Reconstructing the microcirculation

James B. Hoying, PhD FAHA
Cardiovascular Innovation Institute
University of Louisville
Louisville, KY 40202

The intent of microvascular regeneration is the re-establishment of an effective microcirculation; as controlled blood flow is the necessary outcome. While the addition of new vessel segments to the vasculature, typically via angiogenesis, is important in the formation of a new or expanded microcirculation, numerous examples of tissue repair/regeneration in which perfusion is reduced in spite of elevated microvessel densities indicates that additional vascular activities beyond angiogenesis are important. These post-angiogenesis activities are related to the establishment and maintenance of a stable and effective microcirculatory network involving the proper specification and organization of the newly formed, immature microvessels (neovessels) into a perfusion-competent network. An effective microcirculation consists of a microvascular architecture in which the different microvessel types are organized such as to minimize diffusion distances between microvessels, reduced resistance to flow, and eliminated oxygen gradients across a tissue. The final microvascular topology reflects an intrinsic neovascular plasticity and ability to adapt in form and function to input signals (e.g. hemodynamic forces, stromal biomechanics) ultimately giving rise to a network suited to the tissue needs. Leveraging what we've learned concerning the dynamics of this adaptability and neovascular responses, we've developed strategies for building microcirculations (in vivo and in vitro), including approaches to derive tissue-specific microvasculatures.