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Feasibility study of an automatic injection plan for coronary computed tomography angiography using 80 kilovolt and very low iodine dose

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► ***Original article***

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ABSTRACT

Background*:** To explore the feasibility of using various ultra-low contrast flow rates on the coronary CTA (CCTA) when the tube voltage is set at 80KV automatically on 3rd-generation dual-source CT. ***Materials and Methods: A total of 180 patients with suspected coronary atherosclerotic disease were randomly divided into two groups, each subdivided into seven BMI-based subgroups (≤ 25, 25-26, 26-27, 27-28, 28-29, 29 -30, > 30). The experimental group (A) used individualized injection rates (2.8-3.4 ml/s) with 350 mg I/ml contrast agent based on BMI, with a fixed injection time of 10s. The control group (B) used a fixed injection rate of 4.0 ml/s and a fixed injection time of 12s. Both groups employed prospective ECG-gated scanning. Image quality, effective radiation dose, and contrast agent dosage were compared using the Student's t-test. ***Results:*** In Group B, the coronary artery CT value exceeded the optimal diagnostic range (300-450 HU) recommended by experts. Group A had significantly lower CT values, SNR, and CNR compared to Group B ($P < 0.05$), but the enhancement in Group A was closer to the optimal diagnostic range. There was no significant difference in subjective image scores between the groups ($P > 0.05$), with consistent scoring between two directors (ICC: 0.612-0.852). Both groups had similar effective doses ($P > 0.05$). The contrast agent dosage in Group A was significantly lower than in Group B ($P < 0.05$). ***Conclusion:*** The optimized contrast injection scheme can significantly reduce the amount of contrast agent and obtain better image quality.

INTRODUCTION

Coronary Artery CT Angiography (CCTA) is increasingly favored as a noninvasive method for diagnosing coronary heart disease, but faces challenges due to concerns over radiation dose and iodine contrast agent usage [1, 2]. The demand for CCTA examinations continues to rise, prompting research into strategies that minimize these risks while maintaining high-quality diagnostic images.

The advent of 3rd-generation dual-source CT has revolutionized CCTA by integrating automatic tube voltage and current modulation technologies. These advancements consider patient-specific factors such as BMI, chest shape, chest fat and muscle content, and breast morphology [3]. Studies have demonstrated that automatic tube voltage selection surpasses BMI-based methods in reducing radiation dose without compromising image quality [3, 4]. However, Wang et al. highlighted issues with maintaining vascular enhancement stability across various patient profiles within the selected tube voltage range, indicating ongoing challenges in protocol optimization [5]. Before starting this study, a total of 986 patients accepted 80 kV CCTA examination from July 2019 to March 2020 (350mgI/ml,contrast injection rate of 4 ml/s, 12s), with coronary CT value of 580 ± 113HU (467 to 693 HU),which was higher than expert recommendations [6].

For the IDR (iodine delivery rate) as a key element on vascular attenuation [7], the range of optimal coronary enhanced CT values (300-450HU) [8] suggests that the IDR can be further reduced under 80KV. Meanwhile, the BMI range of 80KV population is wide, and according to previous clinical experience, patients with lower BMI may need only a lower contrast injection rate under the same scanning conditions. Therefore, this study set the contrast injection rate of 80kV population to further refine the contrast injection scheme while ensuring the image quality.

Our study uniquely focuses on optimizing contrast injection protocols for 80 kV CCTA, considering both BMI variations and the impact on IDR to achieve optimal vascular enhancement while adhering to recommended coronary CT values. By tailoring contrast administration to patient-specific factors and leveraging advanced CT technologies, we aim to contribute novel insights into enhancing diagnostic accuracy and patient safety in CCTA.

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MATERIALS AND METHODS

General information

From May 2021 to February 2022, 180 patients from the Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University underwent CCTA detection. These patients were randomly assigned to either the experimental group (Group A) or the control group (Group B), as detailed in table 1.

Inclusion criteria: 1) The automatic tube voltage selection is 80KV.Exclusion criteria: 1) Contrast allergy to iodine; 2) Insufficiency of the liver and kidneys (blood creatinine> 12 mol/L); 3) Insufficiency of the heart and severe arrhythmias; 4) Following stenting/bypass grafting of the coronary arteries; 5) Following the implantation of a cardiac pacemaker; 6) Mismatch in breath holding. This study had been reviewed by the ethics committee of our hospital (The ethics committee of Nanjing Medical University, No. 20201012b), and iodine contrast medication informed consent was signed prior to the examination.

Method

CCTA detections were performed on the 3rd-generation dual-source CT (SOMATOM Definition Force; Siemens Healthcare, Forchheim, Germany). All patients accept breathing training before examination. Then patients were placed in the supine position and ECG were connected. An 18G indwelling needle was embedded in the median right cubital vein. Nitroglycerin (0.5mg) was taken under the tongue 3 minutes before scanning. The scan range is from the level 1cm lower than the tracheal fork to the cardiac diaphragm surface. Scanning parameter settings were: prospective ECG gating sequence scanning mode, X-tube speed 0.25s / rotation, image layer thickness 0.75 mm, convolution core b26f. A high pressure twin syringe was injected with ioxol (350 mg I / ml, Beijing Beilu Pharmaceutical Co. LTD, China) through the right anterior cubital vein, followed by 0.9%, 40ml of saline at an injection rate of 4.0ml/s. Use bolus-tracking method and set ROI at the ascending aortic root with a trigger threshold of 60 HU and a delay time of 5s. Tube current is controlled by four-dimensional intel ligent real-time dose control technology (CARE Dose 4D, Siemens Medical system). Tube voltage is automatically provided by the scanner. The injection protocol for the experimental group is shown in table1:

Table 1. The injection protocol of iodinated contrast media.

	BMI	IDR (gI/s)	Flow velocity (mL/s)	Injection time (s)
Experimental group	BMI ≤25	0.98	2.8	10
	25<BMI≤26	1.01	2.9	10
	26<BMI≤27	1.05	3.0	10
	…	…	…	10
	30<BMI	1.19	3.4	10
Control group		1.40	4.0	12

Note: *:BMI: Body Mass Index, IDR: the iodine delivery rate

Image post-processing

Use advanced simulation technology (advanced modeled iterative reconstruction, ADMIRE) to reconstruct images, and the image data is transmitted to Syngo. The post-processing workstation (Siemens Healthcare, Forchheim, Germany) use circulation software with volume reproduction (volume rendering, VR), Multiplan reconstruction (multi planar of each vessel-reformation,,MPR) and surface reconstruction (curved planar reformation, CPR).

Objective evaluation indicators

The CT value of aortic root (AO), left trunk (LM), left anterior descending branch (LAD, proximal, middle, distal), left circumflex branch (LCX) and right coronary artery (RCA, proximal, middle, distal) was recorded. ROI (region of interest) should avoid calcification, plaque and tube wall. Define the standard deviation (SD) of aortic root as image noise: SD <20 HU as excellent, 20~30 HU as good, SD> 30 HU as poor image quality, SD> 40 HU as examination failure (image cannot be evaluated) [8]. The signal to noise ratio (SNR) and contrast noise ratio (CNR) was calculated. The calculation formula is shown in table 2.

Table 2. The formula involved in this study.

1	**SNR**	Luminal CT value/ SD value
2	**CNR**	(Luminal CT value -adjacent soft tissue[a]Average CT value) adjacent to the soft tissue SD value
3	**ED (mSv)**	DLP*k, where k is the conversion factor, In this study, 0.014mSv / (mGy · cm)
4	**Iodine flow rate (mgI/s)**	Iodine contrast concentration (mgI/ml) *Contrast injection flow rate (ml / s)
5	**Total iodine (g)**	Iodine contrast concentration (mgI / ml) *Contrast dose (ml) / 1000

Adjacent tissue: the parasternal muscles were selected as the adjacent tissue in this study. SNR: signal to noise ratio. CNR: contrast noise ratio. ED: effective radiation dose. DLP: dose length product.

Subjective evaluation indicators

Based on the 15 segments of coronary tree recommended by the American Cardiovascular CT Association [9], all 1.5mm diameter coronary artery segments were selected for analysis. The subjective quality is evaluated by 4-point scale: 1 Point: 90% of shaped artery segments are diagnostic without artifacts; 2 Points: 80% of the diagnostic coronary segments have no artifacts; 3 Points: 70% of the diagnostic coronary segments have no artifacts; 4 Points: 60% of diagnostic coronary segments have no artifacts. Vessels with a score of 1-3 were evaluable vessels. The image quality was evaluated by two senior imaging physicians with over 5 years' experience.

Radiation dose and iodine intake

Read and record the value of the CT volume dose index (CTDIvol) and the dose length product (DLP) in the scan dose report, and calculate the effective dose (ED), The calculation formula is shown in table 2.

Contrast dosage (ml) was recorded and total

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iodine and iodine flow rate were calculated (iodine delivery rate, IDR). The amount of contrast agent iodine (gI/s) is injected per second, and the calculation formula is shown in table 2.

Statistical analysis

The results were statistically processed using SPSS 25.0 software. Gender difference, age, BMI, heart rate, $CTDI_{vol}$, DLP, ED, coronary objective parameter values, subjective quality score, contrast dosage and so on were compared. The data that conformed to be the normal distribution were analyzed by ANOVA, and the data with skew distribution were used by *Z*. The consistency of the two physicians was analyzed by inter-class correlation coefficient (ICC). *ICC* <0.40 indicates poor consistency, ICC when 0.40-0.75 or >0.75 means acceptance. All statistical results were considered significant at P <0.05.

RESULTS

General information

Sex, age, BMI, and heart rate varied nonsignificantly between the experimental group (Group A) and the control group (Group B) (P> 0.05, table 3).

Table 3. The comparison of the general data between Groups A and B ($\bar{X}\pm s$).

Group	n	Gender (example) men and women	Age (year)	BMI (kg/m^2)	Heart rate (secondary / min)
Experimental group	90	49 41	62±17	27.9± 4.1	65±16
Control group	90	52 38	63±14	27.3±4.2	66±17
t value		0.059*	-0.506	-0.409	0.793
P value		0.815	0.831	0.901	0.572

Note: *:BMI: Body Mass Index, IDR: the iodine delivery rate

Objective quality evaluation

CT value: the CT value in Group B (602.34±90.42 HU) is higher than the guideline recommended CT range (300-450 HU); the Group A CT value (456.73±76.32 HU) is lower than Group B *P* <0.05, but closer to the guideline recommended CT range (figure 1a).

Noise: The noise of all images does not exceed 30HU, and there is no significant noise difference between group A and B (P> 0.05, figure 1b).

SNR and CNR: The SNR and CNR differed significantly between groups A and B, with group A showing lower values than group B. (*P* <0.05, figure 1c~d).

Subjective quality evaluation

Groups A and B had 4752/4766 vessels segments evaluated and the subjective image quality scores between groups A and B were (1.13± 0.09) and (1.12±0.09), with no significant difference (*Z*=0.169, *P*=0.700; figure 2a~b).The consistency of the coronary image quality scores by 2 physicians was from 0.612 to 0.852, both were more than 0.60, showing good agreement.

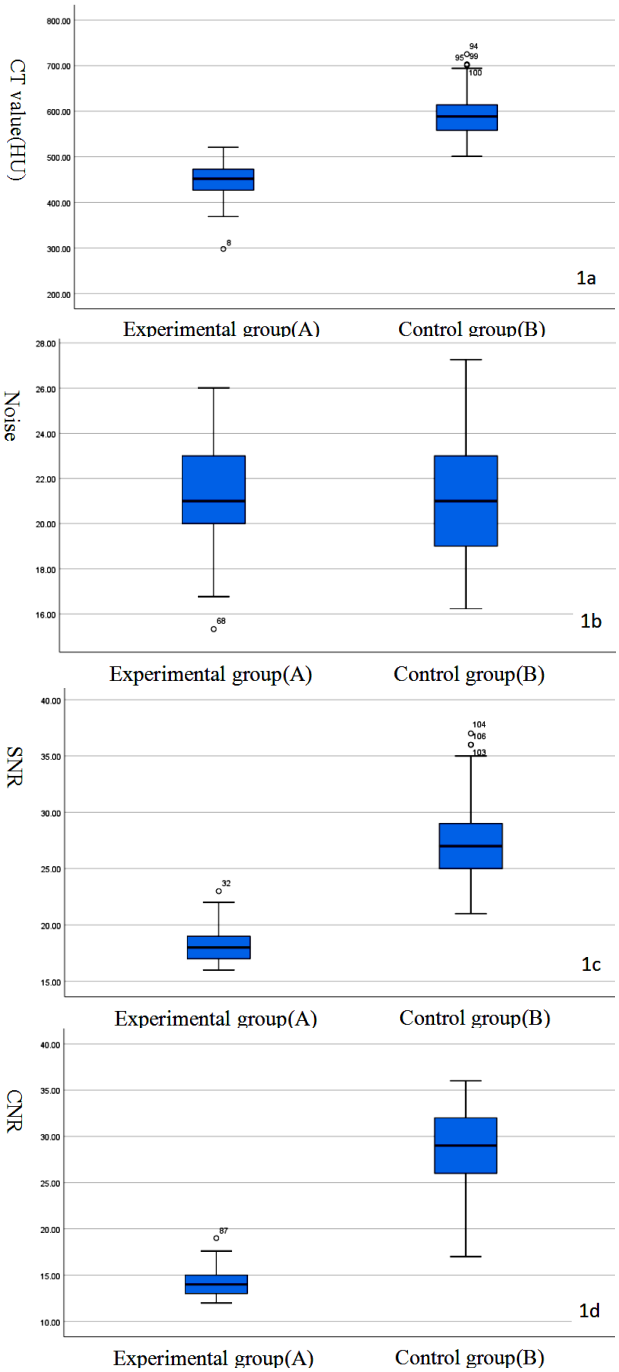


Figure 1. Comparison of the objective quality parameters between groups A and B. **1a:** Comparison of CT value between groups A and B. **1b:** Comparison of noise between groups A and B. **1c:** Comparison of SNR between groups A and B. **1d:** Comparison of CNR between groups A and B.

Radiation dose evaluation

The ED was similar between groups A and B, with no statistically significant difference observed, indicating comparable radiation exposure for both groups. (*P*> 0.05, figure 3).

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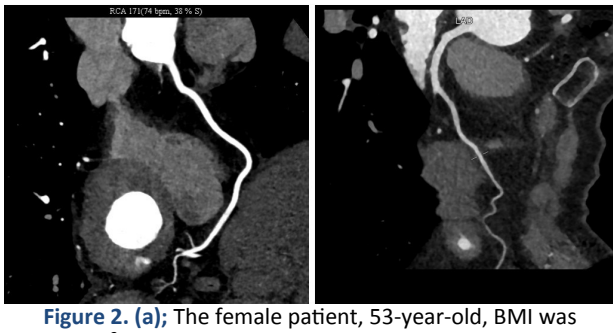


Figure 2. (a); The female patient, 53-year-old, BMI was 27.8kg/m^2, contrast injection rate is 4.0 ml/s, 48ml, contrast dosage, the average CT value of the RCA is 692.1 HU, CPR shows excessive "bright" of the right coronary artery lumen, image quality score is 1 point. **(b);** The female patient, 62-year -old, with a BMI of 27.0kg/m^2, contrast injection rate is 3.0 ml/ s, 30ml contrast dosage, left anterior descending lumen mean CT value of 412.6HU, LAD soft plaque shows clearly, and see calcified plaque (arrow) image quality score of 1 point.

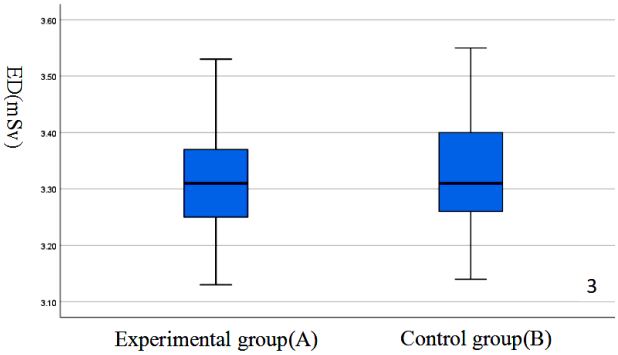


Figure 3. Comparison of ED between groups A and B, The ED was similar between groups A and B.

Evaluation of contrast agent dosage

The amount of contrast agents in groups A and B were (31.5±2.5) ml and 48ml which were significant (t = -13.286, P <0.05).

DISCUSSION

An appropriate coronary artery attenuation interval is the base of accurate diagnosis: low CT value (<200HU) will miss the soft plaque, too high (>500HU) will mask the hardened plaque and cause false negative performance [10-12]. Meanwhile, iodine may lead to allergic symptoms. Though side-reaction is rare to happen, minimized and suitable contrast agent is still required to reduce the probability of occurrence [13].

Our experiment verified that the individualized difference does exist in the actual 3rd-generation dual -source CT excluding the tube voltage photoelectric effect. With ATVS (automatic tube voltage selection) and tube current modulation, the automatic software algorithm (APSCM; Siemens Healthcare, Munich, Germany) focus on radiation dose reduction rather than coronary arteries CT value harmony. The result of control group corresponded to our impression that patients with low BMI could get high artery attenuation: someone's CT values is even 737HU (figure 1a) in the control group. The clinical phenomenon prompt us to adjust the injection parameters by reducing injection time/rate or concentration.

It has been consensus that iodine deliver rate (IDR is the key factor affecting vascular enhancement [14]. For CCTA belongs to short injection without recirculation (duration time < 15s) [6], the concentration of iodine in the blood vessel is a single peak curve [8]. The injection time parameter is related to injection volume. When the time or volume of contrast agent was above the baseline period, adjusting the injection time will not affect the vascular enhancement in the DSCT scanning time window. Meanwhile, if injection flow rate gets higher, although the peak time of intravascular iodine concentration was earlier, with bolus-tracking technology, the scanning window would catch higher attenuation [15].

At present, individualized injection schemes that adjust tube voltage and injection rate according to BMI have been widely studied and accepted [16, 17]. However, in the third-generation DSCT, fixed contrast agent schemes are mostly used according to selected single tube voltage ranges, and increase with the tube voltage [2, 17]. Few studies focus on individualized differences within single tube voltage. On the other hand, some studies focus on the individual indicators such as weight, body surface area (BSA), cardiac output (CO) ignoring the interference of tube voltage [1, 8, 18]. Quantifying voltage effect on vascular enhancement is complex and vague.

The problem of using the weight as the indicator is that the same weight may have different situations [19]. For example, a person with high muscle mass may weigh the same as someone with a higher fat percentage, leading to different clinical implications. Zhu *et al.* [20] had shown that BMI have positive influence on enhancement. One explanation is that fat tissue could have less blood volume than muscle tissue. BSA and CO are also too difficult to calculate for clinical practice. Ng *et al.* [1] had proved that CO have no extra advantage than body weight. Then we still choose BMI as parameters for adjustment. Based on Ruiqiu *et al.*'s research [17], 3.5 ml/s, 10s (IDR 1.22mgI/s) is adequate and still could be reduced. We determined the BMI range of 80KV by pre-experiment which show normal distribution with the peak subgroup 26 < BMI < 27. The center of velocity is 3 ml/s, then flow rate vary with BMI.

The noise difference between the groups A and B is not obvious with less than 30HU (Figure 1b),which showed excellent evaluation, indicating that the tube voltage recommended by the 3rd-generation dual-source CT is relatively reliable, and its iterative reconstruction technology also showed an effective noise reduction efficiency, which is consistent with the researches of Ippolito *et al.* [21].

All 90 patients in group A had obtained relatively

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satisfactory images, the CT value of the coronary artery lumen is closer to the range recommended by the experts (Figure 1a).Then SNR / CNR are the same results based on calculation formula. An intuitive representation is shown in figure 2a/b. However, for the BMI ≤ 25kg /m^2 population, someone's CT value is lower than what we expected. The reduction seemed to get relative critical value on injection rate. It cannot decline indefinitely.

Group A not only reduced the contrast injection rate, but also reduced injection time from 12s to 10s, further reducing the total iodine (table 2). About the effective radiation dose, there was no significant difference between groups A and B (Figure 3), This is because this study only shortened the injection time of the contrast agent, did not affect the time of cardiac data acquisition after the delayed exposure. In both groups A and B, cardiac data in 2-3 cardiac cycles were both collected under prospective ECG gating. The contrast agent volume adjustment will not affect the ED.

ED is mainly related to tube voltage and scan sequence. Wang *et al.* [4] used high-pitch scan mode, with 370 mgI/ml, 3ml/s, 7s (IDR1.11mgI/s), getting the sub-mSv ED. The point is that within 1 cardiac cycle scanning time, the contrast media requirement can be compressed to a very low degree. However, with longer scanning window in normal prospective adaptive sequence, such volume could not meet the aim.

At present, large clinical trials have shown that when 80kV, IDR1.2gI/ml for CCTA is adequate [14]. However, with ATVS technology, Martin *et al.* [2] tried 0.8mgI/s at 80 kV successfully. The result we attempt stands between two of them. One possible guess is that ATVS have the ability of filtering population. Those who suffered 80KV second-generation DSCT examination are partly divided into higher tube voltage in the third generation. They deserve higher IDR. In other words, the voltage selected decide baseline of contrast medium dosage. Similar to our previous study [22], IDR 0.98~1.19mgI/s could be applied with different BMI range in 80kV.

These are some limitations: The sample content of this study was relatively small compared with 70kV study [22], and the BMI < 25kg / m^2 and BMI > 30kg / m^2 populations were not further subdivided. The study results were not compared with the "gold standard" of coronary DSA. These are what to be further improved in future studies.

CONCLUSION

When the third-generation dual-source CCTA select tube voltage 80kV automatically, the contrast injection rate can be optimized according to the BMI range. The optimized contrast injection scheme can significantly reduce the amount of contrast dose and obtain better image quality. The technique is simple and deserves reference in clinical practice.

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***Authors' contributions*:** YY completed the collection of the study data and analyzed the patient data. GS conceived and designed the study and drafted the manuscript. YY and CY evaluated the coronary scores. JCP and GS helped interpret the results and played an important role in revising manuscript.
***Consent for publication*:** Informed consent was obtained from all the participants.

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