The goal of this study was to evaluate the feasibility of [(18)F]Galacto-RGD positron emission tomography (PET)/computed tomography (CT) imaging of αvβ3 expression in human carotid plaques. The integrin αvβ3 is expressed by macrophages and angiogenic endothelial cells in atherosclerotic lesions and thus is a marker of plaque inflammation and, potentially, of plaque vulnerability. [(18)F]Galacto-RGD is a PET tracer binding specifically to αvβ3. Therefore, [(18)F]Galacto-RGD PET/CT imaging of αvβ3 expression in human carotid plaques might provide a novel noninvasive biomarker of plaque vulnerability. [(18)F]Galacto-RGD PET/CT imaging was performed in 10 patients with high-grade carotid artery stenosis scheduled for carotid endarterectomy. Tracer uptake was measured in the stenotic areas of the carotid arteries, as well as on the contralateral side, and was corrected for blood pool activity, measured in the distal common carotid artery (target-to-background [TB] ratio). TB ratio was correlated with immunohistochemistry of αvβ3 expression (LM609), macrophage density (CD68), and microvessel density (CD31) of the surgical specimen. In addition, ex vivo autoradiography of the surgical specimen with [(18)F]Galacto-RGD and competition experiments with an
unlabeled \(\alpha\mathrm{v}\beta3\)-specific RGD peptide were performed. \((18)\text{F}\)Galacto-RGD PET/CT showed significantly higher TB ratios in stenotic areas compared with nonstenotic areas (\(p = 0.01\)). TB ratios correlated significantly with \(\alpha\mathrm{v}\beta3\) expression (\(R = 0.787, p = 0.026\)) and intensity of ex vivo autoradiography (\(R = 0.733, p = 0.038\)). Binding to atherosclerotic plaques was efficiently blocked in ex vivo competition experiments. A weak-to-moderate correlation was found with macrophage density (\(R = 0.367, p = 0.299\)) and microvessel density (\(R = 0.479, p = 0.176\)), which did not reach statistical significance. \((18)\text{F}\)Galacto-RGD PET/CT shows specific tracer accumulation in human atherosclerotic carotid plaques, which correlates with \(\alpha\mathrm{v}\beta3\) expression. Based on these initial data, larger prospective studies are now warranted to evaluate the potential of molecular imaging of \(\alpha\mathrm{v}\beta3\) expression for assessment of plaque inflammation in patients.