

## Digging Deeper With CT Imaging: Slice-by-Micro Slice . . .

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A study being published in this issue of *JACC* (1) has used computed tomography (CT) imaging to characterize the neovascularization in an experimental model of chronic total vascular occlusion (CTO). Over a time period of 24 weeks, a dynamic process beginning with development of circumferentially oriented extravascular microvessels was followed by formation of longitudinal intravascular microvessels. A peal proliferation of extra and intravascular channels was observed at 2 and 6 weeks, respectively, after the occlusion, which progressively declined thereafter. Of interest, connections between these two microvessel platforms developed that could be documented by micro-CT imaging. Interesting conclusions and hypotheses can be deduced from this model. The authors proposed that local hypoxia constitutes an important stimulus for neovessel formation; they also suggest that the extravascular vessels may initiate the development of intravascular channels wherein the connecting microvessels play an important role. Although the study offers substantial pathogenetic leads, the accompanying Editorial Comment (2) cautions about direct extrapolation to clinical CTO for the following reasons: 1) the underlying disease, atherosclerosis, is missing in the animal model; 2) the thrombus induced for arterial occlusion is composed differently; and 3) the healing processes occurs more rapidly in rabbits as compared to humans. Nevertheless, the pathogenetic insights provided by this study should help explore new mechanical or pharmacological intervention strategies for CTO in the acute or delayed stages of the disease process.

We chose this report for the cover story to highlight the imaging technology employed to demonstrate extra and intravascular neovascularization. CT imaging is hardly thought of as a tool that can provide useful information at a microscopic scale. Yet, this report not only very elegantly illustrates 3-dimensional images obtained by CT imaging but also allows the generation of coherent and isotropic information wherein data can be displayed and analyzed in arbitrary orientations and allows definition of the precise spatial relationship of the neovasculature. This offers an advantage over the traditional pathological characterization where 3-dimensional information, especially in a quantitative manner, is difficult to extract. The authors were able to achieve excellent spatial resolution, using a dedicated technology for the CT imaging of small animals. Their report and other sources (3) cite a spatial resolution of 14  $\mu\text{m}$  for such CT systems, which allows visualization and quantification of very small structures. It is pertinent to compare improvised spatial resolution with the conventional CT systems used clinically (typically assumed to be  $0.4 \times 0.4 \times 0.4 \text{ mm}$  [4]) and discuss whether the imaging with a similar degree of precision become possible for clinical application?

A number of issues would need to be considered. First, it is quite difficult to describe the "spatial resolution" of CT. For instance, the spatial resolution of objects with strong contrast is much higher than for low contrast objects. It has therefore been easier to study contrast filled vessels than to characterize the composition of an atherosclerotic plaque. Second, there is a close relationship between spatial resolution and image noise (4,5). In order to achieve high resolution, noise would need to be minimized. And low

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noise means collection of enormous data samples; this explains why the scan time for a single specimen in the study in question was 2.5 h (not even remotely practical for clinical use). It further explains the interaction of radiation exposure and spatial resolution, i.e., in order to increase spatial resolution by a factor of 2 in all spatial orientations, radiation exposure will need to be increased by a factor of 16 (4,5). As such, even a small improvement in spatial resolution is fraught by an enormous increase in radiation exposure, unless

other measures are developed to improve image quality. Technological advances are relentless, and strategies such as “tomosynthesis” (6) and “iterative” reconstruction (7) can provide very high *in plane* resolution at lower noise levels. Although the immediate likelihood of an ability to perform “microscopic” CT imaging in humans seems to be low, the report by Munce et al. (1) reassures that CT imaging will continue to substantially contribute to the understanding of the disease process.

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