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Real-time intravascular catheter detection of protease-generated near-infrared fluorescence (NIRF) signal in atheromata in vivo. A representative experimental rabbit with bilateral iliac atheromata is shown, 24 hours after injection with a cysteine protease-activatable NIRF agent. The yellow circle shows the initial placement of the NIRF catheter in the left distal iliac artery past a moderately severe lesion, as indicated on the angiogram. The NIRF catheter is then manually pulled back to the proximal iliac artery (left panel). The instantaneous NIRF signal is shown in the right panel. As the catheter traverses the plaque, augmented NIRF signal is recorded due to proteasemediated cleavage of the quenched NIR fluorescent agent. In vivo findings were corroborated by ex vivo fluorescence reflectance imaging, fluorescence microscopy, and histopathological measures of inflammation.