The aim of this article is to evaluate the feasibility and results of our peripheral revascularization where we used non-conventional intra-procedural imaging techniques. Between January 2014 and September 2014, 45 patients were imaged with CO2 angiography and/or optical coherence tomography (OCT) or 2D perfusion imaging. The scope was to minimize the use of contrast and obtain additional information to improve the outcome. CO2 angiography was used in all patients with impaired renal function. Two-dimensional perfusion was used in all patients with critical limb ischaemia before and after revascularization to quantify angiosome blood supply improvement at wound level. Optical coherence tomography was performed in superficial femoral arteries and popliteal arteries to disclose vessel microstructure and characterize plaque structure. In all patients, the invasive imaging was feasible and safe. In those patients studied with CO2, the creatinine serum level after procedure increased by 0.11 ± 0.05. None of the patients received dialysis. The procedural success rate was 100% and was no different from the historical sample of the cath lab. Procedural time was not significantly affected by this supplemental technique. The 2D perfusion showed an incremental blood supply at wound level and OCT provided encouraging details regarding dissections and their clinical relevance. Our early experience with supplementary imaging techniques showed safety and feasibility. The peripheral angioplasty success rate was not different from the historical sample and the reduction of the contrast media dose resulted in an encouraging outcome in terms of renal protection. Two-dimensional perfusion added objective information regarding blood supply improvement and guided re-perfusion strategy.

**KEYWORDS**
Peripheral angioplasty; CO2 angiography; Optical coherence tomography; Critical limb ischaemia

**Introduction**
Endovascular treatment of symptomatic atherosclerotic peripheral artery disease (PAD) has gained widespread acceptance and is now recommended as the primary therapeutic strategy in many clinical and interventional situations.1,2 Percutaneous transluminal angioplasty (PTA) of the superficial femoral and/or popliteal and tibial arteries has a high procedural success rate; however, re-stenosis occurs in up to 60% of cases.3 The evaluation of acute procedural result is usually assessed by conventional angiography. Any operator choice is determined by 2D images obtained through the injection of an iodinated contrast agent to obtain monoplane imaging. The imaging modalities have clear and well-known limitations. The purpose of this paper is to report the initial experience with new and more sophisticated invasive procedural imaging modalities in order to reduce patient risk and improve procedural outcome.
Technical description

CO₂ angiography

Carbon dioxide angiography (CO₂ angiography) is a diagnostic procedure to obtain vascular angiography without the use of an iodinated contrast medium. CO₂ is ideal because it is biocompatible, has a very low viscosity, and moves away from the blood quickly, it is not nephro-toxic, nor hepatotoxic and does not have appreciable medical contraindications. CO₂ does not mix with the blood but it displaces it. X-ray absorption of the iodinated contrast is much less (1/10) and it is possible to obtain good quality image if flow parameters optimization are set and a low frame rate digital subtraction imaging technique is used. CO₂ is injected through an automatic pre-settable constant pressure and volume injector to fulfill the vascular space completely. Manual gas injection, widely used, especially in the past, does not permit an optimal control of the gas output. Injection pressure and volume should be set to fulfill the vessel with minimum gas flow fragmentation without the dangerous increase of pressure that could damage the vessel. The use of automated injection standardizes the technique, so reducing the operator variability and training time and improving the imaging quality (Figure 1).

Personal experience

We imaged 45 consecutive patients with PAD by CO₂ angiography. Population demographics and clinical characteristics are displayed in Table 1. In 12 cases, CO₂ angiography was used as a stand-alone technique due to renal insufficiency and GFR value < 30 mL/min/m². In any case dialysis was necessary. Eighteen of them underwent angioplasty of the superficial or popliteal artery, 17 underwent angioplasty of below-the-knee arteries (mostly tibial arteries) and 10 patients underwent both superficial femoral artery (SFA) and tibial arteries. Twenty-five (55.6%) patients were treated for claudication, and 20 (44.4%) were treated for critical limb ischaemia. The imaging procedure was ultimate in all cases without serious patient discomfort. CO₂ angiography was fully diagnostic in all cases showing, appropriately, site and extent of atherosclerotic disease when compared with pre procedural non-invasive imaging and standard angiography in the above-the-knee patients and also in 25 of 27 BTK patients (92.6%). The procedural time was slightly longer (100 ± 45 min) when compared with the historical sample of the cath lab (88 ± 31 min), but the difference was statistically not significant. The planned revascularization strategy was obtained in all 45 patients. Seventeen of 45 pts had GFR < 60 mL/min/m². At 48 h after procedure the creatinine increased by 0.11 ± 0.05.

2D perfusion imaging

Perfusion angiography is a novel X-ray imaging technology that utilizes the high temporal resolution of X-ray angiographic images to assess subtle physiological changes in the parenchymal perfusion level. The technology is successfully being used in neuroradiological interventions. Acquisitions are made on the Philips Allura Xper FD20 system (Philips Healthcare, Best, The Netherlands). No additional exposure to radiation or contrast agent is needed.
needed, as a regular DSA (digital subtraction angiography) run can be used to construct the perfusion image. 2D Perfusion has a 3 frames/second (f/s) acquisition protocol, analysing 30-s acquisition capturing 90 frames. The software captures contrast enhancement changes over time per pixel of the DSA image. During the acquisition, a total of 9 mL radiographic contrast (Visipaque, 320 mg I/mL; GE Healthcare, Oslo, Norway) at 3 mL/s is injected via a 5-Fr catheter. Within seconds after acquisition, the 2D Perfusion image is reconstructed and visualized on the workstation (XtraVision, release 8.8.0 Philips Healthcare, Best, The Netherlands). Immobilization of the leg is crucial when performing perfusion runs, as well as standardization of the injection protocol. With 2D Perfusion, the flow of contrast through peripheral arteries and tissue enhancement can be visualized in a single colour image, where different colours represent the corresponding blood perfusion levels. It also allows comparison of pre- and post-procedural perfusion levels. Within a user defined region of interest, perfusion parameters can be appreciated. Deciding on endovascular treatment endpoint in critical limb ischemia (CLI) patients is far from trivial. Presently, there is no measurement tool available to determine whether the treatment has been successful or whether additional revascularization is needed. Recent work of Jens et al. demonstrates that a dedicated imaging protocol allows for disease specific perfusion imaging and pre- and post-revascularization imaging with 2D perfusion. Significant differences have been demonstrated in the perfusion levels after revascularization in PAD and CLI patients.

**Optical coherence tomography imaging**

Optical coherence tomography is a near-infrared light-based technology that enables to provide cross-sectional images with an axial resolution of up to 10–15 μm resulting in a refined analysis of the vessel wall. The main reason that this technology is not used frequently, is due to the need of additional crystalloid infusion during imaging, and for the low penetration power that is unable to deeply characterize the plaques. The introduction of the user-friendly frequency domain system (FD-OCT) has partially overcome the limitations of the old time domain (TD-OCT). The fast-scanning laser system enables the TD-OCT to achieve images of longer segments (up to 54 mm) and larger arteries without the need of transient balloon occlusion, thus reducing the risk of vascular damage during imaging (Figure 2).

**Personal experience**

Our group firstly described the safety and feasibility of optical coherence tomography (OCT) acquisition during imaging of SFA, using selective saline infusion instead of contrast flush. By manually injecting 50 mL of pure saline solution, we were able to achieve a sufficient substitution of blood and thus were able to detect vessel plaques and dissections as during ioxanol 320 (Visipaque, GE Health Care, Cork, Ireland) infusion performing a FD-OCT (St Jude, Minneapolis, MN, USA) acquisition.

**Discussion**

Standard angiography has been, for a long time, the only procedural imaging technique used during peripheral interventions. It has well-known safety limitations due to renal injury consequent to the iodinated contrast agent effect and resolution drawbacks being limited at a bi-dimensional view, and to its limited spatial resolution. New and more sophisticated imaging modalities are developing, thus enabling to get more detailed information, so leading to clinically relevant intra-procedural decisions.

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**Table 1** Population demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Clinical characteristics (n = 45)</th>
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<tbody>
<tr>
<td>Age (year)</td>
<td>69.5 ± 9.5</td>
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<tr>
<td>Gender: Male, n (%)</td>
<td>30 (66.6)</td>
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<tr>
<td>Diabetes, n (%)</td>
<td>26 (57.7)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>30 (66.6)</td>
</tr>
<tr>
<td>Hyperlipidaemia, n (%)</td>
<td>29 (64.4)</td>
</tr>
<tr>
<td>Current smoker, % (m/n)</td>
<td>15 (33.3)</td>
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<tr>
<td>IDEM Rutherford class, n (%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>11.1 (5/45)</td>
</tr>
<tr>
<td>3</td>
<td>24.4 (11/45)</td>
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<tr>
<td>4</td>
<td>17.7 (8/45)</td>
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<tr>
<td>5</td>
<td>33.3 (15/45)</td>
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<td>6</td>
<td>13.3 (6/45)</td>
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</table>

**Figure 2** OCT images of SFA showing dissection (A) and (B) and thrombus.
CO₂ angiography has demonstrated, in our cohort of patients, to be feasible, safe, and effective in diagnosis. We have been able to obtain the anatomical diagnosis in all patients with SFA and popliteal artery disease, comparably to traditional angiography, and to use less or no iodinated contrast. This assumes particular interest in a subset of patients with poor renal function where we used only CO₂ angiography. It could reduce the rate of contrast induced nephropathy in this particular subset of patients. The use of this alternative modality, with an automatic injector, did not significantly increase the procedural time and radiation exposure time. What is noteworthy, is that the procedural success was not different from the historical sample of the cath lab, showing that it could be an alternative as a stand-alone technique for peripheral revascularization. In below-the-knee patients, particular attention is necessary to optimize the flow, pressure, and volume parameters, to obtain good imaging, especially at foot level. Injection in popliteal and accurate injector setting allowed us to be diagnostic in 92% of the cases.

Critical limb ischemia peripheral endovascular treatment requires both anatomical and physiological assessment of the patient’s vascular pathology and tissue perfusion level. So far only anatomical imaging has been available in the interventional lab. Tissue perfusion information could alter the course of the interventional procedure by demonstrating disease severity, effect, and completeness of treatment. The use of 2D perfusion imaging on CLI patients might offer further and valuable information of foot blood supply of the revascularized angiosome (Figure 3). It is clinically relevant to balance the grade and level of revascularization with the result obtained: further and deeper attempts will be needed only if the tissue perfusion has not improved. This simple technique gives us ‘on-line’ perfusion quantitative information that is not available with other techniques. Perfusion angiography may support intra-procedural decision making. Studies are ongoing to validate the prognostic value of the parameters in CLI patients.

Optical coherence tomography has been mainly evaluated during coronary intervention where its ability to disclose vessel microstructure may lose some of the clinical relevance. In fact, during percutaneous coronary intervention (PCI) the gold standard treatment, in the vast majority, is the stent implantation as a final step, irrespective of the plaque characterization and vessel wall injuries following lesion preparation. Successful percutaneous revascularization of femoral and popliteal arteries differs from PCI because of the several forces such as torsion, compression, flexion, and extension induced by leg movement. These findings might explain the disappointing long-term outcome after peripheral PTA and the high rate of stent fractures at these sites. We believe that in this field, where the role of non-stented techniques such as atherectomy and balloon angioplasty alone, still plays a pivotal role, using an imaging modality able to precisely show the vessel wall response to treatment may provide useful information. Despite this, the significant additional amount of contrast required for OCT evaluation of large muscular arteries might expose this population, frequently affected by major concomitant comorbidities such as diabetes, hypertension, poor renal function, and other cardiovascular disorders to an increased risk of nephropathy. This limitation was overcome by using saline infusion instead of contrast media. We believe that the use of OCT guidance during peripheral artery interventions, where the use of a

Figure 3 2D perfusion imaging: pre-procedural (A) and post-procedural (B) image. Quantitative analysis of tissue perfusion at calcaneal level before posterior tibial artery angioplasty (white line) and post-angioplasty (red line) (C).
stent to seal vessel trauma following balloon inflation or plaque atherectomy is not as obvious as during PCI, and where the response of the vessel wall, may not being detectable by angiography alone, will acquire an important role in future clinical practice.

Conclusions

New imaging modalities are emerging as complimentary to standard angiography during peripheral interventions, so improving image resolution and/or adding further details to guide the procedural decision making.

Conflict of interest: none declared.

References


