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EDITORIAL COMMENT

# Discontinuity

## Is it a Major Cause of Scaffold Thrombosis?*

Renu Virmani, MD, Hiroyuki Jinnouchi, MD, Aloke V. Finn, MD

Very late stent thrombosis (VLST) is an unpredictable and potentially life-threatening complication of percutaneous coronary intervention. In the era of thick strut (i.e., ~140 μm) first-generation drug-eluting stents (DES), delayed healing (i.e., uncovered struts) of the stented segment was the primary cause of late stent thrombosis, which in some series occurred at an annual rate of 1.3% through at least 10 years of follow-up (1). Newer-generation DES are made with thinner struts and have a significantly lower rate of stent thrombosis (ST) than first-generation DES (2). Nonetheless, disadvantages to this type of system remain, including impaired coronary vasomotion, development of early neoatherosclerosis, and long-term retention of polymer-coated metal.

Bioresorbable vascular scaffold (BVS) was developed with the goal of overcoming these shortcomings. The Absorb stent (Abbott Vascular, Santa Clara, California) represents the most advanced attempt to create this type of device. Yet, because its polymeric structure is not as strong as metal, Absorb had to have thicker struts (150 μm) to improve its radial strength, which still is on the order of one-half that of DES. On average, BVS struts occupied 27% of the vessel wall compared with only 13% for most metallic DES.

It was thought that, as long as short-term and mid-term outcomes were at least equivalent to current-generation DES, the advantages of Absorb would begin to appear after 32 months, when the polymer is substantially degraded in vivo. Although initial trial results seemed promising, higher rates of unfavorable outcomes, such as device-related thrombosis in Absorb, especially occurring beyond 1 year, were reported compared with everolimus-eluting metallic stents in a meta-analysis of randomized, controlled trials (3). The device-related VLST for BVS was 0.8% vs. 0.1% ($p = 0.004$) at 24 months (3). Likewise, 2-year data from the pivotal Absorb III clinical trial showed higher rate of ST and target lesion failure in Absorb (4). In a blinded, multicenter, investigator-initiated, noninferiority, randomized, clinical trial (AIDA [Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial]), Absorb had greater device-related ST (3.5%) with mean follow-up of 707 days compared with metallic DES (0.9%; $p < 0.001$) (5).

These data called into serious question the clinical viability of such a stent, especially when metallic DES with thinner struts had far superior outcomes. Indeed, the recent news that Abbott has ended commercial sales of Absorb is not surprising, but does this mean there is no future for BVS? The crucial question remains whether the shortcomings of Absorb can be surmounted by the next-generation BVS. However, to identify these issues, we need to understand better what caused its failure. It is within this context that the study by Yamaji et al. (6) in this issue of the *Journal* is so valuable. The authors report the largest series to date of 36 patients who underwent Absorb implantation and who presented with VLST and had optical coherence tomography (OCT) performed at the

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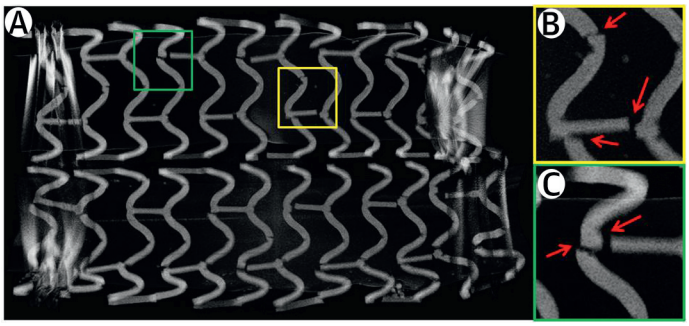
**FIGURE 1 Representative Images of Micro-Computed Tomography After Implantation of Absorb BVS in Porcine Coronary Arteries for 180 Days**




The scaffold has been cut longitudinally and both halves are shown. **(A)** Multiple scaffold fracture (discontinuities) in the Absorb bioresorbable vascular scaffold (BVS). **(B, C)** High-power images of select areas. The **red arrows** show scaffold fractures.

time of catheterization in the INVEST registry (INdependent OCT registry on VEry late bioresorbable Scaffold Thrombosis) (6). Previously, no systematically performed study provided a clear picture of the mechanisms underlying ST in patients who received Absorb.

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The authors report that the most frequent cause of VLST was scaffold discontinuity (42.1%), followed by strut malapposition (18.4%), neoatherosclerosis (18.4%), underexpansion (10.5%), uncovered struts (5.3%), and edge-related progression (2.6%). Discontinuity, malapposed struts, and uncovered struts were found more frequently in thrombosed versus nonthrombosed scaffold regions. The investigators conclude that the leading mechanism behind cases of VLST in Absorb is scaffold discontinuity and suggest that an unfavorable resorption process is the major issue. Although limited by the relatively small number of observations, there seem to be a clear implications for modification of device design, focusing in particular on the role of the absorption process as it relates to scaffold dismantling. However, the interpretation of OCT images is mainly in the eye of the beholder and, thus, results depend almost exclusively on rather subjective interpretation of these images.

## DISCONTINUITY

Discontinued struts were defined as isolated malapposed struts that could not be integrated in the expected circularity of the device in at least a cross-section or those with an abrupt loss on longitudinal scaffold between 2 adjacent frames (6). How this could occur and cause thrombosis despite a very high percentage of tissue strut coverage (87.9% of lesions) seems difficult to comprehend. Indeed, discontinuous embedded struts in the neointima have been frequently reported with Absorb (25% of lesions at 2 years and 42% at 3 years), but were not associated with adverse sequelae in ABSORB B (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions) and ABSORB Japan studies (7,8). The idea that discontinuous embedded struts fall into the lumen, causing malapposition, and provoking thrombosis is also inconsistent with preclinical data. We have performed micro-computed tomography in our laboratory in porcine studies and show a large number of struts with discontinuities at 180 days (**Figure 1**). We have not seen evidence of struts falling into the lumen nor have these isolated discontinuous struts been associated with thrombosis.

## COVERAGE

A major shortcoming of the present manuscript focuses on the authors' definition of strut coverage. Many of the images shown by the authors in cases of scaffold thrombosis do indeed show covered struts, but it remains unclear what exactly is the nature of the tissue that is covering these struts. In a paper written by us examining cases of ST after first-generation DES, we showed that uncovered struts were the most important predictor of ST, but our definition was based on evidence of neointimal tissue covering struts (9). Here the authors, by their own admission, admit coverage in their definition might include thrombus or fibrin, 2 hallmarks of delayed and incomplete healing. The failure to adequately distinguish between the 2 types of coverage (fibrin/thrombus vs. neointima) by OCT, is a central issue of contention in the manuscript. It is entirely believable that thrombus/fibrin might not prevent dismantled scaffold from falling into the lumen and causing thrombosis, but not when there is tissue coverage by neointima. The failure to recognize this difference also raises the issue of whether the most important problem causing device failure in Absorb is lack of healing (i.e., fibrin/thrombus) or device dismantling. For these reasons, the possibility of overestimation of neointimal coverage in BVS cannot be excluded. Scaffold struts are more likely to be surrounded by fibrin due to a high incidence of fractures or discontinuities inducing thrombogenicity, whereas