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Weight-adapted ultra-low-dose pancreatic perfusion CT: radiation dose, image quality, and perfusion parameters

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Abstract

Purpose We evaluate the reliability and feasibility of weight-adapted ultra-low-dose pancreatic perfusion CT.

Methods A total of 100 (47 men, 53 women) patients were enrolled prospectively and were assigned to five groups (A, B, C, D, and E) with different combination of tube voltage and tube current according to their body weight. Radiation dose parameters including volume CT dose index (CTDI) and dose-length product (DLP) were recorded. Image quality was evaluated both subjectively and objectively (noise, signal-to-noise ratio, contrast-to-noise ratio). Perfusion parameters including blood flow (BF), blood volume (BV), and permeability (PMB) were measured. The dose, image quality measurements, and perfusion parameters were compared between the five groups using one-way analysis of variance (ANOVA).

Results Radiation dose reached 8.7 mSv in patients under 50 kg and was 18.9 mSv in patients above 80 kg. The mean subjective image quality score was above 4.45 on a 5-point scale with good agreement between two radiologists. Groups A–D had equivalent performance on objective image quality ($P > 0.05$), while Group E performed even better ($P < 0.05$). No significant differences emerged in comparison with perfusion parameters (BF, BV, PMB) of normal pancreas parenchyma between the five groups.

Conclusion Weight-adapted ultra-low-dose pancreatic perfusion CT can effectively reduce radiation dose without prejudice to image quality, and the perfusion parameters of normal parenchyma are accurate and reliable.

Keywords Perfusion computed tomography · Image quality · Perfusion parameters · Dose reduction

Introduction

Volume perfusion computed tomography (VPCT) is an advanced functional CT imaging technique for the quantification of tissue perfusion [1]. It is an ideal noninvasive method to detect and locate insulinomas, the most common hyperfunctioning pancreatic endocrine tumors. Insulinomas are generally benign and curable with surgery [2], and precise preoperative localization of insulinomas allows for minimally invasive surgeries [3]. Multi-detector computed tomography (MDCT) is the first-line imaging modality for insulinoma detection with a sensitivity ranging from 63.3% to 94.4% according to different studies [4–7]. Positive MDCT results are mainly based on the typical enhancement pattern of insulinomas (hyperattenuating in the arterial phase), so false negative results may occur when facing insulinomas with missed transient hyperenhancement or non-hyperenhancement [8]. Non-hyperenhancement insulinomas, or isoattenuating insulinomas, account for about a quarter of all insulinomas and can be detected by perfusion CT because they have increased blood flow [9]. Previous study has proved that the addition of pancreatic perfusion CT can improve the diagnostic performance of MDCT, sensitivity/specificity increasing from 88.1%/85.7% to 94.6%/94.7% [10]. Although 3T MRI with DWI has been proven to have equivalent insulinoma detection accuracy and even higher tumor conspicuity, not all patients can undergo MRI [11]. Moreover, perfusion CT may aid in predicting pancreatic necrosis in patients with acute pancreatitis, in

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differentiation between chronic pancreatitis with and without exocrine pancreatic insufficiency (EPI), and in differentiation between mass-forming chronic pancreatitis and pancreatic adenocarcinoma [12–15]. Because of all these promising advantages, VPCT is routinely performed as additional scans to conventional enhanced CT, which leads to higher radiation dose, larger amount of contrast material, as well as longer examination time, limiting its widespread use in clinical practice [16]. At present, radiation exposure is of foremost concern. With the development of equipment, a third-generation dual-source CT (SOMATOM Force) allows for ultra-low-dose scans and more rapid scans at the same time, and it has been applied on imaging examination of different parts of the body, such as chest CT and coronary CT angiography [17–21], proving its feasibility and advantages in clinical practice. So far, no multi-group weight-adapted ultra-low-dose pancreatic perfusion CT protocol has been established aiming at a gradual dose reduction as patient's weight declines. Under these circumstances, whether image quality remains stable and whether the perfusion parameters measured keep reliable need further investigation.

Thus, the aim of this study is to evaluate the reliability and feasibility of weight adapted ultra-low-dose pancreatic perfusion CT.

Materials and methods

Patient inclusion and exclusion criteria

This prospective HIPAA compliant study was approved by the institutional review board and complies with the Declaration of Helsinki. Informed consent was obtained from all patients. Patients with suspicion of pancreatic insulinoma were enrolled in this study if they fulfilled the following inclusion criteria: (1) clinical request of pancreatic perfusion CT examination; (2) no known history of iodine contrast material allergy; (3) normal renal function according to ESUR Contrast Media Safety Committee guidelines [22]. Exclusion criteria were as follows: (1) pancreatic lesion larger than 2 cm; (2) diffuse pancreatic disease; (3) poor image quality for measurement of perfusion parameters due to image artifacts. From December 2015 to March 2017, a total of 100 consecutive patients were included and were assigned to 5 groups according to their body weight, undergoing dose-saving volume perfusion CT scan with different combinations of tube voltage and tube current (Fig. 1). As for the design (kVp and mAs) of the five groups, the present routine protocol (80 kVp, 150 mAs) served as baseline. Then, the lower target effective dose we wanted to achieve was set compared to that, and tube current or tube voltage was computed accordingly with one of which was set to achieve the target effective dose. In this study, we evaluated the feasibility of lowering tube current first (Group A, B) and then tube voltage (Group C, D). To be more specific, considering the patient weight reduction in Group C compared with that of Group A, we hoped a one-third dose reduction in Group C by means of reducing tube voltage to 70 kVp; thus, the value of tube current was computed to be 189 mAs. The setting of Group E seemed special. That was because the result of preliminary scanning, in which the image quality of 80 kVP and that of 70 kVP under the same target dose were compared. The image quality of 80 kVp was much better subjectively.

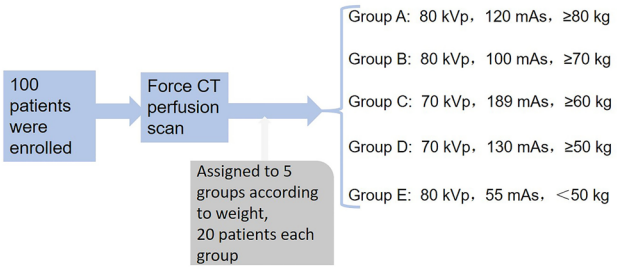

Fig. 1 Flowchart of study design

CT scanning protocol

Non-contrast scan of upper abdomen was done first to decide the scanning range of perfusion scan. CT perfusion (Somatom Force; Siemens Healthcare Sector, Forchheim, Germany) of the pancreas started 6 s after contrast injection and a total of 28 continuous dynamic acquisitions were performed with a scan interval of 1.5 s (the last interval was 3 s), resulting in a total acquisition time of 42 s. Scan parameters were as following: gantry rotation time 0.5 s, pitch 0.6, collimator 192 × 0.6 mm, total z coverage 176 mm, 512 matrix size and kernel Br 36. For contrast injection, a bolus of 45 mL iodinated contrast medium (iodine concentration 370 mg/mL, Ultravist 370, Bayer, Berlin, Germany) was injected in an antecubital vein with a flow-rate of 5 mL/s, followed by a 40-mL saline chaser injected at the same flow rate. All patients were instructed to hold their breath throughout the scan or to perform shallow breath if they had difficulty with breath hold in order to minimize motion.

Radiation dose calculation

For each group, the volume CT dose index (CTDI) and the dose-length product (DLP) were recorded. The estimating effective dose was calculated using the following formula:

$$\text{Estimating effective dose} = \text{DLP} \times 0.015\ (\text{mSv})$$

0.015 is the dose conversion coefficient for the abdomen according to the International Commission on Radiological Protection [23].

Subjective and objective image quality evaluation

The perfusion images with a slice thickness of 1.5 mm were separately evaluated by two radiologists with more than 3 years of experience for subjective image quality analysis. The image quality was assessed using a 5-point scale: (1) 5 = very clear anatomic structure and detail, no artifact, excellent for diagnosis; (2) 4 = fairly clear anatomic structure and detail, slight artifact and image noise, good for diagnosis; (3) 3 = clear in most anatomic structure and detail, obvious artifact and image noise, poor-quality image locally, not enough for definite diagnosis; (4) 2 = not clear anatomic structure and detail, not enough for diagnosis, cannot exclude the possibility of space-occupying lesions; (5) 1 = blurred anatomic structure and detail, heavy artifact and image noise, no diagnosis possible [24]. Motion artifact from patients was not included in the analysis.

For objective image quality analysis, axial images of the "plain phase" (0 s after perfusion scan began), the "arterial phase" (20 s after perfusion scan began), and the "late arterial phase" (42 s after perfusion scan began) were selected from each patient's perfusion CT image sets from Picture Archiving and Communication System (PACS) and measured by one radiologist independently. The CT values (Hounsfield units [HU]) of various anatomic regions and the background image noise (standard deviation of CT value of air outside the abdomen on the level of the celiac artery) were measured for calculation of signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR). Regions of interest (ROI) with an area of 80 ~ 100 mm^2 were placed on the abdominal aorta, the main portal vein, liver, pancreas, and muscle. Blood vessels and regions with obvious beam hardening artifact were avoided with all efforts during this process. Every ROI was measured twice, and the average value was obtained.

The SNR and CNR were calculated using the following formulae:

$$\mathrm{SNR} = \mathrm{CT}_{\mathrm{ROI}} / \mathrm{SD}_{\mathrm{air}} \quad (1)$$

$$\mathrm{CNR} = \left(\mathrm{CT}_{\mathrm{ROI}} - \mathrm{CT}_{\mathrm{pancreas}}\right) / \mathrm{SD}_{\mathrm{air}} \quad (2)$$

Perfusion parameters measurement

The perfusion images with a slice thickness of 3 mm were transferred to a post-processing workstation (Syngo MMWP, VE 36A, Siemens Healthcare, Forchheim, Germany), and perfusion parameters were measured using a perfusion post-processing software (Syngo Volume Perfusion CT Body) by one radiologist. The software, equipped with an automatic motion correction and a 4D noise reduction algorithm, automatically chose the abdominal aorta as the input artery to form an Arterial Input Function (AIF), resulting in a Time Attenuation Curve (TAC) and a perfusion pseudo-color image was constructed at last. When choosing a round ROI on normal pancreas parenchyma away from lesions (if existed), the following areas were avoided: blood vessels, bile ducts, edge of pancreas, pancreatic ducts, fat-infiltration area. ROI was drawn three times in the pancreas head, body, and tail, respectively, and the average value was obtained. The blood flow (BF), blood volume (BV), and permeability (PMB) were measured using a deconvolution method, with results being expressed as mean ± standard deviation (SD).

Statistical analysis

Statistical analysis was performed using SPSS 21.0 (IBM SPSS, Armonk, New York, USA). Differences in patients' ages as well as subjective image quality scores between the five groups were analyzed using the Kruskal–Wallis test, the objective image quality measurements and perfusion parameters were compared using one-way analysis of variance (ANOVA), and the Chi square test was used to evaluate the significance of difference in sex constituent ratio between groups. After one-way ANOVA, the unpaired t test with Bonferroni correction was used to identify differences between pairs of groups. An unpaired t test was conducted to analyze perfusion parameters between images with and without space-occupying pancreatic lesions within each group. For all statistical analysis, P values lower than 0.05 were considered statistically significant. The agreement between the two radiologists on subjective evaluation of image quality was estimated using kappa values: (1) excellent: $k > 0.81$; (2) good: $k = 0.61 \sim 0.80$; (3) moderate: $k = 0.41 \sim 0.60$; (4) suboptimal: $k = 0.21 \sim 0.40$; (5) poor: $k < 0.20$ [25].

Results

Patients characteristics

The demographic data of the 100 patients (47 men, 53 women, average weight 64.0 ± 13.8 kg) included in this study are shown in Table 1. There were no statistically significant differences in age and sex constituent ratio of patients between the five groups ($P > 0.05$). A total of 46 people were diagnosed with insulinoma according to their CT perfusion results, among which 31 were pathologically confirmed.

Table 1 Demographic data of patients in five groups ($n=100$) and comparison of radiation dose between each group

Group	Gender[a]		Age (year)[b]	Space occupying lesions		CTDI	DLP	Effective dose (mSv)	Effective dose reduction %
	Male	Female		Yes	No				
a*	–	–	–	–	–	95	1477	22.2	–
A	13	7	47.8 ± 11.6	12	8	66	1260	18.9	14.9
B	9	11	48.2 ± 12.4	11	9	55	1049	15.7	29.3
C	14	6	44.0 ± 16.3	7	13	51	993	14.9	32.9
D	6	14	46.3 ± 12.3	10	10	44	831	12.5	43.7
E	5	15	44.7 ± 20.6	6	14	30	577	8.7	60.8
Average	–	–	–	–	–	49.2	942	14.1	36.5

CTDI CT dose index, *DLP* dose-length product

*a is our hospital's routine perfusion protocol (tube voltage 80kVp, tube current 150mAs)

[a]$P=0.187$ by Chi square test

[b]$P=0.982$ by Kruskal–Wallis test

Table 2 Subjective image quality scores of each group from the two radiologists and the agreement between the two evaluators

Group	Mean score from Radiologist 1	Mean score from Radiologist 2	Kappa value	*P* value*
A	4.70	4.60	0.778	0.656
B	4.70	4.70	0.747	
C	4.65	4.60	0.683	
D	4.55	4.45	0.816	
E	4.60	4.45	0.718	

*Kruskal–Wallis test

Radiation dose

We reached a gradual radiation dose reduction as patient's weight declined (Table 1), radiation dose being 8.7 mSv in patients under 50 kg and 18.9 mSv in patients above 80 kg. The setting of 80 kVp and 55 mAs for Group E yielded the lowest dose. The average radiation dose of all groups was 14.1 mSv, decreasing by 36.5% compared with our hospital's routine perfusion protocol (80 kVp, 150 mAs).

Subjective and objective image quality

The agreement between the subjective scores on evaluation of image quality from the two radiologists was good, with kappa values ranging from 0.683 to 0.816, and there was no statistically significant difference in subjective scores between the five groups (Table 2). The mean subjective image quality score was above 4.45 points, indicating good image quality subjectively (Fig. 2).

All groups except Group E had equivalent performance on objective image quality, with no significant differences in measurements of SD, SNR, and CNR. Group E had better image quality than other groups, with statistically lower SD and higher SNR and CNR. The preceding results remained consistent for all the three scan phases. See details in Fig. 3. Besides, Fig. 4 exhibits representative perfusion CT axial images of the "arterial phase" from each group.

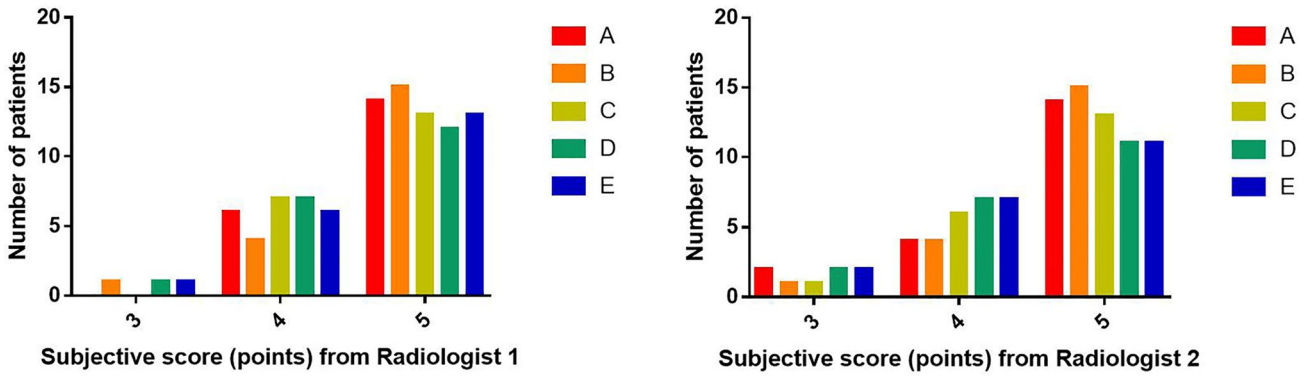

Fig. 2 Subjective scores from both radiologists mainly distributed at 4–5 points

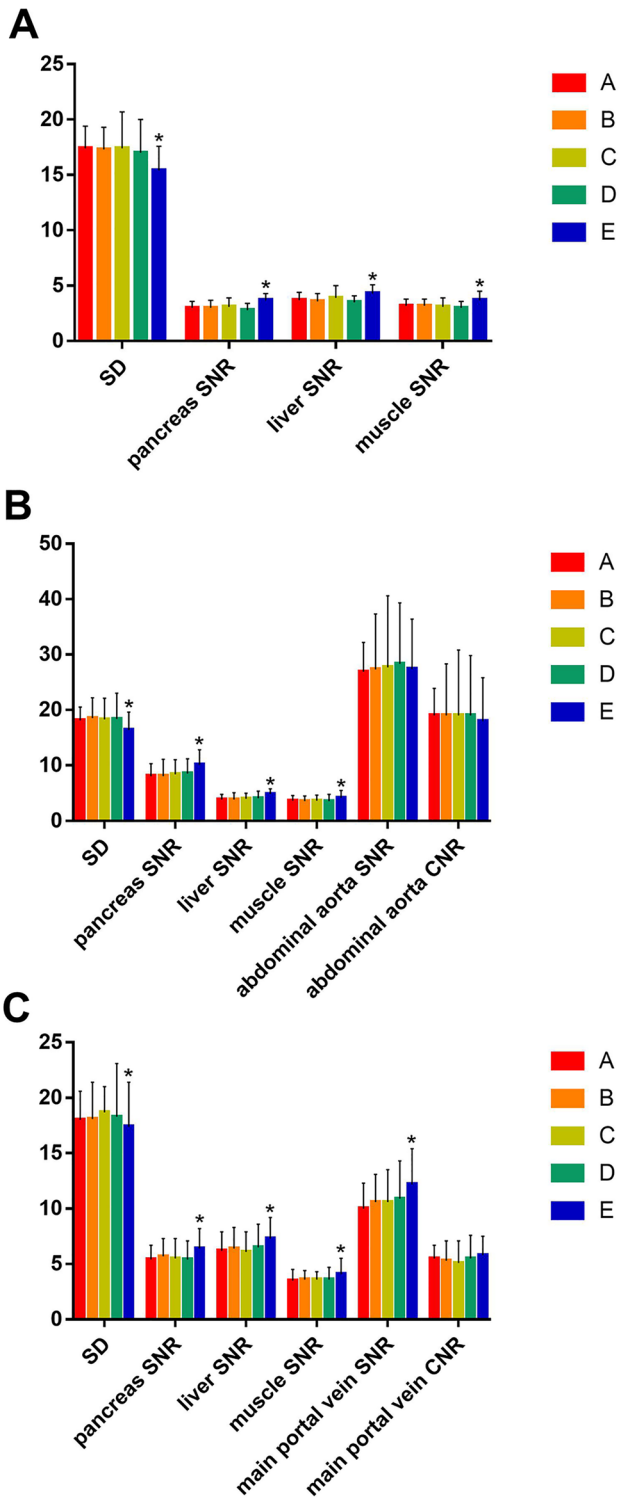

Fig. 3 Bar charts illustrating comparison of objective image quality parameters of the plain phase (**a**), the arterial phase (**b**), the late arterial phase (**c**) between the five groups. $P > 0.05$ on comparison of all parameters between Group A, B, C, and D. (*) in the figure means $P < 0.05$ on comparison of certain parameters between Group E and the other groups using unpaired t test with Bonferroni correction. *SD* standard deviation (of CT value of air outside the abdomen as background image noise), *SNR* signal-to-noise ratio, *CNR* contrast-to-noise ratio

Perfusion parameters

In order to eliminate the possible effect of space-occupying lesions on perfusion parameter measurement of normal pancreas parenchyma, comparison of perfusion parameters between patients with and without lesions within each group was conducted first. All space-occupying lesions turned out to be neuroendocrine tumors and their constituent ratio in each group is demonstrated in Table 1. No statistically significant differences were found in perfusion parameters between patients with and without lesions (Fig. 5).

Since pancreatic lesions had no influence on perfusion parameter measurement, comparison of these parameters between the five groups was simply carried out and no significant differences emerged (Table 3).

Discussion

Perfusion CT is an advanced imaging technique which can quantify tissue perfusion and hence is an ideal noninvasive method to detect insulinomas. At present, radiation dose is the main concern in its way to broad clinical routine. In this study, we for the first time established a weight-adapted ultra-low-dose pancreatic perfusion CT protocol with good image quality and accurate perfusion parameter measurement.

As known, radiation dose is mainly determined by three factors: tube voltage, tube current, and scan duration [26, 27]. Accordingly, we effectively reduced the radiation dose of perfusion CT by means of lowering tube voltage and (or) tube current and shortening scan duration. And we verified that reducing tube voltage led to a more effective dose drop than reducing tube current: the effective dose of Group A (80 kVp, 120 mAs) was 18.9 mSv, while that of Group B (80 kVp, 100 mAs) was 15.7 mSv and that of Group C (70 kVp, 189 mAs) was 14.9 mSv. This result was consistent with previous studies [26, 28]. The scan duration was minimized to 42 s with 28 acquisitions in the premise of adequate time points to ensure a complete and smooth perfusion curve. This duration was long enough to detect most tumors, meeting clinical demands of lesion identification and localization, and caused no excessive radiation exposure. Besides, scan field (z coverage) is another key factor. Therefore, the CSG recommendations on limiting ionized radiation dose are made based on specific coverage, which suggest the dose within 20 mSv for 4 cm coverage and 30 mSv for wider coverage [29]. The reported mean radiation dose for liver or pancreas CT perfusion ranged from 10.1 to 39 mSv with z coverage ranging from 160 mm to 350 mm and time-point acquisitions ranging from 13 to 23 [26, 30–36]. And by further narrowing z-axis and reducing acquisitions, lower radiation doses have been achieved. However, it might increase

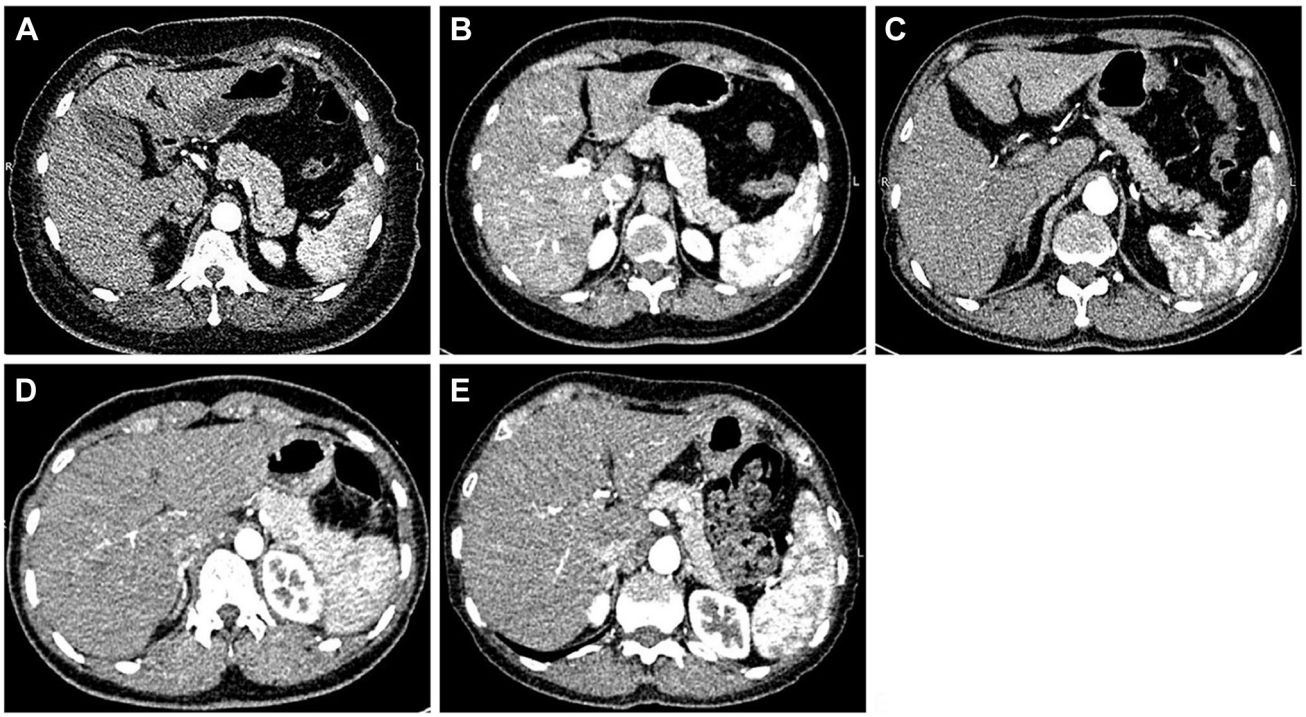

Fig. 4 Representative perfusion CT "arterial phase" (20 s after perfusion scan began) images of each group: **a** patient weighed 85 kg; **b** patient weighed 73 kg; **c** patient weighed 62 kg; **d** patient weighed 57 kg; **e** patient weighed 45 kg

the risk of hindering diagnostic performance. Our weight-adapted protocol (z coverage 176 mm, 28 acquisitions) realized a gradual dose reduction as patient's weight declined and reached an average dose of 14.1 mSv, decreasing by 36.5% compared with routine protocol. This novel protocol might not be a lowest-dose one, but according to the good image quality and accurate perfusion parameter measurement in this study, we can infer that it has great promise to meet needs of clinical diagnosis as a substitute for the present protocol. But still, we see possibility of further dose reduction by omitting some time-point acquisitions [37] and narrowing z-axis coverage [26].

The reduction in radiation dose will inevitably increase image noise, thus degrading image quality. In order to maintain image quality, we have adopted relatively softer reconstruction kernel and less image matrix [38]. In this study, the image quality kept stable and comparable both subjectively and objectively as radiation dose decreased gradually. The mean subjective score was above 4.45 on a 5-point scale, enough for clinical diagnosis. Besides, Group E had better objective image quality than other groups, suggesting that dose could be reduced further on low-weight patients (weight < 50 kg), which needs to be verified by further studies.

CT perfusion parameters are influenced by multiple factors, such as mathematical model of perfusion, concentration of contrast material, injection velocity, position, and size of ROI; thus, we have kept these factors consistent when analyzing and comparing perfusion parameters between all groups. Although CT allows for thin slice acquisition (1.5 mm), thicker slice reconstruction (3 or 5 mm) is often used to derive perfusion parameters for the purpose of reducing noise and processing time while increasing parameter accuracy. However, it will increase partial volume effect, which inevitably hinders the depiction of small lesions such as insulinoma. Thus, we adopted the thinnest reconstructed slice widths acceptable to post-processing workstation, which is 3 mm. In order to avert possible impact of lesions on measurement of normal parenchyma, we excluded patients with large lesions when recruiting participants. Consequently, all of the space-occupying lesions in our study were smaller than 2 cm and turned out to be insulinomas, which were avoided intentionally when measuring parameters. Our results exhibited no significant differences in parameter measurements between all groups, and our measurements were within the range of values reported in the literature [38–40], revealing that our low-dose protocol did not undermine the accuracy and reliability of perfusion parameter measurement. This is reasonable because the calculation of perfusion parameters is based on the change in tissue density in ROI along with time [41], rather than individual images.

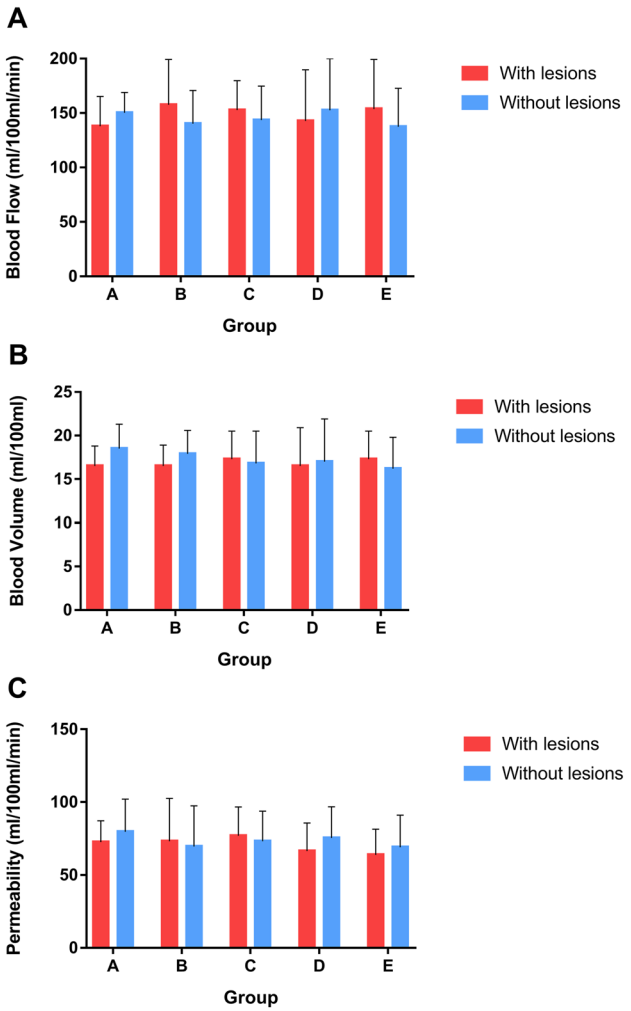

Fig. 5 Comparison of blood flow (**a**), blood volume (**b**), permeability (**c**) between patients with and without lesions within each group. $P > 0.05$ on every comparison using unpaired t test

As mentioned before, VPCT is routinely performed in addition to conventional enhanced CT, which brings about many drawbacks. In conventional multiphase enhanced CT, an optimal timing of each phase is hard even using bolus tracking technique due to variability in individual's circulation. This problem can be easily solved in perfusion CT, in which the optimal enhancement can be selected according to the Time Attenuation Curve (TAC). X. Wang et al. have proved that mean temporal images from VPCT can replace conventional enhanced CT and exhibit superior image quality [16], and our study here provides a weight-adapted ultra-low-dose protocol with stable image quality, both laying a foundation for further studies on low-dose VPCT images being used for three-dimensional reconstruction, a critical step in VPCT's way toward its complete substitution of conventional enhanced CT.

There are several limitations in our study: (1) The number of patients in each group was relatively small, but this was an exploratory study, and the results of our study laid a foundation for future research. (2) Our parameters were measured by only one radiologist. Although measurement of perfusion parameters is usually done by two radiologists to double check the results according to previous studies [26], measurement by one radiologist can also be seen and is considered acceptable [34, 38, 42]. Besides, every result was the average of triple measurements. (3) Only one combination of tube voltage and tube current was applied to one specific weight group, but whether it was the optimal choice still needs further studies to confirm. (4) We did not establish a control group of our hospital's routine protocol when comparing image quality. However, we did prove that the image quality kept stable as radiation dose declined, and further comparisons regarding image quality as well as diagnostic performance between low-dose protocol and routine protocol wait to be investigated.

In conclusion, our study has established a weight-adapted ultra-low-dose pancreatic perfusion CT protocol, which can effectively reduce radiation dose without prejudice to image quality, and the perfusion parameters of normal parenchyma measured in this circumstance are accurate and reliable.

Table 3 Comparison of perfusion parameters of normal pancreas parenchyma between the five groups

	A	B	C	D	E	*P* value*
BF (mL/100 mL/min)	141.5 ± 27.2	145.4 ± 34.1	146.7 ± 30.8	149.7 ± 46.3	143.2 ± 38.9	0.520
BV (mL/100 mL)	17.2 ± 2.6	17.5 ± 2.6	17.0 ± 4.4	16.9 ± 4.7	16.6 ± 3.4	0.138
PMB (mL/100 mL/min)	78.3 ± 21.0	70.6 ± 27.6	74.6 ± 19.8	72.7 ± 20.7	67.2 ± 20.3	0.164

BF blood flow, *BV* blood volume, *PMB* permeability

*One-way ANOVA

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest to disclose.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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