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RESEARCH CORRESPONDENCE

Is There Light at the End of the Thin-Strut Tunnel?

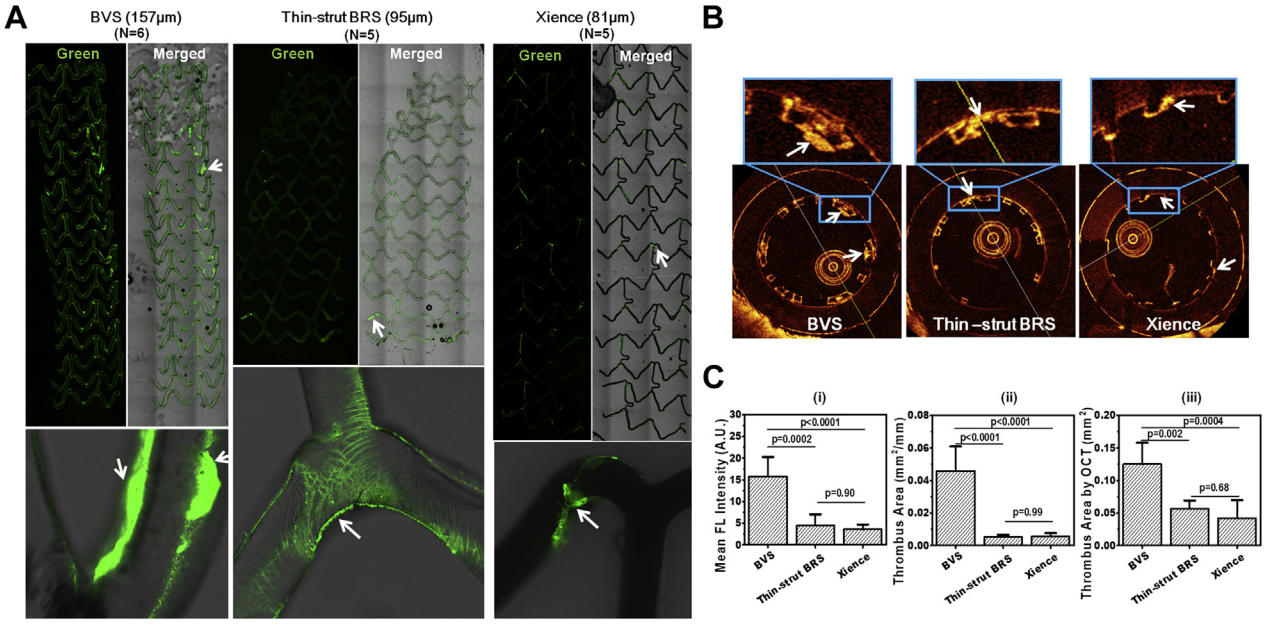
In Vitro Insights on Strut Thickness Impact on Thrombogenicity in Bioresorbable Stents or Scaffolds

The first generation of bioresorbable stents or scaffolds (BRS) have significantly larger strut thickness compared with metallic drug-eluting stents (DES). This results in more flow disturbance, thus potentially increases scaffold thrombogenicity. Stent or scaffold thrombosis (ST) remains a major and undesirable clinical complication in percutaneous coronary interventions. Current BRS with larger strut thickness have demonstrated similar efficacy to metallic DES in moderate angiographic severe lesion scenarios but the higher ST rate of the Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California) is a major concern, as seen in the recent ABSORB trials (1). Newer-generation of BRS have reduced strut thickness (<120 μm) but the effect of a thinner strut on scaffold thrombogenicity remains unclear.

The role of strut thickness on stent or scaffold thrombogenicity has been previously shown in several pathological and computational model studies (2). Large strut thickness increases the amount of foreign material in the lumen and results in increased flow disturbance, flow separation, and areas of recirculation, thereby possibly increasing the thrombogenic risk of the device (3). Perturbed flow patterns around large, protruding struts are associated with increased platelet adhesion, inflammatory responses, and reduced re-endothelialization.

Three types of 3.0-mm DES and scaffolds (XIENCE everolimus-eluting stent [Abbott Vascular]: strut thickness = 81 μm [n = 5]; Absorb BVS: strut thickness = 157 μm [n = 6]; ArterioSorb BRS [Arterius Limited, Leeds, United Kingdom]: strut thickness = 95 μm [n = 5]) were individually deployed in 3-mm silicone coronary models. The samples were perfused with porcine blood in a flow loop for 4 min at a flow rate of 200 ml/min. Adherent platelet

FIGURE 1 Impact of Strut Thickness on Thrombogenicity



(A) Representative longitudinal section antiplatelet immunofluorescence images and **(B)** optical coherence tomography (OCT) cross-sectional frames of the bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California), thin-strut ArterioSorb (Arterius Limited, Leeds, United Kingdom), and XIENCE (Abbott Vascular) after perfusion. High-magnification images are also shown in **A** and **B**, correspondingly. **Arrows** indicate the clots on the stent samples. **(C)** Quantification of thrombogenicity on the stents or scaffolds: 1) average fluorescence (FL) intensity; 2) thrombus area from immunofluorescence images; and 3) average cross-sectional thrombus area from OCT pullback analysis of samples. A.U. = arbitrary units; BRS = bioresorbable scaffolds.

aggregates on the stent after perfusion were immunohistochemically stained with mouse anti-pig CD61 primary antibody, followed by Alexa Fluor 488 goat anti-mouse secondary antibody, and then observed under confocal microscopy. The extent of platelet adherence and thrombus formation on the stents was evaluated using immunofluorescence analysis and optical coherence tomography (OCT).

From the in vitro perfusion coronary model, we observed that the thin-strut BRS showed significantly smaller thrombus area in immunofluorescence images as compared with the thicker-strut BVS (0.005 mm^2/mm vs. 0.046 mm^2/mm; $p < 0.0001$), while no difference was found between a thin-strut BRS and metallic XIENCE stent (0.005 mm^2/mm vs. 0.006 mm^2/mm; $p = 0.99$). Similar patterns were observed in cross-sectional thrombus area in OCT images and mean fluorescence intensity, indicating activated platelets adhering on the stent surfaces (**Figure 1**).

The initial enthusiasm for the concept of BRS has been tempered by current clinical data on ST in both early and late phases. A recent meta-analysis involving 4 studies revealed that the pooled incidence rate of ST through 3 years was clearly higher in the BVS group than in the metallic everolimus-eluting stent group (2.4% vs. 0.6%), despite a relative closer rate of target lesion failure (11.7% vs. 8.1%) (1).

Possible mechanical causes of ST can be categorized into 3 pathophysiological mechanisms: 1) disturbance of laminar blood flow and alteration of shear stress in the subacute phase; 2) high thrombogenicity of the biodegradation products; and 3) an inflammatory environment around the struts during degradation of the polymer. Scaffold struts thickness can potentially mitigate all 3 mechanisms. Bulky stent struts have been reported to introduce significant hemodynamic changes, which have an impact on endothelial coverage and thrombosis (4).

Small strut thickness decreases protrusion and improves embedment of the struts, and hence could theoretically contribute to less flow disturbance compared with the thick struts of the current BVS. Computational fluid dynamics reconstructions show the impact of strut thickness on shear rate patterns and blood flow velocity profiles. Thin-strut BRS protrusion led to less flow disturbance than did the larger-strut BVS, which had a larger area with shear rate more than 1,000/s. Regions with high shear rate activates von Willebrand factor binding to glycoprotein Ib and glycoprotein IIb or IIIa receptors, thereby increasing platelet adherence. In addition, there was 7- and 14-fold reduction of recirculation area in the thin-strut BRS and XIENCE stent respectively, as compared with the thick-strut BVS.

It has also been demonstrated previously that better embedment of struts and lesser alteration of physiologic shear stress enhance re-endothelialization (2). Although the thrombogenicity of the biodegradation by-products is biomaterial related, scaffold dismantling with macroscopic structures protruding into the lumen has been also a concern in terms of ST risk. In this aspect, thin-strut BRS have potential advantages of faster degradation and less material dismantling into the vessel. Moreover, thinner struts translate into less foreign material being implanted, thereby reducing inflammation and fibrin deposition. Koppara et al. (5) demonstrated a significant increase of inflammatory cell adhesion as well as platelet aggregation in thick-strut BVS as compared with thin-strut DES in the acute phase (<28 days), emphasizing the importance of stent geometry and struts thickness with regard to activation of coagulatory pathways.

The results suggest that a thinner BRS strut may improve the hemodynamic milieu around the BRS struts, which is important in the subacute phase after implantation. Whether thin-strut BRS will help also in reducing inflammation and thrombus formation during the late degradation phase until complete polymer resorption still requires in-depth examination.

In vitro perfusion model experiments suggest that strut thickness can impact flow profile and acute thrombogenic response on stent strut. In comparison with current larger strut BVS, a thin-strut BRS was shown to decrease acute platelet adherence and clot formation.

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