

Now you see me, now you don't: The bioabsorbable stent in clinical practice

From *heartwire*

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Washington, DC - Predicting the future is a fool's game, and predicting successful drug and device therapy in cardiovascular medicine is just as tricky.

When bioabsorbable stents emerged on the radar of interventionalists this past decade, some dared to dream that they might one day have a stent that would do its job, then disappear, eliminating the long-term use of dual antiplatelet therapy, without a subsequent risk of stent thrombosis.

In addition, bioabsorbable stents wouldn't interfere with diagnostic evaluations using noninvasive imaging, such as MRI and computed tomography (CT). Equally important, the technology offered the promise of doing away with vessels loaded up with multiple stents, the so-called full metal jacket, which has the potential to interfere with future coronary surgery.

After a number of years, one stent, a fully bioabsorbable everolimus-eluting stent (BVS, Abbott Vascular) shows promise and is furthest along in clinical development, but not everybody is sure of the role the vanishing scaffolds will play in everyday practice. Some experts see a more expansive role for the devices, even implanting the stents into vulnerable arteries that are not yet significantly closed, with the intention of making an unhealthy vessel healthy again. Others, however, see interventionalists implanting the stents only in a minority of patients.

"These stents won't be for everyone," **Dr. Renu Virmani** (CVPath Institute, Gaithersburg, MD) told *heartwire*. "There will probably be 10% to 20% of the population in whom they'll work, but most of the patient cases are severe now and have a fair amount of calcification, except for the patient who comes in with acute myocardial infarction. [AMI patients] don't tend to have much calcification at the site, so it could be that it works there. But overall, I'm skeptical. This is a thick-strut [stent], and yes, it will dissolve in two years, but after two years even bare-metal stents have healed."

During this year's TCT 2010 summit on next-generation drug-eluting stents, bioabsorbable stents, and drug-eluting balloons, Virmani outlined her misgivings. In animal models, she noted, there is an almost full degradation of the stent at two to three years and a full absorption by four years. Like most first-in-human trials, however, much of the early clinical work has been carried out in easier-to-treat patients, those with lesions <60% narrowed and in lesions with minimal calcification.

“In the calcified lesions, the question is, Are [bioabsorbable stents] as strong as bare-metal stents?” asked Virmani. “I’m not convinced of that. And they have to be appropriately placed. The lumen is not perfect all the time, and they don’t always adhere to the vessel wall, so there might some malapposition. Then what happens? I’m a little concerned.”

Speaking with *heartwire*, **Dr. Gregg Stone** (Columbia University, New York) concedes the limited data at this stage of the game but does envision a future where cardiologists are implanting the stents into more and more patients. The current-generation bioabsorbable stents, however, are unlikely to ever make their way into the arteries of heavily calcified lesions, bifurcations, or small vessels.

“It depends on how one defines workhorse, but I do think they they’ll be able to be used in a majority of cases,” said Stone. “I don’t think they’ll be used in all patients, at least not the first-generation bioabsorbable stents. . . . It’s going to take years before we have adequate data showing how they respond in bifurcation lesions, overlap situations, and so on, but I would think that for garden-variety lesions, which are most of the lesions that we treat, they should be quite acceptable.”

The clinical need

Dr. Ron Waksman (Washington Hospital Center, Washington, DC) told *heartwire* that a stent, metal or otherwise, serves a temporary role, that being to open the vessel, to provide some support, “but after that it’s basically a nuisance, with the potential to develop stent thrombosis, atherosclerosis, and restenosis.” Stent thrombosis, he pointed out, still occurs at a rate of 0.2% to 0.3% per year even with the second-generation stents. A bioabsorbable scaffold has the advantage of letting the stent do its job, then disappear, allowing the vessel to return to its natural functionality in term of vasomotion and eliminating the risk of inflammation.

To *heartwire*, **Dr. John Ormiston** (Mercy Angiography and Auckland City Hospital, New Zealand) noted that in preclinical testing, inflammation with the everolimus-eluting bioabsorbable stent is less than that observed with the Cypher stent. Moreover, 10-year data on another stent that uses the same poly-L-lactide polymer (the Igaki-Tamai stent [Kyoto Medical Planning]) suggested minimal inflammation.

Dr. Robert Schwartz (Minnesota Heart Institute, MN) points to the fact that there continues to be restenosis with the traditional stents and that first-generation stents are experiencing late catch-up, maybe as late as seven, eight, or nine years on. Also, if the scaffold degrades and is no longer in the artery, there is nothing that can cause inflammation, which would reduce the risk of stent thrombosis.

“Wouldn’t it be nice to have a stent that disappears in six months, and we could use dual antiplatelet therapy for just six months instead of two years?” asked Schwartz. “Or maybe put something into the bioabsorbable stent where you don’t need dual antiplatelet therapy at all.”

Dr. Raoul Bonan (Montreal Heart Institute, QC) said the new technology needs to balance absorption and inflammation and that absorption needs to be slow enough to prevent increased inflammation. Currently, it takes about two years for the stent to be absorbed, and “that’s too long,” said Bonan.

According to Ormiston, three to six months would be ideal. “The trouble is you just can’t flip a switch and have the stent go away. It takes time for the body to absorb it,” he said.

According to Waksman, the field is moving in the right direction. He notes that the Abbott stent has very good biocompatibility, and even though some of the earlier models had problems with regard to radial force and recoil, the newer models are improving. Early data on the stent showed it was equivalent at six months to the Xience stent in terms of late loss, restenosis, and clinical and angiographic outcomes.

“I think the stents have to perform, in terms of efficacy, as well as the best drug-eluting stents,” Waksman told *heartwire*. “Otherwise, they’re not going to be well received. The interventional community is not going to tolerate 15% target lesion revascularization rates. The second challenge is that these stents need to be as deliverable as the best stents that we have.”

Goals and expectations

An important drawback of bioabsorbable stents today is their profile and deliverability, but Ormiston, for one, believes these drawbacks are less and less with newer and newer generations. The crossing profile of the Abbott stent is 1.4 mm compared with 1.2 mm of contemporary stents, and this could pose a problem with jagged, calcified plaque protruding into the lumen, as the calcium might catch on the device, stopping it from being delivered.

“The device does compare favorably with metallic stents, such as the Xience stent, for flexibility and radial strength, and we’re relatively impressed by how well it delivers,” he said. “Some people will say that it has a very thick strut. Strut thickness with the polymer is similar to that of Cypher stent, which was the first-generation metallic drug-eluting stent. So, it delivers pretty well, interestingly enough. However, these are not calcified lesions, so we don’t know how it performs in that setting. That’s a question mark, and we don’t know what percentage of patients the device will be applicable to, but it could easily be more than 50%.”

Stone, however, predicts strut thickness will remain an issue. “These are probably going to be higher profile than the best-in-class metallic-based stents.”

Several experts *heartwire* spoke with noted that bioabsorbable stents could help eliminate the “full metal jacket,” a situation where a patient with multivessel disease is treated with multiple metallic stents. One of the proposed benefits of having a bioabsorbable stent in this setting would be that surgeons could operate on vessels that had returned to “normal,” with no metal casing, should the patient later need cardiac surgery.

But Virmani questioned whether or not bioabsorbable stents can fill even this clinical need. For one, surgeons typically place anastomoses for vein grafts or internal mammary artery bypass grafts distal to lesions, yet it’s not clear that bioabsorbable stents, with struts that are 150 μm thick, could even be placed in these distal arteries. What’s more, Virmani points out that no studies have demonstrated that an anastomosis can be placed at a site where a stent has previously dissolved.

Transforming the sick artery into a healthy one

One of the more speculative hypotheses with the bioabsorbable stents is that a stent that leaves nothing behind might prove useful in patients with vulnerable plaques/arteries. Rather than wait for the disease to advance to stenosis or plaque rupture, some experts envision the stent as preventive, which would expand use of the stents to more and more patients.

“Specifically, treating new patients in the context of those who have vulnerable histology, that is a truly preventive function of the stent, with advanced imaging showing us that the patient is at risk for an event and yet does not have a severe stenosis, no chest pain, and no symptoms,” Schwartz told *heartwire*. “In a perfect world, you might see a stent like this turn a high-risk artery into a low-risk or no-risk region.”

Imaging studies, he explained, have shown that bioabsorbable stents can limit restenosis and provide satisfactory mechanical support, traditional roles for the devices, but they might also safely and reliably transform the histology, the cellular architecture, of the artery. These early data suggest it might be possible to transform an atherosclerotic artery into one that functions reasonably well.

“This opens up the option, I don’t want to say it too loudly yet, where we can treat regions of vulnerable plaque,” said Schwartz. “Vulnerable plaque forms in regions that are diseased, where there are large necrotic nodules, where there are calcified nodules, and where there is sick endothelium that allows hemorrhage and plaque erosion to occur. One can imagine a drug-eluting scaffold that disappears, where that nasty, bad, ugly pathobiology is replaced by

a healthy chunk of vessel.”

Ormiston said that for an artery to be considered healthy, it needs to be subjected to the pulsatile forces and shear stresses of a normal artery, and that none of this can happen if there is a metal cage in it. Implanting a stent that goes away allows the vessel to expand and contract normally, subject to the natural pulsatile forces, which allow it to become healthy again. There are also data suggesting plaque regression with the Abbott stent, although he and other experts cautioned that this needs to be studied further.

Stone is cautiously optimistic.

“If you imagine what the vessel looks like at the beginning, say with 70% plaque burden stenosis, and then put a bioabsorbable stent in it, and come back two years later when the stent has completely degraded,” Stone told *heartwire*. “You don’t see the stent, and there does seem to be some plaque regression, where you end up with, say, 30% plaque burden. We don’t have enough cases like that yet, and we don’t know if that’s going to be the typical experience, but Patrick Serruys has shown some cases like that with the earliest first-in-human data.”

The biggest push for bioabsorbable stents might come from patients themselves. Psychologically, nobody wants a metal stent left in their bodies for the rest of their lives. Like the analogy proponents of the new stents like to use, people can break their arms, but they don’t wear the cast for life. The same thinking should also be applied during coronary interventions of diseased arteries, they say.

Virmani consults for GlaxoSmithKline, Lutonix, Arsenal, Terumo Medical Corporation, CoreValve, Medtronic, Abbott Vascular, WL Gore and Associates, and Atrium. Stone reports being on the advisory board for and receiving honoraria from Boston Scientific and Abbott Vascular and being a consultant for the Medicines Company. Waksman reports research support from the Medicines Company, Boston Scientific, and Medtronic and consulting for Abbott Vascular and Biotronik. Schwartz reports research support from Boston Scientific, Abbott Vascular and Vital Images and consulting for Boston Scientific, Abbott Vascular, Medrad, Edwards Lifesciences, Cappella, and Arsenal. Bonan reports consulting for Medtronic. Ormiston reports consulting for Abbott Vascular and Boston Scientific.