

# Is Magnetic Resonance Image Guidance the Key to Opening Chronic Total Occlusions?

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Through progressive plaque growth or fibrotic organization of occlusive thrombus, atherosclerosis may result in chronic total occlusion (CTO) of a major arterial conduit. If CTO develops slowly, collateral pathways may supply sufficient perfusion to retain tissue viability despite occlusion of the major inflow conduit. However, such collateral-mediated perfusion rarely matches that provided by an open main conduit, particularly during the peak demand of regional muscular activity. Although strategies to limit regional oxygen demand (eg,  $\beta$ -blockers for the treatment of angina pectoris) or to enhance collateral function (eg, a walking program for superficial femoral occlusion, experimental angiogenesis) may be of some benefit, these approaches generally offer less complete return of normal physiology and relief of ischemic symptoms than does direct revascularization of the occluded vessel. With surgical bypass, the nature of the occlusion (its length, duration, tortuosity, calcification) is less important than the presence of a suitable distal anastomotic target. On the other hand, with catheter-based techniques, success depends heavily on these lesion characteristics. In fact, crossing such occluded segments with a guidewire remains the dominant barrier to catheter-based treatments of occluded arterial segments. Once the guidewire has been passed successfully into the distal true lumen, the process of dilating and stenting the segment is usually straightforward and durable, at least with the use of drug-eluting stents in coronary CTOs.<sup>1,2</sup>

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Devices designed to cross CTOs should have 3 key features: an ability to distinguish a true luminal path from one created within (dissection) or through (perforation) the vessel wall of the occluded segment, an ability to change direction (steer) to correct deviations from the desired path through the occlusion, and an ability to penetrate the frequently fibrotic and focally calcific substance of the occlusion through the use of either mechanical stiffness or an alternative energy modality (laser, radiofrequency, ultrasound, blunt microdissection).

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Despite these seemingly simple requirements, devices that have emphasized only the third feature—penetrating power—have generally failed to deliver significant enhancements in their ability to cross the occluded segment and reenter the distal true lumen, because they can easily enter a vessel wall dissection plane (the path of least resistance) within the occlusion and then remain next to (rather than within) the distal true lumen.<sup>3</sup> Fluoroscopic or intravascular ultrasound-guided devices can then be used to attempt puncture back into the distal true lumen to augment the success of such devices. Secondary success for crossing lesions that are uncrossable with conventional guidewire, however, is only 50% to 60%. On the other hand, if the energy source leads to frank perforation of the vessel wall, safe conclusion of the procedure may be difficult (except in the superficial femoral, where it may be possible to negotiate along side the occluded segment and then reenter the distal true lumen, salvaging success by stenting the path with covered stents).<sup>4</sup>

It thus appears that any successful device for crossing CTOs must also incorporate strong performance in the second feature—steering—to continually readjust direction of the device toward the desired true lumen path. The recent introduction of specialized guidewires for crossing CTOs has demonstrated that coupling exceptional tip stiffness (the ability to deliver up to 12 g of force with the distal 1 cm of the wire compared with 0.5 to 1.0 g for conventional angioplasty wires), precise tip shaping, and steering with partial coverage by lubricious coatings can increase the success of crossing CTOs to 85% to 90% in the most skilled hands.<sup>1,2</sup>

Still, the availability of devices with precise steering and potent advancement capability do not make up for the lack of the first feature—guidance—to allow the operator to understand the instantaneous device trajectory relative to both the occluded lumen and the distal reconstituted true lumen. In clinical practice, operators rely on a combination of x-ray fluoroscopy and tactile feel of the guidewire. One major advance has been the use of simultaneous contrast injection into both the occluded vessel and a contralateral (collateral-supplying) vessel to allow estimation of the position of the guidewire relative to the interpolated missing segment in between. Using such double injections in different projections frequently requires very high contrast and x-ray doses for procedural success. Attempts to use forward-looking ultrasound have been unsuccessful, but a recent device (the Safe-Cross-RF Guidewire, Intraluminal Therapeutics) has used optical coherence reflectometry via a 0.014-in intermediate-stiffness steerable guidewire to determine whether amorphous plaque or organized vessel wall layers lie immediately ahead of the guidewire tip.<sup>5</sup> The penetrating

power of the wire can then be enhanced by delivering a train of radiofrequency energy pulses to the wire tip.

Against this backdrop, the development of an imaging modality that can visualize the position of the guidewire relative to the proximal and distal true lumen and relative to the vessel walls within the occluded segment would constitute a major advance. If this could be combined with technologies that allow precise wire steering and effective wire advancement, the triad of capabilities required to elevate the success of crossing CTOs (coronary and peripheral) to the 95% to 98% success rate now achieved for subtotal stenosis would be in place. In this issue of *Circulation*, Raval et al<sup>6</sup> from the cardiovascular branch of the National Heart, Lung, and Blood Institute share a provocative preliminary animal study suggesting that magnetic resonance imaging (MRI) fluoroscopy, coupled with catheters and guidewires equipped to serve as active antennas within the MRI system, may be able to fulfill that goal.

MR-guided vascular intervention is appealing for its freedom from ionizing radiation, superior soft tissue contrast that allows it to display the vascular lumen (with or without the use of gadolinium-based rather than more toxic iodine-based contrast materials), and tomographic capability that permits 3-dimensional display of the vascular path. If these are combined with methods to visualize catheters and guidewires under MR, real-time navigation of those devices relative to the vascular true lumen, including the latent true lumen within the occluded segment, would be enabled. But many technical challenges exist. MR-guided intervention demands rapid acquisition of real-time imaging data to track the motion of the interventional devices. Needed pulse sequences such as the steady-state free precession (also known as TrueFisp, Fiesta, or balanced FFE) may deposit enough radiofrequency energy to heat commercial ferromagnetic materials (eg, stainless steel guidewires) significantly. In addition, any ferromagnetic metal elements embedded in catheters may distort the magnetic field and obscure adjacent structures.<sup>7</sup> Active catheters with embedded signal pickup coils can interface with the coil inputs of the MR scanner, allowing the catheters to be displayed on the MR image in faux colors, but this requires dedicated multiple receiver channels and MR-imaging pulse sequences.

Despite these considerable challenges, Raval et al<sup>6</sup> have demonstrated feasibility of using MRI guidance to recanalize carotid artery CTO in a swine model. Several technical developments were required: Nonmagnetic materials (MP35N, nitinol) were used to build custom guidewires, loopless and microcoil active antennas were created on the guidewires and catheters to allow real-time detection of these devices, and the microcoils and their associated circuitry were detuned and decoupled to prevent device heating during real-time MRI. Similar to other reports, echo-sharing data acquisition was used to improve temporal resolution, allowing capture of device motion during manipulation, whereas an interactive flat-panel display inside the scanner room allowed superimposed multiplanar display of real-time images from the active devices combined with anatomic images acquired from the surface coils. For higher resolution before and after intervention, subtraction MR angiography of the carotid

artery was achieved at an in-plane resolution of 0.3×0.5 mm. In this particular model, MR-guided intervention actually had a higher success rate than conventional fluoroscopic techniques.

The authors should be commended for the latest in their ongoing efforts at developing MR-guided intervention and for their encouraging preclinical results. But, significant hurdles remain in implementing MR-guided vascular intervention clinically. High-field ( $\geq 1.5$  T) MRI systems are required to achieve adequate signal-to-noise ratio and speed for real-time data acquisition and display. Conventional x-ray fluoroscopy may be required as an adjunct to facilitate initial catheter placement, to verify procedural success, and to manage emergency bailout situations. In some applications, this may require the construction of combined MRI/x-ray fluoroscopy interventional units with intermodality patient-transfer capability. Other challenges include claustrophobia and limited patient access within closed-bored magnets, although major vendors have designed newer short-bore or more spacious MRI systems that may partially overcome this problem. Cathode-ray tubes (x-ray image intensifiers or even conventional monitors) do not function adequately within the high-magnetic-field MRI environment, and the vibration of the image coils during pulse sequencing creates relatively high levels of acoustic noise, making custom-built interactive flat-panel display systems and special communication equipment a requirement to move MRI-guided intervention beyond specialized research centers such as the NIH facility.

Although improved real-time “passive” visualization of conventional catheters can be achieved by filling the catheters with gadolinium<sup>8,9</sup> or CO<sub>2</sub> contrast,<sup>10</sup> the various active designs<sup>11–15</sup> that incorporate MRI receiver coils provide better device positioning and motion tracking. To reduce heating risk, detuning or decoupling the conductive wire<sup>16</sup> or replacing metal circuitry with fiberoptic connections is required. Although vascular stents made of nonmagnetic or weakly ferromagnetic materials (eg, nitinol, titanium, titanium alloy) are considered safe in the MRI environment,<sup>17</sup> the clinical safety of deploying vascular stents made from ferromagnetic materials (eg, stainless steel) under MR guidance requires further evaluation.

Beyond the challenges of the imaging system, moving to the MR environment also requires adapting or modifying many of the existing clinical systems and devices. Although the patient’s ECG can be reliably monitored for rhythm and gated image acquisition, it is not possible to monitor ST-segment changes inside the scanner room because of artifacts generated by aortic blood flow in the magnetic field. A designated area outside the scanner room should always be available in case of patient emergency, because resuscitative equipment such as the defibrillator cart may be pulled violently into the magnet if brought inside the scanner room.

It is also important to appreciate how hard it may be to move from the relatively static carotid artery studied by Raval et al<sup>6</sup> to cardiac or coronary intervention. Several groups have demonstrated preclinical success in MRI-guided cardiac interventions, including left and right heart catheterization,<sup>18</sup> targeted injections of intramyocardial contrast<sup>19,20</sup> and stem

cells,<sup>21</sup> catheter-based closure of atrial septal defect,<sup>22,23</sup> atrial septal puncture,<sup>24</sup> abdominal aortic aneurysm repair,<sup>25</sup> and even transcatheter aortic valve replacement.<sup>26</sup> MRI is also useful in assessing myocardial perfusion, tomographic visualization of coronary anatomy, and potentially even coronary plaque morphology. Although preliminary human experience in MR-guided cardiac intervention also exists,<sup>10</sup> to be competitive with current x-ray-guided coronary procedures, a 3- to 4-fold improvement in spatial and temporal resolution is needed. Second, the operator needs to work in a single (although selectable) MR imaging plane that contains the catheter, so real-time 3-dimensional data acquisition and multiplanar or “stacked” layered display of the local coronary anatomy may be required. Third, it is unlikely that the device industry will undertake the development of a whole suite of MR-enabled and MR-compatible devices without a demonstration of strong clinical demand (driven by improved outcomes or equal outcomes with elimination of x-ray exposure) and the potential growth of a critical mass of suitably equipped interventional MR or MR/x-ray fluoroscopy suites.

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