Systemic monocyte activation and arterial macrophage infiltration are thought to contribute to heightened cardiovascular disease risk in HIV. Current in vivo investigative techniques including ¹⁸F-FDG uptake on PET/CT do not allow for quantification of macrophage-specific arterial inflammation.

**Methods**

We performed a first-in-human investigation testing whether systemic administration of ⁹⁹mTc-tilmanocept (which specifically binds CD206+ macrophages) would enable quantification of arterial macrophage infiltration. Our primary outcome measure, aortic ⁹⁹mTc-tilmanocept uptake on SPECT/CT, was assessed among 6 HIV-infected subjects with subclinical atherosclerosis and 3 non-HIV-infected subjects with similar Framingham Risk Scores (FRS). The clinical significance of aortic ⁹⁹mTc-tilmanocept uptake was established through relation to atherosclerotic plaque burden on computed tomography angiography and to measures of systemic immune activation.

**Results**

Study subjects were males 58 ± 5 years old with baseline demographics including Framingham Risk Scores that did not differ significantly between groups (FRS: 9% vs. 8%, P=0.55; HIV vs. non-HIV). Among HIV-infected subjects, duration since HIV diagnosis was 23.3 ± 8.1 years, logVL was 1.4 (1.3, 2.8) copies/mL, and CD4 count was 534 ± 138 cells/mm². ⁹⁹mTc-tilmanocept uptake localized to three regions: kidney, liver, and aorta. High-level ⁹⁹mTc-tilmanocept uptake (≥5x uptake in muscle as a reference region representing non-specific tissue and blood pool uptake) was apparent across 20.4% of the aortic surface volume in HIV-infected subjects versus 4.3% in non-HIV-infected subjects (P=0.009) (Figure 2).

**Conclusion**

Macrophage-specific imaging strategies may help elucidate immune mechanisms of macrophage-mediated end-organ damage in HIV and may identify HIV-infected patients at risk for such complications.