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# One-year clinical and computed tomography follow-up after implantation of bioresorbable vascular scaffolds in patients with coronary chronic total occlusions

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**Disclosures / Conflicts of Interest**

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## ABSTRACT

**Objectives** To assess the safety and efficacy of everolimus-eluting bioresorbable scaffolds (BRS) in the treatment of chronic total occlusions (CTO) using non-invasive Multislice Computed Tomography (MSCT) angiography at one-year follow-up.

**Background** Current evidence regarding the safety and efficacy of BRS for the percutaneous treatment of CTO is limited.

**Methods** Between September 2013 and January 2016, patients who received one or more ABSORB BRSs were included at three centers. MSCT (including quantitative analysis) and clinical follow-up were performed at one year.

**Results** Forty-one CTO patients were included. Mean age was  $60\pm 11$  years and the majority was male (83%). Average Japanese CTO (J-CTO) score was  $0.9\pm 0.9$ . Seventy-one BRS were implanted in total with, on average,  $1.7\pm 0.8$  scaffolds/patient, and a total length of  $43\pm 20$ mm and diameter of  $3.1\pm 0.4$ mm. One non-cardiac death took place. MSCT angiography was performed in 34 (83%) patients: all scaffolds were patent, except in one patient, in whom a patent target vessel was present on subsequent diagnostic angiography. MSCT quality was sufficient for quantitative analyses in 27 patients (46 scaffolds): median reference versus scaffold minimal lumen diameter and minimal lumen area were measured, and showed a small difference of 0.1mm (-0.2-0.4) (lumen diameter stenosis=3.0%) and  $0.5\text{mm}^2$  (-1.0-2.0) (lumen area stenosis=4.2%) respectively.

**Conclusions** The low number of events and high patency rate at 1 year are encouraging the further use of the ABSORB scaffold for CTOs with low J-CTO score. Non-invasive MSCT angiography is a valid tool to assess scaffold patency, although its image resolution limits the use for quantitative measurements.

**Abbreviations:**

BRS: Bioresorbable scaffold

CTO: Chronic total occlusion

FU: Follow-up

J-CTO: Japanese CTO score

MLD: Minimal lumen diameter

MLA: Minimal lumen area

MSCT: Multislice computed tomography

PCI: Percutaneous coronary intervention

## INTRODUCTION

To overcome the issue of permanent artery caging and reduce the risk for (very) late stent thrombosis with drug-eluting stents, bioresorbable scaffolds (BRS) have been developed. BRS provide transient vessel support to resist acute recoil, have drug delivery capability to avoid re-stenosis, and disintegrate over a period of approximately 12 months, whilst disappearing over an expected period of two to three years. Because of their re-absorptive properties, these scaffolds potentially promote vessel healing, permit vascular remodelling, late lumen enlargement, and restoration of vasomotion (1, 2).

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Up to now, experience with BRS has mainly focused on the ABSORB scaffold (ABBOTT Vascular, Santa Clara, CA). Although several large randomized trials have been performed (3-6), data specifically focussing on the use of BRS in chronic total occlusions (CTO) are limited. However, BRS are especially attractive for use in CTOs, as these lesions often require long segments to be stented, and thus carry a greater risk for in-stent re-stenosis and re-occlusion, stent fracture and thrombosis (7, 8).

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The available reports currently focus on clinical outcomes, short/mid-term (non-invasive) follow-up (FU) ( $\pm 6$  months) without (or limited) quantitative analyses, and/or invasive imaging strategies (i.e. quantitative angiography or optical coherence tomography) (9-18). Therefore, this multicenter, prospective study aimed to assess the feasibility and safety of BRS when used for the interventional treatment of CTOs, by analyzing the outcomes and scaffold patency at one year, both clinically and via use of non-invasive multislice computed tomography (MSCT) imaging. Given the polymer-based construction of BRSs, these scaffolds are invisible when performing coronary MSCT imaging (19). In addition, quantitative MSCT imaging was performed for determining diameter and area stenosis during FU.

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## **METHODS**

### **Study population and design**

Between September 2013 and January 2016, patients were prospectively and consecutively included in three centers (Ziekenhuis Oost-Limburg, Genk, Belgium; Institut de Chirurgie Cardiaque et de Cardiologie Interventionelle, Luxembourg, Luxembourg; Onze-Lieve-Vrouw Ziekenhuis, Aalst, Belgium) if they underwent a successful percutaneous coronary intervention (PCI) of their CTO, followed by the implantation of one or more ABSORB BRSs. All procedures were performed by experienced CTO operators. Baseline, angiographic, procedural, outcome and FU data were collected for all patients using a case report form. Clinical follow-up and non-invasive MSCT imaging studies were planned at one year. There were no specific patient or lesion exclusion criteria, although BRS use was not advised ~~when for CTOs with very long~~ lesion lengths, or when subintimal tracks ante- or retrograde were performed. In addition, patients on new oral anticoagulants or Acenocoumarol and known allergy to Aspirin or Clopidogrel were excluded. All authors conformed to the institutional guidelines. The study was granted ethical permission and all patients gave written informed consent.

### **Study device and scaffolding procedure**

All patients were pre-treated with Clopidogrel 300mg one day in advance of the index procedure and on the day of the index procedure. Patients not pre-treated the day before, received 600mg of Clopidogrel on the index procedure date. All patients were treated post-procedural with dual antiplatelet treatment (including Clopidogrel 75mg) for at least 12 months. The ABSORB BRS consists of a polymer backbone of poly-L-lactide, coated with a thin layer of a 1:1 mixture of poly-D,L-lactide polymer and the antiproliferative drug everolimus. Radiopaque markers at the tip of both ends provide visualization of the BRS during implantation. BRS implantation was performed according to standard clinical practice, including appropriate sizing, aggressive lesion preparation, and high pressure post-dilatation with non-compliant balloons having a balloon-to-artery ratio of  $\pm 1.0$ . Multiple BRSs were implanted in a marker-to-marker fashion from the distal to the proximal part of the target vessel. The

use of intravascular ultrasound was not mandatory. Although not preferred/recommended, non-ABSORB metallic stents could be implanted as bail-out, in addition to the study device; the decision of which was left at the discretion of the operator.

### **MSCT angiography**

MSCT scans were performed at each site at 12 months, using 64-slice dual-source CT (Definition, Siemens AG, Forchheim, Germany), 128-slice dual-source CT (Definition Flash, Siemens), and 128-slice CT (Discovery CT750 HDI, GE Healthcare, Milwaukee, Wisconsin) scanners. Standard acquisition techniques were used, at the discretion of the individual sites. Tube settings were adjusted to patient size (80-140kV), and axial scan protocols for patients with lower heart rates were applied to reduce radiation doses. Beta-blockers were administered to patients with a heart rate >75bpm and routine breath-hold instructions were given during acquisition. Images were reconstructed using thin slices (0.5-0.75mm) and medium smooth reconstruction filters. One or several phases were included depending on the scanning protocol. All data were stored on DVD media for core laboratory analysis (as given below).

### **MSCT analysis**

All MSCT data were collected at the core laboratory center (Ziekenhuis Oost-Limburg, Genk) and were analyzed by a study investigator (JM) and an independent non-invasive cardiologist (DV) separately. The average of the measurements performed by both investigators was taken. A dedicated workstation was used for all analyses (SyngoVia, Siemens AG). The outer vessel/lumen borders were manually traced to approximate the total vessel/lumen size. For each scaffold, the minimal lumen diameter (MLD) and minimal lumen area (MLA) were measured. Within 5mm proximal or distal of each scaffold, the reference MLD and MLA were measured. In case of a single scaffold, a proximal reference point was taken, unless not feasible (i.e. ostial lesion, proximal lesion bifurcation, etc.). If so, measurements were performed in the distal reference point. In case of two scaffolds, a proximal reference point was taken for the proximal scaffold. Similarly, the reference MLD and MLA of the distal

BRS were measured distally from the second scaffold. In case of >2 scaffolds, the reference MLD and MLA for the middle scaffold(s) were calculated from the average of the proximal and distal reference values, corresponding to those of the proximal and distal scaffolds respectively. This technique was applied to account for the tapering of the vessel and the inability to measure in-between scaffolds due to the marker-to-marker implantation fashion. Apart from this, a visual estimation of target vessel and/or scaffold (re-)stenosis on MSCT was performed.

### Definitions and endpoints

A CTO was defined as a lesion of a native coronary artery, which exhibited Thrombolysis in Myocardial Infarction antegrade flow equal to zero, for >3 months. Calcification was present if visible on fluoroscopy. CTO complexity was graded using the Japanese CTO (J-CTO) score (20). Technical success was considered when a patent target vessel with <30% residual stenosis and a Thrombolysis in Myocardial Infarction flow grade 3 was obtained. Procedural success was technical success in the absence of any periprocedural adverse events. Major Adverse Cardiac Events included death, myocardial infarction (incl. (non-)ST-segment elevated myocardial infarction), target vessel failure (i.e. in-stent re-stenosis or occlusion with or without target vessel revascularization), and target vessel revascularization with PCI or coronary artery bypass graft surgery, and were counted mutually exclusive. Myocardial infarction was clinically-based on the presence of recurrent chest pain, with or without electrocardiogram changes and positive troponins. Other complications included major bleeding (Bleeding Academic Research Consortium criteria (21)) and major vascular complications (incl. coronary perforation necessitating the use of unplanned endovascular (coronary graft or covered stents, coils, fat embolization) or surgical interventions). Visual estimation of the degree of target vessel and/or scaffold (re-)stenosis on MSCT was performed, and was defined as follows: no visible re-stenosis (<30%), mild (≥30%), moderate (≥50%), and severe (≥70%) re-stenosis. All adverse events were collected post-discharge. However, in-hospital events were reported separately according to the definitions above.

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The primary endpoint of this study was the incidence of target vessel failure during follow-up. A new cardiac catheterization was advised in the presence of recurrence of symptoms or if MSCT imaging showed a non-patent target vessel. Secondary endpoints were the assessment of BRS patency and performance of quantitative MSCT imaging for determining diameter and area stenosis at one-year FU.

### **Statistical analyses**

Baseline, angiographic, and MSCT data were analyzed using descriptive statistics. Numerical values were expressed as mean  $\pm$  standard deviation or median (interquartile range) as appropriate, while categorical variables were expressed as percentages. Normality was assessed using the Shapiro-Wilk statistic. All statistical analyses were carried out using SPSS Statistics version 22 (IBM SPSS Inc.).

## **RESULTS**

### **Demographic and angiographic characteristics**

Forty-one patients have been included during the study inclusion period, of whom 83% (n=34) were male. Mean age corresponded to  $60\pm 11$  years and mean body mass index equaled  $29\pm 4.8\text{kg/m}^2$ . A high percentage of patients suffered from hypertension (73%, n=30) and dyslipidemia (73%, n=30). Diabetes was present in 29% (n=12) (Table I). On angiography, more than half of the patients had a normal left ventricular function (ejection fraction  $>60\%$ ), and one in four patients suffered from multivessel disease. CTO-PCI was performed most commonly on the right coronary artery. The average J-CTO score was low ( $0.9\pm 0.9$ ) (Table II), suggesting lesion selection (24% of all CTO lesions treated during the study period).

### **Scaffold implantation characteristics**

Included patients were treated successfully with a true lumen crossing strategy, and had Thrombolysis in Myocardial Infarction flow 3 on angiography at the end of the index procedure. A cumulative 71 ABSORB scaffolds were implanted in 41 patients, with an average of  $1.7\pm 0.8$  scaffolds per patient. The mean total scaffold length corresponded to  $43\pm 20\text{mm}$  and the mean scaffold diameter was  $3.1\pm 0.4\text{mm}$ . In one patient, a  $2.75\text{*}12\text{mm}$  Cre8 (Alvimedica) drug-eluting stent was implanted in the distal right coronary artery, in addition to a proximal and middle ABSORB scaffold. No intravascular ultrasound or optical coherence tomography were used to optimize scaffold implantation. All patients were free of any in-hospital events.

### **Clinical and MSCT outcomes**

One-year clinical FU was available for 98% (n=40/41) patients (Figure 1). During this period, all 40 patients remained free from target vessel failure. One patient suffered a non-cardiac death. No other events or complications took place.

At 12 months, MSCT imaging was performed in 83% (n=34/41). Five patients withdrew consent for the MSCT scan, one patient died (as above), and one patient dropped-out due to a loss of contact (went abroad) (Figure 1). On MSCT, all vessels and scaffolds were patent (Figure 2), except in one patient, who underwent a subsequent diagnostic angiography that showed a mildly “toothed” proximal BRS stent but an otherwise patent target vessel. Despite the use of true lumen crossing and scaffold implantation techniques, MSCT imaging showed the presence of a remaining dissection in two patients (Figure 3). In one patient, a small right lung lesion was noted on MSCT, which was further investigated and confirmed to be metastatic. The patient received surgical and oncological treatment subsequently.

#### **MSCT analyses**

Due to motion artefacts, heavy coronary calcifications with resulting blooming artefacts, poor resolution, and/or suboptimal antegrade contrast flow (n=1), the MSCT quality in seven patients was deemed insufficient for accurate quantitative measurements. MSCT scans of 27 patients - having a total of 46 scaffolds - were therefore available for further analysis (Figure 1, 4A-D). An average of  $1.7 \pm 0.9$  scaffolds were implanted in this subgroup, having an average total scaffold length and diameter of  $42 \pm 20$  and  $3.2 \pm 0.3$  mm respectively. In 21 patients (36 scaffolds), MSCT image quality was considered optimal for quantitative analyses, based on the operators’ opinions and radiology report. In the other six patients (10 scaffolds), image quality was adequate for such analyses. MLD and MLA were assessed for each individual scaffold (and reference point). The measurements of one scaffold and three references were excluded due to interfering motion artefacts, a “bias-generating” reference location, and an additional drug-eluting stent implanted distally (Table III). Overall, a median MLD and MLA of 3.3 mm (2.8-3.6) and  $12.0 \text{ mm}^2$  (9.0-15.0) were measured in the reference segments respectively. Median MLD and MLA were 3.2 mm (2.8-3.5) and  $12.0 \text{ mm}^2$  (9.5-13.5) in the scaffold segments respectively, resulting in a small difference in median MLD and MLA of 0.1 mm (-0.2-0.4) (lumen diameter stenosis = 3.0%) and  $0.5 \text{ mm}^2$  (-1.0-2.0) (lumen area stenosis = 4.2%) respectively.

In addition to the computational measurements, all analyzable scaffolds and vessels (n=27) were assessed qualitatively on MSCT for the presence of any (focal) re-stenosis. A mild (focal) re-stenosis was observed in nine scaffolds, implanted in seven patients. A moderate re-stenosis was observed in one scaffold. In five proximal references, either a mild (n=3) or moderate (n=2) focal stenosis was visible. None required further treatment.

## DISCUSSION

The main findings of this study are that (1) the implantation of BRS in CTO with a low J-CTO score is safe, both at short (i.e. in-hospital) and intermediate-term FU; and (2) non-invasive MSCT imaging is a valuable tool to assess vessel and scaffold patency during FU; although (3) further investigation is needed to assess patency at long term (beyond one year) and enhance the reliability and reproducibility of MSCT-based vessel and lumen assessments.

Given the temporary elution and scaffolding of BRS, the return of vessel vasomotion, adaptive shear stress, late expansive remodeling, and late luminal enlargement can potentially be promoted (22, 23). This suggests that BRS are interesting for use in complex lesions, such as CTOs, which often require long stented segments (7, 8). Previous literature has shown greater stent length to be associated with an increased risk for adverse events during FU (24). However, only limited data on the use of BRS in CTOs are currently available. At present, the largest study focusing on BRS in CTO is the multicenter BONITO registry (11), which found a similar risk for target vessel failure between patients treated with BRS (n=153) and second-generation drug-eluting stents (n=384) at long-term FU, and a trend towards higher risk of ischemia-driven target lesion revascularization in BRS. As discussed by the authors, the absence of significance regarding the latter can potentially be found in the underestimation of this event, due to the absent use of imaging modalities at FU. This is especially true for asymptomatic re-stenosis or re-occlusion, which can occur in CTO lesions. Due to the increased risk for target vessel failure after CTO-PCI, there currently exists an unmet clinical need to perform an accurate FU (i.e. via imaging techniques) in these patients.

Some smaller studies have assessed vessel/scaffold patency of BRS in CTO via imaging techniques. Similar to our study, a high rate of technical scaffold implantation success and low rate of cardiac events have been reported (9, 10, 12, 17, 18). However, these were (1) single-center studies, (2) limited to mid-term FU (i.e. MSCT at 6 months), and/or (3) based on invasive quantitative coronary angiography, which inherently carries a greater risk of complications. For these reasons, our study

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focused on the assessment of adverse events, and scaffold and vessel patency after treatment of CTO with BRS at one year FU, by performing clinical and non-invasive MSCT imaging. The synergy between BRS and non-invasive MSCT (as opposed to metallic stents) could enable clinicians to successfully treat and follow up on these patients. Furthermore, the compatibility of BRS and non-invasive MSCT could provide a means for investigators to safely include imaging FU to clinical studies with a similar study design, eliminating potential underestimation of clinical (asymptomatic) events.

CTO lesions are frequently characterized by (severe) calcifications, a tortuous vessel anatomy (especially after bypass surgery), and often require long scaffolds. Despite the less favorable crossing profile of BRS versus new-generation drug-eluting metallic stents, all scaffolds had good cross-ability and no peri-procedural complications took place. At one-year, no clinical events occurred, except for one non-cardiac death. MSCT imaging was performed in >80% of the patients. All vessels and scaffolds were patent on MSCT, except for one case, which had absent contrast flow most likely due to body movements during the MSCT scan, as subsequent diagnostic angiography demonstrated vessel patency. The absence of scaffold thrombosis is particularly noteworthy as higher rates of late scaffold thrombosis in BRS compared to second-generation everolimus-eluting stents have been reported in non-CTO lesions (25, 26). Apart from known issues such as incomplete lesion coverage, malapposition, scaffold under-expansion, and strut discontinuities (27-29), the lower (long-term) use of dual antiplatelet therapy was likely related to the prevalence of these late events (25, 26). Given the higher lesion complexity and greater need for longer scaffolds, as well as the increased risk for late events after dual antiplatelet therapy discontinuation (especially beyond the one-year FU time point, of this study), a prolonged use of dual antiplatelet therapy (>12 months) after BRS implantation in CTOs might be needed (30).

Although CTO complexity in our series was low, these favorable study outcomes could potentially support the use of BRS for higher CTO lesion complexity as well. Of note however, the ABSORB scaffolds are currently available with a maximum length of 28mm. Since CTO lesions often

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require long stented segments, this would necessitate implantation of multiple adjacent overlapping scaffolds. Present data demonstrated multiple stents in overlap increases the risk for scaffold thrombosis (26, 30, 31). In addition, no data are currently available for BRS use in the subintimal space, which is commonly used as part of a dissection and re-entry strategy in more complex CTO lesions. Thus, in the absence of clear evidence on BRS in more complex CTO lesions, the use of BRS in this setting should be evaluated within study protocols.

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Quantitative MSCT imaging analysis for the determination of diameter and area stenosis was also performed. Since BRS are radiolucent – except for the platinum markers – MSCT imaging could potentially prove as a relevant technique for performing non-invasive assessments (10). Previously, Bruining et al. (32) found a positive correlation between the quantitative results of 2D and 3D quantitative coronary conventional angiography, 3D intravascular ultrasound, and MSCT immediately after the procedure and at six months. Furthermore, Onuma et al. (33, 34) performed serial quantitative MSCT assessments in non-CTO patients, supporting the feasibility of the technique for quantitative assessments in BRS.

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In our study, quantitative MSCT analyses demonstrated an overall small percentage of lumen diameter and area stenosis, potentially underscoring the long-term safety of the ABSORB BRS device(s) when used in CTOs. However, only a subset (79%) of MSCT scans was available for quantitative assessments, and even less (78%) had “optimal” image quality. The reasons for the inability to perform reliable quantitative assessments are multifaceted (Figure 4):

First, motion artefacts were not uncommon despite the use of standard acquisition techniques. Second and not surprisingly, calcific plaques were commonly encountered, which often result in blooming artefacts on MSCT. Likewise, the platinum radiomarkers (37µm) may also result in “blooming”, thus hampering accurate assessments, especially in the overlap areas (10, 32). We reviewed the procedure angiograms systematically to localize the scaffold markers. However, standard baseline (postpre-implantation) MSCT imaging could facilitate better marker localization and calcific

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discrimination (old vs. new). Third and most importantly, even in the absence of the above, image quality was still variable between studies. Besides patient characteristics (e.g. body mass index) and the use of different MSCT imaging scanners (i.e. different slice numbers (64-slice/128-slice)), the inherent limited in-plane (spatial) resolution of MSCT hampers accurate (cross-sectional) delineation of vessel and/or lumen and reliable quantitative measurements, particularly when vessel size is small. In this study, MSCT assessments were performed manually, which might result in greater inter-operator variability. In previous studies, (semi-)automatic computational models were used for these assessments (32). However, the accuracy and/or applicability of these models will vary amongst different scenarios (e.g. circular model is less accurate for oval shapes post-scaffolding (14.9%) (35), or when late (expansive) vessel remodeling or even re-stenosis has potentially occurred). In either case (manual or (semi-)automatic assessment), under- and overestimation of coronary lumen dimensions is inevitable. Therefore, the applicability of MSCT, other than for assessment of patency, is limited and needs further investigation and development.

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## STUDY LIMITATIONS

This non-randomized study included a small group of patients with a low CTO complexity, and extrapolation of the study results for a larger group of patients, including those with higher CTO complexity – which are frequently associated with more comorbidities and multivessel disease – might therefore be limited. Furthermore, operators were free in their choice of stent type (BRS vs. drug-eluting stent). Therefore, if deemed unfeasible to implant a BRS, these patients were not included. MSCT imaging at one-year was not performed in all patients, and asymptomatic in-scaffold re-stenosis or re-occlusion could have potentially remained undetected in these cases. Also, late malapposition, BRS strut discontinuations, and focal aneurysms are potential important imaging observations which cannot be visualized by MSCT. Furthermore, no direct comparisons between MSCT and invasive angiography were performed. On the other hand, for patients being asymptomatic and with a patent vessel on CT, there will be reluctance to perform an additional angiogram. Although standard MSCT acquisition techniques were used, the scan protocol was adjusted for the specific MSCT scanners used at each site. Together with the presence of multiple “blooming” (due to calcification, scaffold markers) and/or motion artefacts, notable variations in image quality were observed, which may have affected MSCT analyses and the assessment of re-stenosis. This was further limited by the absence of ~~postpre~~-implantation (baseline) MSCT imaging, due to practical and financial reasons. The absence of the latter also limits potential determination of late recoil, neo-intima formation and distal lumen enlargement.

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## CONCLUSIONS

This multicenter study demonstrated the implantation of the ABSORB BRS in CTOs with a low complexity score is safe, directly post-implantation and at intermediate-term FU. In addition, MSCT imaging is a valuable tool to evaluate vessel and scaffold patency, and thus provides a patient-friendly means in case imaging FU is warranted or to improve the strength and validity of clinical study results.

-Notwithstanding, the applicability of MSCT imaging for the assessment of coronary lumen dimensions needs further investigation.

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## FIGURE LEGENDS

**Figure 1: Patient flow chart of one-year clinical and MSCT follow-up.** (MSCT, multislice computed tomography).

**Figure 2: Case example of a patent vessel and scaffolds at one-year MSCT follow-up** – The patient had a blunt CTO in the left anterior descending artery (A) that was successfully treated by a 3.0x28mm and 2.5x28mm ABSORB (ABBOTT Vascular) scaffold (white arrows) (B). Angiography post-implantation confirms good scaffold deployment and Thrombolysis in Myocardial Infarction flow 3 (C). MSCT imaging at one-year demonstrated patent vessel and scaffolds (white markers) (D). Cross-sectional slice of the proximal scaffold (E). (MSCT, multislice computed tomography)

**Figure 3: Case example of the dissection lesion at one-year MSCT follow-up** – The CTO in the right coronary artery of this patient (A) was successfully treated by a 3.5x28mm and 3.5x18mm ABSORB (ABBOTT Vascular) scaffold. Scaffold markers indicated by the white arrows (B). MSCT imaging at one-year shows vessel and scaffold patency. Scaffold markers indicated by the white arrows (C). Small dissection lesion present on MSCT (D). (MSCT, multislice computed tomography)

**Figure 4: Limiting factors for MSCT analysis** – (A) Major imaging artefact in the proximal RCA ABSORB scaffold, limiting MSCT analyses. However, the contrast delineated the distal vessel well, indicating a patent target vessel. (B) Case example of low quality MSCT imaging, especially in the proximal part of the RCA. Clear interfering “motion” artefact in the second ABSORB scaffold (white arrow). (C) Case example of a badly delineated RCA (cross-sectional view), resulting in unreliable MSCT measurements. (D) Same patient as in C, showing multiple proximal calcifications in the RCA, impeding scaffold marker assessment and MSCT analysis. (E) Patent ABSORB scaffold in the proximal/ostial LAD. Location of the left main branch proximal and first diagonal bifurcation distal bias MSCT reference measurements. Scaffold markers indicated by the white arrows (CX, circumflex; D1, first diagonal branch; LAD, left anterior descending artery; LMCA, left main coronary artery; MSCT, multislice computed tomography; RCA, right coronary artery) [Table 1: Baseline characteristics of the study population.](#)

| <b>Patients (n=41)</b>             |                 |
|------------------------------------|-----------------|
| <u>Age (years)</u>                 | <u>60 ± 11</u>  |
| <u>Male</u>                        | <u>34 (83)</u>  |
| <u>BMI</u>                         | <u>29 ± 4.8</u> |
| <u>Current smoker</u>              | <u>9 (22)</u>   |
| <u>Hypertension</u>                | <u>30 (73)</u>  |
| <u>Dyslipidemia</u>                | <u>30 (73)</u>  |
| <u>Diabetes mellitus</u>           | <u>12 (29)</u>  |
| <u>Previous MI</u>                 | <u>10 (24)</u>  |
| <u>Previous CABG</u>               | <u>3 (7)</u>    |
| <u>Previous PCI</u>                | <u>11 (27)</u>  |
| <u>Peripheral vascular disease</u> | <u>3 (7)</u>    |
| <u>Previous stroke</u>             | <u>2 (5)</u>    |

Variables expressed as n (%) or mean ± standard deviation.

BMI, body mass index; CABG, coronary artery bypass graft surgery; MI; myocardial infarction; PCI, percutaneous coronary intervention.

*Table II: Angiographic characteristics of the study population.*

|  | <b>Patients (n=41)</b>          |
|--|---------------------------------|
| <u>Normal LVEF</u>                           | <u>23 (56)</u>                  |
| <u>CTO target vessel</u>                     |                                 |
| <u>RCA</u>                                   | <u>21 (51)</u>                  |
| <u>LAD</u>                                   | <u>14 (34)</u>                  |
| <u>CX</u>                                    | <u>6 (15)</u>                   |
| <u>MVD</u>                                   | <u>11 (27)</u>                  |
| <u>Proximal cap side-branch</u>              | <u>8 (20)</u>                   |
| <u>Lesion length <math>\geq 20</math>mm</u>  | <u>13 (32)</u>                  |
| <u>Blunt stump</u>                           | <u>8 (20)</u>                   |
| <u>Calcification</u>                         | <u>8 (20)</u>                   |
| <u>Tortuosity <math>\geq 45^\circ</math></u> | <u>3 (7)</u>                    |
| <u>Re-attempt</u>                            | <u>3 (7)</u>                    |
| <u>J-CTO score</u>                           | <u>0.9 <math>\pm</math> 0.9</u> |
| <u>Average # of scaffolds</u>                | <u>1.7 <math>\pm</math> 0.8</u> |
| <u>Average total scaffold length (mm)</u>    | <u>43 <math>\pm</math> 20</u>   |
| <u>Average scaffold diameter (mm)</u>        | <u>3.1 <math>\pm</math> 0.4</u> |

Variables expressed as n (%) or mean  $\pm$  standard deviation.

CX, circumflex artery; CTO, chronic total occlusion; J-CTO, Japanese CTO score; LAD, left anterior descending artery; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MVD, multivessel disease; RCA, right coronary artery.

*Table III: Quantitative MSCT assessments at 12 months.*

|  | <u>Reference segment</u> | <u>Scaffolded segment</u> | <u>Difference</u>      |
|--|--------------------------|---------------------------|------------------------|
| <i>Proximal scaffolds (n=29)*</i>          |                          |                           |                        |
| <u>Minimal lumen diameter (mm)</u>         | <u>3.5 (2.9-3.7)</u>     | <u>3.2 (2.8-3.5)</u>      | <u>0.1 (0.0-0.5)</u>   |
| <u>Minimal lumen area (mm<sup>2</sup>)</u> | <u>12.0 (9.5-16.0)</u>   | <u>12.0 (10.0-13.5)</u>   | <u>1.0 (-0.4-2.5)</u>  |
| <i>Middle scaffolds (n=5)</i>              |                          |                           |                        |
| <u>Minimal lumen diameter (mm)</u>         | <u>3.6 (3.1-3.6)</u>     | <u>3.3 (2.9-3.8)</u>      | <u>-0.1 (-0.2-0.5)</u> |
| <u>Minimal lumen area (mm<sup>2</sup>)</u> | <u>13.0 (11.5-15.0)</u>  | <u>12.0 (10.0-16.0)</u>   | <u>1.0 (-1.0-1.5)</u>  |
| <i>Distal scaffolds (n=11)<sup>a</sup></i> |                          |                           |                        |
| <u>Minimal lumen diameter (mm)</u>         | <u>3.0 (2.6-3.4)</u>     | <u>3.2 (2.8-3.5)</u>      | <u>0.1 (-0.2-0.2)</u>  |
| <u>Minimal lumen area (mm<sup>2</sup>)</u> | <u>10 (7.8-13.3)</u>     | <u>12 (9-14)</u>          | <u>-0.5 (-2.0-1.0)</u> |
| <i>All scaffolds (n=45)</i>                |                          |                           |                        |
| <u>Minimal lumen diameter (mm)</u>         | <u>3.3 (2.8-3.6)</u>     | <u>3.2 (2.8-3.5)</u>      | <u>0.1 (-0.2-0.4)</u>  |
| <u>Minimal lumen area (mm<sup>2</sup>)</u> | <u>12.0 (9.0-15.0)</u>   | <u>12.0 (9.5-13.5)</u>    | <u>0.5 (-1.0-2.0)</u>  |

Variables expressed as median (interquartile range).

\* In one case, a scaffold was implanted in the ostial LAD, with the distal end of the scaffold located at the bifurcation with the first diagonal. Therefore, the proximal reference was located in the left main coronary artery and the distal reference in the smaller, post-bifurcation LAD or diagonal. The reference for this scaffold was excluded from the analysis to avoid bias.

<sup>a</sup> One scaffold (and distal reference) was excluded due to a motion artefact. In one case, the distal reference measurements were excluded as a third drug-eluting stent was implanted distal (and adjacent) to the distal (second) bioresorbable scaffold. In one case, a distal reference was preferred over a proximal reference, given the ostial Circumflex scaffold implantation site.

LAD, left anterior descending artery.

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*Supplemental Table 1: Baseline characteristics of the study population versus the non-ABSORB CTO population.*

|                                    | <u>ABSORB (n=41)</u> | <u>OTHER (n=100)</u> | <u>p value</u> |
|------------------------------------|----------------------|----------------------|----------------|
| <u>Age (years)</u>                 | <u>60 ± 11</u>       | <u>66 ± 10</u>       | <u>0.007</u>   |
| <u>Male</u>                        | <u>34 (83)</u>       | <u>87 (87)</u>       | <u>0.529</u>   |
| <u>BMI</u>                         | <u>29 ± 4.8</u>      | <u>29 ± 4.5</u>      | <u>0.704</u>   |
| <u>Current smoker</u>              | <u>9 (22)</u>        | <u>22 (22)</u>       | <u>0.995</u>   |
| <u>Hypertension</u>                | <u>30 (73)</u>       | <u>54 (54)</u>       | <u>0.035</u>   |
| <u>Dyslipidemia</u>                | <u>30 (73)</u>       | <u>81 (81)</u>       | <u>0.302</u>   |
| <u>Diabetes mellitus</u>           | <u>12 (29)</u>       | <u>23 (23)</u>       | <u>0.434</u>   |
| <u>Previous MI</u>                 | <u>10 (24)</u>       | <u>30 (30)</u>       | <u>0.502</u>   |
| <u>Previous CABG</u>               | <u>3 (7)</u>         | <u>16 (16)</u>       | <u>0.170</u>   |
| <u>Previous PCI</u>                | <u>11 (27)</u>       | <u>54 (54)</u>       | <u>0.003</u>   |
| <u>Peripheral vascular disease</u> | <u>3 (7)</u>         | <u>20 (20)</u>       | <u>0.008</u>   |
| <u>Previous stroke</u>             | <u>2 (5)</u>         | <u>9 (9)</u>         | <u>0.407</u>   |

Variables expressed as n (%) or mean ± standard deviation.

BMI, body mass index; CABG, coronary artery bypass graft surgery; MI, myocardial infarction; PCI, percutaneous coronary intervention.

*Supplemental Table II: Angiographic characteristics of the study population versus the non-ABSORB*

*CTO population.*

|                                    | <b>ABSORB (n=41)</b> | <b>OTHER (n=100)</b> | <b>p value</b> |
|------------------------------------|----------------------|----------------------|----------------|
| Normal LVEF                        | 23 (56)              | 68 (68)              | 0.239          |
| <i>CTO target vessel</i>           |                      |                      | 0.679          |
| RCA                                | 21 (51)              | 57 (57)              |                |
| LAD                                | 14 (34)              | 27 (27)              |                |
| CX                                 | 6 (15)               | 14 (14)              |                |
| MVD                                | 11 (27)              | 52 (52)              | 0.006          |
| Proximal cap side-branch           | 8 (20)               | 40 (40)              | 0.020          |
| Lesion length $\geq 20$ mm         | 13 (32)              | 53 (53)              | 0.021          |
| Blunt stump                        | 8 (20)               | 44 (44)              | 0.006          |
| Calcification                      | 8 (20)               | 52 (52)              | <0.001         |
| Tortuosity $\geq 45^\circ$         | 3 (7)                | 20 (20)              | 0.064          |
| Re-attempt                         | 3 (7)                | 17 (17)              | 0.135          |
| J-CTO score                        | 0.9 $\pm$ 0.9        | 1.9 $\pm$ 1.2        | <0.001         |
| Final DR technique applied         | 0 (0)                | 34 (34)              | <0.001         |
| Average # of scaffolds             | 1.7 $\pm$ 0.8        | 2.2 $\pm$ 1.0        | 0.006          |
| Average total scaffold length (mm) | 43 $\pm$ 20          | 66 $\pm$ 31          | <0.001         |
| Average scaffold diameter (mm)     | 3.1 $\pm$ 0.4        | 3.1 $\pm$ 0.4        | 0.892          |

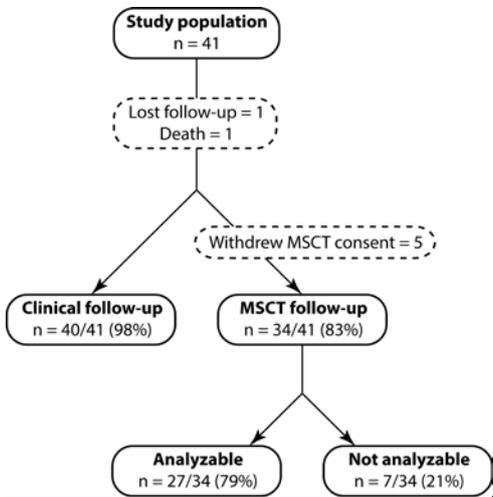
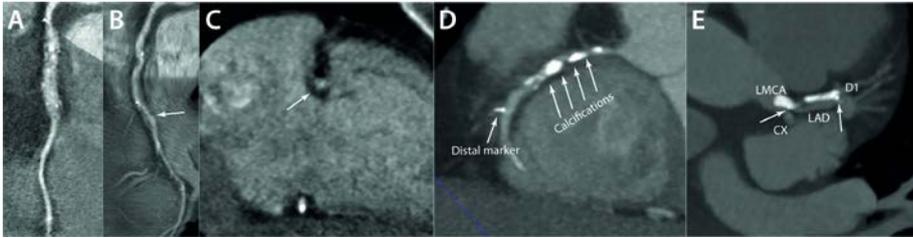
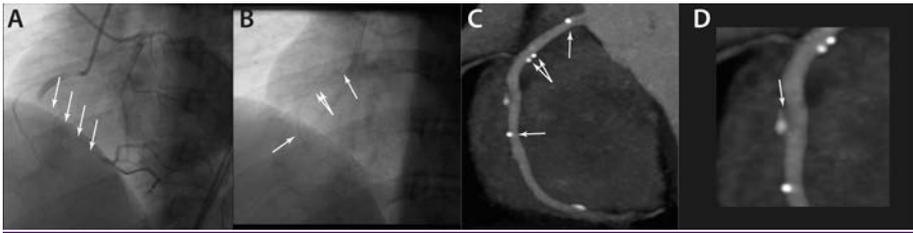
Variables expressed as n (%) or mean  $\pm$  standard deviation.

CX, circumflex artery; CTO, chronic total occlusion; DR, dissection and re-entry; J-CTO, Japanese CTO score; LAD, left anterior descending artery; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MVD, multivessel disease; RCA, right coronary artery.

Supplemental Table III: Clinical outcomes of the study population versus the non-ABSORB CTO population after one year post-discharge.

|  | <u>ABSORB (n=41)</u> | <u>OTHER (n=100)</u> | <u>p value</u> |
|--|----------------------|----------------------|----------------|
| <u>Major Adverse Cardiac Events</u>    | <u>1 (2.4)</u>       | <u>15 (15.0)</u>     | <u>0.035</u>   |
| <u>Death</u>                           | <u>1 (2.4)</u>       | <u>3 (3.0)</u>       | <u>0.6846</u>  |
| <u>Myocardial infarction</u>           | <u>0 (0)</u>         | <u>0 (0)</u>         | <u>-</u>       |
| <u>Target vessel failure</u>           | <u>0 (0)</u>         | <u>12 (12)</u>       | <u>0.022</u>   |
| <u>Target vessel revascularization</u> | <u>0 (0)</u>         | <u>11 (11)</u>       | <u>0.029</u>   |
| <u>Variables expressed as n (%).</u>   |                      |                      |                |

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