**IN VIVO OPTICAL MOLECULAR - STRUCTURAL IMAGING OF CORONARY ARTERY STENT INFLAMMATION PREDICTS THE SITE-APECIFIC RESTENOSIS RISK**

Poster Contributions
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**Background:** Restenosis after coronary stent placement leads to repeat procedures and adverse outcomes. While inflammation tracks with neointimal smooth muscle cell ingrowth, a detailed in vivo understanding of local inflammation on stent restenosis is unknown. Using intravascular optical molecular-structural near-infrared fluorescence (NIRF)-optical coherence tomography (OCT), we quantified the evolution of in vivo inflammation during coronary artery stent healing, and assessed if early stent inflammatory protease activity predicts site-specific late neointimal hyperplasia.

**Methods:** Clinical cobalt chromium bare-metal stents (3.5x12mm; N=12) were implanted in the aorta of healthy rabbits. At 2 and 6 weeks, intravascular NIRF-OCT was performed 24 hours following ProSense VM110 administration (4mg/kg IV; ex/em 750/780 nm) to enable molecular NIRF imaging of inflammatory cathepsin protease activity. Co-registered structural OCT stent neointimal formation was simultaneously assessed every 400 μm throughout the stent. Stents then underwent ex vivo fluorescence imaging, histopathology, and mRNA analysis.

**Results:** At 2 weeks, NIRF protease inflammation was significantly enhanced at the stent edges compared to the mid stent zone and unstented aorta, respectively (32.6±7.3 vs. 20.1±2.6 vs. 7.6±0.7 nM; p<0.0001). Stent NIRF inflammatory activity uniformly diminished between 2 and 6 weeks (delta NIRF -0.39±0.06). Serial OCT from 2 to 6 weeks demonstrated greater neointimal formation at the stent edges (delta OCT neointimal area 0.61±0.25 stent edge vs. 0.33±0.13 mm2 stent middle; p<0.01). Stent NIRF inflammation at week 2 strongly predicted site-specific delta OCT neointimal formation (R=0.72; p=0.001). Ex vivo analyses revealed enhanced cathepsin expression at neointimal smooth muscle cells exhibiting high NIRF inflammation.

**Conclusion:** We demonstrate a new approach to quantitatively evaluate coronary stent inflammation using molecular-structural intravascular NIRF-OFDI. Inflammation predominates at stent edges and predicts restenosis measured by serial OCT. This translatable approach offers the opportunity to identify subjects at elevated risk of restenosis.