Shedding Light on Bioabsorbable Stent Struts Seen by Optical Coherence Tomography in the ABSORB Trial

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Optical coherence tomography (OCT) is an emerging intracoronary imaging technology that obtains depth-resolved images of light backscattered from the coronary wall with an axial resolution of \( \approx 10 \ \mu m \). First demonstrated in 2001 in patients, \(^1\) intracoronary OCT is now commercially available and is beginning to be adopted in cardiac catheterization laboratories worldwide. An important application of OCT is the investigation of intracoronary stents; \( \approx 100 \) articles have been published over the past 5 years in which OCT was used for this purpose. OCT is well suited for such studies because (1) its contrast and resolution enable delineation of fine details including device and arterial wall structures; (2) stent healing occurs near the luminal surface, where OCT is most effective; and (3) relative to other imaging modalities, OCT has fewer imaging artifacts that interfere with the appearance of stent struts and surrounding tissues.

Recently, researchers have found that OCT may also be well suited for investigating the fate of bioabsorbable stents, including bioabsorbable vascular scaffolds (BVS). \(^2\)–\(^9\) These new devices are of particular interest because they offer the potential to facilitate coronary revascularization while subsequently being dissolved and assimilated into the artery wall. Resorption in this manner may overcome many of the limitations of bare-metal and drug-eluting stents by leaving behind a revascularized coronary artery without any residual “foreign” material that can promote restenosis or precipitate late stent thrombosis. Given the recent introduction of new generations of bioabsorbable stents, it is critical to understand and monitor what happens to these devices over time in vivo, how the tissue responds to the stent/scaffold, and the manner in which the artery returns to structural/biological normalcy.

A team of investigators at the Thoraxcenter, Rotterdam, Netherlands, has made pioneering contributions to the assessment of bioabsorbable stents. The BVS used in their studies are composed of a poly-L-lactide backbone and poly-D,L-lactide coating that contains and governs the release of everolimus, an antiproliferative drug that inhibits neointimal growth. \(^5\)–\(^9\) Because the rectangular polymer BVS struts are optically transparent, they can be easily distinguished from the highly scattering vascular wall. As a starting point in their analysis, the Thoraxcenter investigators have defined a useful terminology describing OCT features associated with various stages of BVS strut evolution: an intact strut footprint appears as a “preserved box,” the first OCT change in the strut footprint is termed an “open box,” and “black” and “white” dissolved boxes designate struts with a degraded footprint that merges into the artery wall. \(^5\)–\(^9\) In a longitudinal, 30-patient clinical study, named ABSORB, \(^5\)–\(^9\) these same researchers reported a time course for bioabsorption of the BVS studied and observed that the preserved box remains until \( \approx 6 \) months and the struts predominantly become either indiscernible or integrated into the artery wall (open, black dissolved, white dissolved boxes) within 2 years. Still unknown after the ABSORB study are the histological correlates of these OCT findings and whether or not the OCT appearance of BVS struts corresponds to changes in polymer content.

In the present issue of Circulation, \(^10\) the authors provide key answers to these questions through the results of a study in which BVS were implanted in swine coronaries and imaged by OCT at time points ranging from 0 to 4 years in vivo. After imaging, the swine arteries were analyzed with gold standards histology and gel permeate chromatography to quantify polymer content. Their findings show that the clear, rectangular OCT appearance of the BVS struts that correspond to a preserved box could represent the presence of intact polymer struts or complete resorption of the polymer with replacement by proteoglycans. It appears that the proteoglycans, which replace the polymer, are as transparent as the polymer, making it difficult to differentiate between the two on the basis of light scattering or attenuation. Another interesting finding by OCT and confirmed by histology is that the stent strut outline is preserved even when the polymer is fully resorbed and replaced by proteoglycans. Possible explanations of this phenomenon include maintenance of the strut footprint by a rim of calcium that forms at the interface of the strut and the surrounding tissue or the fact that the structural integrity of the footprint may be provided by the proteoglycans themselves.

Although the authors found that current OCT technology was unable to provide details on the changes in polymer during the resorption process, it was, however, possible to determine when the BVS struts were “integrated” within or “assimilated” into the artery wall. OCT images of BVS corresponding to dissolved boxes or indiscernible struts were...
found by histology to comprise cells and/or connective tissue that had replaced the regions that were previously occupied by the struts. Other valuable findings of the study include documentation that the stent-implanted coronary arteries in this swine model were nearly devoid of polymer after 24 months. It is interesting to note that there were clear differences between the time course of strut evolution between these animals and human patients in the ABSORB trial; OCT integration of struts in humans was nearly complete at 2 years, whereas the same took longer for this swine model. However, these temporal differences do not likely affect the OCT findings of this study.

Even though OCT as implemented in this work was incapable of characterizing polymer content, it is possible that this technology could be configured to better distinguish polymer from proteoglycan in the future. First, the refractive index, which governs the speed of light through a material, may be different between the poly-L-lactic acid polymer and the proteoglycan. Changes in refractive index will make the axial thickness of the strut appear larger if the index is larger and smaller if the index is lower. If differences in the refractive indices of these 2 materials existed, then the thicknesses or areas of individual struts could in principle be followed over time to provide an estimate of polymer/proteoglycan concentration. Another property that can be assessed by OCT is a parameter termed dispersion. Dispersion refers to the degree to which different wavelengths of light travel at different speeds within a material. Like refractive index, if the dispersion of the polymer were different from the dispersion of the proteoglycan, then there would be a relative distortion in the OCT signal that could, in principle, be quantified from the OCT data. Birefringence is another property of a material that can be measured by OCT and that may allow differentiation of polymer from proteoglycan. Birefringence refers to the change in polarization of the light as it propagates through material comprised of oriented molecules. This change in polarization can be measured from a modified form of OCT known as polarization-sensitive OCT, previously shown to be capable of measuring collagen content within plaque ex vivo.11–13 Finally, future-generation bioabsorbable devices could be developed to intentionally incorporate a small amount of scattering that can be detected by OCT; measurement of the OCT signal within the strut region could then be used to quantify polymer content.

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References

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