Monitoring the Inflammatory Response in Stented Mice Aortas Using Novel Fluorescence-Based in vivo Imaging Techniques

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Abstract:

Explant studies have revealed that some stents undergo corrosion in vivo, with significant release of metallic ions into surrounding tissues [1]. A direct link between corrosion and in-stent restenosis (ISR) has not been clearly established. In order to examine the vessel inflammatory response to stent implantation, miniature nitinol coil stents were implanted in mice aortas. In vivo imaging techniques were used to assess the proliferation of vascular smooth muscle cells and the accumulation of activated monocytes at the implantation site.

The surface chemistry of stents was modified by oxidizing heat treatment in order to mimic in vivo corrosion. Stents without corrosion (normal) or with severe corrosion were surgically implanted in the abdominal aortas of male CD1 mice via femoral access (sham-stent control included). Fluorescently labeled (lipophilic membrane dye, DiD) isolated peripheral blood monocytes (PBMs) were injected via tail vein in each group of mice, 14 days post-operatively. Mice were then monitored by in vivo flow cytometry in order to track DiD-labeled PBMs in circulation. Subsequently, DiD-labeled PBM accumulation in stented aortas was assessed by fluorescence reflectance imaging. At 28 days post-operatively mice were again imaged in vivo, following injection of matrix metalloproteinase (MMPSense-680).

Significant differences were found at the implantation site between the tested groups with respect to the numbers of DiD-labeled activated monocytes (Fig. 1). The dynamic monitoring of cellular recruitment and accumulation at the site of inflammation in real time and in the native environment of the implanted stents has provided new insight into mechanisms that regulate this response. Fluorescence reflectance imaging analysis revealed a significant increase in MMP activity in corroded stented aortas with respect to the normal stented aortas. The increase in MMP activity was associated with higher numbers of in-stent neointimal vascular smooth muscle cells (VSMCs) at the site of injury. The results of the dual analysis provide a direct link between stent corrosion and metallic ion release with vascular inflammation and VSMCs proliferation, factors thought to initiate in-stent restenosis.

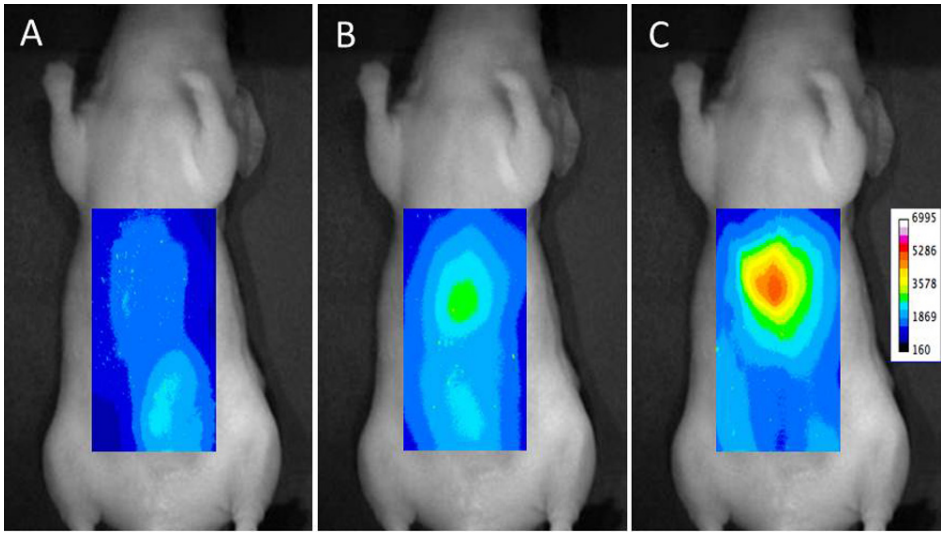

Figure 1. DiD-labeled PBM accumulation 14 days post-operatively. (A): Sham, (B): Normal, (C): Corroded stent.

Reference:

1. D. Halwani, P. Anderson, J. Lemons, W. Jordan, A. Anayiotos, B. Brott. In-vivo Corrosion and Local Release of Metallic Ions from Vascular Stents into Surrounding Tissue. J INVASIVE CARDIOL 2010;22:528-535.