Selective Intra-arterial Dual-energy CT Angiography (s-CTA) in Lower Extremity Arterial Occlusive Disease

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WHAT THIS PAPER ADDS
Detailed preoperative imaging of the infrapopliteal arteries is crucial for patient selection and procedural planning in patients with critical limb ischemia. Sometimes, however, the use of conventional contrast enhanced imaging methods (CTA and MRA) is limited by the contraindications of the iodine and gadolinium contrast media. In this study, a novel imaging method (s-CTA) is presented that provides high-quality arterial phase images with ultra-low dose iodine contrast media, useful also for patients unsuitable for conventional contrast enhanced imaging methods because of renal insufficiency.

Objective: In patients with peripheral arterial occlusive disease, renal impairment is a common contraindication to iodine and gadolinium contrast media, which limits the utility of conventional computed tomography angiography (CTA) and magnetic resonance angiography (MRA). It is proposed that selective intra-arterial dual-energy CT-angiography (s-CTA), that is CTA with intra-arterial injection of an ultra-low dose iodine contrast media, is a feasible, safe and accurate alternative imaging method to conventional non-invasive contrast enhanced vascular imaging in this patient group. The aim of this study was to report a preliminary experience of s-CTA in patients with critical limb ischemia and renal insufficiency with respect to safety, feasibility, and diagnostic accuracy.

Materials and methods: Ten non-consecutive patients with ischemic foot ulcers underwent s-CTA of one leg. Procedure related complications were recorded and imaging results were compared with conventional digital subtraction angiography (DSA).

Results: A median 17 mL (range 10–19 mL) contrast media (400 mg I/mL) was used. The median baseline plasma creatinine was 163 μmol/L (range 105–569) pre s-CTA versus 153 μmol/L (range 105–562) post s-CTA (p = .24). There was no puncture site complication. Among the patients selected for intervention (n = 6 with 30 arterial segments) the s-CTA findings correlated well with the DSA findings; the diagnostic sensitivity was 100%, the specificity 89%, and the accuracy 93%.

Conclusion: In this pilot study, a novel imaging method (s-CTA) is presented that provides high-quality arterial phase images with ultra-low dose iodine contrast media useful also for patients unsuitable for conventional contrast enhanced imaging methods because of renal insufficiency.

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INTRODUCTION
Accurate and detailed preoperative mapping of the infrapopliteal arteries is essential in patient selection (candidate for revascularization) and pre-procedural planning (open or endovascular, target artery for bypass, antegrade/crossover/pedal access, sizing of angioplasty balloons etc).

Magnetic resonance angiography (MRA) and computed tomographic angiography (CTA) with intravenous contrast injection are two cornerstones in preoperative arterial mapping, which have been shown to be accurate and tolerable for most patients. However, in patients with peripheral arterial occlusive disease (PAOD), concomitant renal impairment may limit the use of iodine and gadolinium contrast media, and thus the utility of conventional contrast enhanced CTA and MRA. The third cornerstone is duplex ultrasound (DUS), which is a safe and widely used alternative to contrast enhanced sectional imaging, that does not require any use of nephrotoxic contrast media. Although DUS has a high overall accuracy in detecting tibial vessel patency or occlusion, it is less reliable in subjects with...
extensive occlusive disease, compared with digital subtraction angiography (DSA), which is the gold standard.

Thus, there is a need for a minimally invasive contrast enhanced imaging technique that can reduce the amount of contrast media used while retaining high diagnostic accuracy. Ideally, such a technique should be able to visualize medium to small diameter arteries with a low blood flow, and be able to separate the vessel lumen from the vessel wall in the presence of calcification, as well as be safe and tolerable to the patient. By using CT with selective intraarterial contrast media injection, the required injected amount can be considerably reduced, thereby reducing the risk of renal impairment.

The aim of this study was to report an initial experience with selective intra-arterial dual energy CT-angiography (s-CTA), a novel minimally invasive vascular imaging method, in patients with lower extremity arterial occlusive disease unsuitable for conventional contrast enhanced imaging.

MATERIALS AND METHODS

Patients

Ten non-consecutive patients (nine males and one female; median age 73 years; age range 48–95 years) with chronic ischemic foot ulcers were examined with s-CTA between December 2010 and March 2012. The study was approved by the ethics committee of the Uppsala/Orebro Region. All subjects gave informed consent prior to the investigation.

Patients with a detected arterial lesion of clinical significance were scheduled for conventional angiography and attempted revascularization. The intraoperative angiograms were used to validate the s-CTA images. Pre and post s-CTA plasma creatinine levels were compared and puncture related complications were recorded.

CT technique

Nine examinations were performed on a Somatom Definition Flash 64-slice Dual Source CT-scanner (Siemens Healthcare, Forchheim, Germany). Tube voltages were set to 140 kV (tube A) and 80 kV (tube B). Tube A was operated with a quality reference milliampere-seconds (QRmAs) of 55, and the QRmAs of tube B was automatically adjusted according to tube A and scout image parameters. Automatic tube current modulation (CARE Dose 4D) was used. Tube rotation time (TR) was 0.5 s. The detector collimation was 64 × 0.6; pitch was 0.6 in five examinations, and 0.7 in the remaining five cases. Separate datasets were calculated for each tube voltage with a soft kernel specific for dual energy (D30), with slice thickness 1.5 mm and a reconstruction increment of 1.0 mm. The scan delay varied between 3 and 6 seconds after the beginning of the contrast injection. The median scan time required to cover the entire leg with this technique was 45 seconds (range 37–55).

One study was performed on a Somatom Definition Flash 128-slice Dual Source CT-scanner (Siemens Healthcare, Forchheim, Germany). Tube voltages were 80 kV (Tube A) and 140 kV (Tube B). The QRmAs of tube A was set to 300, and that of tube B was automatically adjusted according to tube A and scout image parameters. CARE Dose 4D was used. TR was 0.33 s. The detector collimation was 64 × 0.6; pitch was 0.7. Separate 80 kV and 140 kV datasets were calculated using kernel D30 with a slice thickness of 1.5 mm and a reconstruction increment of 1.0 mm. The resulting scan time was 27 seconds with these settings.

Arterial puncture and contrast injection

After sterile preparation and draping of the ipsilateral groin, the common femoral artery was punctured using a 4 French micro-puncture set (Cook Medical, Bloomington, IN, USA) (Fig. 1). After administration of local anaesthetic, the coaxial catheter was introduced into the external iliac artery over a 0.018 inch Nitinol wire, using the Seldinger technique. The catheter was connected to a Stellant DualFlow dual-headed CT contrast injector (Medrad Inc, Warrendale, PA, USA) via a 150 cm long extension tube, with an intrinsic volume of 10 mL, and simultaneous injection of the iodine contrast media (CM) iomeprol 400 mg I/mL (Iomeron, Bracco, Milan, Italy) and normal saline 0.9% (NS) was performed in three phases. The injection duration, and thereby also the total contrast volume, was tailored to match the scan time, so that adequate contrast density would be maintained throughout the scan. Typically, 7 mL of CM along with 13 mL of NS was injected during 10 seconds, immediately followed by 10.5 mL of CM and 19.5 mL of NS during 30 seconds, and finally 40 mL of NS bolus to clear the extension tube of contrast. In this way, a total of 17.5 mL of iomeprol 400 mg I/mL was injected during 50 seconds. The contrast/saline ratio was 35%, equalling an iodine concentration of 140 mg I/mL.

In the examination that was performed on the Somatom Definition Flash 128-slice Dual Source CT-scanner, 5 mL of CM along with 15 mL NS was injected during 10 seconds, followed by 5 mL CM and 15 mL NS injected during 20 seconds, resulting in an injection duration of 30 seconds. In this case an immediate repeat scan from the knee joint to the foot was obtained to make sure that sufficient time had elapsed to opacify arterial segments with slow flow.

Figure 1. MPR-reformat showing the contrast injection site at s-CTA. A 4 French × 7 cm micro-puncture catheter has been inserted into the common femoral artery, and is connected to the contrast injector extension tube.
Upon completion of the examination, the 4 French micro-puncture catheter was removed and a QuikClot haemostatic pad (Z-Medica Corporation, Wallingford, CT, USA) was applied, and the puncture site was manually compressed for 10 minutes. The patients were allowed to ambulate after 1 hour and were discharged after 2 hours, unless they were admitted for other reasons.

**Image analysis**

Post-processing was performed on a Carestream PACS workstation (Carestream, Genova, Italy), version 11.1 P003, equipped with the commercially available post-processing program SyngoVia 64 (Siemens, Forchheim, Germany), capable of handling Dual Energy datasets. The default workflow “CT-vascular” was utilized in all cases. 3D vascular reconstructions as well as maximum intensity projection (MIP) reformats were reviewed in various projections with and without automatic subtraction of scanner table, body bone removal, and hard plaques removal tools; as well as axial source images.

Intra-arterial contrast enhancement was assessed by drawing circular regions of interest (ROI:s) within the arterial lumen of a visually non-calciﬁed segment of the popliteal artery, one of the crural arteries in the middle part of the lower leg, and the dorsalis pedis artery or plantar artery below the ankle. Contrast density values were measured in the 80 kV dataset and are given in Hounsﬁeld Units (HU). The infrapopliteal arteries were subdivided into ﬁve segments: (1) popliteal artery below knee, (2) tibioperoneal trunk, (3) anterior tibial artery, (4) posterior tibial artery, and (5) peroneal artery, and were assessed for signiﬁcant arterial lesions, deﬁned as a localized >50% stenosis or occlusion.

**Statistics**

Statistical evaluation of the data was carried out with computer software package (SPSS PC version 20.0, SPSS, Chicago, IL, USA). Values are presented as median (range) and the sensitivity, speciﬁcity, and accuracy were calculated for s-CTA compared with DSA. For comparison of pre- and post s-CTA creatinine levels, Wilcoxon Signed Rank Test was used. A p value <.05 was considered signiﬁcant.

**RESULTS**

Ten patients were included; eight patients were considered unsuitable for conventional contrast enhanced vascular imaging, such as MRA and CTA because of renal impairment (median plasma creatinine 163 μmol/L, range 139—374 μmol/L), of whom one had end stage renal insufﬁciency treated with hemodialysis with a residual renal function important to preserve. One patient had end stage renal insufﬁciency treated with hemodialysis (creatinine 569 μmol/L), and one patient had only moderate renal impairment (creatinine 105 μmol/L).

The median (range) total contrast volume used at s-CTA was 17.1 mL (10—19 mL) iomeprol 400 mg I/mL, which corresponds to 6.8 g iodine (4.0—7.6 g). The median intra-arterial contrast enhancement was 1125 HU (317—2611) in the popliteal artery, 914 HU (357—2389) below the knee, and 630 HU (200—1224) below the ankle. The median scanning time was 42 seconds (27—55 seconds).

No in-hospital puncture site complication (such as hematoma) occurred and no patient showed any signiﬁcant increase in plasma creatinine level a median 27 days (8—50 days) post s-CTA; the median baseline plasma creatinine level was 163 μmol/L (range 105—569) pre s-CTA versus 153 μmol/L (range 105—562) post s-CTA (p = .24) with a median change of −7% (~30% to +12%).

Six of the ten patients examined with s-CTA were found to have an infrapopliteal arterial lesion of signiﬁcance justifying a revascularization attempt, and subsequently underwent selective antegrade femoral DSA and angioplasty with low proﬁle guide wires (0.014” or 0.018”) and balloon catheters, if a signiﬁcant arterial lesion was conﬁrmed (Fig. 2). In total, 30 infrapopliteal arteries were examined with both s-CTA and DSA. Of 18 arterial lesions detected with s-CTA, 16 were conﬁrmed with DSA (2/18 false positive) (Fig. 3). Twelve arteries showed no sign of occlusive disease at s-CTA, all conﬁrmed at DSA (0/12 false negative). Thus, the sensitivity was 100%, the speciﬁcity 89%, and the accuracy 93%.

**DISCUSSION**

The diagnostic value of a CT angiographic examination largely depends on the degree of intra-arterial contrast enhancement within the arterial segment of interest.⁵,⁶ Numerous intravenous contrast injection protocols exist, all with the goal of optimizing the intra-arterial contrast density in the target vessel bed. High contrast doses (100 mL 400 mg I/mL or more, 40 g I) are often required.⁷ Nevertheless, a high-quality peripheral CT arteriogram may still be diﬃcult to obtain, because of contrast timing issues, especially in the presence of arterial occlusions.

In the present pilot study, selective intra-arterial contrast injection was utilized, which resulted in a very high intra-arterial contrast density, even in the periphery (crural and pedal arteries) despite a relatively low total contrast dose (10—19 mL 400 mg I/mL, 4—8 g I). In fact, the intra-arterial contrast density was extremely high in some of the studies (above 2000 HU in the popliteal and crural arteries, and above 1000 HU below the ankle). In conventional (“single energy”) CT angiography, such a high contrast density may not be desirable, as it makes the distinction between the high-attenuating contrast media and vessel wall calcium more diﬃcult. Although dual energy CT-technique has the potential to discriminate iodine from calcium, misinterpretation may occur for various reasons. For example, arterial branches that run in the axial image plane may be interpreted as occluded because of partial volume effects, if the original slices are not thin enough. In the authors’ experience, the origin of the anterior tibial artery, the anterior and posterior perforating branches of the peroneal artery, and the dorsalis pedis artery, seem to be particularly prone to this artefact. Another possible pitfall is blooming artefacts,
either from vessel wall calcium or high intra-arterial iodine concentrations. This inherent weakness of CT-angiography usually tends to exaggerate stenotic lesions. The problem is less severe when high (e.g. 140 kV) compared with low x-ray tube voltages (e.g. 80 kV) are employed. For this reason, dual-energy CTA may have an advantage compared with conventional single energy (100–120 kV) CTA in this respect.

In all forms of contrast enhanced arteriography, the timing of contrast injection and image acquisition is crucial. The contrast bolus must not be too diluted, and the peak contrast density should ideally be reached early enough to avoid the concomitant venous return, especially in peripheral vascular beds. Minimizing the distance between the contrast injection site and the target vessel to be studied work towards these goals, a fact well recognized among radiologists. Additionally, much less contrast material is required to achieve adequate arterial contrast enhancement with this approach.

In the absence of significant occlusive arterial disease, contrast timing is generally straightforward. However, when flow-limiting arterial lesions are present, the contrast bolus transit time may be difficult to predict, especially below the knee, where the tibioperoneal arteries may be affected asymmetrically by vascular disease. This is less of an issue in dynamic imaging studies such as conventional DSA or time-resolved MRA, than in CT angiography, in which the scan table speed should ideally parallel the blood flow velocity, with some delay to allow for contrast filling of slow flow

Figure 2. Diabetic patient with renal insufficiency and chronic heel ulcer, examined with s-CTA using 17.5 mL iomeron 400 mg I/mL (a, b) and DSA (c). Dual-energy MIP reformats with automatic body bone removal shows total occlusion of the posterior tibial artery (white arrow), partial occlusion of the plantar arteries (white star), and significant stenoses in the tibioperoneal trunk (upper black arrow) and the peroneal artery (lower black arrow). The short interruption of the posterior perforating branch is a bone subtraction artefact, not present on axial source images (white thin arrow). The pedal arteriogram is somewhat obscured by venous contrast filling, which is caused by a relatively long scan time (50 seconds). (c) Selective infrapopliteal DSA confirms the findings of s-CTA. The perfusion of the wound area depends on the peroneal artery in this case.

Figure 3. s-CTA (left) showing occlusion of the anterior and posterior tibial arteries, with reconstitution of the dorsalis pedis and the lateral plantar artery through collaterals from the peroneal artery. Super-selective DSA during recanalization of the occluded anterior tibial artery confirms that the dorsalis pedis is patent.
segments. However, a long scan time requires a relatively higher contrast volume and carries a risk of venous filling obscuring the arteriogram. A short scan time, on the other hand, requires a lower contrast dose and has less risk of venous contrast contamination, but may not allow for the contrast to fill all arterial segments sufficiently. These timing issues are less problematic with s-CTA than with conventional intravenous CTA, both because of proximity of the contrast injection to the target vessel bed, as well as the high contrast density that contributes to reaching diagnostically acceptable contrast enhancement at an earlier stage, even in low-flow arteries.

As stated earlier, optimal timing of the scan and contrast injection are subject to individual variation. The authors’ current practice is a scan time of 25—30 seconds (whole leg) together with an injection of 50 mL 25% contrast medium over 25 seconds (12.5 mL 400 mg I/mL with simultaneous injection of 37.5 mL normal saline at 2 mL/s followed by a 40 mL saline bolus at 2 mL per second) and a scan delay of 14 seconds, which is the authors’ experience works well for most patients.

The aim of the present pilot study was to describe and report a preliminary experience with s-CTA (selective intraarterial dual energy CT angiography), a novel minimally invasive arterial imaging method, with respect to feasibility and safety, in patients with critical lower limb ischemia and renal insufficiency. In this small series, no procedure-related adverse event was observed. These preliminary results also indicate that s-CTA is accurate with a high sensitivity and specificity, although statistically robust conclusions were difficult to reach because of the limited number of vessel segments (n = 30) that were examined with both CTA and DSA. A limitation of the proposed method is the need for an arterial puncture, which requires active participation of the radiologist during the exam, in contrast with conventional CTA. There may also be a slightly higher risk of bleeding complications than with regular i.v. cannulation. All procedures were carried out on an out-patient basis, and all patients could be discharged within 2 hours.

Detailed and accurate preoperative imaging of the infrapopliteal arteries is crucial for successful revascularization. The results of this pilot study are encouraging and s-CTA may become a valuable adjunct to the existing arsenal of vascular imaging modalities, especially for the small cohort of CLI patients who do not tolerate conventional CTA or MRA because of advanced renal disease, and in whom extensive tibial occlusive disease compromises the accuracy of duplex scanning. The high-quality arterial phase images obtained also suggest that s-CTA may provide more detailed and informative arterial mapping than other imaging techniques available, and thus has the potential to be of value for all patients with distal arterial lesions, regardless of the renal function. Also, the high peripheral contrast enhancement that was obtained with intra-arterial contrast injection may prove valuable in CT perfusion studies and other CTA applications where a short and high contrast peak is desired. Further evaluation of the method is warranted.

Conclusion
In this pilot study, a novel imaging method (s-CTA) is presented that provides high-quality arterial phase images with ultra-low dose iodine contrast, useful also for patients unsuitable for conventional contrast enhanced imaging methods because of renal insufficiency.

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CONFLICT OF INTEREST
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REFERENCES
4 Seidlinger SI. Catheter replacement of the needle in percutaneous arteriography; a new technique. Acta Radiol 1953;39: 368—76.
9 Fleischmann D, Rubin GD. Quantification of intravenously administered contrast medium transit through the peripheral arteries: implications for CT angiography. Radiology 2005;236: 1076—82.