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Feasibility study of the best monitoring time-interval to track contrast agent bolus in dual-source coronary computed tomography angiography

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► ***Original article***

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Keywords: *Dual source computed tomography, coronary computed tomography angiography, bolus tracking, radiation dose.*

ABSTRACT

***Background*:** To identify the best time-interval for dual-source coronary computed tomography angiography (CCTA) with bolus tracking automatic trigger technique. ***Materials and Methods*:** 120 patients were randomly divided into four groups (A, B, C and D), with 30 patients in each group. Monitoring was begun 10 seconds after injection, and the monitoring time-intervals for groups A, B, C and D were 1.14, 1.47, 2.00 and 3.00 seconds, respectively. CCTA acquisition was triggered as the monitored concentration in the region of interest (ROI) exceeded 100 HU. The monitoring times, CT and dose length product (DLP) values of the four groups were compared statistically. The quality of recorded CCTA images was evaluated objectively, and the image quality of blood vessel segments was accessed subjectively. ***Results*:** there were no statistically significant differences in objective evaluations between the four groups (P>0.05). Subjective evaluation results showed no statistically significant differences between groups A (1.879±0.042), B (1.876±0.043) and C (1.881±0.052). Group D showed the highest subjective score (2.923±0.069), which was significantly different from groups A, B, and C (P<0.01). The monitoring times for groups A, B, C and D were 4.78±2.37, 3.76±1.39, 2.77±0.99 and 2.38±0.64, respectively; and the DLP values were 4.13±2.22, 2.18±0.80, 1.50±0.51 and 1.48±0.43 mGy·cm, respectively. DLP increases with increased monitoring times. ***Conclusion*:** When performing dual-source CCTA, a monitoring time-interval of 2 seconds with trigger scanning technique is the best choice, since it effectively reduces the radiation dose while providing satisfactory images.

INTRODUCTION

Dual-source coronary computed tomography angiography (CCTA) is a noninvasive diagnostic method offering fast scanning speed [1-5]. The latest dual-source computed tomography (CT) systems allow improved temporal resolution to 83 ms [6]. Initial reports demonstrated high diagnostic accuracy [7, 8] and good quality vessel images with this technique, even in the presence of high and irregular heart rates [9-14].

Although CCTA is a valuable tool for the clinician, the dangers from radiation exposure cannot be ignored [15-19]. It has been a challenging problem to ensure that CT images meet diagnostic requirements while at the same time reducing the risk of exposure to a maximum radiation level during the procedure. Solving this problem has become a hot research topic and a focus of investigation in recent years. In dual-source CCTA, the radiation dose received by the patient is not only caused by the inherent characteristics of the method, but also by the condition of the individual patient, the technician's operation of the equipment, and by the scanning parameters [20-26].

There are two kinds of computed tomography angiography (CTA) contrast agent bolus methods [27-29]: 1. Test bolus: Test bolus uses a small dose to measure the time-to-peak in blood circulation, then adds 4~6 seconds of experience value to the scan delay time. A total of 15~20 ml of contrast agent is injected. With this method the radiologist can obtain the dynamic blood curve of the patients. The time-density curve is used to calculate the time to peak. The peak time is accurately determined with this method, but the workflow is complicated, and the dose of contrast agent is large, so it is seldom applied in the clinic [30]. 2. Bolus-tracking: the region of interest (ROI) and a threshold value are set, and the scan is triggered when it reaches the threshold value

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[31]. This method involves injection of contrast agent only once to complete the enhanced inspection, the workflow is easy, and it reduces the radiation dosage. The bolus-tracking technique is commonly used in CCTA.

Previous studies have seldom investigated ways of reducing the radiation dose received during bolus tracking once the contrast agent arrives at the coronary artery field. In the bolus-tracking technique, the time-interval for bolus tracking is one of the most important parameters affecting radiation dose and image quality. Short time intervals increase the radiation dose, while long time intervals may miss the best CTA scanning period, when the contrast agent concentration peaks in the coronary artery. At present, there are few studies investigating the relationship between the interval and the radiation dose. In the spirit of the ALARA (As Low as Reasonably Achievable) principle, the authors aim was to determine the best monitoring time-interval in dual-source CCTA, to ensure the best image quality with the lowest CT radiation dose.

MATERIALS AND METHODS

Clinical data

A total of 120 patients suspected of having coronary heart disease were prospectively followed from April 2016 to April 2017 at Tianjin Third Central Hospital. Inclusion criteria included the following: (1) no iodine allergy history; (2) no coronary artery lumen angioplasty and stent implantation, no bypass history; (3) heart rate < 90 times/min, smooth rhythm of the heart; (4) a body mass index (BMI) >18 kg/m2 and <25 kg/m2; (5) ejection fraction >50% and <70% by ultrasonic cardiogram.

The 120 patients were randomly divided into four groups (A, B, C and D), with 30 patients in each group. The groups consisted of the following: (1) Group A: 18 males, 12 females; aged 25 to 81 years, with an average age of 61±11 years; (2) Group B: 19 males, 11 females; aged 24 to 78 years, with an average age of 59±12 years; (3) Group C: 17 males, 13 females; aged 29 to 86 years, with an average age of 60±10 years; (4) Group D: 19 males, 11 females; aged 23 to 78 years, with an average age of 63±8 years. This study was approved by the medical ethics committee of Tianjin Third Central Hospital (IRB2019-023-01).

CCTA imaging method

We used a Siemens Healthcare Definition Flash dual-source CT (Germany) system, with the prospective heart switch trigger control sequence activated. Additional specifications include the following: full exposure dose range 35–85% R-R interphase, automatic tube voltage scanning technology and CAREdose4D, reference tube voltage 100 kV, reference tube current 320 mAs, collimation 128×0.6 mm2, rotation rate 0.28 seconds per circle, temporal resolution 75 ms, and field of view (FOV) determined by the patient's size. The scan range was from 1 cm under the carina of the trachea to the diaphragmatic surface of the heart. The scan duration was automatically determined by the CT machine. Prior to conducting the scan, 60 ml of contrast agent (iohexol, ionic, 350 mg/ml) was injected into the vein of the right forearm at a rate of 5 ml/s using a double-cylinder, high pressure syringe (American LF OptiVantage™ DH). 40 ml of normal saline solution was then injected at the same flow rate. Using bolus tracking automatic trigger technology with enhanced monitoring, the ROI was established as the ascending aorta from 1 cm under the carina of the trachea, and the area of the ROI was larger than 50% of the cross-sectional area of the aortic root.

During the monitoring scan, the X-ray tube voltage was 100 kV, and the tube current was 80 mAs. When the value of the ROI reached or exceeded a preset threshold of 100 HU, the scan of the coronary artery was started in 5 seconds. The equipment automatically generated a density-enhancement curve during the monitoring process. Monitoring started after a 10 seconds delay following injection of the contrast agent. The monitoring time-intervals for groups A, B, C and D were 1.14, 1.47, 2.00 and 3.00 seconds, respectively.

CT images were processed via sinogram affirmed iterative reconstruction (SAFIRE). The restructuring value was three, and the convolution kernels were medium smooth ASA. The image layer thickness was 0.75 mm with a space-interval of 0.50 mm. The thin-layer data was transferred to an evaluation system, and the image post-processing was performed using the maximum intensity projection (MIP), multi-planar reformat (MPR), and volume-rendering (VR) methods.

Evaluation of image quality

Two radiologists with at least five years of experience performed blindly a subjective and objective evaluation of the images and examined the phenomenon of inflection in the time-density curves.

Objective evaluation

Measurements were taken of the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the aortic root, and the CNR of the left main (LM) and right coronary artery (RCA). The largest possible ROIs in the lumen of the aortic root (AO), LM and RCA were delimited, avoiding soft plaque and calcification in the lumen. To account for the standard deviation (SD) of the average CT value in the ROI of the AO manifesting as image noise, the CT value of surrounding adipose tissue (AT) in the vessel wall was measured. The ROI should be kept the same as the ROI of the coronary artery lumen when measuring the CNR. The SNR of the AO (SNR_{AO}) was calculated using the equation (1) [19]:

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$SNR_{AO}=CT_{AO}/SD_{AO}$ (1)

Where CT_{AO} is the CT value of the AO and SD_{AO} is the SDof the AO.

The CNR of the LM (CNR_{LM}) and the CNR of the RCA were calculated using equation (2) and equation (3), respectively [19], where CT_{LM} is the CT value of the LM, CT_{AT} is the CT value of the AT, SD_{AT} is the SD of the AT and CT_{RCA} is the CT value of the RCA

$CNR_{LM}=(CT_{LM}-CT_{AT})/SD_{AT}$ (2)
$CNR_{RCA}=(CT_{RCA}-CT_{AT})/SD_{AT}$ (3)

Subjective evaluation

Adopting the 18-segment standard recommended by American Heart Association [32], missing blood vessels, occlusive blood vessels and terminal blood vessels were excluded from this research. The procedure for grading the quality of coronary artery images was obtained from the literature [33] and was as follows: Score 1, vessels and boundaries are clear without pulsation artifacts or vascular disruption; Score 2, vessels show light pulsation artifacts; Score 3, vessels show medium pulsation artifacts; Score 4, vessels are unclear or show serious pulsation artifacts. Scores 1–3 indicate that the vessels can be evaluated; Score 4 indicates that the vessels cannot be evaluated.

Monitoring and radiation dose

The CT dose during the bolus-tracking technique was recorded to determine the dose length product (DLP). The radiation dose was simply the dose received while in auto-tracking technology without considering the scout view and the coronary artery CTA scan dose. The monitoring times were recorded, as well as the CT values, CT dose index volumes (CTDivol) and the DLP, once the CT values at the ROI of the four groups reached the threshold value.

Statistical analysis

Data were analyzed using IBM SPSS Statistics software (SPSS, Inc., Chicago, USA) 19.0 software. Results are expressed as the mean±SD. One-way analysis of variance (ANOVA) was used to compare the objective evaluation values, monitoring results and DLP between the four groups. Pairwise comparison using the Chi-square test was processed in an inter-group fashion. P values less than 0.05 were considered statistically significant.

RESULTS

Evaluation of image quality

As shown in figure 1, several specific ROIs in all the selected CCTA images were evaluated objectively and subjectively.

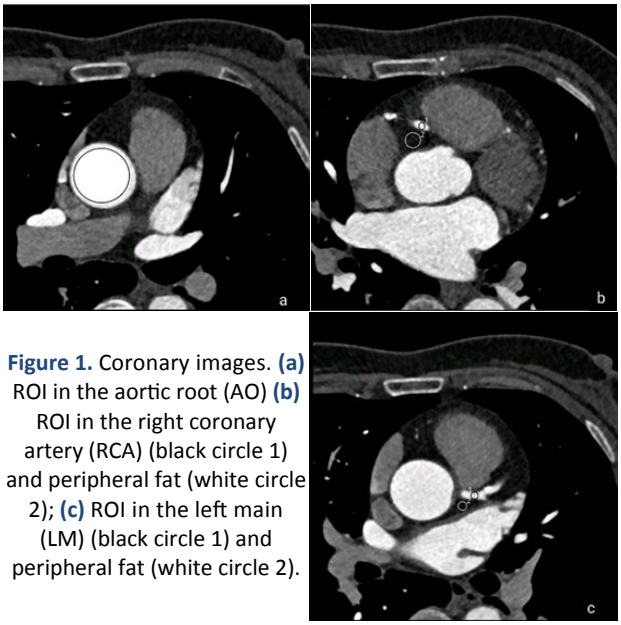


Figure 1. Coronary images. **(a)** ROI in the aortic root (AO) **(b)** ROI in the right coronary artery (RCA) (black circle 1) and peripheral fat (white circle 2); **(c)** ROI in the left main (LM) (black circle 1) and peripheral fat (white circle 2).

Objective evaluation

The results of the statistical analysis of the objective evaluation scores for the AO, RCA, and LM are shown in table 1. After comparing the quality of the images obtained with different time-intervals, the results showed no statistically significant differences (P>0.05).

Table 1. Objective image quality evaluation of the ROIs in the four groups with different monitoring time-intervals (mean±SD).

Group	AO				RCA		LM	
	CT (HU)	Noise	SNR	CNR	CT (HU)	CNR	CT (HU)	CNR
A	486±5	34±5	14.4±3.2	23±10	471±64	25±7	479±21	21±3
B	465±65	32±4	15.6±2.1	20±8	455±95	28±13	450±65	23±6
C	494±59	33±4	14.8±1.3	25±5	455±62	28±5	486±96	25±6
D	474±55	33±5	14.3±1.8	24±7	456±62	27±5	475±57	24±3
F-value	2.111	2.651	2.125	2.734	1.299	1.200	2.646	3.031
P-value	0.127	0.076	0.125	0.070	0.278	0.306	0.076	0.053

* Monitoring time-interval for Groups A, B, C and D were 1.14, 1.47, 2.00and 3.00 seconds, respectively.

Subjective evaluation

The results of the statistical analysis of the subjective evaluation scores for the four groups are shown in table 2. There were no statistically significant differences between groups A (1.879±0.042), B (1.876±0.043), and C (1.881±0.052). The highest subjective score was for group D (2.923±0.069). Based on the calculated P-values (P<0.01), there were statistically significant differences between group D and groups A, B, C. As shown in figure 2, longer monitoring times (over 2 seconds), were associated with reduced image quality. As shown in figure 2(a), with a time-interval of 2 seconds the contrast agent was evenly

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distributed in the right coronary artery, producing good visibility and clear boundaries of blood vessels. In contrast, with a time-interval of 3 seconds, the contrast agent concentration was significantly higher at the proximal end of the right coronary artery than at its distal end [figure 2(b)]. The contrast agent was unevenly distributed inside the vessels, a phenomenon which could increase the risks of an incorrect diagnosis.

Table 2. Subjective quality scores of the images for the four groups.

G	S.N.	Score 1		Score 2		Score 3		Score 4		Average score
		SN	percent	SN	percent	SN	percent	SN	percent	(Mean± SD)
A	629	317	50.3%	152	24.2%	79	12.6%	81	12.9%	1.879± 0.042
B	631	320	50.7%	150	23.8%	80	12.7%	81	12.8%	1.876± 0.043
C	631	319	50.5%	150	23.8%	80	12.7%	82	13.0%	1.881± 0.052
D	512	85	16.6%	94	18.4%	108	21%	225	44%	2.923± 0.069*

[1]Monitoring time-intervals for Group A, B, C and D were 1.14, 1.47, 2.00 and 3.00 seconds, respectively. [2], there were statistically significant differences between group D and groups A, B, and C ($P < 0.01$). [3]G denotes group; P denotes percentage; SN denotes segment number.

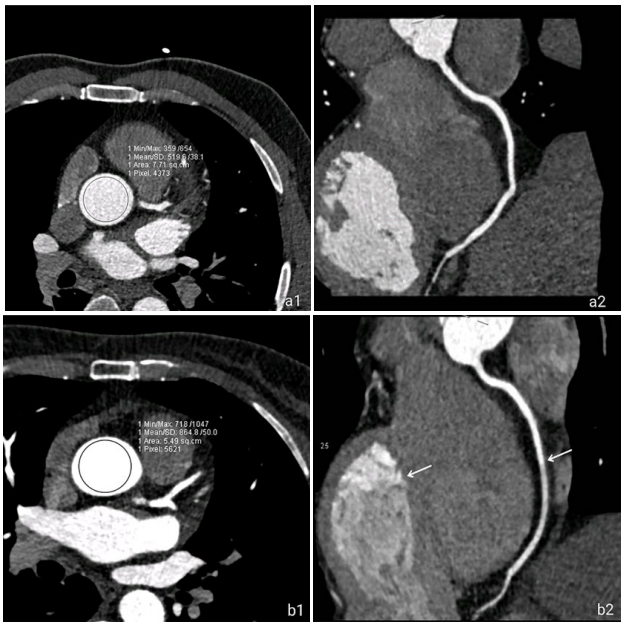


Figure 2. Comparison of images at time-intervals of 2 seconds and 3 seconds. **(a1)** Image monitoring time-interval of 2 seconds; monitored four times; last CT value (146 HU) reached the threshold. **(a2)** CT value is 519.6 HU for the aortic root scan; the contrast agent fills the right coronary artery evenly; blood vessels show clear boundaries. **(b1)** Image monitoring time-interval of 3 seconds; monitored three times; last CT (328 HU) reached the threshold. **(b2)** CT value is 864.8 HU for the aortic root scan; the contrast agent concentration in the proximal end of the right coronary artery is significantly higher than in the distal end of the right coronary artery; the arrows indicated where the contrast agent is unevenly distributed in the vessels.

Monitoring index and radiation dose

This analysis was performed to demonstrate that several indicators change during monitoring and that the radiation dose is reduced by extending the time interval.

Bolus tracking results

Time-density curves were generated to show the quality of the bolus tracking. The CT values for the ROI were recorded by X-ray scans during monitoring and are shown in figure 3. The curve in figure 3(c) shows ideal bolus tracking results, with no reversal of CT values. In contrast, there were two reversals of CT values in figure 3(a). Even though there were no CT value reversals in figure 3(b), the bolus tracking results were not ideal, when compared with the curve in figure 3(c).

Based on the time-density curves, the percentage of reversal phenomena in groups A, B, C and D gradually decreased: 30% (9/30), 20% (6/30), 0.7% (2/30) and 0.03% (1/30) respectively.

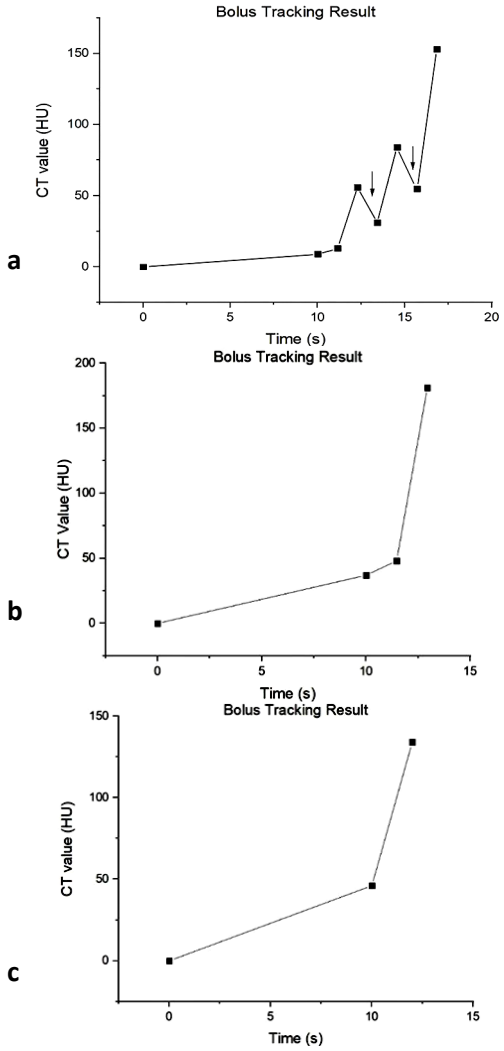


Figure 3. Bolus tracking results for **(a)** 39-yr-old male, Group A, two reversals (indicated by the arrows), time-enhancement curve, DLP=4 mGy·cm; **(b)** 67-yr-old female, Group B, no reversals, not the ideal state, DLP=2 mGy·cm; **(c)** 72-yr-old male, Group C, no reversals, the ideal state, DLP=1 mGy·cm.

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Monitoring and radiation dose results

The statistical analysis of several monitoring and radiation dose indicators for the four groups is shown in table 3. In terms of CT values (the CT value for the ROI once it reached the threshold), there were no statistically significant differences between groups A, B and C. However, there were statistically significant differences between group D and groups A, B and C (P<0.01). Compared with group D (3 seconds), the patients in group A (1.14 seconds) received about three times more radiation. DLP increases with increased monitoring times.

Table 3. Monitoring index and radiation dose for the four groups with different monitoring time-intervals (mean±SD).

Group	Case	Monitoring index		
		M times	CT (HU)	DLP (mGy·cm)
A	30	4.78±2.37	133±24	4.13±2.22
B	30	3.76±1.39	142±39	2.18±0.80
C	30	2.77±0.99	137±26	1.50±0.51
D	30	2.38±0.64	204±46*	1.48±0.43

*M times: monitoring times; CT value: the measured CT values when the ROIs reached the threshold. *DLP denotes dose length product. * There were statistically significant differences between Group D and Groups A, B and C (P<0.01).

DISCUSSION

The goal of this study was to identify the optimal time intervals to obtain good quality CCTA images while reducing the radiation dose, thus conforming to the ALARA (As Low as Reasonably Achievable) principles.

CCTA has high accuracy in detecting coronary artery stenosis and is an important non-invasive inspection method. There are two kinds of CTA contrast agent bolus methods: test bolus and bolus tracking [27-29]. There are a large number of studies including hardware, software, and optimization of scanning schemes to reduce radiation dose [34, 35]. In terms of optimizing the scanning plan, Masuda *et al.* [36] found that the 100-kVp CCTA protocol can help reduce radiation dose without reducing the diagnostic accuracy; Moradi *et al.* [37] resulted that the Bolus tracking technology has a smaller radiation dose than the test bolus technology when there is no statistical difference in the diagnosis; Achenbach *et al.* [38] used prospective ECG trigger acquisition technology, and Nakaura *et al.* [29] used a low-dose short injection duration scheme protocol reduce radiation dose. They all focused on reducing the radiation dose during the enhancement period, because the radiation dose during this period accounted for the vast majority of the total dose in the CCTA examination. Previous studies have neglected the radiation dose of the contrast agent monitoring scan. In this study, the optimization of the bolus-tracking scheme was studied.

Few studies investigated ways of reducing the radiation dose received during bolus tracking once the contrast agent arrives at the coronary artery field. The selection of the time interval to trigger acquisition with the bolus -tracking technique is critical. With this method, a short time interval may result in acquisition of data too early, before the contrast agent in the aorta reaches a stable peak, and frequent exposure makes no sense. On the other hand, a long time interval may result in the acquisition of data too late, after the contrast agent peak in the aorta has passed. This may affect image quality in CCTA.

In our study, the monitoring time-intervals of the four groups were 1.14, 1.47, 2.00 and 3.00 seconds, respectively. The results show that setting the monitoring time interval at 2 seconds when performing dual-source CCTA with bolus-tracking technique ensures good image quality while reducing the radiation dose.

In a report by Lell *et al.* [39], the contrast agent concentration in vessels increased sharply to 200 HU after slowly increasing to 100 HU, and then steadily reached its peak. Since the CT scanning threshold trigger in our study was 100 HU, the sharply increasing curve from 100 to 200 HU was not observed. In the slow-ascending segment of the curve (up to 100 HU), groups A and B often showed reversal phenomena, instead of an ideal increase. Only 2 cases in group C showed a reversal of the CT value curve, and it is possible that the long time interval (2 seconds) and reduced monitoring times decreased the rate of triggering by CT value fluctuations.

The potential reasons are: 1. when the contrast agent bolus advances inside the aorta, the front is constantly diluted and mixed with blood. If the monitoring time interval is too short and the front of the contrast agent bolus (with an unstable iodine concentration) is monitored too frequently, this may lead to a fluctuation of the CT value for the ROI in the aortic root. 2. A highly concentrated contrast agent bolus may rapidly enter into the superior vena cava, forming beam-hardening artifacts and contaminating the adjacent aortic arch root, resulting in errors of the CT value. Because of these two reasons, increased monitoring times were associated with more reversal phenomena.

Our study did not address patients who required additional doses of contrast agentor higher injection flow rates. Whether this technology can be adapted to patients with arrhythmia or cardiac dysfunction still requires further study.

CONCLUSION

It is feasible to identify the best time interval for dual-source CCTA with bolus tracking automatic trigger technique. Compared with the traditional time interval of 1 seconds, a 2 seconds time interval produces satisfactory images, but the radiation dose is significantly reduced.

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***Conflicts of Interest*:** The authors declare that they have no conflicts of interest.

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***Author contribution*:** Conceptualization, (L.H), (Y.H), and (T.W); methodology, (L.H); software, (C.Y), (R.L), (Z.L) and (T. Z); validation, (C.Y), (R.L), (Z.L), and (T.Z); data curation, (T.W), (Y.H), and (L.L); writing-original draft preparation, (L.L), (Y.H), and (T.W); writing-review and editing, (L.L), (T.W) and (Y.Han); supervision, (L.H).

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