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Live imaging of collagen remodeling during angiogenesis.

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Abstract
To better understand interstitial matrix remodeling during angiogenesis, we probed endogenous optical signatures of collagen fibrils and cells with multiphoton microscopy to noninvasively visualize, in real-time, changes to fibril organization around angiogenic sprouts and growing neovessels. From analyses of the second-harmonic generation signal from fibrillar collagen and two-photon excited fluorescence, as well as coherent transmitted light from vascular cells, we found that microvessel fragments interacting with the collagen matrix exhibited two key features: a strong association of fibrillar collagen around the parent vessel fragment during vessel construct reconstitution and a substantial collagen fibril reorganization by sprout and neovessel tips. Results indicate that angiogenic sprouts and growing neovessels actively and differentially remodel existing collagen fibrils. This imaging approach to assess local changes in matrix organization may have a broader impact on tissue biology and mechanics during angiogenesis and allow for new insights in cardiovascular, diabetes, and cancer research.

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