

ORIGINAL STUDIES

Serial invasive imaging follow-up of the first clinical experience with the Magmaris magnesium bioresorbable scaffold

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Abstract

Objectives: To assess the performance of the commercially available Magmaris sirolimus-eluting bioresorbable scaffold (BRS) with invasive imaging at different time points.

Background: Coronary BRS with a magnesium backbone have been recently studied as an alternative to polymeric scaffolds, providing enhanced vessel support and a faster resorption rate. We aimed to assess the performance of the commercially available Magmaris sirolimus-eluting BRS at different time points.

Methods: A prospective, single-center, nonrandomized study was performed at the Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands. Six patients with stable de novo coronary artery lesions underwent single-vessel revascularization with the Magmaris sirolimus-eluting BRS. Invasive follow-up including intravascular imaging using optical coherence tomography (OCT) was performed at different time points.

Results: At a median of 8 months (range 4–12 months) target lesion failure occurred in one patient. Angiography revealed a late lumen loss of 0.59 ± 0.39 mm, a percentage diameter stenosis of $39.65 \pm 15.81\%$, and a binary restenosis rate of 33.3%. OCT showed a significant reduction in both minimal lumen area (MLA) and scaffold area at the site of the MLA by 43.44 ± 28.62 and $38.20 \pm 25.74\%$, respectively. A fast and heterogeneous scaffold degradation process was found with a significant reduction of patent struts at 4–5 months.

Conclusions: Our findings show that the latest iteration of magnesium BRS suffers from premature dismantling, resulting in a higher than expected decrease in MLA.

KEYWORDS

bioresorbable scaffolds, constrictive remodeling, Magmaris sirolimus-eluting bioresorbable scaffold, scaffold bioresorption, scaffold collapse, scaffold recoil

Abbreviations: AMS, absorbable magnesium scaffolds; BRS, bioresorbable scaffold; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; DS, diameter stenosis; LA, lumen area; LLL, late lumen loss; MLA, minimal lumen area; MSA, minimal scaffold area; NC, noncompliant; OCT, optical coherence tomography; post-PCI, post-percutaneous coronary intervention; pre-PCI, pre-percutaneous coronary intervention; QCA, quantitative coronary analysis; RVD, reference vessel diameter; SA, scaffold area; SE-MEA, scaffold expansion according to manufacturer's expected area; SE-RVA, scaffold expansion according to reference vessel area.

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1 | INTRODUCTION

Bioresorbable scaffolds (BRS) provide short-term vessel scaffolding while avoiding long-term consequences of metallic drug-eluting stents (DES). Recent studies demonstrated higher rates of clinical events with polymeric BRS as compared to contemporary metallic DES.¹ In order to improve BRS performance, alternative backbone materials such as magnesium are currently under investigation. First generations of absorbable magnesium scaffolds (AMS-1 and AMS-2; Biotronik, Berlin, Germany) failed to maintain vessel support due to rapid degradation process.² Later iterations of the device (DREAMS and DREAMS 2G; Biotronik AG, Bülach, Switzerland) demonstrated safety and efficacy in the BIOSOLVE I and BIOSOLVE II trials.^{3,4} The Magmaris sirolimus-eluting BRS (Biotronik AG) represents the latest generation and is currently being tested in the BIOSOLVE III and IV studies.

We present the findings of clinical and intravascular imaging at different time points following the commercial use of the Magmaris sirolimus-eluting BRS.

2 | MATERIALS AND METHODS

All commercial cases treated with the Magmaris BRS (six cases) in the Thoraxcenter of the Erasmus Medical Center, Rotterdam, The Netherlands, from September 2016 to April 2017 were included in the analysis. Angiographic follow-up was available for all patients at a median of 8 months (range 4–12 months). Quantitative coronary analysis (QCA) and optical coherence tomography (OCT) imaging analysis were performed offline. In-device measurements are reported and presented as mean \pm 1 standard deviation (SD) or percentages. Wilcoxon's signed rank test was used to analyze paired comparisons between continuous values. The coefficient of correlation of Pearson (r) was used to determine the linear relationship between quantitative variables. A value of $p < .05$ was considered statistically significant. Statistical analysis was conducted using SPSS for Windows version 21 (SPSS Inc., Chicago, IL) (see Supporting Information, Methods).

3 | RESULTS

All patients presented with stable angina and noncomplex single-vessel coronary artery disease. Mean age was 57.2 years and 50% were male. One scaffold per patient was implanted; mean BRS diameter and length were 3.08 ± 0.20 and 20.00 ± 4.47 mm, respectively. High-pressure predilatation and post-dilatation was implemented in all cases using non-compliant (NC) balloons. (see Tables S1 and S2). OCT post-procedure was performed in five cases. Procedural and device success was 100%. Patients were discharged on dual antiplatelet therapy (DAPT) for at least 12 months along with high-intensity statin treatment.

Offline pre-percutaneous coronary intervention (pre-PCI) QCA revealed a lesion length of 16.50 ± 4.61 mm, percentage diameter stenosis (%DS) of $61.95 \pm 5.30\%$, and a reference vessel diameter (RVD) of 2.75 ± 0.25 . Pre-dilatation balloon diameter/RVD ratio was 1.10

± 0.10 . BRS diameter/RVD ratio was 1.13 ± 0.10 , and post-dilatation balloon diameter/BRS diameter ratio was 1.14 ± 0.10 . Residual %DS was $22.41 \pm 8.13\%$. Acute recoil was $5.34 \pm 3.99\%$. Offline post-percutaneous coronary intervention (post-PCI) OCT showed a minimal lumen area (MLA) of 5.64 ± 1.47 mm² and a minimal scaffold area (MSA) of 5.62 ± 1.60 mm². Scaffold expansion (SE) according to reference vessel area (SE-RVA) was $91.04 \pm 18.13\%$ and scaffold expansion according to manufacturer's expected area (SE-MEA) was $73.84 \pm 16.33\%$. Eccentricity index and symmetry index were 0.88 ± 0.01 and 0.32 ± 0.08 , respectively. Incomplete strut apposition was $3.16 \pm 4.22\%$ (Table 1). No edge dissections were found.

At a median of 8 months (minimum 4 months, maximum 12 months), all patients were under DAPT and target lesion failure occurred in one patient (patient #5, see Figure S1) based on severe constrictive remodeling. All other patients remained asymptomatic.

Offline QCA of the invasive follow-up procedure revealed a late lumen loss (LLL) of 0.59 ± 0.39 mm, %DS of $39.65 \pm 15.81\%$, and a binary restenosis rate of 33.3%. Offline OCT at follow-up demonstrated a decrease in MLA by $43.44 \pm 28.62\%$ ($p = .042$), along with a significant decrease in scaffold area (SA) at the site of the MLA by $38.20 \pm 25.74\%$ ($p = .043$) (Figure 1 and Table 1). Percentage lumen area (%LA) stenosis was 56.64% with a binary restenosis rate of 83.3%.

In a per-scaffold subsegment analysis, a strong linear correlation between SA at baseline and %LA reduction at follow-up was found ($r = -.87$, $p = .001$). Furthermore, a similar correlation was present between SE at baseline and %LA reduction at follow-up according to both RVA and MEA ($r = -.86$, $p = .001$ and $r = -.85$, $p = .002$, respectively) (see Figure S2a–c). Attenuation and backscattering analysis demonstrated a numerical reduction of maximum indices that correspond with strut degradation. Yet, both high and low values were within the same scaffolded segment at follow-up illustrating a heterogeneous strut degradation process (see Figures S3 and S4). No evidence of edge dissection or thrombosis was found.

4 | DISCUSSION

Sufficient radial force to overcome elastic recoil and plaque resistance is an essential feature of contemporary stents. The mechanical properties of coronary stents are influenced by backbone/polymer material, geometry, and strut thickness⁵; recently, with the advent of BRS, the resorption time was also added to this equation. Driven by the presentation of case #5 with severe early scaffold collapse at 4 months, and the recent data on adverse events related to Absorb Bioresorbable vascular scaffold (BVS), our hospital institutional board mandated us to call back all previous cases treated with the commercially available Magmaris BRS and to perform invasive control in order to assess the performance of this device. This resulted in imaging assessment at different follow-up time points.

The Magmaris BRS starts its degradation process as soon as 3 months and completes at 12 months.⁶ Our results revealed a significant decrease in patent struts with a heterogeneous resorption pattern as soon as 4–5 months postimplantation; the latest was

TABLE 1 QCA and OCT measurements

	Post-PCI	Follow-up	Absolute difference	Relative difference (%)	p value
QCA measurements ^a					
Lesion length (mm)	19.79 ± 4.48	20.12 ± 4.64	-0.33 ± 0.41	-1.59 ± 1.97	.116
Reference vessel diameter (mm)	2.92 ± 0.26	2.74 ± 0.39	0.18 ± 0.21	6.47 ± 7.05	.080
Minimal lumen diameter (mm)	2.25 ± 0.20	1.66 ± 0.48	0.59 ± 0.39	26.33 ± 19.52	.028
Mean lumen diameter (mm)	2.67 ± 0.23	2.30 ± 0.35	0.37 ± 0.22	14.00 ± 8.79	.028
In device diameter stenosis (%)	22.41 ± 8.13	39.65 ± 15.81	-17.24 ± 16.48	-99.88 ± 103.13	.046
Acute recoil (%)	5.34 ± 3.99	NA	NA	NA	NA
OCT measurements					
MLA (mm ²) ^b	5.64 ± 1.47	3.24 ± 1.85	2.41 ± 1.51	43.44 ± 28.62	.042
Mean lumen area (mm ²) ^b	7.03 ± 1.91	6.82 ± 3.79	0.22 ± 2.64	5.49 ± 36.04	.686
MSA (mm ²)	5.62 ± 1.60	NA	NA	NA	NA
Mean SA (mm ²)	6.87 ± 1.73	NA	NA	NA	NA
SA at MLA site (mm ²) ^c	6.06 ± 1.70	3.76 ± 1.77	2.30 ± 1.48	38.20 ± 25.74	.043
ISA (%) ^d	3.16 ± 4.22	0.44 ± 0.88	2.72 ± 3.37	70.25 ± 47.68	.109
SE-RVA (%)	91.04 ± 18.13	NA	NA	NA	NA
SE-MEA (%)	73.84 ± 16.36	NA	NA	NA	NA
Eccentricity index	0.88 ± 0.01	NA	NA	NA	NA
Symmetry index	0.32 ± 0.08	NA	NA	NA	NA
Maximum attenuation values ^b	16.4 ± 2.63	8.71 ± 5.38	7.70 ± 5.74	46.62 ± 30.7	.080
Maximum backscattering values ^b	8.97 ± 0.33	8.13 ± 0.59	0.84 ± 0.68	9.23 ± 7.22	.080

Note: Paired comparison of the pooled data measurements at baseline post-intervention (post-PCI) and at a median follow-up of 8 months by QCA and OCT. Data are expressed as mean ± SD.

Abbreviations: ISA, incomplete strut apposition; MLA, minimal lumen area; MSA, minimal scaffold area; OCT, optical coherence tomography; post-PCI, post-percutaneous coronary intervention; QCA, quantitative coronary analysis; SA, scaffold area; SE-MEA, scaffold expansion according to manufacturer's expected area; SE-RVA, scaffold expansion according to reference vessel area.

^aComparison made for six patients.

^bComparison made for five patients.

^cComparison made for five patients with the SA at baseline and follow-up matching the same cross-sectional area.

^dComparison made for four patients.

demonstrated by an important reduction of attenuation and backscattering indices; this is in line with a serial OCT imaging analysis performed in the BIOSOLVE II trial, showing a significant decrease in MLA of 28.3% at 6 months, and reduction of attenuation and backscattering values with fewer struts remnants visible.^{3,7} A rapid bioresorption rate might induce nonuniform vessel support and loss of radial strength, which has been corroborated with the first generation of Absorb BVS and magnesium BRS.^{2,8} The present report suggests that the most recent version of magnesium BRS also suffers from premature dismantling.

Whether the high LA reduction as found in our study could be attributed to a lower radial strength secondary to rapid bioresorption, an excessive neointimal formation, or both, is yet to be proven. Complete SA and neointimal volumes throughout the scaffolded segment could not be determined due to the difficulty in recognizing patent struts; however, when the SA was analyzable, a significant reduction of SA was found compared to the postimplantation result at the same location. These findings are in line with seven recently published case reports on severe lumen reduction and scaffold collapse after Magmaris BRS implantation.⁹⁻¹⁵ Furthermore, acute recoil was only

5.3%, in line with current generation metallic DES and BVS.^{16,17} Pre-clinical data have suggested that increased local inflammation is responsible for the higher LLL obtained during the Magmaris degradation process, and a switch to a progressive positive vessel remodeling once the bioresorption is completed might be expected.¹⁸ The latest warrants for serial invasive evaluation of the vessel response beyond 12 months. Nevertheless, vessel constrictive remodeling occurs between 1 and 6 months after PCI; therefore, assuring optimal radial support for at least 6 months after device implantation seems to be crucial.¹⁹

Although careful lesion preparation and systematic high-pressure post-dilatation with NC balloons were routinely performed in all cases, a trend toward enhanced lumen loss in the distal scaffold edges was noticed. The latter appeared to be strongly linked to the post-procedural SA and lower SE at the most distal scaffold subsegments, compared to the middle and proximal subsegments. This discrepancy could be explained by the presence of smaller vessel diameter in the distal subsegments leading to scaffold oversizing, and potentially less aggressive post-dilatation due to the challenge in visualizing the tantalum markers. OCT assessment of magnesium BRS has shown an

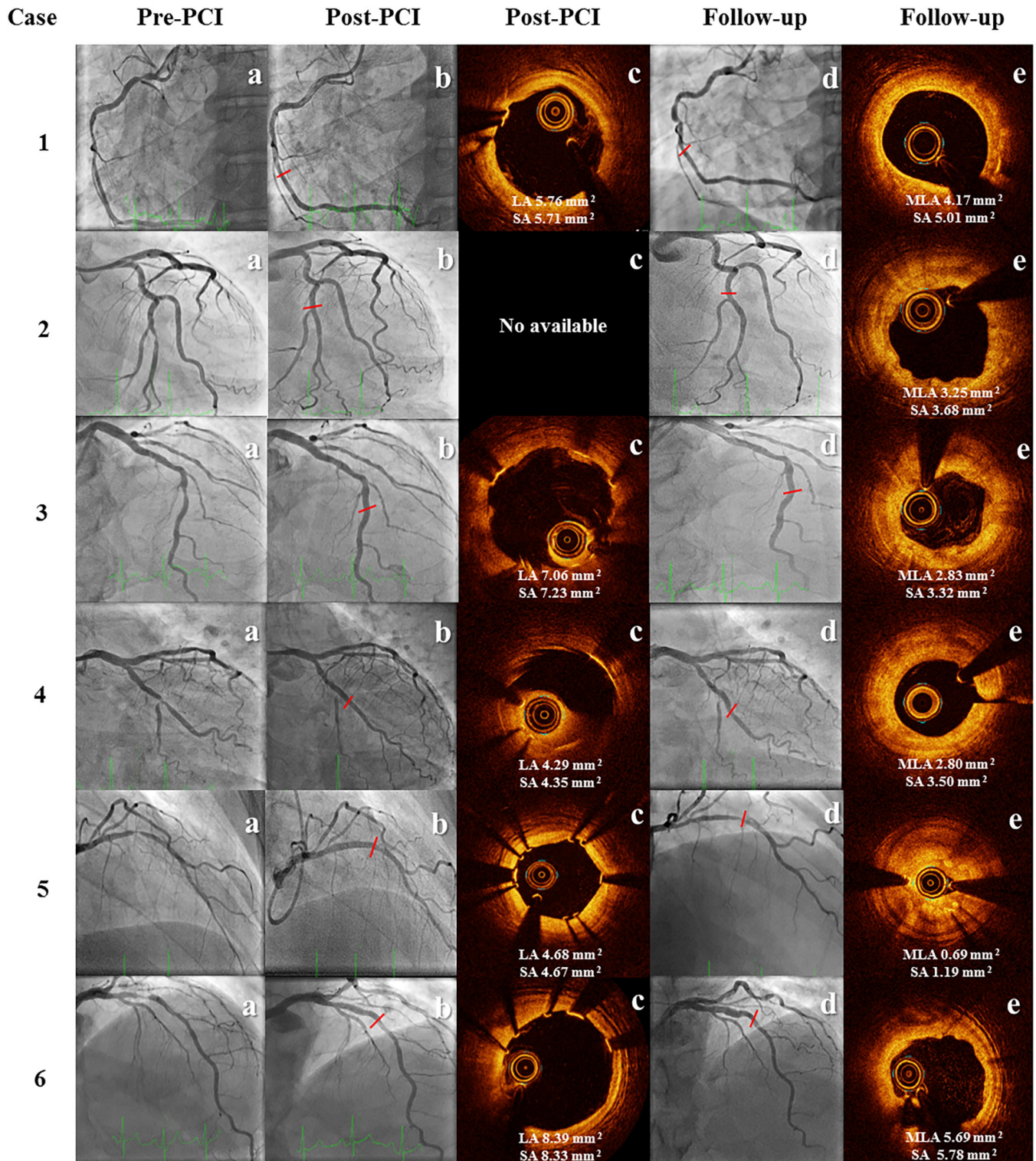


FIGURE 1 Angiography and OCT imaging at baseline and follow-up. Angiography imaging available for six patients showing target vessel at baseline before intervention (pre-PCI), post-intervention (post-PCI) and at invasive control (follow-up). OCT imaging available for five patients at post-intervention (post-PCI) and for six patients at invasive control (follow-up). Comparison of cross-sectional image at follow-up with the MLA matched with the same cross-sectional image at baseline. LA, lumen area; MLA, minimal lumen area; OCT, optical coherence tomography; post-PCI, post-percutaneous coronary intervention; pre-PCI, pre-percutaneous coronary intervention; SA, scaffold area [Color figure can be viewed at wileyonlinelibrary.com]

increase of lumen volume loss when expansion index is >1 ,²⁰ and previous data on Absorb BVS have correlated implantation in small vessel diameter with a higher rate of in-device restenosis,²¹ eccentricity, and

asymmetry.²² Performing pre-procedural intracoronary imaging for vessel sizing and lesion characterization might help to further improve lesion/device selection.²³ On the other hand, increasing device

visibility under fluoroscopy for future BRS generations could boost expansion optimization.

4.1 | Study limitations

This is a nonrandomized single-center study with small sample size. Patient and lesion selection was at the operator's discretion. Pre-PCI intracoronary imaging was not systematically performed. The heterogeneity of the invasive follow-up time points might have resulted in high SD caused by extreme values, and the lack of serial invasive imaging after 12 months prohibited statements on potential long-term lumen enlargement. The difficulty of identifying patent struts at follow-up did not allow us to perform methodical analysis of the entire scaffold and precluded any detailed analyses on neointimal hyperplasia volumes.

5 | CONCLUSIONS

The latest magnesium BRS iteration suffers from premature dismantling with subsequent loss of vessel support; together with incomplete distal device expansion, could have contributed to a higher than expected lumen loss. While our findings need to be confirmed in a randomized fashion, it seems imperative to follow the European working group recommendations on BRS and limiting their use to clinical trials or registries with adequate follow-up.²⁴ Finally, our results suggest that clinical and angiographic follow-up alone might not be sufficient to establish the safety and long-term efficacy of new BRS, and warrants the use of serial invasive coronary imaging at baseline and follow-up.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Tovar Forero MN, van Zandvoort L, Masdjedi K, et al. Serial invasive imaging follow-up of the first clinical experience with the Magmaris magnesium bioresorbable scaffold. *Catheter Cardiovasc Interv.* 2020;95: 226–231. <https://doi.org/10.1002/ccd.28304>