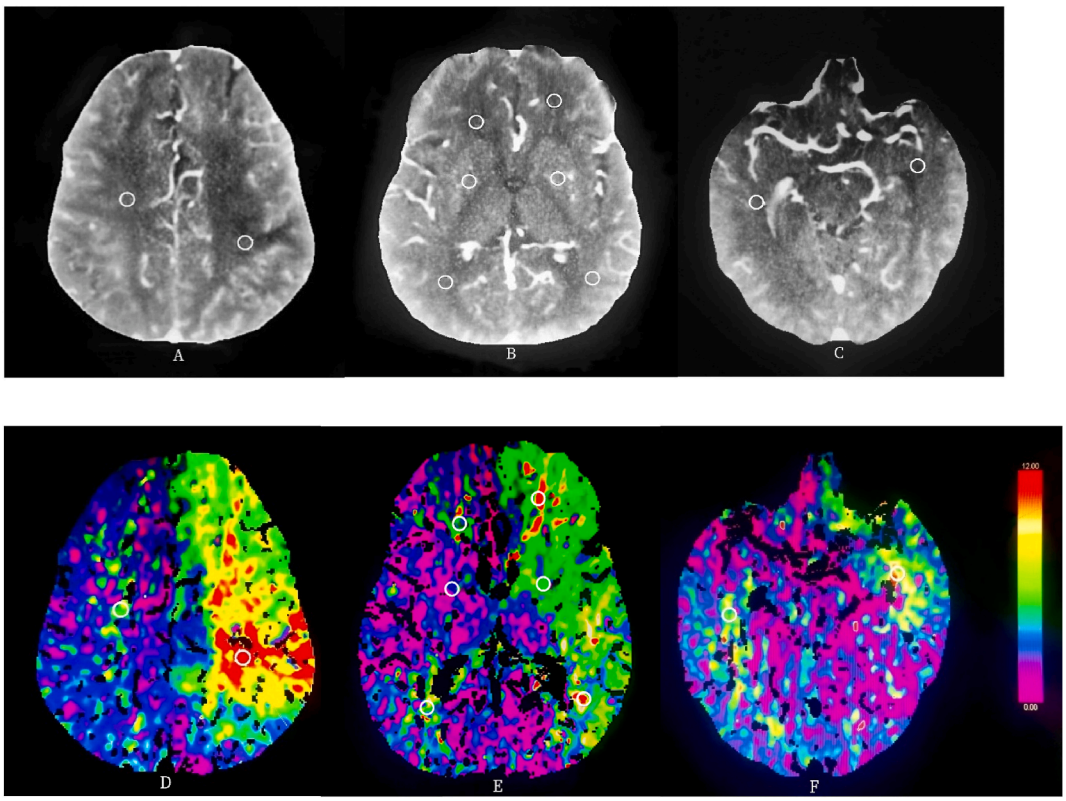

Fig. 3. ROI Placement Diagram. The positions for placing regions of interest (ROIs) at the semioval center (A, D), basal ganglia area (B, E), and arterial ring level are indicated (Fig. 3-C, F),including the infarct zone, hypoperfusion zone, and healthy region. A, B, C represent MIP images. D, E, F represent Tmax images.

2.4. Statistical analysis

Statistical analysis was performed using SPSS (IBM SPSS Statistics, IBM Corporation, Armonk, New York) and MedCalc (MedCalc Statistics, MedCalc Software Ltd., v20.100). For each group, normality and homogeneity of variances were assessed initially. If the data followed a normal distribution (expressed as the mean ± standard deviation, X ± S) and met the assumption of homogeneity of variances, analysis of variance (ANOVA) and post hoc comparisons using the least significant difference (LSD) method were applied. In

cases where the data did not adhere to a normal distribution (represented as median, M), nonparametric tests were employed for comparison. The second to fourth groups were compared to the first group in various regions, including the left and right cerebral hemispheres of healthy individuals, as well as the infarcted and noninfarcted regions in patients. Multivariate linear regression analysis was employed to assess the impact of delay trigger time on Tmax in relation to patient age, heart rate, height, triglycerides, systolic blood pressure, and diastolic blood pressure. A significance level of $P < 0.05$ was considered to indicate significant differences. The groups in the noninfarcted area were averaged for statistical analysis.

3. Result

Forty-five suspected stroke patients underwent CTP scans, with each individual undergoing standard scanning at intervals of 1.5 s in the control group comprising all 45 patients. All patients underwent three different interval processing methods (with a uniform interval of 3 s, an interval of 1.5 s between the arterial and venous peak vertices with a scanning interval of 1.5 s that was retained before and after the peak, and the remaining intervals of 4.5 s, with a uniform interval of 4.5 s), and the perfusion parameters of these three different processing methods were compared with the control group. Two patients underwent multiple scans.

3.1. Testing for normality and homogeneity of variance

The CBF of Group 1 in the right cerebral hemisphere, the CBV of Group 1 in the left cerebral hemisphere, the CBF of Group 3 in the infarcted area of the patient, the CBV of Group 1, the MTT of the whole group, the CBF of Group 2 in the noninfarcted area of the patient, the CBV of Groups 1–3, and the Tmax of Groups 1–3 did not conform to the normal distribution, and the rest of the groups conformed to normality. Each group that conformed to a normal distribution also satisfied the homogeneity of variance. The results are shown in Table 2.

3.2. ANOVA, non-parametric tests

The results of the analysis of variance show that there is no significant difference between the CBV groups in the right hemisphere of the brains of healthy individuals ($P > 0.05$). However, there were significant differences between the groups in terms of MTT and Tmax $P < 0.05$. The post hoc comparisons revealed that there was no significant difference in MTT and Tmax between the first group and the second group or between the first group and the third group ($P > 0.05$), but there was a significant difference between the first group and the fourth group ($P < 0.05$). In healthy individuals, there was no significant difference in CBF and Tmax between the left hemisphere and the control group ($P > 0.05$). However, there was a significant difference in MTT between the left hemisphere and the

Table 2
Testing for normality and homogeneity of variance.

	CBF		CBV		MTT		Tmax	
	P-value	*x ± s/M*	*P-value*	*x ± s/M*	*P-value*	*x ± s/M*	*P-value*	*x ± s/M*
Right cerebral hemisphere in healthy people								
Group 1	0.003	41.581	0.071	2.728 ± 0.313	0.481	4.554 ± 0.481	0.402	2.985 ± 0.701
Group 2	0.575	43.941 ± 4.823	0.385	2.729 ± 0.336	0.847	4.430 ± 0.397	0.916	3.134 ± 0.677
Group 3	0.105	44.327 ± 5.271	0.137	2.796 ± 0.356	0.479	4.325 ± 0.417	0.785	3.056 ± 0.564
Group 4	0.132	45.739 ± 6.281	0.083	2.783 ± 0.411	0.967	4.049 ± 0.297	0.797	3.818 ± 1.078
Homogeneity of variance			0.571		0.678		0.071	
Left cerebral hemisphere in healthy people								
Group 1	0.515	42.523 ± 5.101	0.044	2.702	0.188	4.407 ± 0.402	0.977	2.836 ± 0.402
Group 2	0.787	43.776 ± 4.723	0.313	2.674 ± 0.349	0.277	4.286 ± 0.312	0.565	3.016 ± 0.553
Group 3	0.771	43.887 ± 5.351	0.868	2.725 ± 0.215	0.608	4.306 ± 0.441	0.059	2.957 ± 0.351
Group 4	0.169	46.668 ± 10.285	0.162	2.916 ± 0.684	0.180	3.993 ± 0.266	0.458	3.023 ± 0.692
Homogeneity of variance	0.059				0.365		0.095	
Patient infarct zone								
Group 1	0.051	31.080 ± 12.358	0.031	2.340	0.000	4.74	0.214	7.369 ± 2.650
Group 2	0.092	32.127 ± 13.185	0.922	2.255 ± 0.896	0.000	4.76	0.730	7.030 ± 2.627
Group 3	0.033	28.430	0.594	2.224 ± 0.836	0.000	4.98	0.590	7.102 ± 2.621
Group 4	0.059	36.736 ± 16.258	0.286	2.278 ± 0.899	0.000	4.02	0.203	7.097 ± 2.369
Homogeneity of variance								0.917
Non-infarcted area of the patient								
Group 1	0.071	44.134 ± 6.836	0.029	2.764	0.139	4.562 ± 0.549	0.000	3.130
Group 2	0.043	43.250	0.013	2.649	0.817	4.404 ± 0.394	0.001	3.263
Group 3	0.087	45.232 ± 7.536	0.009	2.710	0.385	4.447 ± 0.527	0.001	3.231
Group 4	0.390	46.035 ± 9.303	0.322	2.823 ± 0.564	0.101	4.377 ± 0.634	0.205	3.877 ± 0.726
Homogeneity of variance					0.157			

Note - x ± s: mean ± standard deviation; M: median. The first group had a continuous scan with a uniform interval of 1.5 s, which served as the control group. The second group had a uniform interval of 3 s between scans. The third group had scans taken at intervals of 1.5 s between the peak values of the arterial and venous waves, with an additional 1.5 s of scanning before and after each peak. The remaining intervals in this group were 4.5 s. The fourth group had a uniform interval of 4.5 s between scans. The Shapiro-Wilk test was used to assess the normality of the data.

control group ($P < 0.05$). The post hoc comparison showed that there was no significant difference in MTT between the first group and the second group or between the first group and the third group ($P > 0.05$), but there was a significant difference in MTT between the first group and the fourth group ($P < 0.05$). $P > 0.05$ between the groups for Tmax in the infarcted area of patients and between the groups for MTT in the noninfarcted area of patients. The nonparametric test results showed that there was no significant difference in the right hemisphere CBF, right hemisphere CBV, patient infarct zone CBV, noninfarct zone CBF, or CBV between healthy individuals and patients ($P > 0.05$). $P < 0.05$ for the infarct area CBF and MTT between the Groups; for the pairwise comparison: $P > 0.05$ between the first group and the second group and between the first group and the third group; $P < 0.05$ between the first group and the fourth group; $P < 0.05$ between the groups for Tmax in the noninfarct area; for the pairwise comparison: $P > 0.05$ between the first group and the second group and between the first group and the third group; and $P < 0.05$ between the first group and the fourth group. The results are shown in Table 3.

3.3. Bland-Altman concordance analysis

The first group, the second group and the third group were in the left and right cerebral hemispheres of healthy people, respectively, and the perfusion parameters CBF, CBV, MTT, and Tmax in the infarcted and noninfarcted areas of the patients had good consistency (Table 4).

3.4. Radiation dose

In the first group, the initial data was used, with a continuous scan of 37.5 s, a time interval of 1.5 s, and continuous scan exposure of 25 times. The ED was 2.49 mSv, and the average ED per exposure was 0.100 mSv. The number of exposures, ED and the percentage of the ED to the standard scan for each group are shown in Table 5.

3.5. Head and neck CTA 20 mL contrast pre-injection Scan.Multivariate stepwise linear regression analysis of Tmax and individual factors

Based on the results of the analysis of variance, individual factors that met the criteria and contributed significantly to Tmax were selected to enter the regression equation (see Table 6). The individual factor with the smallest F value, which also met the criteria for removal, was excluded from the model. This process led to a well-fitting regression equation ($R2 = 0.449$, $F = 17.905$, $P < 0.01$):

$$\text{Tmax (s)} = 0.290 \times \text{Height (cm)} - 0.226 \times \text{Heart rate (beats/min)} + 0.216 \times \text{Age (years)} - 1.901 \times \text{Triglycerides (mmol/L)} - 0.061 \times \text{Systolic blood pressure (mmHg)} - 7.216$$

Table 3
Statistical results of perfusion values in each group.

	CBF		CBV		MTT		Tmax	
		P-value		*P-value*		*P-value*		*P-value*
Right cerebral hemisphere in healthy people								
Comparison between groups	1.700[c]	0.637	0.121[b]	0.947	3.410[b]	0.026	2.924[b]	0.044
Comparing Group1 with Group2					0.123[a]	0.459	−0.148[a]	0.644
Comparing Group1 with Group3					0.229[a]	0.172	−0.071[a]	0.824
Comparing Group1 with Group4					0.505[a]	0.004	−0.833[a]	0.012
Leftt cerebral hemisphere in healthy people								
Comparison between groups	0.804[b]	0.498	3.200[c]	0.362	2.908[b]	0.045	0.337[b]	0.798
Comparing Group1 with Group2					0.122[a]	0.416		
Comparing Group1 with Group3					0.101[a]	0.497		
Comparing Group1 with Group4					0.415[a]	0.007		
Patient infarct zone								
Comparison between groups	16.098[c]	0.001	3.707[c]	0.295	34.026[c]	0.000	0.160[b]	0.923
Comparing Group1 with Group2	−0.447[d]	0.093			0.404[d]	0.129		
Comparing Group1 with Group3	−0.489[d]	0.066			0.490[d]	0.066		
Comparing Group1 with Group4	−1.064[d]	0.000			1.489[d]	0.000		
Non-infarcted area of the patient								
Comparison between groups	3.971[c]	0.265	6.200[c]	0.102	0.489[b]	0.691	15.000[c]	0.002
Comparing Group1 with Group2							−0.286[d]	0.473
Comparing Group1 with Group2							−0.143[d]	0.720
Comparing Group1 with Group2							−1.381[d]	0.001

Note-a: Mean difference. b: F-value. c: chi-square value. d: Test statistics. Nonparametric test: Friedman test. ROIs at the center of semiovale, basal ganglia and arterial ring include white matter and gray matter. Patients with stroke also include the ischemic area. There are 10 ROIs in total for each patient (Number of ROIs: 2 in semiovale, 2 in basal 6 node areas, 2 arterial ring areas), a total of 340 ROIs; The average value of the data of each group was taken for healthy people and non-infarcted areas of patients for analysis; left and right cerebral hemispheres of healthy people: 12 groups each, non-infarcted areas of patients: 21 groups, and infarcted areas: 47 groups. The first group: the scanning interval was 1.5s as the standard control group; the second group: the scanning interval was 3s evenly; the third group: the scanning interval was 1.5s in the middle period of the arterial and venous peak peaks, and the interval in the rest periods was 4.5s. CBV: blood flow; CBV: blood volume; MTT: mean transit time; Tmax: peak time.

Table 4
Bland-Altman concordance analysis.

	CBF		CBV		MTT		Tmax	
	P-value	*Arithmetic Mean*	*P-value*	*Arithmetic Mean*	*P-value*	*Arithmetic Mean*	*P-value*	*Arithmetic Mean*
Right cerebral hemisphere in healthy people								
Comparing Group1 with Group2	0.367	0.722	0.973	0.002	0.175	−0.124	0.082	0.147
Comparing Group1 with Group3	0.079	1.108	0.283	0.070	0.054	−0.230	0.457	0.071
Lefft cerebral hemisphere in healthy people								
Comparing Group1 with Group2	0.118	1.253	0.774	0.022	0.199	−0.123	0.123	0.181
Comparing Group1 with Group3	0.056	1.365	0.147	0.047	0.283	0.102	0.070	0.119
Patient infarct zone								
Comparing Group1 with Group2	0.061	1.048	0.126	0.105	0.068	−0.317	0.091	−0.339
Comparing Group1 with Group3	0.513	0.495	0.205	0.074	0.361	−0.079	0.120	−0.267
Non-infarcted area of the patient								
Comparing Group1 with Group2	0.389	0.571	0.103	−0.060	0.091	−0.158	0.075	−0.107
Comparing Group1 with Group3	0.081	1.098	0.090	0.060	0.266	−0.114	0.292	−0.089

Note-consistency analysis verification for two groups with no statistical difference. Compare the second group with the first group, and the third group with the first group.

Table 5
Exposure times, ED values, and percentage of standard scan ED values for each group.

Index	Group1	Group2	Group3	Grop4
Exposure times	25	13	12	9
ED value H/mSv	2.49	1.29	1.20	0.90
Percentage of standard ED value (%)	100	51.84	48	36

Table 6
Individual factors in the head and neck CTA-Tmax regression model.

Related Factors	Unstandardized Coefficients		Standardized Regression Coefficients	*t*	*P*
	B	Standard Errors			
Constant (Intercept)	−7.216	12.937		−0.558	0.578
Heart Rate	−0.226	0.050	−0.326	−4.498	<0.001
Triglycerides	−1.901	0.484	−0.281	−3.929	<0.001
Age	0.216	0.051	0.322	4.238	<0.001
Heigh	0.290	0.065	0.328	4.463	<0.001
Systolic Blood Pressure	−0.061	0.023	−0.199	−2.635	0.010

3.6. Correlation with ASPECTS score

Parsons et al. [5] described the CBV-ASPECTS within 6 h of symptom onset, which more accurately predicts irreversible tissue damage than the NCCT ASPECTS. Sillanpaa et al. [6,7] found that MTT/CBV ASPECTS mismatch within 3 h of symptom onset is highly correlated with the volume of at-risk tissue in patients. Additionally, within 8 h of symptom onset, CBV ASPECTS outperforms NCCT ASPECTS in distinguishing patients with favorable outcomes. CBV and MTT ASPECTS have been identified as significant predictors of adverse clinical outcomes in univariate analysis [8]. CTP ASPECTS is superior to Auto and NCCT-ASPECTS in detecting acute ischemic stroke, with CTP ASPECTS $\geq$6 being a good predictor of favorable clinical outcomes at 90 days of follow-up [9,10]. Some scholars have suggested that in patients with acute ischemic stroke, placing the region of interest at the proximal or contralateral hemisphere proximal and distal to the thrombus has minimal impact on the CBV. The use of deconvolution algorithms with delay-insensitive techniques has minimal impact on the perfusion values [11]. When performing cerebral vascular imaging, for patients with mild to moderate stenosis of the internal carotid artery, the cerebral arteries can be chosen as the input artery. For patients with severe stenosis or complete occlusion of the internal carotid artery, choosing the contralateral middle cerebral artery or basilar artery has a smaller impact on the perfusion results [12]. Therefore, the author believes that ASPECTS scores of 1–2, indicating extensive unilateral cerebral ischemia, may affect the placement of ROIs, leading to inaccurate perfusion results. However, if there is a large vessel occlusion and some segments or contralateral vessels can still be visualized, the placement of ROIs may not affect perfusion results.

4. Discussion

With the continuous development of CT equipment, CT examinations have become an indispensable part of clinical diagnosis and

treatment. Currently, CT scanners can cover the entire brain, thus solving one of the problems associated with CT perfusion technology. However, high levels of radiation exposure continue to limit its application in clinical settings, as high radiation doses can increase the risk of patient illness. As a result, methods must be taken to reduce the radiation dose. The most commonly used methods include reducing the tube voltage, lowering the tube current, and increasing the collection time interval (reducing the number of collections). Reducing the tube voltage and tube current can affect the image quality and is also limited by the equipment performance; thus, they cannot be reduced too much. Increasing the collection time interval can significantly reduce the radiation dose, but there is no consensus as to how much of an interval is necessary to achieve the final perfusion result without affecting the image. Kämena et al. [13,14] suggested that a sampling interval of 2 s does not affect the image quality, while Wiesmann et al. [15] proposed that the scanning acquisition time can be extended to 3–4 s. Wintermark et al. [16,17] also recommend a temporal resolution of 3 s when using 40 mL contrast agent in their study. However, Goh et al. [18] argued that the sampling interval should not exceed 3 s, as it significantly reduces the image quality and affects the diagnostic results. Cao et al. [19] proposed using irregular interval scanning to reduce the radiation dose instead of a fixed sampling interval. In this study, a sampling interval of 3 s was set to verify the results of Wiesmann et al. [15] and to explore the limit of the sampling interval. These studies all used uniform sampling. Based on the existing data, this study innovatively explored which method of taking different sampling intervals in personalized time intervals can further reduce the radiation dose without affecting the perfusion effect.

The subject's heart rate and the injection rate of the contrast agent affect the time to peak on the time-density curve, and the duration of sustained blood enhancement is related to the amount of contrast agent injected [20]. Some researchers suggest that using a contrast agent dose of 40 mL results in a lower dose [17], and in combination with deconvolution algorithms, a lower injection rate of 4 mL/s can be employed [21]. Therefore, in this study, a contrast agent dose of 40 mL and an injection rate of 4 mL/s were utilized, effectively eliminating the influence of contrast agent dosage and injection speed. The DC method has higher spatial and temporal resolution, does not require special requirements for the contrast agent injection rate and is less affected by cardiac function. In addition, a few assumptions were made in establishing the organizational perfusion model. Therefore, the perfusion parameters derived from this method are closer to the actual physiological variables, which is why we chose the deconvolution algorithm. Blood flow based on Fick's law is given by the formula $BF = [d/dt\ Ct_{(t)}|max]/[Ca_{(t)}|max]$, where Ct is the concentration of contrast agent in tissue and Ca is the concentration of contrast agent in the artery [22]. It can be seen that some parts of the contrast agent passing process may be less sensitive to the sampling frequency, such as the rising part and the falling part before the peak vertex, and it is a good choice to reduce the sampling rate in these parts. Keeping the artery through key parts of the tissue, other "omitted" parts can be exchanged for a dose reduction. Therefore, according to the characteristics of arterial and venous TDC, the apex range of the tissue perfusion curve can be retained, and the sampling interval can be extended appropriately in other parts to reduce the radiation dose. We reserved the peak apex of the arteriovenous and continuous scans, as well as one scan point before and after the peak, to ensure the integrity and accuracy of TDC. This is the theoretical basis for the establishment of the third group of scanning protocols. Because of the third-generation dual-source CT we used, the standard sampling interval was 1.5 s, so the sampling interval of our fourth group was 4.5 s. We compared samples taken at different intervals from the left and right hemispheres of healthy individuals, as well as from the infarct and noninfarct areas of patients, to prevent experimental data bias. To increase the accuracy of our research, we chose to use the mean values of each group for the statistical analysis.

In this study, the set ROIs encompassed the nonischemic region, ischemic penumbra, and core infarct zone. The obtained perfusion parameter values from these ROIs were compared and analyzed against values from continuous scans. The consistency between the results of the ischemic penumbra and core infarct zone detection in relation to the continuous scanning approach was excellent. Given the current advocacy for a one-stop stroke imaging protocol involving CTP (CT perfusion) and CTA (CT angiography), where CTA examination requires a target vessel CT value exceeding 300 Hounsfield units (HU), our approach involves continuous scanning during the cerebral arterial peak phase. This ensures that the acquired density is sufficient to capture the phase suitable for CTA reconstruction of the vessels. In CTA scanning, the closer the vessel of interest is to the target area, the higher the accuracy, so we chose the carotid artery as the ROI placement area. During the examination, the patient was instructed to cooperate as much as possible and refrain from swallowing. The Test-Bolus method was used to manually remove individual areas with larger CT value errors. We used IR to optimize the imaging data, thereby reducing noise and artifacts. Utilizing the third-generation Siemens dual-source CT and setting SAFIRE to 3, previous research has shown that SAFIRE 3 and 4 provide better reconstruction sensitivity and edge sharpness, with the highest subjective ratings [23]. Compared to traditional reconstruction methods such as filtered back projection (FBP), our approach exhibits fewer image artifacts, reduces radiation dosage, and can be employed for scans with limited sampled data. The ED value of conventional CTP scans is 3.78H/mSv per exposure, while our first group has an ED value of 2.49 H/mSv, which is lower than the typical dose of conventional CTP scans. The third scanning protocol reduces the radiation dose to 1.20 H/mSv. By utilizing this algorithm, our scanning protocol allows for lower radiation doses while maintaining a consistent image quality. In combination with the IR algorithm, low-dose CTP has been shown to be effective in the clinical environment for most acute stroke patients [24].

According to the calculation formula of blood flow [25], the apex of the arteriovenous peak of TDC is an important time point for calculating perfusion parameters, so the acquisition interval beyond the peak of the arteriovenous peak can be extended appropriately. Since several scholars [15,16,26] have reached experimental conclusions on CT perfusion scanning with a sampling interval of 3 s, their research results are consistent with previous conclusions, and there is no significant difference between them and standard scanning with a sampling interval of 1.5s. Different from the conclusion of Kämena et al. [13], the author considers that it may be influenced by some factors. For example: (1) this can be influenced based on whether there is ROI placement in input arteries and output veins. (2) Perfusion software packages and mathematical models of CT perfusion from different manufacturers are different. (3) Different scanning protocols, patient cohorts, and CTP thresholds can also be factors. (4) Statistical analysis methods are different. For example, t tests, Wilcoxon tests, and ANOVA were used in these studies [13,15,17], none of which accounted for repeated measures

and thus failed to properly distinguish the sources of variation resulting from both secondary sampling and the heterogeneity between patients. Consequently, our findings differ from those of Kämena et al. [13]. The key to CT perfusion imaging lies in acquisition. Information on the dynamic image changes from before the contrast enters the selected level to the venous sinus period. After the TDC arterial and venous curves have been generated, the selection of the last image frame before the contrast enters the selected level and the first image frame when the contrast first exits the venous sinus may differ due to the unsmoothness of the image and the increase in the sampling interval, resulting in a different starting point for the correction curve and therefore the area under the curve. The time point shift of the TDC curve rise can only affect MTT because the time when the contrast agent just passes through the blood vessel will inevitably change. A larger time interval may lead to missing the peaks of the arterial and venous phases, causing changes in the shape of the TDC (Fig. 2). An optimization criterion for deconvolution algorithms is to keep the CBV constant when calculating the arrival time of the contrast agent in the blood vessels. Since the CBV is equal to the area under the TDC curve, this can affect the curve width, leading to inaccurate MTT calculations. Missing the time points of arterial and venous peaks may also cause a shift in the location of the arterial and venous enhancement peaks, reducing their peak heights. This can introduce errors when calculating the corresponding Tmax in the fourth group. It can also lead to increased noise. The author believes that this is also a reason for the significant differences in MTT and Tmax between the fourth group and the standard scanning group.

In CTA, Tmax is influenced by various factors, such as the subject's cardiac function, blood properties, height, weight, medical condition, contrast agent injection rate, injection site, patient position during injection, scanning direction, and properties of the contrast agent itself [27,28]. However, under the use of certain contrast agents and standardized CTA techniques, they are mainly related to the individual factors of the subjects. The effects of height, heart rate, triglycerides, systolic blood pressure, and age on Tmax have been studied by scholars [29–31], and the author conducted a statistical analysis on 286 patients who underwent head and neck CTA examination based on previous studies and combined these influencing factors to obtain the calculation formula of Tmax. Due to the random selection of patients, this study has generalizability. The third set of acquisition schemes includes points before and after the static and dynamic peaks. The calculation formula we obtained will basically not miss the patient's arterial peaks.

One limitation of this study is the relatively small sample size of CTP scans, which could introduce some computational bias. Further validation of the research findings would require a substantial increase in the sample size. Second, this study only focused on patients with acute ischemic stroke, and other diseases need to be further studied. Finally, this study obtained conclusions through a retrospective analysis and did not conduct prospective scanning for research. CTP is designed to detect early acute ischemic stroke, and CTP ASPECTS $\geq$6 is superior to Auto and NCCT-ASPECTS in detecting acute ischemic stroke [9]. We conducted a methodological study, placing regions of interest based on anatomical locations, and retrospectively analyzed the differences in the perfusion values at the same level of interest through processing. Therefore, this study did not include patients with ASPECTS scores of 1–2.

Through this experimental study, it was found that the scanning scheme (with a sampling interval of 3 s for scanning, continuous scanning between the peak points of the arterial and venous TDC, and retention of one continuous sampling point before and after the peak points of the arterial and venous TDC, with the remaining sampling interval of 4.5s) is consistent with the perfusion parameters of the 1.5s standard sampling scheme and is the maximum time limit for CTP scanning. By incorporating the peak time prediction from this study, this method has the potential to become a truly applicable scanning protocol in a clinical setting.

Data availability statement

Data will be made available on request. Data included in article/supp. material/referenced in article.

Informed consent statement

All patients signed informed consent forms.

Ethics statement

This study was reviewed and approved by the Ethics Committee of Tianjin Medical University General Hospital, with the approval number: 3332. All participants provided informed consent to participate in the study.

CRediT authorship contribution statement

Yaxin Duan: Writing – original draft, Visualization, Supervision, Methodology, Formal analysis. **Jia Yao:** Resources, Methodology. **Yingjian Jiang:** Writing – review & editing, Software. **Wen Sun:** Validation, Software. **Fengtan Li:** Supervision, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Fengtan Li reports financial support was provided by Tianjin Bureau of Science and Technology.

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