Coronary chronic total occlusions (CTOs) are a persistent challenge within the field of interventional cardiology. In the post-COURAGE trial and occluded-artery trial era, some cardiologists may question the need to perform intervention in CTOs. However, as with any procedure, patient selection and recognizing the limitations of therapy are key. CTO is defined as an occlusion to antegrade flow that is characterized by TIMI 0 or TIMI 1 flow, as assessed by coronary angiography. The occlusive lesion should have been present for >3 months. CTOs are visualized in approximately one third of diagnostic cardiac catheterizations, of which between 8% and 15% undergo percutaneous coronary intervention (PCI). The rate of recanalization by PCIs for a CTO is approximately 70%. The low rate of attempted interventions is likely influenced not only by the technical challenge of the CTO but by the relatively lower rates of success, as compared to PCI of a nonocclusive lesion. However, as technologies begin to expand, there has been increased success in CTO revascularization. One such technology is optical coherence reflectometry.

### CTO Histopathology
CTOs are a continuum of atherosclerotic progression leading to plaque rupture with thrombus formation. Over time, this thrombus tissue will be converted to fibrous tissue composed mainly of collagen and, in the later phase, calcium. Histopathologically, CTOs are characterized by inflammation, neovascularization, and the extent of calcification. The plaque that forms a CTO is also categorized as soft, hard, or mixed. Soft plaque is primarily composed of cholesterol-laden cells and foam cells that are generally more amenable to wire passage. The hard plaques are composed of dense, fibrous tissue with fibrocalcific regions that are more resistant to wire passage.

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**Figure 1.** Interaction of the Safe-Cross catheter (Kensey Nash, Exton, PA) with a CTO, with optical coherence reflectometry waveforms above. Left to right: the real-time monitoring apparatus as the catheter approaches the CTO within the lumen; the wire as it approaches the arterial wall with a red light indicator; and the wire having been steered away from the arterial wall with the green indicator.
**PATIENT SELECTION**

Procedural success in treating CTOs is predicated on the selection of the proper patient, which typically relies on the age of the lesion, lesion morphology, absence of bridging collaterals, and side branches at the site of occlusion. Lesion morphology, length of missing segment, lack of lesion angulation (<45º), and multiple lesions have been shown to be predictors for outcome in CTO recanalization.7-9

Although emerging technologies allow interventionalists to address more complex lesion characteristics, a determination must be made as to which patients truly benefit from treatment of a CTO. The most common presentation for the patient with a CTO involves progressive symptoms or stable angina. Approximately 11% to 15% of patients with CTO who present for intervention are asymptomatic.6 Previous studies have shown that with recanalization of a CTO, patients may achieve improved left ventricular remodeling, reduction in angina, reduction in arrhythmias, increased survival, decreased need for coronary artery bypass grafting (CABG), and increased tolerance to subsequent coronary events.10,11

Baks et al11 demonstrated that among patients who underwent cardiac MRI before and after PCI to a CTO, there was an improvement in left ventricular function. The TOAST-GISE investigators, one of the largest clinical trials of CTOs, showed a significant increase in angina-free periods after successful PCI to CTOs (88.7% vs 75%; P=.008). The study also demonstrated a significant reduction in patients requiring CABG among successfully recanalized CTOs (2.45% vs 15.7%; P<.0001). Suero et al10 found that among patients with recanalized CTOs, there was a 10-year survival benefit compared to the failure group (73.5% vs 65%; P=.001). The stent era has generated significant data to support the use of stents in CTOs. The GISSOC trial showed a significant increase in freedom from major adverse cardiac events (MACE) in stent versus balloon angioplasty-alone patients (76% vs 60%).12 The introduction of drug-eluting stents has also led to reductions in restenosis similar to those found in nonocclusive lesions that receive stent intervention.13,14 The benefits of CTO recanalization are apparent in the appropriately selected patient. However, ultimately, the success or failure of the procedure depends on the ability to cross the CTO. The overwhelming reason for failure to recanalize a CTO is related to an inability to cross the lesion in approximately 75% of cases.7 In addition, the increased risk of perforation and vessel dissection associated with CTO occlusion has led to an emergence of technology specifically aimed at meeting that challenge. Optical coherence reflectometry is one such technology that assists in safely crossing the difficult CTO.

**WHAT IS OPTICAL COHERENCE REFLECTOMETRY?**

Optical coherence reflectometry offers a forward-looking fiber-optic guidance system to navigate across CTOs. A reference beam and sampling beam of near-infrared light emanate from the wire tip. The reference beam serves as a measure as this light is reflected at a determinable distance. The light within the sample beam is reflected and backscattered to a degree dependent on the tissue that is encountered. The reflected and scattered light information is returned to the interferometer. The interference intensity of the backscattered light is measured against the reference. The reflected backscatter is affected by the tissue characteristics of the arterial (plaque vs media vs adventitia).15 The result is a system that can distinguish calcified from noncalcified plaque and atherosclerotic lesions from arterial wall. The signals are then interpreted on a monitor in real time in which a green bar indicates lumen and a red bar indicates arterial wall. The green light indicates a safe approach to advance a wire, whereas the red light warns against potentially entering the vessel wall. This technology serves as the platform from which the Safe-Steer TO (total occlusion)
crossing system (Kensey Nash) is able to function. In one study involving 28 patients with CTOs and ischemia, the device was successful in recanalizing 86% of the patients. The most significant limitation of the Safe-Steer TO device was its inability to steer easily.

The Safe-Steer TO system was the forerunner to the Safe-Cross device. Relying on similar optical coherence reflectometry, the Safe-Cross device incorporates radiofrequency ablation technology to the wire tip. The apparatus can deliver between 3 and 5 watts of radiofrequency ablative energy only if there is no evidence of arterial wall within 1 mm of the wire tip. A green bar on the monitor indicates that radiofrequency energy can be delivered. A red bar indicates contact with arterial lumen, thus disabling radiofrequency energy (Figure 1). The Safe-Cross device has also significantly improved steering performance relative to its predecessor. Hoye et al18 showed more modest results in 29 patients with CTOs, with a success rate of approximately 52%. In the Guided Radiofrequency Energy Ablation of Total Occlusions registry study (GREAT), 116 patients with CTOs underwent intervention with the Safe-Cross after failed attempts to cross with conventional wires. Success in the trial was based on device delivery into the true lumen. The trial demonstrated an overall success rate of 54.3%, leading to subsequent CE mark approval in Europe (Figure 2).19

CONCLUSIONS

Technology continues to grow in the field of interventional cardiology. The evolution of newer wires, stents, support catheters, and forward-looking devices, such as the Safe-Cross, will continue to improve success rates in treating CTOs. Success, however, will improve only in the appropriately selected patient. The question of routine intervention for CTOs was effectively answered by the Occluded Artery Trial (OAT) investigators, who demonstrated no reduction in death, reinfarction, or heart failure with routine intervention to persistently occluded arteries after myocardial infarction.20 The ideal patient is one who has persistent angina with suitable lesion anatomy consisting of a tapered occlusion, angulation <45°, a single lesion, and lesion length <15 mm. Successful intervention will afford patients increased survival, decreased arrhythmias, decreased referral to CABG, and decreased angina. The appropriately selected patient can now look forward to increased successful recanalization and safety during treatment of CTOs using the Safe-Cross System, which is unique in its ability to assess the intraluminal tissue in real time. The hope is that it will continue to add safety and increase success across these difficult-to-cross lesions. Inevitably, the ideal patient will not always be encountered, and the interventionist’s decision to proceed or refrain from attempting to cross a CTO is the most important tool at his or her disposal.

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