

revascularization are needed. We also agree with Conti's opinion that, unless ischemia is present, collaterals do not appear angiographically; if the collateral provides excellent blood flow to ischemic myocardium, the collaterals will remain (2). Werner et al. (3) reported that even collaterals that appear well developed on angiography are not able to fully replace antegrade blood flow; therefore, restoring flow reserve does little to prevent myocardial ischemia. Our hypothesis was that well-developed collateral flow in patients with stable CTO lesions may partially protect the myocardium and the revascularization may allow complete maintenance of viable myocardium (4), and we identified long-term survival benefits of aggressive revascularization compared with medical therapy in our study. Unfortunately, because we did not routinely perform contralateral injections after successful revascularization of CTO in our practice, we could not identify the existence or disappearance of collaterals after CTO revascularization, as mentioned in Conti's letter. However, we agree with his hypothesis that the change of collateral flow after CTO revascularization in coronary angiography might correlate with whether ischemia of viable myocardium occurs or not. This hypothesis requires further detailed study.

As stated by Barbato and Wijns (1), our study might have reported a higher rate of successful percutaneous coronary intervention (PCI) or coronary bypass grafting (CABG) compared to previous studies of CTO revascularization. However, remarkable developments in the survival benefits posed by CTO revascularization are rapidly becoming a reality because CTO PCI techniques have improved and the experience of CABG has also increased. We anticipate that the survival benefits of aggressive reduction of remnant ischemia by revascularization or intensive medication in patients with CTO lesions will be verified by future large-scale randomized trials.

Woo Jin Jang, MD
Jeong Hoon Yang, MD, PhD
*Seung-Hyuk Choi, MD, PhD
Young Bin Song, MD, PhD
Joo-Yong Hahn, MD, PhD
Jin-Ho Choi, MD, PhD
Wook Sung Kim, MD, PhD
Young Tak Lee, MD, PhD
Hyeon-Cheol Gwon, MD, PhD

*Division of Cardiology
Department of Medicine, Cardiac and Vascular Center
Samsung Medical Center
Sungkyunkwan University School of Medicine

#50, Irwon-dong, Gangnam-gu
Seoul 135-710
Republic of Korea
E-mail: sh1214.choi@samsung.com
<http://dx.doi.org/10.1016/j.jcin.2015.05.012>

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose. The first two authors contributed equally to this work.

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Fate of Bioresorbable Vascular Scaffold Metallic Radio-Opaque Markers at the Site of Implantation After Bioresorption



The use of bioresorbable vascular scaffolds (BRS) is increasing in patients with coronary artery disease undergoing percutaneous coronary interventions. Because the devices are radiolucent on fluoroscopy, 2 adjacent cylindrical platinum markers are incorporated in the proximal and distal edges of the polymeric devices for precise scaffold deployment and post-dilation during the procedure. In addition, the metallic radio-opaque markers (MRMs) also provide anatomic landmarks for long-term follow-up when all the polymeric struts have been bioresorbed. There has been concern about the potential risk of MRM beads becoming dislodged from the device and embolized into the coronary bed after complete bioresorption of the polymeric struts. Beyond the biological hazard of MRMs embolization, the additional inconvenience is that the embolization may result in the incapacity to locate the coronary segment where the fully bioresorbed scaffold was implanted. Invasive assessment of BRS such as quantitative coronary angiography (QCA), intravascular ultrasound (IVUS), or optical coherence tomography (OCT) may be unable to detect the precise location of the MRMs either because of the

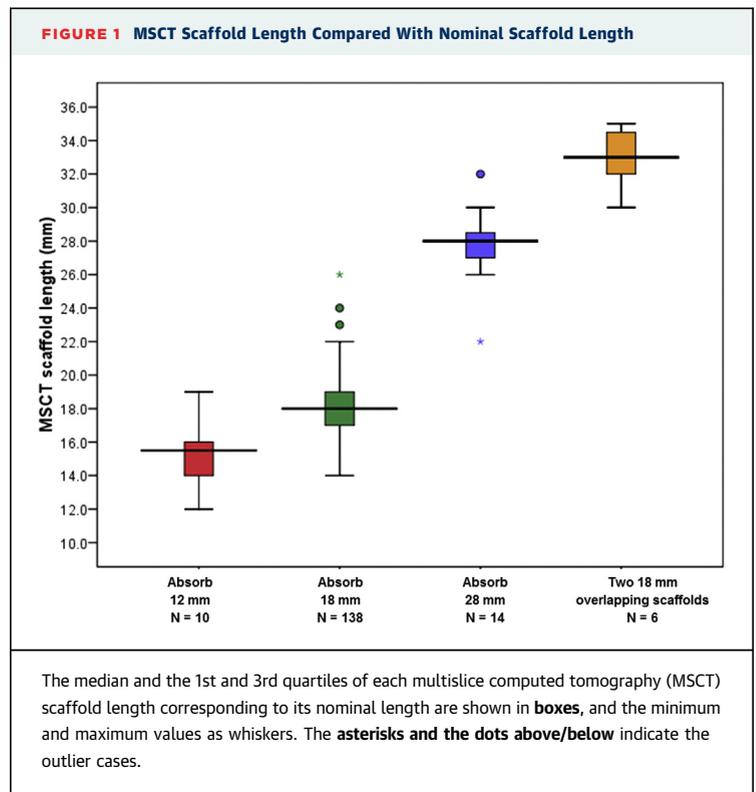
resolution of the imaging technique (QCA) or as a result of wire artifact (IVUS, OCT) or mimicry by heavy calcium (IVUS). Multislice computed tomography coronary angiography (MSCT) has provided reliable assessment of the angiographic results up to 3 to 5 years (1,2) after scaffold implantation with accurate detection of the position of MRMs and their blooming effect without being dependent on the rate of image acquisition and wire artifact. In order to dispel the question of embolization of MRMs, we evaluated the persistent presence and location at 18 months of the MRMs following implantation of these fully bioresorbable scaffolds.

We retrospectively pooled data from the ABSORB trials (ABSORB Cohort A, ABSORB Cohort B, and ABSORB EXTEND) in which 943 patients with de novo native coronary artery lesions were treated with the fully resorbable everolimus-eluting Absorb scaffold (Abbott Vascular, Santa Clara, California); the details and primary outcome of each trial have been published (2-4). Of these 943 patients, 165 patients with 168 lesions underwent MSCT at 18 months. A list of the MSCT scanners, the acquisition protocol, and the MSCT analysis are described in the [Online Appendix](#).

To establish the persistent presence of the MRMs in MSCT, both qualitative and quantitative evidence were required. The qualitative evidence was the ability to identify both proximal and distal MRMs position. Because calcified nodules (CN) could mimic MRMs, 4 criteria were used to identify the position of the radio-opaque markers: 1) typical location and orientation of the MRMs; 2) marker-to-marker length; 3) topographical relationship of the radio-opaque markers with anatomic landmarks visualized on MSCT and conventional coronary angiography; and 4) blooming artifact and its peak attenuation. The description of criteria and examples of MSCT images by using these 4 criteria are provided in [Online Figure 1](#). The quantitative evidence is the MSCT scaffold length compared with its nominal length.

The statistical analysis is detailed in the [Online Appendix](#).

A total of 168 lesions (12 lesions in ABSORB Cohort A, 61 lesions in ABSORB Cohort B, and 95 lesions in the ABSORB EXTEND study) were analyzed, and the study profile is shown in [Online Figure 2](#). A total of 348 MRMs were evaluated by both quantitative and qualitative analyses; all MRMs were detected at the implantation site; and there was no evidence of marker embolization to distal vascular beds. The median MSCT scaffold length was 18.0 mm (ranging from 12 mm to 36 mm; interquartile range [IQR]: 17 to 19 mm) as well as the median nominal scaffold length was 18.0 mm (ranging from 12 mm to 28 mm) ([Figure 1](#)).



The median difference in length between MSCT scaffold length and nominal scaffold length was 0.0 mm (IQR: -1.0 to 1.0 mm). There was a moderate correlation between MSCT mean lumen area (Mean LA) and QCA Mean LA ($r = 0.54, p < 0.0001$). A good correlation was observed between MSCT Mean LA and IVUS Mean LA, and between MSCT Mean LA and OCT Mean LA ($r = 0.74$ and $r = 0.73$, respectively; $p < 0.0001$) ([Online Figure 3](#)). The Mean LA measured by MSCT was comparable to QCA, but statistically lower than IVUS and OCT ([Online Table 1](#)). The reproducibility of the 4 criteria to identify MRMs from CN was good, $r = 0.97; p < 0.0001$ ([Online Figure 4](#)).

The attenuation of MRMs was approximately 30% higher than dense CN attenuation, but there was nevertheless a modest overlap of the attenuation values; MRM attenuation was sometimes lower than 1,000 HU as a result of the partial volume effect. The median peak density of MRMs was 1,368 HU (IQR: 1,158 to 1,715 HU) in contrast to the median peak density of CN that was 946 HU (IQR: 844 to 1,133 HU).

The main findings of this study are the following: 1) according to the criteria, all MRMs were identified and located at the site of the initial implantation; 2) the MSCT Mean LA was comparable to the Mean LA measured by QCA but lower than OCT and IVUS; and 3) the reproducibility in detecting of MRMs by using 4 criteria was high.

However, the distinction between calcified spots and metallic markers with computed tomography is also not easy to determine compared with OCT. The possible advantages of OCT are the ability to: 1) distinguish the MRMs from underlying calcium more clearly than MSCT; 2) measure the embedment of the struts; and 3) evaluate the thickness of neointima because of a higher axial resolution of around 10 to 15 μm as compared with MSCT.

The limitation in this study is that the study result was able to confirm the persistent presence of MRMs only at medium-term follow-up, and the long-term results still require investigation.

In conclusion, MRM recognition by MSCT is critical for precise noninvasive assessment of the coronary location of all MRMs. On the basis of our study criteria, there was no evidence of MRMs dislodgement and embolization 18 months after scaffold implantation.

Pannipa Suwannasom, MD
Yoshinobu Onuma, MD, PhD

Carlos M. Campos, MD

Shimpei Nakatani, MD

Yuki Ishibashi, MD, PhD

Hiroki Tateishi, MD, PhD

Maik J. Grundeken, MD

Bojan Stanetic, MD

Koen Nieman, MD, PhD

Hans Jonker, BSc

Hector M. Garcia-Garcia, MD, PhD

*Patrick W. Serruys, MD, PhD

on behalf of the investigators of ABSORB Cohort A, B and EXTEND trials

*International Center for Circulatory Health

NHLI, Imperial College London

London, United Kingdom

P.O. box 2125

Rotterdam 3000CC

the Netherlands

E-mail: patrick.w.j.c.serruys@gmail.com

<http://dx.doi.org/10.1016/j.jcin.2015.04.010>

Please note: The ABSORB trials were sponsored by Abbott Vascular. Dr. Nieman has received institutional research support from Siemens Medical Solutions, GE Healthcare, and Bayer HealthCare. Mr. Jonker is an employee of Cardialysis. Drs. Garcia-Garcia, Onuma, and Serruys are members of the Advisory Board of Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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APPENDIX For supplemental methods, statistical analysis, table, and figures, please see the online version of this article.

3-Year Follow-Up of the Balloon Elution and Late Loss Optimization Study (BELLO)



The optimal treatment of de novo small-vessel coronary artery disease remains unclear. The use of drug-eluting stents in this patient group are limited by high rates of restenosis (1) and the requirement of prolonged treatment with dual antiplatelet therapy. The use of drug-coated balloons (DCB) might be an alternative treatment option. There are currently limited data with regard to the long-term efficacy of this strategy (2), and currently no randomized data to support this approach. The BELLO (Balloon Elution and Late Loss Optimization) study (3) was an investigator-initiated, prospective, multicenter, single-blinded, active-treatment controlled clinical trial. In BELLO, 182 patients undergoing percutaneous revascularization of small coronary vessels (reference vessel diameter <2.8 mm by visual estimation) were randomly assigned in a 1:1 ratio to treatments with: 1) In.Pact Falcon paclitaxel DCB (Medtronic, Inc., Santa Rosa, California) dilation and provisional bare-metal stenting; or 2) paclitaxel-eluting stent (PES) (Taxus Liberté, Boston Scientific, Marlborough, Massachusetts) implantation as per standard clinical practice. We have shown that treatment of small-vessel disease with a paclitaxel DCB is associated with less angiographic late loss and similar rates of restenosis and revascularization as PES is at 1 year. Here we report the final pre-defined, protocol-mandated 3-year clinical follow-up results of this study population.

A total of 182 patients were enrolled at 15 Italian centers and randomized to treatment with DCB (n = 90) in 94 lesions or PES (n = 92) in 98 lesions. Patients were eligible if ≥ 18 years of age, with a diagnosis of stable or unstable angina or documented ischemia and a maximum of 2 angiographically significant de novo lesions <25 mm in length in native coronary arteries with a visually estimated reference