

# Innovations in imaging for chronic total occlusions: a glimpse into the future of angiography's blind-spot

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Chronic total occlusions (CTOs) are a subset of lesions that present a considerable burden to cardiovascular patients. There exists a strong clinical desire to improve non-surgical options for CTO revascularization. While several techniques, devices, and guide wires have been developed and refined for use in CTOs, the inability of angiography to adequately visualize occluded arterial segments makes interventions in this setting technically challenging. This review describes the current status of several invasive and non-invasive imaging techniques that may facilitate improved image guidance during CTO revascularization, with the goals of improving procedure safety and efficacy while reducing the time required to complete these interventions. Cardiac imaging also has important potential roles in selecting patients most likely to benefit from revascularization as well as pre-procedural planning, post-procedural assessment of revascularized segments and long-term outcomes studies. Modalities discussed include non-invasive techniques, such as CT (computed tomography) angiography and cardiac magnetic resonance imaging (MRI), as well as invasive techniques, such as intravascular ultrasound, optical coherence tomography, intravascular MRI, and conventional angiography. While some of these techniques have some evidence to support their use at present, others are at earlier stages of development. Strategies that combine imaging techniques with the use of interventional therapies may provide significant opportunities to improve results in CTO interventions and represent an active area of investigation.

## Keywords

Chronic total occlusions • Image-guided interventions • Cardiac MRI • Optical coherence tomography  
• Intravascular ultrasound • CT coronary angiography

## Introduction

Chronic total occlusions (CTOs) are defined as occlusions greater than 1 month old with angiographic TIMI 0 or TIMI 1 flow. Successful revascularization of CTOs by either surgical or percutaneous means has been associated with improved LV function<sup>1,2</sup> and possibly reduced mortality.<sup>3,4</sup> Patients who present with an ST-elevation myocardial infarction (STEMI) and are found to have an underlying CTO in a non-infarct related artery are known to have poor outcomes with >30% mortality at 1

year. Furthermore, CTOs appear to account substantially for the poor prognosis in patients with multivessel disease who suffer an STEMI<sup>5</sup> compared with their single-vessel disease cohorts.

Recent data from the occluded artery trial (OAT) and total occlusion study of Canada (TOSCA-2) trials<sup>6,7</sup> demonstrate that routine percutaneous coronary revascularization of sub-acute total occlusions (3–28 days old) does not reduce the combined endpoint of death, myocardial re-infarction, or NYHA class IV heart failure. However, these studies did not address CTOs (>1 month old) and excluded patients with multi-vessel disease,

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**Table 1** Comparison of described visualization techniques

Technique	Resolution ( $\mu\text{m}$ ) (approximate)	Invasive	Visualize occluded lumen	Maturity	Salient features
Angiography	300–500	Yes	No	+++++	Real-time; broad availability
Computed tomography (CT) angiography	500	No	No	++++	Good assessment of calcifications; increasing availability
Cardiovascular magnetic resonance imaging (MRI)	500–700	No	In periphery	+++	Strong soft tissue contrast; excellent assessment of function and viability
Conventional intravascular ultrasound (IVUS)	50–200	Yes	Yes	++++	Assessment of revascularized CTO; cannot see through calcium; may be combined with tissue characterization techniques such as virtual histology
Forward-looking IVUS	30–200	Yes	Yes	+	Forward-looking configurations more appropriate for most CTOs; good compromise between resolution and tissue penetration ( $\sim 4\text{--}8\text{ mm}$ ) but cannot see through calcium
Forward-looking optical coherence tomography (OCT)	4–15	Yes	Yes	+	High resolution and contrast; easily integrated with laser-based interventions; limited tissue penetration ( $\sim 400\text{--}700\ \mu\text{m}$ )
Intravascular MRI	150–250	Yes	Yes	+	Excellent soft tissue contrast; broader field of view than OCT or IVUS

A summary of the several imaging techniques described, with descriptions of their most salient features.

angina at rest or severe inducible ischemia. Randomized controlled trial data for either routine or selective revascularization of CTOs, including these important subgroups are currently not available.<sup>8</sup>

Revascularization by percutaneous coronary intervention is often a technical challenge. The manipulation of wires and devices through a CTO during percutaneous coronary intervention (PCI) without a means to visually identify vessel wall boundaries involves an inherent risk of complications such as arterial dissection, perforation and cardiac tamponade. Prolonged procedural times for CTOs increases the likelihood of contrast nephropathy and radiation skin injury. Finally, the unpredictable and lengthy amount of time required for these procedures complicates the scheduling and efficiency of catheterization labs. A large proportion of patients are treated with medical management alone. Reductions in restenosis rates with drug eluting stents in CTOs<sup>9</sup> suggest markedly improved long-term patency over bare metal stents. Thus, the main limitation to PCI in CTOs is the ability to negotiate the CTO. Improvements in guidewire technology, interventional devices and revascularization techniques are helping to increase the likelihood of success with PCI for CTOs. A recent series of review articles further describes the background, significance and treatment methods for this highly relevant subset of lesions.<sup>10–13</sup>

### The developing roles of imaging in the management of chronic total occlusions

The most important clinical roles for imaging in CTOs include (i) identifying the CTO; (ii) predicting whether or not the patient is likely to derive clinical benefit from revascularizing the occluded segment; (iii) predicting the ease with which a CTO can be

crossed; (iv) pre-procedural planning; (v) visualization during the procedure; (vi) post-procedural assessment of the revascularized arterial segments and affected myocardium, and (vii) long-term follow-up. In addition, imaging of coronary and peripheral CTOs may help us better understand their pathophysiology and natural history, and provide important insights into devising future strategies to facilitate their management.

Improvements in patient selection, procedural success rates, myocardial function, and long-term morbidity and mortality are important goals that may be facilitated by cardiac imaging in the context of CTOs. Other secondary but important goals include reductions in both procedure times and the frequency of complications.

Angiography provides real-time interactive guidance and will likely continue as the primary imaging technique for CTOs. It is widely available and serves as the *de facto* imaging technique most familiar to interventional cardiologists. Indeed, the contemporary definition of a CTO is dependent on a lesion's angiographic appearance. The use of adjunctive imaging techniques to guide the penetration of a wire or other device through a CTO to improve procedural outcomes is an unrealized but very desirable goal.

Proposed imaging techniques for CTOs can be broadly categorized into (i) large field of view and modest resolution [such as cardiac MRI (magnetic resonance imaging) or CT (computed tomography) angiography] and (ii) small field of view and high resolution (Table 1). High-resolution methods include forward-looking adaptations of intravascular ultrasound (IVUS), optical coherence tomography (OCT), and intravascular MRI. Many of these imaging modalities can be coupled with interventional techniques, and thus improve upon the guidance provided by angiography during revascularization. Characterizing a CTO before

**Table 2** A summary of imaging findings and their relevance based on currently available clinical evidence for the management of chronic total occlusions (CTCA, computed tomography coronary angiography)

		Modality	Supportive references	Non-supportive references
Features with demonstrated value				
Length > 15–20 mm	Negative predictor of successful crossing	Angiography, CTCA	Olivari, Noguchi, Maiello, Mollett	Tan
Calcification	Negative predictor of successful crossing	Angiography, CTCA	Olivari, Noguchi, Soon, Mollett	
Multivessel disease	Negative predictor of successful crossing	Angiography	Tan, Olivari, Noguchi, Ivanhoe, Suero	Maiello
Tapered stump	Positive predictor of successful crossing	Angiography, CTCA	Tan, Mollett, Soon, Maeillo, Olivari, Ivanhoe	
Emerging features with potential value				
Myocardial viability	Predicts improvement in myocardial function	Magnetic resonance imaging (MRI)	Baks	
Features of debated value				
Proximity to a side branch	Negative predictor of successful crossing	Angiography	Mollett, Tan	Olivari, Maiello
Vessel Size < 3 mm	Negative predictor of successful crossing	Angiography	Tan	Olivari, Noguchi
Bridging collaterals	Negative predictor of successful crossing	Angiography, CTCA	Tan, Maiello	Kinoshita, Olivari, Noguchi

intervention, such as with non-invasive techniques, may provide information about mechanical and geometric properties that would influence interventional strategies. Post-intervention imaging may help assess the resulting lumen and predict outcomes such as long-term patency and need for follow-up.

## Angiography

As mentioned previously, angiography will continue as the primary imaging technique for procedural guidance during CTO interventions into the foreseeable future. Angiographic characteristics of CTOs can strongly predict the likelihood of a successful intervention (Table 2). Features that consistently correlate with failure to cross a lesion with a guidewire include lesion length greater than 15–20 mm, multi-vessel disease, calcifications, and absence of a tapered stump.<sup>1,4,14–17</sup> Other features with conflicting results in terms of their predictive value include the presence of bridging collaterals, proximity to a side branch, tortuosity, and lack of visibility of the distal vessel.<sup>4,15–18</sup> Contralateral (and simultaneous) injections of both the right coronary artery (RCA) and LCA will often permit simultaneous visualization of the entry point and exit point via collaterals. Multiple projections or bi-plane angiography are often used to further augment visualization of the coronary anatomy. While angiography is very useful for guidance purposes, it still has considerable limitations that stem from its two-dimensional projection format and the lack of soft tissue contrast. Angiography does not provide sufficient information about the geometry, composition or vessel borders of an occluded segment. Additional safety concerns include excessive

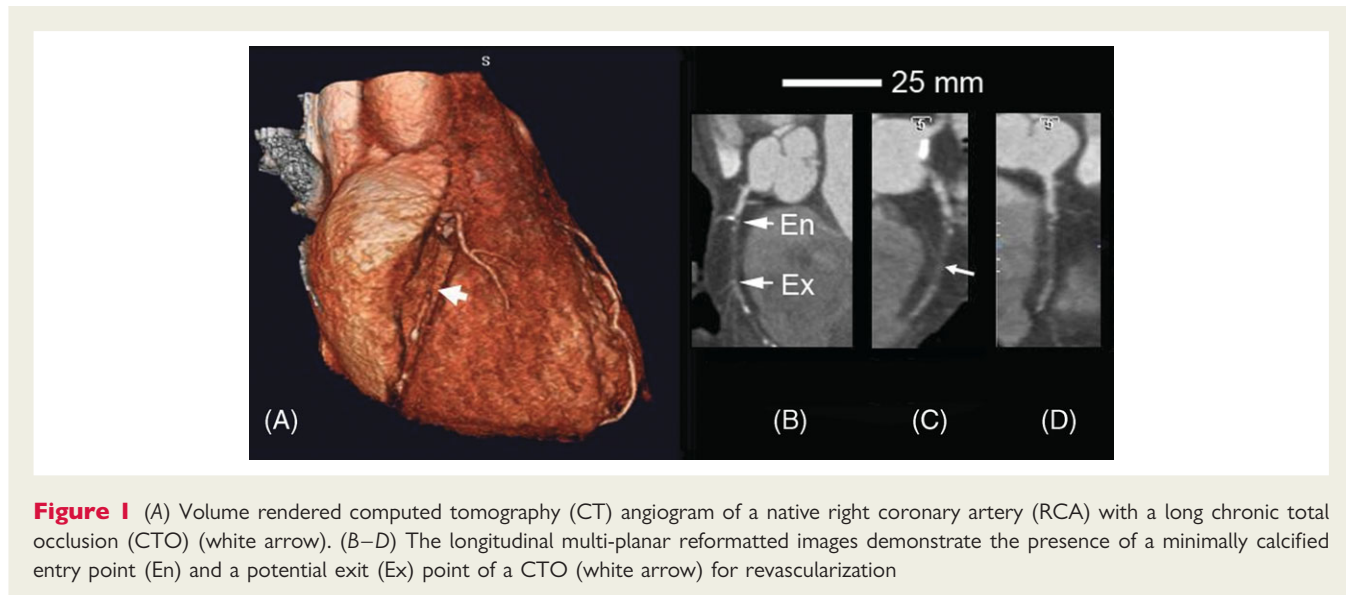
X-ray exposure (>40 min fluoroscopy time) and contrast loads averaging 350 mL.<sup>19,20</sup>

Resolution remains another significant limitation of angiography. Even in angiographic CTOs with TIMI grade 0 or 1 antegrade flow, ~50% are <99% stenotic by histopathology.<sup>21</sup> Intraluminal micro-channels measuring 100–500 µm, beyond the resolution of angiography, are commonly found in both human pathological samples and in animal models of CTOs.<sup>22</sup> These micro-channels may have importance in characterizing the age and mechanical properties of a CTO. We suspect that they may also serve as useful landmarks for other higher resolution imaging methods to facilitate successful guidewire passage through CTO and may provide conduits that facilitate delivery of lesion-modifying agents such as collagenase.<sup>23</sup>

## Computed tomography angiography

Multi-slice or multi-detector CT coronary angiography (CTCA) is rapidly gaining in popularity for assessing coronary artery lesions. A single venous injection of less than 100 mL is used for most scans. CT angiography is more accurate in identifying severe stenoses<sup>24</sup> compared with less significantly diseased segments, although severe calcification reduces the ability to distinguish the vessel lumen from calcified deposits. An example of a CTO with minimal calcification is shown in Figure 1, with a potential exit point visualized near the distal end of the occluded segment.

A recent study demonstrated that procedural success for crossing CTOs could be predicted based on several features identifiable by CT angiography.<sup>25</sup> Occlusion length >15 mm and severe



**Figure 1** (A) Volume rendered computed tomography (CT) angiogram of a native right coronary artery (RCA) with a long chronic total occlusion (CTO) (white arrow). (B–D) The longitudinal multi-planar reformatted images demonstrate the presence of a minimally calcified entry point (En) and a potential exit (Ex) point of a CTO (white arrow) for revascularization

calcification were negative predictors of success, while tapered stump morphology was a positive predictor. In particular, heavy transluminal calcification (occupying >50% of the cross-sectional area of the lumen) may be an important predictor of procedural failure.<sup>26</sup> CT angiography provides measurements of occlusion length that can exceed measurements obtained using conventional angiography, likely due to the absence of foreshortening effects. As a three-dimensional imaging technique, features such as vessel tortuosity, bridging collaterals, and the extent of calcifications within the occlusion may provide important information in pre-procedural planning of interventional strategies. Yokoyama *et al.*<sup>27</sup> reported on the use of CT angiography for pre-procedural planning. This strategy identified the location of calcifications and regions of sharp bends along the course of a CTO to help guide their interventions.

Disadvantages of CT angiography include the lack of soft tissue contrast, which can impair localization of the luminal borders of the CTO, and a relatively high degree of radiation exposure, especially when the doses delivered by both a pre-procedural CT angiogram and a potential subsequent interventional procedure are taken into account.<sup>28</sup>

Incorporation of ECG-pulsed modulation of the tube current can significantly reduce radiation dose,<sup>29</sup> and becomes most practical in dual-source CT scanners.<sup>30</sup> Dual-source CT scanners can acquire data at twice the speed as single source multi-detector CT systems, obviating the need for heart rate control prior to scanning and improving the likelihood of interpretable imaging data.<sup>31</sup> Dual-energy CT uses two different tube voltages to generate a pair of imaging datasets that may improve tissue characterization.<sup>32</sup> Its potential role to improve discrimination between calcifications and iodine contrast in vessels is under investigation. Indeed, rapid advances in CT technology are contributing significantly to CT angiography's popularity. Further data regarding its suitability for CTO identification, characterization, and pre-procedural planning is anticipated.

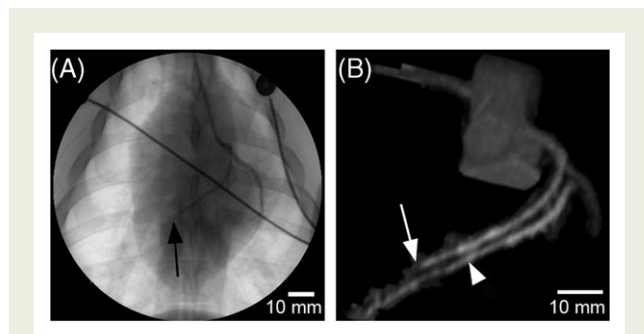
## Cardiac magnetic resonance imaging

At present, cardiac magnetic resonance (MR) has its most significant clinical relevance for CTO management in assessing myocardial function and predicting the potential of a myocardial bed to regain contractility after CTO intervention. Delayed hyper-enhancement imaging by contrast-enhanced MRI has been shown to predict the recovery of myocardial function in dysfunctional segments by surgical revascularization<sup>33,34</sup> and in the setting of acute myocardial infarctions.<sup>35,36</sup> It can also predict functional improvement in patients undergoing PCI of CTOs,<sup>37</sup> and may therefore play an important role in selecting patients who are most likely to benefit from intervention. While positron emission tomography has a long history of evidence to support its accuracy in detecting myocardial viability, MRI has the advantages of broader availability, and better resolution with comparable sensitivity and specificity.<sup>38,39</sup>

Non-invasive characterization by CMR of cardiac structure and function also are very useful for assessing the natural history of myocardium in areas affected by CTOs, for post-procedural studies and to provide long-term follow-up after CTO interventions. For example, CMR has been used to demonstrate a reduction in infarct size and improvement in left ventricular function with the concomitant delivery of progenitor cells to target regions that were previously rendered ischaemic by CTO.<sup>40</sup>

Several techniques to non-invasively detect significant coronary artery stenoses are available using CMR. First-pass contrast studies to image tissue perfusion<sup>41</sup> and dobutamine stress CMR to detect regions of ischemia with changes in myocardial contractility<sup>42</sup> provide indirect evidence of significant coronary stenoses. However, there is no evidence to suggest that either of these techniques can differentially identify a total occlusion from a partial occlusion.

The use of cardiac MRI to directly assess coronary plaque via CMR angiography continues to undergo active development.<sup>43</sup> CMR angiography utility is currently limited to ruling out left



**Figure 2** (A) Conventional angiogram of an experimentally induced chronic total occlusion in a porcine left anterior descending artery (LAD) (black arrow) 30 days after implanting a biodegradable occlusion. (B) Occlusion at the distal end of patent portion of the LAD (white arrow) and the neighbouring great cardiac vein (white arrowhead) by magnetic resonance (MR) angiography with an intravascular contrast agent

main or multivessel disease<sup>44</sup> and for assessing coronary artery bypass graft patency.<sup>45</sup> The sensitivity and specificity for identifying coronary CTOs has not been studied. Cardiac and respiratory motions contribute to technical difficulties in achieving ideal resolutions and signal-to-noise ratios with non-invasive characterization of coronary plaque. Nonetheless, steady improvements in overcoming these obstacles continue to develop with success via the use of surface coils, stronger magnetic fields, and novel scanning sequences. *Figure 2* demonstrates an example of a coronary CTO imaged *in vivo* in an experimental porcine model using a 1.5T scanner and an intravascular contrast agent.

CMR remains attractive for future work due to its inherent soft tissue contrast and its non-invasive nature. Its real-time images, flow measurement, various contrast-weighting schemes and imaging planes provide a great deal of potential for future CTO research. Data from our laboratory has shown that intravascular MR contrast agents can assess intraluminal perfusion through the CTO and possibly even identify micro-vessels that are undetectable by conventional angiography in peripheral CTOs, as seen in *Figure 3*. Extravascular agents simultaneously enhance both the lumen and the surrounding myocardium, while intravascular agents preferentially enhance the lumen and may thus improve the diagnostic performance of CMR angiography in humans.<sup>46</sup> MR contrast agents are also rapidly maturing in animal models of disease, including agents that target molecules frequently found in atherosclerotic activity.<sup>47</sup>

Another variant of cardiac MRI that may have relevance to the assessment of CTOs is direct thrombus imaging<sup>48</sup> (MRDTI). MRDTI allows for the estimation of the extent and age of thrombi without the use of an exogenous contrast agent and is being refined for use towards coronary lesions.

### Intravascular magnetic resonance imaging

The ability to characterize coronary plaque composition using MRI remains limited by the inherent resolution of the technique and artefacts generated by cardiac and respiratory motion.

Intravascular coils improve the signal-to-noise ratio sufficiently to attain a resolution that allows for the identification of structural layers within a plaque<sup>49</sup> and could be used to confirm intraluminal position of devices during CTO revascularization. Recently, a 0.014 inch MRI imaging guidewire has been developed and tested *in vivo*.<sup>50</sup>

Previous efforts of intravascular MRI development have been directed towards side-viewing orientations.<sup>51</sup> However, most CTOs will require forward-looking coils to guide penetration during the intervention. We have recently developed intravascular coils with sufficient sensitivity as far as 5 mm ahead of the catheter tip for that purpose.

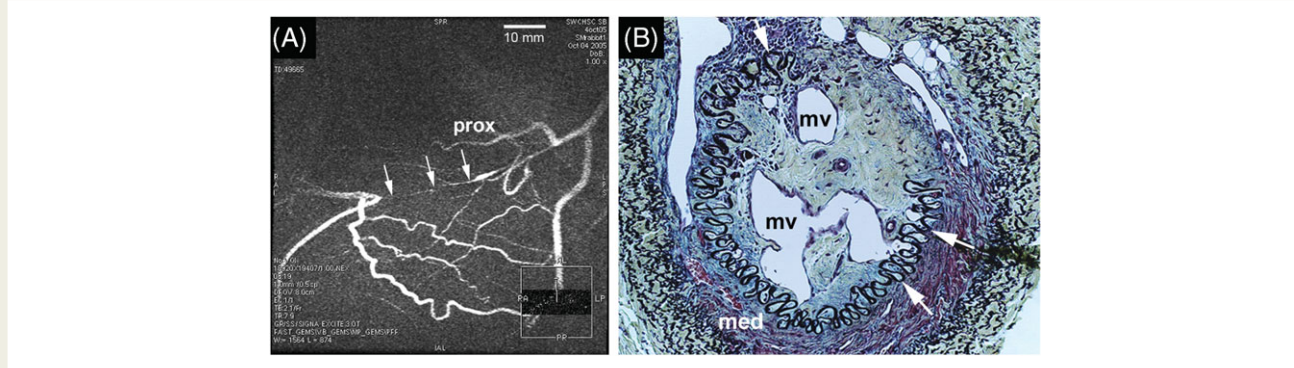
The inclusion of MR-compatible receiver coils in catheters is also very helpful for tracking the catheter motion during CMR-guided interventions,<sup>52</sup> as most conventional catheters and devices are not well visualized under MRI. MR sensitive coils in guide wires, catheters, and devices have been used to guide the recanalization of a long CTO in a carotid swine model.<sup>53</sup> Finally, the use of intravascular MR receiver coils remains controversial, as these devices can be subject to significant *in vivo* heating under specific conditions.<sup>54</sup> There are many ways to reduce the severity and likelihood of this potential hazard, but very few studies have been performed in humans using intravascular MRI to date.<sup>55</sup>

### Intravascular ultrasound

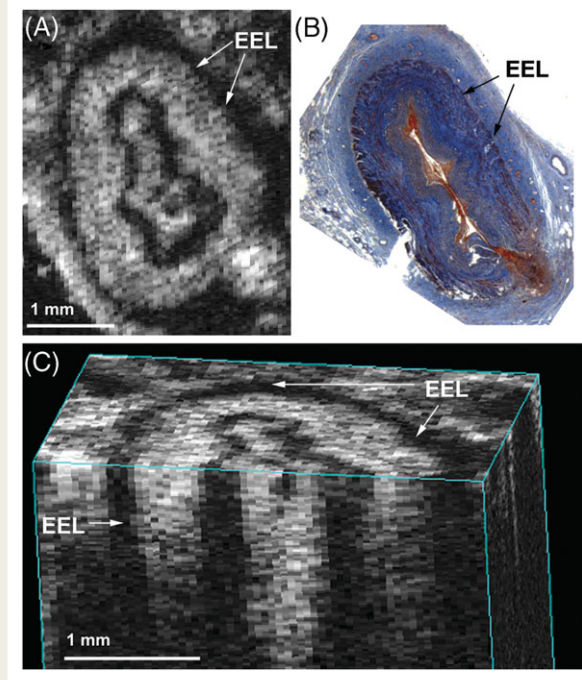
IVUS is a particularly appealing imaging modality for image guidance purposes due to its high resolution, reasonable penetration depth, and its ability to readily identify the external elastic lamina in the absence of calcifications. Conventional IVUS systems are side-viewing, and are commonly used in non-occluded vessels. Alternative configurations of IVUS with the imaging transducer focused in a forward-looking manner, rather than side-viewing, would be more suitable for imaging of CTOs.<sup>56–58</sup> Examples of forward-looking ultrasound images collected from a peripheral CTO in an *ex vivo* setting are shown in *Figure 4*. Frequencies of 25–60 MHz would likely provide useful resolution in the order of 30–200  $\mu\text{m}$ , while still retaining sufficient penetration depth in the order of 2–10 mm. The development of capacitive micro-machined ultrasound transducers may have a role in improving the performance of forward-looking IVUS,<sup>59</sup> although adequate imaging quality has not yet been demonstrated with this particular technology. IVUS-based techniques such as elastography,<sup>60,61</sup> radio-frequency (RF) tissue characterization or virtual histology<sup>62–64</sup> can be incorporated with forward-looking IVUS systems to identify the mechanical properties and composition of CTOs. However, many properties of ultrasound signals are affected by the direction in which the beam approaches the tissue being imaged. Therefore, these techniques would have to be revised and revalidated in a forward-looking configuration. Forward-looking IVUS systems can also be combined with ablation or other strategies for altering vascular tissues.

Conventional side-viewing IVUS has also been applied on rare occasions to provide real-time interventional guidance. Ito *et al.*<sup>65</sup> have described techniques for guiding a wire through the proximal cap of CTO by placing an IVUS catheter in a side branch of the occluded lumen. Guidance of an intervention





**Figure 3** (A) Magnetic resonance (MR) angiogram of an experimentally induced chronic total occlusion in rabbit right femoral artery taken with a 3.0T scanner and intravascular contrast agent. The MR angiogram detected a microvessel (white arrows) not detected by conventional angiography. (B) Histology confirms the presence of microvessels (mv) and also demonstrates disruption of the internal elastic lamina (white arrows) and the media (med) within the occluded segment



**Figure 4** (A) Cross-sectional image of a human peripheral chronic total occlusion acquired ex vivo using a bench-top forward-looking micro-ultrasound system with a centre frequency of 55 MHz. (B) Histological cross-section of the same sample stained with Masson's Trichrome. (C) Three-dimensional image, including cross-sectional and longitudinal cuts. The external elastic lamina (EEL) separates the media from the surrounding adventitia and is visible in the histology and micro-ultrasound images

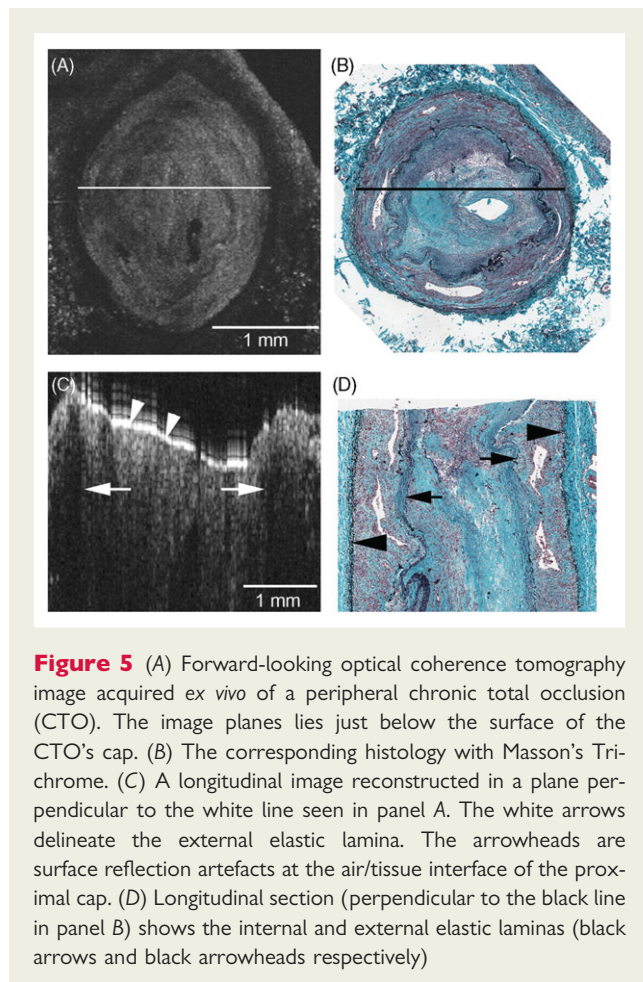
within the true lumen by placing the IVUS catheter into a previously created false lumen has also been described.<sup>66</sup> However, operators must be very mindful of complications that can arise during the manipulation of a conventional IVUS catheter within a false lumen.

IVUS can be used in its side-viewing configuration to image CTOs once they have been revascularized in order to assess properties of the new lumen that may require further intervention.<sup>67</sup> It can also be used to identify important features at follow-up for revascularized CTOs such as restenosis and late-stent malapposition.<sup>68</sup> A recent study using IVUS to assess CTOs immediately after they had been recanalized demonstrated intramural haematomas in as many as 34% of the lesions,<sup>69</sup> supporting the notion that current techniques lack sufficient guidance to minimize vessel trauma. Conventional IVUS has also demonstrated a positive correlation between the extent of calcification and duration of an occlusion, thus providing some insight into the difficulties experienced when attempting to cross older CTOs.<sup>70</sup>

### Optical coherence tomography

OCT produces images in a manner analogous to ultrasound using light rather than sound waves.<sup>71</sup> Its primary advantage is increased resolution (in the order of 4–15  $\mu\text{m}$ ) at the cost of poorer penetration through tissue and blood.<sup>72</sup> Saline flushing is often required to improve visualization. OCT has significant potential in the area of image-guidance for CTOs, as demonstrated by bench top testing of forward-looking OCT with ex vivo specimens of peripheral CTOs. *Figure 5* illustrates an image of a CTO generated using forward-looking OCT alongside the corresponding histology. Forward-looking OCT has more than sufficient resolution to clearly depict microvessels and the different layers of the vessel wall.<sup>73</sup> As a result of lower flow rates in regions adjacent to a CTO (as compared with non-occluded regions) the requirement for frequent or prolonged saline flushes to obtain meaningful images should be less problematic.

While the penetration depth of OCT is intrinsically poor, it would be helpful in guiding initial wire penetration or in guiding laser ablation<sup>74</sup> to create an initial entry hole or divot into the cap of the occlusion. Forward looking OCT could then be applied in an iterative fashion to guide along the length of CTO in small increments of a few millimeters at a time. In such a scenario, a lesion-modifying intervention would be applied at each



**Figure 5** (A) Forward-looking optical coherence tomography image acquired *ex vivo* of a peripheral chronic total occlusion (CTO). The image plane lies just below the surface of the CTO's cap. (B) The corresponding histology with Masson's Trichrome. (C) A longitudinal image reconstructed in a plane perpendicular to the white line seen in panel A. The white arrows delineate the external elastic lamina. The arrowheads are surface reflection artefacts at the air/tissue interface of the proximal cap. (D) Longitudinal section (perpendicular to the black line in panel B) shows the internal and external elastic laminae (black arrows and black arrowheads respectively)

increment, such as balloon angioplasty, laser ablation, or the advancement of a micro-dilator through the lesion.

Several variants of conventional side-viewing OCT exist that could be adapted to forward-looking implementations. Optical frequency-domain imaging is a form of OCT that enables a dramatically more rapid scan time and would facilitate volumetric imaging to guide CTO procedures.<sup>75</sup> Polarization sensitivity imaging is another variant of OCT, which provides a method to assess the concentration of collagen within coronary artery plaques.<sup>76</sup> Elastography using OCT rather than IVUS has also been investigated in preparation for future efforts to assess the mechanical properties of plaque.<sup>77</sup> OCT-based Doppler techniques are possible,<sup>78</sup> and may help assess the presence of flow in the microvessels of a CTO.

A method to optically assess CTOs using optical coherence reflectometry (OCR) has previously been combined with an RF ablation probe in a single guidewire (SafeCross, IntraLuminal Therapeutics, Carlsbad, CA, USA).<sup>79</sup> OCR uses OCT along a single line of sight rather than producing a true image. Clinical results from the use of the SafeCross wire have resulted in device success rates in the order of 50–60% in CTOs not crossable using conventional techniques. While these results illustrated the potential of additional guidance strategies to facilitate CTO interventions, considerable room for improvement remains.

### Image fusion: incorporating three-dimensional image roadmaps

Image guidance for crossing CTOs is markedly different from the guidance required for the treatment of stenoses or acute occlusions. In vessels that are either non-occluded or contain a soft, thrombotic occlusion, the mechanical integrity of the vessel wall helps contain the wires and devices within the vessel's boundaries. CTOs, on the other hand, are more difficult to navigate. For example, an intraluminal calcification or heavily fibrotic region may deflect a guide wire out of the lumen. Similarly, disruption of the normal three-layer architecture of the vessel wall that occurs within some occlusions may make it easier for a wire to exit the vessel boundaries. The practical value of three-dimensional image guidance becomes more significant in this setting, and many interventionalists will either use bi-plane angiography or alternate between orthogonal views in frequent attempts to identify wire position relative to the presumed path of the true lumen.

CTCA and MR coronary angiography provide opportunities to collect three-dimensional datasets of the coronary anatomy that could potentially augment guidance during CTO interventions. The fusion of cardiac MR or CT images with angiography would combine the real-time capabilities of angiography with additional three-dimensional information and, in the case of MR, soft tissue contrast. Image fusion is presently more developed for electrophysiological applications, but could be applied to CTO interventions using similar principles. There may also be a select role for catheterization suites with combined fluoroscopic and cardiac MR imaging equipment<sup>80</sup> so that both datasets are acquired during the same procedure, which may improve the accuracy of registering the two datasets.

### Comparison with vulnerable plaque imaging

A major focus of imaging research over the past five years has been the identification of locations of the vasculature that will develop plaque disruption leading to significant clinical events such as myocardial infarction. Imaging of such vulnerable plaques has been studied with many of the modalities described above, such as IVUS (with or without virtual histology), elastography, OCT, elastography, and thermography.<sup>81</sup> Potential clinical benefits from adjunctive imaging techniques for CTO revascularization may be easier to demonstrate than clinical benefits from vulnerable plaque imaging. For example, changes in clinical outcomes such as procedural success rates, ventricular function and resolution of angina as a result of CTO revascularization may be easier to measure than effects that may result from the identification and/or stabilization of vulnerable plaques. Additionally, with the high incidence of CTOs in the peripheral vasculature that lead to significant morbidity, such as claudication and amputation due to critical limb ischemia, there is a large opportunity to use the peripheral vascular bed to refine CTO imaging techniques prior to use in the coronaries.

## Conclusions

The imaging techniques described above are at different stages of maturation and their roles (present and anticipated) in the characterization and treatment of CTOs are similarly diverse. In addition to developments in imaging techniques, there have been significant improvements in guide wire technology. The integration of these new imaging techniques with advances in guide wires, steering mechanisms, drug eluting stents, and other plaque modification strategies may enable impressive improvements in CTO revascularization and significantly expand the complexity of CTOs attempted by percutaneous techniques. Importantly, imaging may help identify situations in which it is most appropriate to attempt these challenging lesions. Further development and validation of these techniques are required before integration into routine practice.

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