

**Uniform Vascular Enhancement of Lower-extremity Artery on CT Angiography
Using Test-Injection Monitoring at the Central Level of the Scan Range: A Simulation
Flow Phantom Study with Clinical Correlation**

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Rationale and Objectives: To evaluate the efficacy of variable contrast injection durations and scanning delay determined by test-injection analysis of CT angiography (CTA) of peripheral arteries.

Materials and Methods: We used a flow phantom that simulates the hemodynamics in a lower-extremity artery. We set the flow rate at the pump to 2.0- or 5.0 L/min. In protocol 1, we adopted a variable contrast injection duration based on the peak enhancement time of the test injection monitoring at the central level of the scan range. In protocol 2, we adopted a fixed contrast injection duration. The scanning delay was determined with a conventional bolus-tracking technique monitoring at the top of the scan range. Mean arterial attenuation and difference between the maximum and minimum attenuation values were calculated. To verify the phantom study results clinical study including 16 patients was performed under protocol 1.

Results: The mean attenuation values under protocols 1 and -2 were comparable (563.6 HU and 535.0 HU, respectively) at a pump flow rate of 2.0 L/min; at 5.0 L/min they were 289.4 HU and 328.8 HU. The difference between the maximum and minimum attenuation values was smaller under protocol 1 than protocol 2 (76.8 HU vs 184.9 HU) at a pump flow of 2.0 L/min and also smaller under protocol 1 than protocol 2 (79.7 HU vs 203.8 HU) at 5.0 L/min. In clinical study, the mean attenuation value was 332.6 ± 51.9 HU, and the difference between the maximum and minimum attenuation values was 55.1 ± 24.4 HU.

Conclusion: The object-specific injection duration based on test injection at the central level of the scan range provides sufficient and constant vascular enhancement at CTA.

Key Words: CT angiography; injection method; peripheral artery

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INTRODUCTION

CT angiography (CTA) is an accurate modality to assess the presence and extent of peripheral arterial disease (PAD) (1-3). At CTA of peripheral arteries it is important to evaluate not only arterial stenosis but also the run-off vessels. Coexisting cardiovascular disorders and blood flow obstruction or aneurysms may delay opacification of peripheral arterial trees (4, 5). Moreover, the actual flow speed of the injected contrast material through the peripheral arteries is highly variable in patients with PAD (4). As high-speed multi-detector computed tomography (MDCT) scanning can outpace the flow of the contrast bolus, resulting in inadequate vascular enhancement of peripheral arteries, the contrast injection method should take into account the arterial transit speed.

To achieve satisfactory enhancement of a wide range of aortoiliac and lower-extremity arteries, adequate enhancement must be maintained for a certain period depending on the CT data acquisition time. Time-to-peak arterial enhancement is theoretically equal to the contrast injection duration for a given arterial arrival time when the injection duration is longer than the arterial peak time of the test bolus (6, 7). Therefore, we applied time-to-peak arterial enhancement of the test injection to the injection duration at CTA to achieve sufficient and constant vascular enhancement. Moreover, we set the monitoring level of the test injection at the central level of the scan range to avoid outpacing the scanning.

To investigate the time-density curve of the optimal CTA protocol we used a flow phantom that simulates the hemodynamics of contrast material in vivo. The purpose of our study was to evaluate the efficacy of contrast material protocols with variable injection durations and scanning delay times determined by test-injection analysis of MDCTA of the peripheral arteries.

MATERIALS AND METHODS

Phantom Study

Phantom configuration

Our flow phantom consists of a plastic cistern, a pump, a flow meter, an acrylic container, a hermetic metallic tank, and connecting tubes. The precise configuration of our flow phantom is described elsewhere (8). The volume of circulating water was set at 6.5 L to simulate a human weighing 60 kg (8). A long acrylic hollow cylinder (2 cm in diameter, 100 cm in length) simulating a lower-extremity artery was used (Figs. 1A and B). Water was delivered with the pump at a pulsating flow rate of 60 bpm. We set the flow rate at the pump at 2.0 or 5.0 L/min, values equivalent to the cardiac output flow in a human with- or without heart failure, respectively. CT imaging was from the top to the end of the simulated lower-extremity artery.

CTA Protocols

All CT examinations were performed on a 64-row MDCT scanner (Brilliance 64, Philips Healthcare). The acquisition parameters were: tube voltage 120 kV, tube current 400 mA, 120 kV, collimation 0.625×64 mm, beam pitch 0.798, rotation time 0.5 sec. The contrast material was administered with a double-head power injector (Dual Shot, Nemoto-Kyorindo).

We compared the contrast protocol using variable injection durations based on the test bolus injection (protocol 1) with a conventional protocol that used a fixed injection duration and a bolus tracking technique (protocol 2). We delivered 90 mL of contrast material (Iopamiron 300, Bayer HealthCare) in each of the protocols. In protocol 1, we adopted a variable contrast injection duration based on the peak enhancement time of the test injection. In the test injection, 10 mL of contrast material were injected at a rate of 5 mL/sec; this was followed by a 15-mL saline flush delivered

at 5 mL/sec. Single-level repeated CT scans (30 mA) were acquired in the central level of the scan range every 2 sec from 10 - 60 sec after the start of contrast injection. A region of interest (ROI) was placed on CT images at the monitoring level and a time-density curve was generated by connecting the time points. We measured the arterial arrival time to arterial peak enhancement from the start of contrast injection. Bae (7) demonstrated that when the injection duration was longer than time-to-peak test bolus enhancement, the time to peak aortic enhancement increased linearly with the injection duration and occurred shortly after the completion of injection. Therefore, positing that time-to-peak enhancement of the test injection can be converted to time-to-peak at CTA, we applied the peak enhancement time of the test injection to the injection duration at CTA. To determine the scanning delay time (T_{delay}) at CTA we used the equation

$$T_{\text{delay}} = T_{\text{arrive}} + T_{\text{peak}} - 1/2 T_{\text{acquisition}},$$

where T_{arrive} and T_{peak} are the arterial arrival time and the time-to-peak enhancement of the test injection, respectively, and $T_{\text{acquisition}}$ is the data acquisition time for CTA. The monitoring level of the test injection was set in the central level of the scan range. We subtracted $1/2 T_{\text{acquisition}}$ from $T_{\text{arrive}} + T_{\text{peak}}$ for the determination of the delay time.

The schematic for protocol 1 is presented in Fig. 2. In protocol 2, we adopted a fixed contrast injection duration (20 sec) because a fixed injection duration provides constant arterial enhancement regardless of patient weight and injection rate (9) and it is widely used in clinical practice (10). The scanning delay was determined with a real-time bolus tracking system. The monitoring level was set in the top of the scan range based on the previous clinical studies (2, 3) (Fig. 1). The trigger threshold was set at 200 Hounsfield units (HU) for the arterial ROI.

Data Analysis

One board-certified radiologist with 12 years of experience measured the attenuation values on CTA images using 20 circular ROIs placed at 5-cm intervals along the simulated lower-extremity artery (100-cm length) from the top (ROI-1) to the end (ROI-20). The size of all arterial ROIs was 100 mm². Mean arterial attenuation, indicative of the magnitude of the contrast column, was calculated as the average of the mean attenuation values from ROI-1 to ROI-20. The difference between the maximum and minimum attenuation values along the z-axis, indicating the uniformity of the contrast column, was also calculated. Based on acquired data we selected an enhancement value of 250 HU to indicate adequate arterial attenuation. In both protocols we applied Bland-Altman analysis to delineate the variability of vessel attenuation using MedCalc software (MedCalc).

Patient Study

The clinical study was comprised of 16 consecutive patients, 12 males and 4 females ranging in age from 53 to 81 years (mean 69.0 ± 7.8 years). Their body weight was 62.9 ± 7.2 kg. They underwent CTA of the aortoiliac and lower-extremity arteries for suspected PAD. Based on the phantom study results, CTA was performed with protocol 1. After the delivery of 1.8 mL/kg of contrast material (300 mgI/mL) one board-certified radiologist with 12 years of experience measured the attenuation values on CTA images using circular ROIs placed in (1) the juxta-renal abdominal aorta, (2) the aortic bifurcation, (3) the right and left common femoral arteries, (4) the right and left popliteal arteries, and (5) the right and left mid-posterior tibial arteries. The size of the ROIs in the arteries was identical in each patient. An attempt was made to select an ROI area of approximately 40 mm² for the aortoiliac artery, 20 mm² for the

femoral and popliteal artery, and 10 mm^2 for the lower-extremity artery, i.e., large enough to avoid an effect by pixel variability and small enough to avoid contact with vessel edges. Attenuation values in the left and right femoral-, popliteal-, and posterior tibial arteries were averaged. Mean arterial attenuation and the difference between maximum and minimum attenuation values of 8 ROIs were calculated. Based on a previous study [8] we adopted an attenuation value of 250 HU as an index of adequate arterial attenuation.

CTA images were visually evaluated consensually by 2 board-certified radiologists with 12 and 13 years of experience. First they examined CTA images of each patient to determine whether the CT scan had outpaced the flow of the bolus contrast material through the aortoiliac and lower extremity arteries. Second, they divided the CT angiographic images into 3 segments, the aortoiliac-, femoral-, and lower leg segment. Each segment was evaluated for diagnostic quality and rated based on the visualization of arteries and on venous contamination. Image findings were rated as follows: 3 (good) = sufficient visualization and no or minimum venous contamination, 2 (fair) = assessable visualization of arteries and moderate venous contamination that did not interfere with a clinical diagnosis, and 1 (poor) = insufficient visualization of arteries and severe venous contamination that interfered with a clinical diagnosis. In cases with different ratings on the right and left side segments, the worse rating was used.

Our institutional review board approved the clinical study. We explained the purpose of our study to all patients and obtained their prior informed consent.

RESULTS

Phantom Study

The mean attenuation values of the simulated peripheral artery under protocols 1 and 2 were 563.6 HU and 535.0 HU, respectively, at a pump flow rate of 2.0 L/min; at a flow rate of 5.0 L/min they were 289.4 HU and 328.8 HU. The difference between the maximum and minimum attenuation values along the z-axis was smaller under protocol 1 than protocol 2 (76.8 HU vs 184.9 HU) at a pump flow rate of 2.0 L/min and also smaller under protocol 1 than protocol 2 (79.7 HU vs 203.8 HU) at a pump flow rate of 5.0 L/min.

The arterial attenuation value profile along the z-axis under protocol 1 showed a more constant level during CT imaging at either pump flow rate (Fig. 3).

Bland-Altman plots revealed the relationship between the differences and the averages of protocols 1 and 2 that the difference tended to be greater and exceeded 95 % limit of agreement interval when the average vascular attenuation was low at either pump flow rate (Fig. 4).

Patient Study

Scans and test injection procedures were successful in all 16 patients. The mean scanning delay and mean data acquisition times were 36.5 ± 7.6 sec (range, 25 – 52 sec) and 19.8 ± 2.1 sec (range, 18 – 24 sec), respectively. The scanning range was 114.0 ± 8.9 cm (range, 97 – 123 cm), the contrast material volume used 100.5 ± 10.8 mL (range, 81 – 110 mL), the injection duration 28.1 ± 3.9 sec (range, 25 – 37 sec), and mean arterial attenuation was 332.6 ± 51.9 HU. The mean attenuation of each arterial ROI and the average value of all ROIs are summarized in Table 1. All arterial segments in 15 of the 16 patients showed attenuation of more than 250 HU. In the other patient, the attenuation values in the popliteal- and posterior tibial artery were less

than 250 HU. The difference between the maximum and minimum attenuation values along the z-axis was 55.1 ± 24.4 HU.

In no cases did CT scans outpace the flow of bolus contrast material. Scans of all 16 patients were classified as yielding “good” visualization in the aortoiliac and the femoral artery segments. A score of good was recorded for 15 patients and a score of fair for one patient with respect to visualization of the lower leg segment. The visual evaluation score was 8.94 ± 0.25 . No patient in our study population was judged to present with poor visualization in either arterial segment.

DISCUSSION

The introduction of 64-row MDCT has led to an increase in the scanning speed. Therefore, scanning timing must be adjusted to the appropriate temporal window after contrast injection. Sufficient and constant vascular enhancement during CTA is necessary, especially for the evaluation of PAD. It has been reported (4) that aortopopliteal bolus transit speeds differ widely (29 – 177 mm/sec) and may be slower in patients with PAD. As the time to arterial peak enhancement is theoretically equal to the injection duration for a given arterial arrival time (6), we suggest that the injection duration should be tailored to the arterial transit speed.

Our phantom study revealed that the patient-specific injection duration and scanning delay based on test injection analysis is effective for sufficient and constant vascular enhancement at CTA of the peripheral artery. It is possible that vascular enhancement was sufficient because the injection duration under protocol 1, which was equal to the time-to-peak enhancement on the test injection, is convertible to the time-to-peak plateau enhancement at CTA. Also, the observed constancy in vascular enhancement may be attributable to our setting the level of the monitoring scan of the test injection in the central level of the scan range. We did this to avoid outpacing by CT data acquisition of the flow rate of the contrast bolus. Moreover, subtracting $1/2 T_{\text{acquisition}}$ from $T_{\text{arrive}} + T_{\text{peak}}$ for determination of the scanning delay time may allow for peak arterial enhancement at the start of data acquisition as well as in the middle.

In the management of patients with PAD it is important to assess not only inflow but also the flow in runoff arteries. Our phantom study demonstrated that the arterial attenuation value profile along the z -axis under protocol 1 showed a more constant level. Although the difference between two protocols seemed to be not so large (Fig. 3), the difference exceeded 95 % limit of agreement interval when the average vascular attenuation was low (Fig. 4). This implies that protocol 1 provided higher vascular

attenuation even in the lower level of the scanning range. Based on our phantom study results we applied protocol 1 in our subsequent clinical pilot study. That investigation revealed good arterial visualization in each segment from the abdominal aorta to the lower legs, findings that supported our phantom study results. Although the method used under protocol 1 may result in venous overlap in the lower leg in patients with a high arterial transit speed, venous overlap did not result in poor visualization in any of our patients.

An earlier study (4) demonstrated that an injection duration of at least 35 sec, combined with a reduction in the acquisition speed or an increase in the scanning delay, produced adequate opacification of the entire peripheral arteries in most PAD patients. However, a longer injection duration may increase the contrast volume unnecessarily and result in venous overlap. A considerable number of PAD patients present with impaired renal function and are at risk of contrast-induced nephropathy (11). In our clinical study the mean injection duration was approximately 28 sec, among our patients there were substantial differences of more than 10 sec in the injection duration. Adjusting the patient-specific injection duration may allow for adequate vascular enhancement regardless of the arterial transit speed and may avoid the delivery of unnecessarily high doses of contrast medium.

There are some limitations in our study. Our clinical investigation included a small number of patients and no control group subjected to conventional techniques for determining the scanning delay time for CTA. We are in the process of assembling a larger patient population for further study.

In conclusion, the test injection using a monitoring scan for determining the scanning delay and injection duration at the central level of the scan range proved to be useful for 64-row MDCTA of the peripheral arteries of patients with suspected PAD.

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Table 1. Attenuation values from the abdominal aorta to the lower-extremity artery in our patient study (n=16)

Arterial segment	Mean (HU)	Range (HU)
Abdominal aorta	313.9 (54.8)	249 - 436
Aortic bifurcation	329.1 (48.9)	281 - 433
Femoral artery	347.9 (49.5)	291 - 448
Popliteal artery	354.9 (68.3)	235 - 467
Posterior tibial artery	318.6 (60.5)	204 - 441
Average	332.6 (51.9)	274 - 430

Note. Numbers in parentheses indicate standard deviation.

Fig. 1A

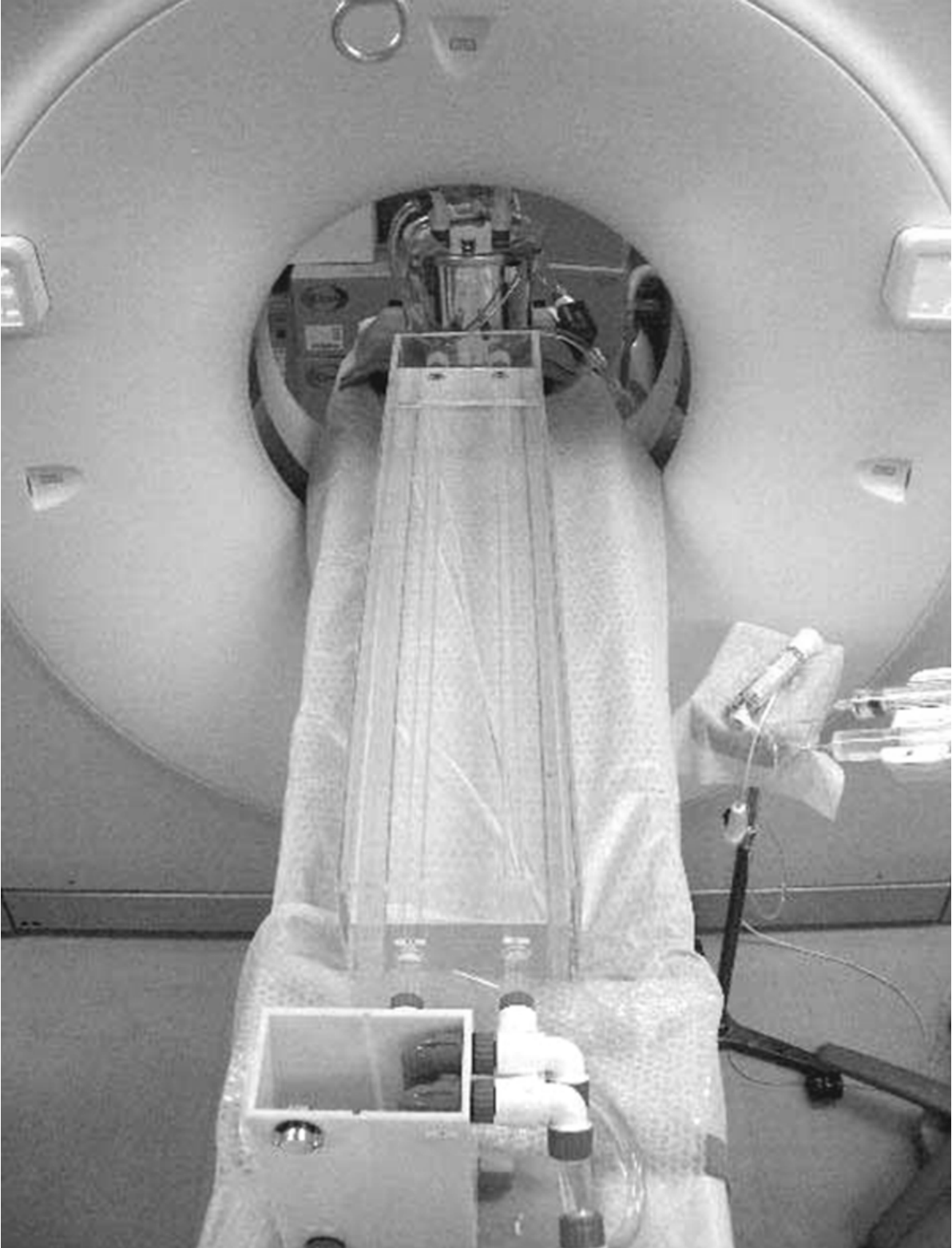


Fig. 1B

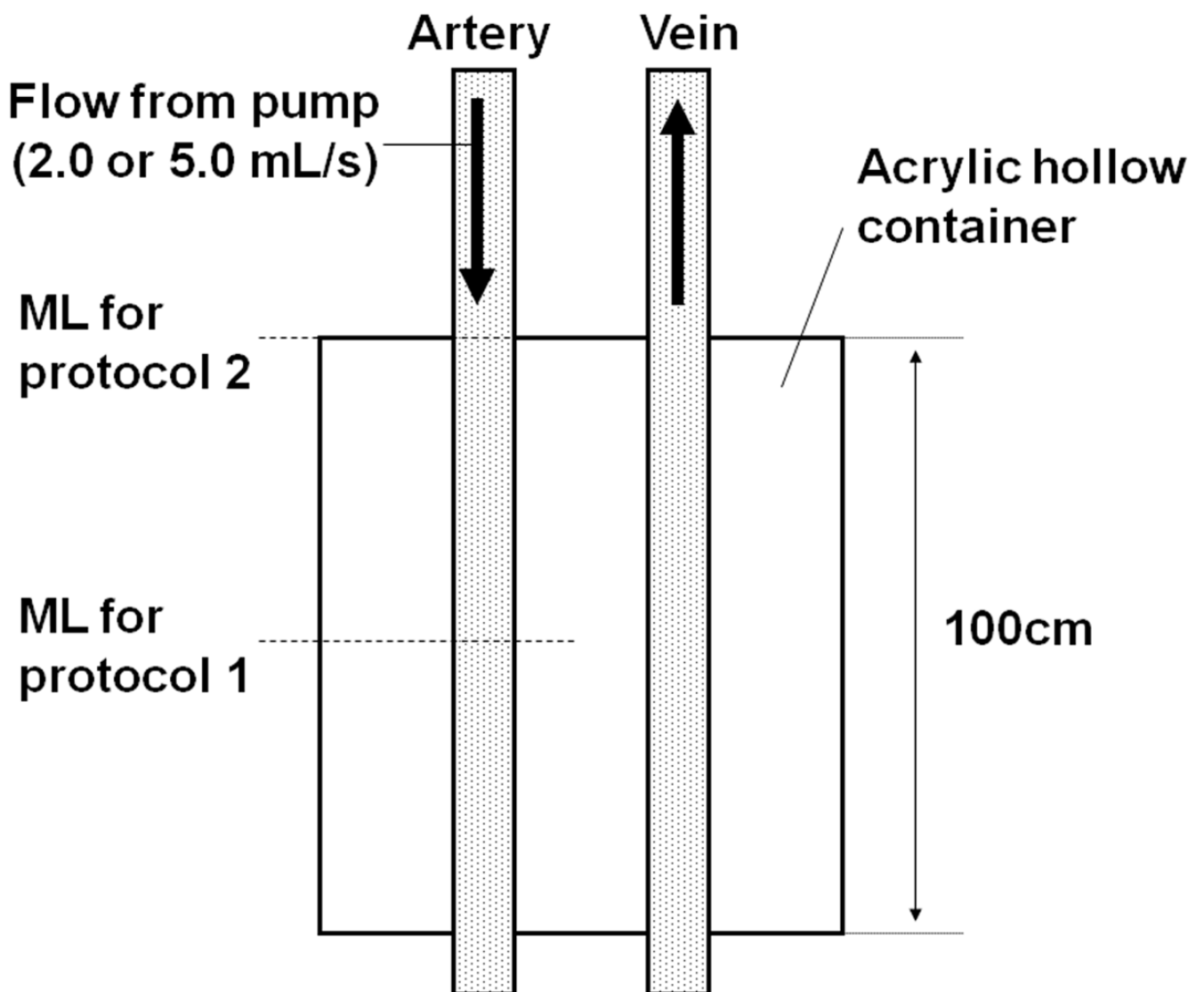


Fig. 2

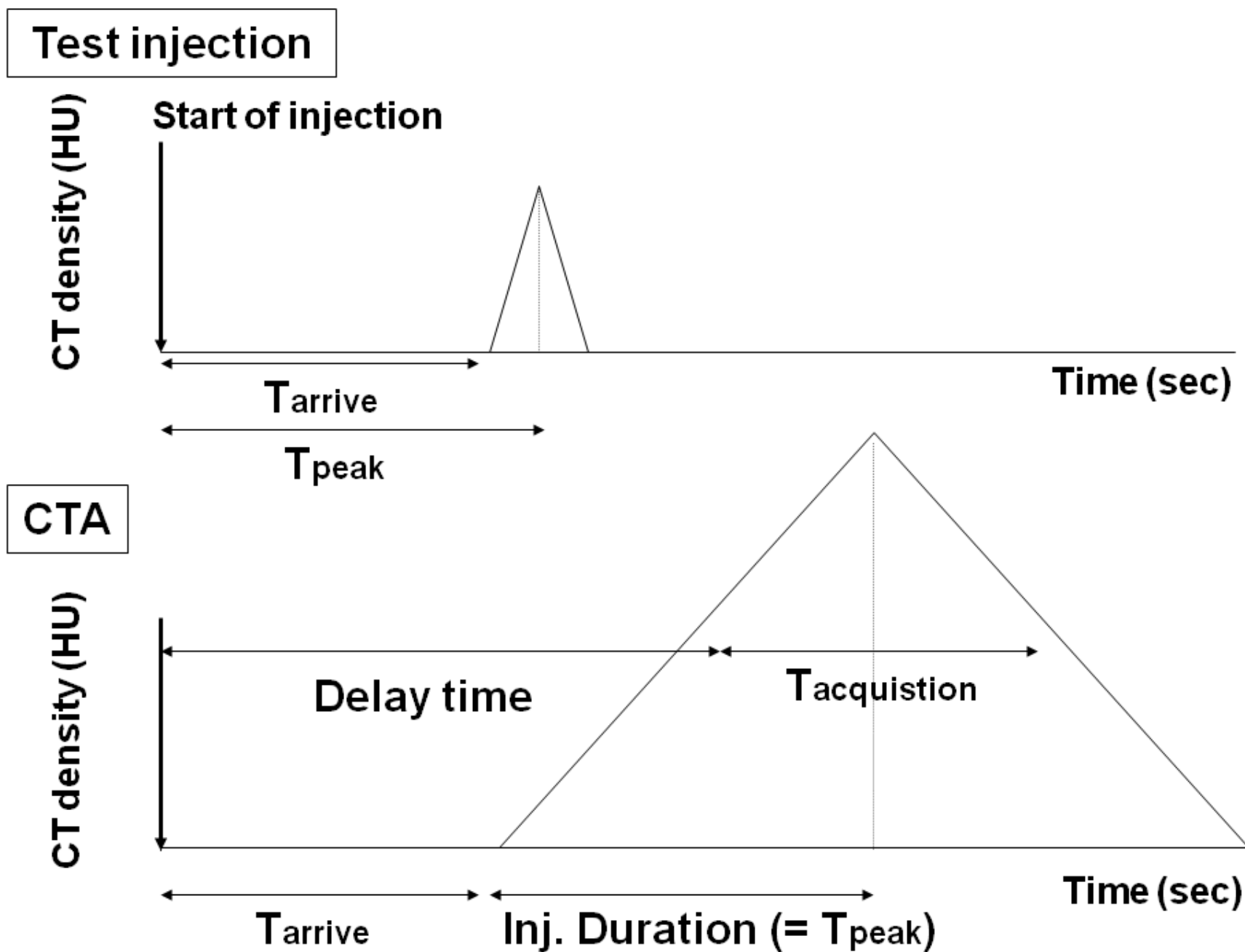


Fig. 3A

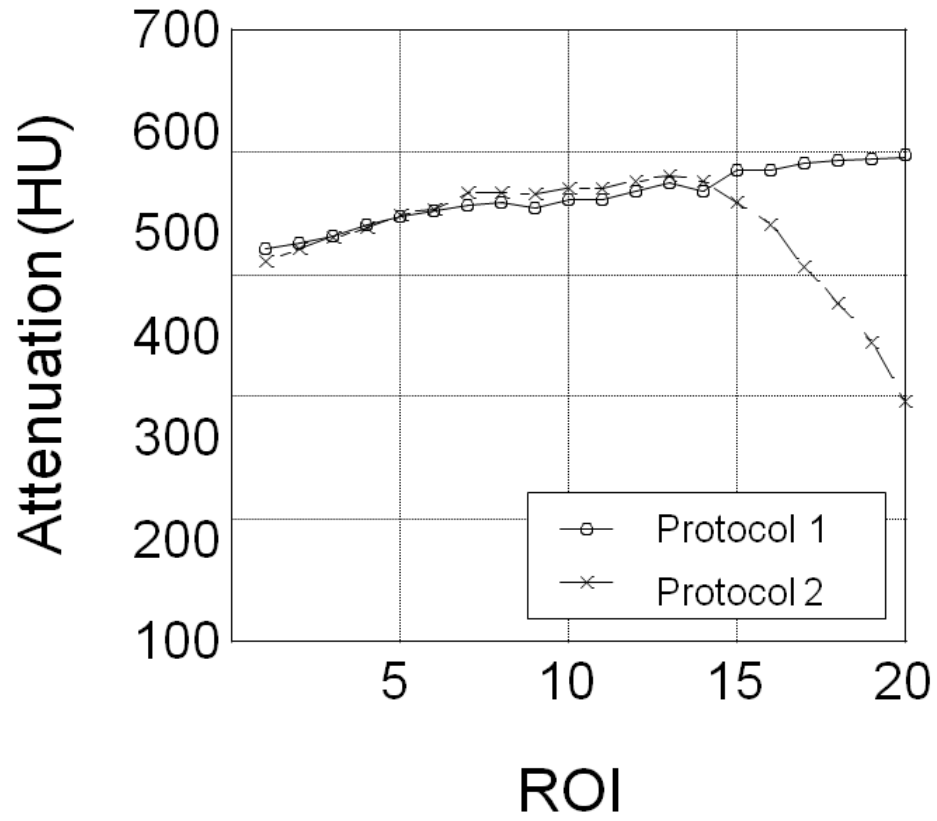


Fig. 3B

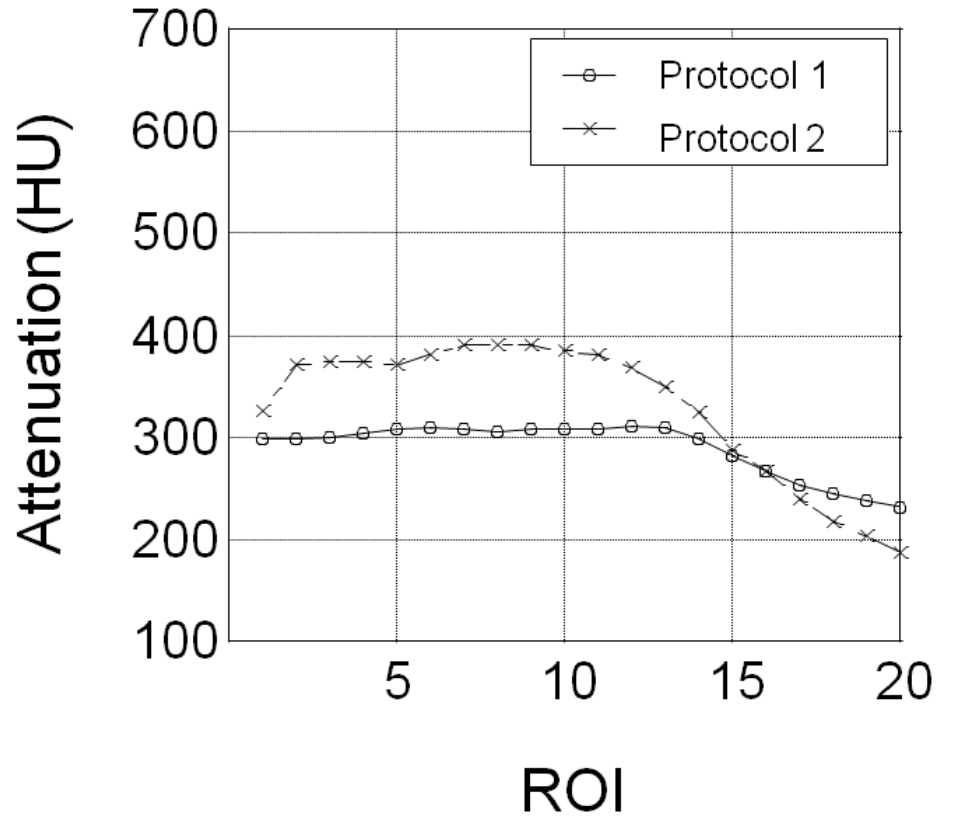


Fig. 4A

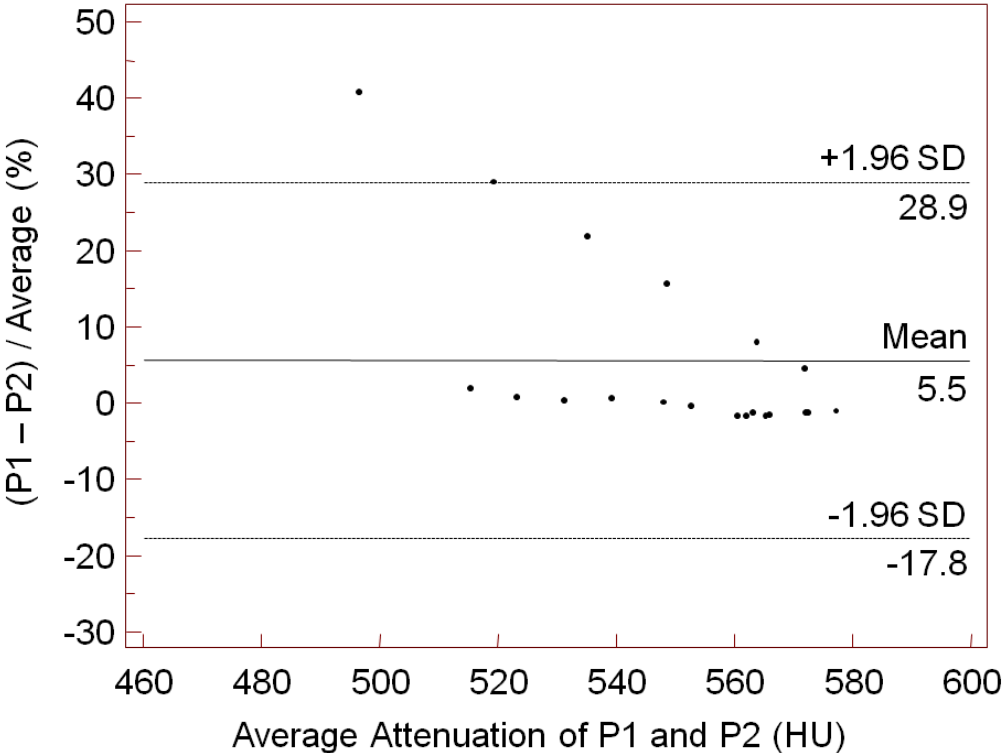


Fig. 4B

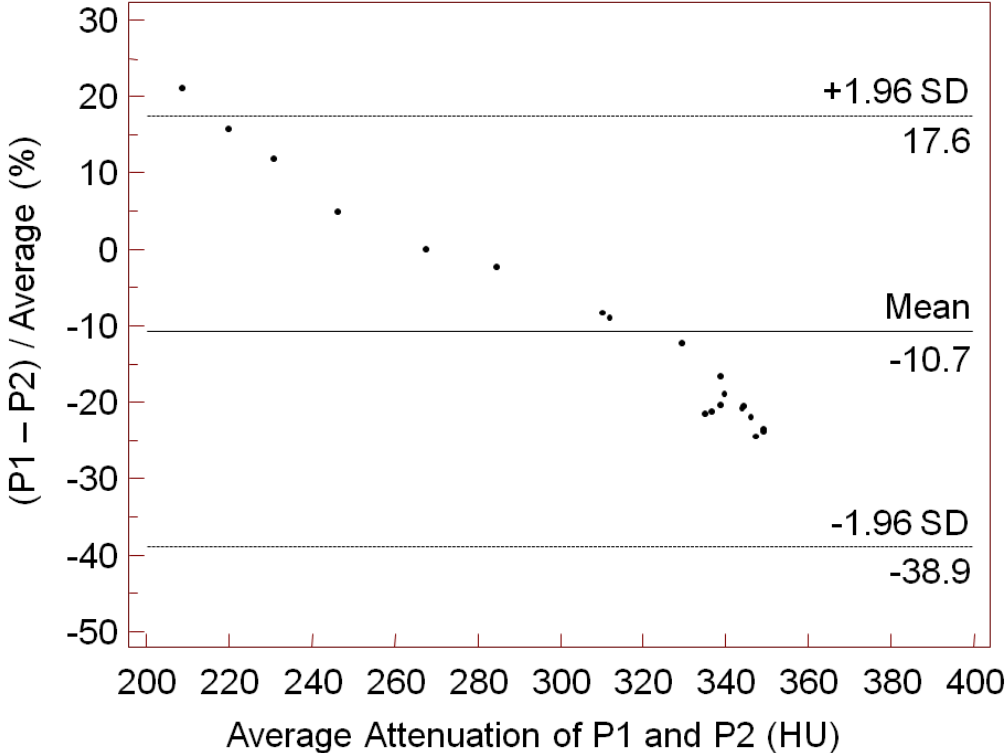


Figure Legends

Fig. 1. Schematic (A) and photograph (B) showing the configuration of the flow phantom simulating the lower extremity artery. The pump flow rate was set at 2.0 L/min or 5.0 L/min, values equivalent to the cardiac output flow of a human with- and without heart failure, respectively.

Note: ML = monitoring level

Fig. 2. Schematic of test injection and CTA under protocol 1.

Note: T_{arrive} = arterial arrival time; T_{peak} = time to peak enhancement after test injection;

$T_{\text{acquisition}}$ = data acquisition time of CTA

Fig. 3. Arterial attenuation-value profiles along the z -axis under protocols 1 and 2.

The pump flow rate was 2.0 L/min (A) and 5.0 L/min (B).

Fig. 4. Bland-Altman plots illustrating the relationship between differences and averages of protocols 1 and 2 at the pump flow rate of 2.0 L/min (A) and 5.0 L/min (B).

The solid line indicates the mean difference between two protocols. The dashed lines show the 95% limits of agreement interval (mean \pm 1.96 standard deviation [SD]).

Note. _P1 = protocol 1; P2 = protocol 2