In this Institutional Review Board-approved investigation, an 82-year-old male underwent carotid endarterectomy for a >80% asymptomatic carotid stenosis. Six weeks prior, the subject had undergone carotid endarterectomy of the contralateral carotid artery for a symptomatic >70% stenosis. Approximately 1 hour before surgery, the patient was injected with 7.9 mCi [18]Fluorodeoxyglucose (FDG). After resection of the plaque using a surgical technique that maintained its integrity, the specimen was imaged using micro-positron emission tomography (PET) (Siemens Inveon) and magnetic resonance imaging (3T Philips Achieva). Subsequently, the specimen was fixed in formalin, sectioned at 1 mm intervals, and stained with hematoxylin and eosin. Immunocytochemistry was performed using antibodies to detect macrophages (HAM-56, Dako, 1:100), leukocytes (CD-45, Dako, 1:200), and smooth muscle cell actin (anti-α-actin Sigma, 1:100).

The Figure shows matched cross-sections from magnetic resonance imaging, FDG-PET, and histology obtained at the carotid artery bifurcation and internal carotid artery. The FDG-PET images were first registered and fused with the magnetic resonance imaging results, then reformatted to match the corresponding histology sections. FDG uptake is seen to be highly variable with focal hot spots. The maximal standardized uptake value for the entire specimen was 3.50 g/cc and occurred in the internal carotid artery (Figure, right). In this zone of high uptake, histology indicated the presence of a necrotic core with recent intraplaque hemorrhage and significant macrophage infiltration, particularly around the periphery of the intraplaque hemorrhage. Other zones of high uptake (Figure, left) were associated with deposition of loose extracellular matrix with concomitant neovascularization and inflammatory infiltrate including macrophages and leukocytes.

To investigate the common features of regions with high standardized uptake value, 12 cross sections were analyzed at 2 mm intervals with matched histology. Sixteen regions with standardized uptake value in excess of 2.0 were identified by thresholding and the histological features of all 16 regions were recorded. Ten regions (63%) exhibited substantial inflammatory infiltrate including >30 macrophages per high-power (600×) field. Five regions (31%) exhibited extensive neovascularization with >6 vessels per high-power field. All 5 of these regions also exhibited loose extracellular matrix. Accumulations of smooth muscle cells were observed in only 2 regions. Necrotic cores with intraplaque hemorrhage were observed in only 2 regions on consecutive slices, which also contained loose matrix and significant numbers of macrophages and neovessels. None of the regions contained calcifications.

Figure. Ex vivo appearance of carotid atherosclerosis after presurgical injection of [18]fluorodeoxyglucose in an 82-year-old male. A maximum intensity projection (MIP) image of the positron emission tomography (PET) volume is shown in the center, with arrows indicating zones of high uptake. PET, magnetic resonance imaging (MRI), fused PET/MRI, and histology (hematoxylin and eosin [H&E] and HAM-56 at 100×) transverse cross sections are shown for the lower arrow at left and for the upper arrow at right. High PET signals are encoded as yellow, which show spatial correspondence with dense accumulations of macrophages by HAM-56 immunohistochemistry.
Strong uptake of FDG associated with atherosclerosis has previously been reported and associated with extensive inflammatory activity.\textsuperscript{1,2} The low in vivo resolution of FDG-PET, however, has precluded exact colocalization of the FDG signal with specific pathology. In fact, some studies suggest that the signal may originate outside of the vessel wall.\textsuperscript{3} One study used microPET to investigate carotid endarterectomy specimens bathed in FDG,\textsuperscript{4} but this may not accurately reflect uptake of a perfused plaque in vivo. By injecting FDG before surgery, this study was able to definitively localize the FDG signal relative to magnetic resonance imaging and histology.

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References

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High-Resolution [18]Fluorodeoxyglucose-Positron Emission Tomography and Coregistered Magnetic Resonance Imaging of Atherosclerotic Plaque From a Patient Undergoing Carotid Endarterectomy

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