Mechanism of Success and Failure in Chronic Total Occlusion Angioplasty:
Lessons from the histology of CTO

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Chronic total occlusion remains one of the major obstacles toward complete revascularization in patients with multivessel coronary artery disease undergoing percutaneous intervention. Despite improvements in the approach to a chronic total occlusion using conventional wires and angioplasty approaches, the failure rate for this lesion remains substantial. Many failures are mediated by vessel dissection or perforation. While neither of these complications is ordinarily clinically catastrophic for the patient, each leads to an end point in the procedure.

A careful examination of the histology of chronic total occlusions leads to significant insight regarding the reasons for these two common modes of PCI failure in this lesion. As chronic total occlusion develops, the character of the lesion changes significantly over the first months to year following vessel occlusion. While initially is comprised of loose fibrous tissue, over time this organizes and the length and hardness of the fibrous tissue increases. Dispersed, loose tissue is seen early while later there is calcification and coalescence of fibrotic tissue into a harder material.

Many chronic total occlusions develop neovascularization. Neovascular channels will appear with a distribution ranging from the center of the vessel all the way out to the adventitia. Nutrient vessels and growth factors from the vaso-vasorum contribute to the growth of the intimal channels, thus the channels typically form from the adventitia or grow toward the adventitia rather than occupying a central luminal location. Neovascular channels are usually too small to allow passage of a PTCA wire. The growth of these channels towards the adventitia makes a path of least resistance toward the outer wall of the vessel and this explains the tendency toward either dissection or perforation as the result of attempts to cross these channels with a wire.

The plaque constituency changes during the first year or so. Soft plaque is comprised of about 50% cholesterol and less than one-quarter collagen while harder plaques are more than half of collagen and as much as one-quarter calcium. Medial inflammation is common in soft plaques and thus more prone to recanalization. This explains the obvious tendency of younger total occlusions to have a higher probability for revascularization success.
Neovascular channels grow in proportion to inflammation by T-lymphocytes and macrophages in the chronic total occlusion lesion. It is important to appreciate that the total occlusion is a highly dynamic lesion.

The dimensions of neovascular channels typically range from 150 to 200 microns for smaller channels, while larger channels may be over 250 microns. These dimensions are remarkably small, although multiple neovascular channels in a single lesion may appear angiographically to represent a continuous lumen. This explains the potential to see a good pathway through a lesion but find that a wire will not traverse these micro-channels.

The histology of chronic total occlusion demonstrates a dynamic lesion which changes significantly over time. The key features of these lesions are a loose connective tissue early in the development of the total occlusion followed by dense fibrosis and calcification and later neointimal channel formation. Neointimal channels may commonly develop around the adventitial surface of the vessel or grow toward the adventitial surface. This makes a path of least resistance towards the outer wall of the vessel which leads to the common complications of dissection and perforation during attempts to cross chronic total occlusions with a guide wire.

New devices that are able to interrogate tissue type and allow for more directed wire movement in conjunction with radiofrequency ablation that will effectively treat the dense fibrosis and calcification common to these lesions will be necessary for significant improvements in our approach to the chronic total occlusion lesion.

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