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Titel des Beitrags:
Multispectral optoacoustic tomography of matrix metalloproteinase activity in vulnerable human carotid plaques.

Abstract:
Elevated expression of cathepsins, integrins and matrix metalloproteinases (MMPs) is typically associated with atherosclerotic plaque instability. While fluorescent tagging of such molecules has been amply demonstrated, no imaging method was so far shown capable of resolving these inflammation-associated tags with high fidelity and resolution beyond microscopic depths. This study is aimed at demonstrating a new method with high potential for noninvasive clinical cardiovascular diagnostics of vulnerable plaques using high-resolution deep-tissue multispectral optoacoustic tomography (MSOT) technology. MMP-sensitive activatable fluorescent probe (MMPSense(TM) 680) was applied to human carotid plaques from symptomatic patients. Atherosclerotic activity was detected by tuning MSOT wavelengths to activation-dependent absorption changes of the molecules, structurally modified in the presence of enzymes. MSOT analysis simultaneously provided morphology along with heterogeneous MMP activity with better than 200 micron resolution throughout the intact plaque tissue. The results corresponded well with epi-fluorescence images made from thin cryosections. Elevated MMP activity was further confirmed by in situ zymography, accompanied by
increased macrophage influx. We demonstrated, for the first time to our knowledge, the ability of MSOT to provide volumetric images of activatable molecular probe distribution deep within optically diffuse tissues. High-resolution mapping of MMP activity was achieved deep in the vulnerable plaque of intact human carotid specimens. This performance directly relates to pre-clinical screening applications in animal models and to clinical decision potential as it might eventually allow for highly specific visualization and staging of plaque vulnerability thus impacting therapeutic clinical decision making.