THE EFFECT OF STRUT PROTRUSION ON SHEAR STRESS DISTRIBUTION: HEMODYNAMIC INSIGHTS FROM A PROSPECTIVE CLINICAL TRIAL

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After scaffold implantation, local flow dynamics, particularly endothelial shear stress(ESS) is restored by newly constituted luminal surface. Scaffold design and strut embedment/protrusion-which is related to the underlying atherosclerotic plaque type, have impact on the local flow behaviors(1). Disrupted coronary flow in the vicinity of struts induces recirculations and stagnation zones with lower shear stress that triggers biological mechanisms of platelet aggregation and neointimal hyperplasia(1). In the present study, we investigated strut protrusion in two different bioresorbable scaffolds(BRS) and its implication on ESS distribution.

The present analysis processed data from the patients enrolled in the Mirage first-in-man trial. During implantation, all lesions were predilated, post-dilatation was left at the operator's discretion. Nine patients treated with Absorb and 11 patients treated with Mirage scaffolds were selected for computational fluid dynamic(CFD) study. Case selections were based on the orthogonal(≥30°) angiographic projections with minimal foreshortening and clearly documented lumen on OCT. Scaffold designs are described elsewhere(2). The struts of Absorb were automatically detected by OCT software,QCU-CMS(Leiden University Medical Center,Netherlands). Since QCU-CMS has no automatic detection for circular struts of Mirage,the struts of Mirage were depicted as part of the lumen contours and interpolation of the true lumen contour allows the assessment of the protrusion of the Mirage struts(2, 3). In OCT,plaque composition was characterized and predominant plaque type was determined when several plaque types were identified in one cross-section. The eccentricity index(EI) and expansion index were calculated in OCT. Three-dimensional(3D) reconstruction was performed using a validated methodology(2). CFD techniques were employed to process 3D-models.ESS was estimated around the circumference of the lumen per 5^{o}-interval and along the axial-direction per 0.2mm-interval. As the data have multilevel structure, mixed linear model was used for comparisons of continuous variables in cross-section level analysis.

All scaffolds were 3.0x18mm in both groups. Mean luminal area(7.12±1.24mm^2 vs. 7.10±1.31mm^2,p=0.98) and mean scaffold area(7.48±0.94 mm^2 vs. 7.16±1.14 mm^2,p=0.87) were comparable between Absorb and Mirage. Mean strut area per cross-section was significantly higher in Mirage(0.31±0.03mm^2) compared to Absorb(0.18±0.06mm^2) (p<0.0001). EI was higher in Absorb(0.90±0.06) compared to Mirage(0.86±0.08)(p<0.001). In Absorb, EI for fibro-calcific plaques,fibroatheromas,fibrous plaques and normal vessel segments were 0.87±0.05, 0.87±0.06, 0.91±0.05 and 0.89±0.04, respectively($p_{overall}$<0.0001).In Mirage,EI for fibro-calcific plaques,fibroatheromas,fibrous plaques and normal segments were 0.80±0.08, 0.82±0.08, 0.86±0.08 and 0.93±0.02, respectively($p_{overall}$<0.0001).Strut protrusion was significantly less in Mirage (77±23µm)(62±19% of strut thickness) compared to Absorb(145±31µm)(92±20% of strut thickness)(p<0.0001). Lowest strut protrusion was noted in fibro-atheromas**(Figure)**. At cross-section-level analysis,mean ESS was significantly higher in Mirage(2.46±2.17Pa) than in Absorb(1.39±0.66Pa)(p<0.0001). In 5°-level analysis, 49.30% of the luminal surface in Absorb and 24.48% in Mirage was exposed to low-ESS(<1.0 Pa)(p<0.0001). CFD results demonstrated higher ESS in fibroatheromas in both scaffolds. Lowest ESS levels were documented in fibrous and fibro-calcific plaques**(Figure)**.

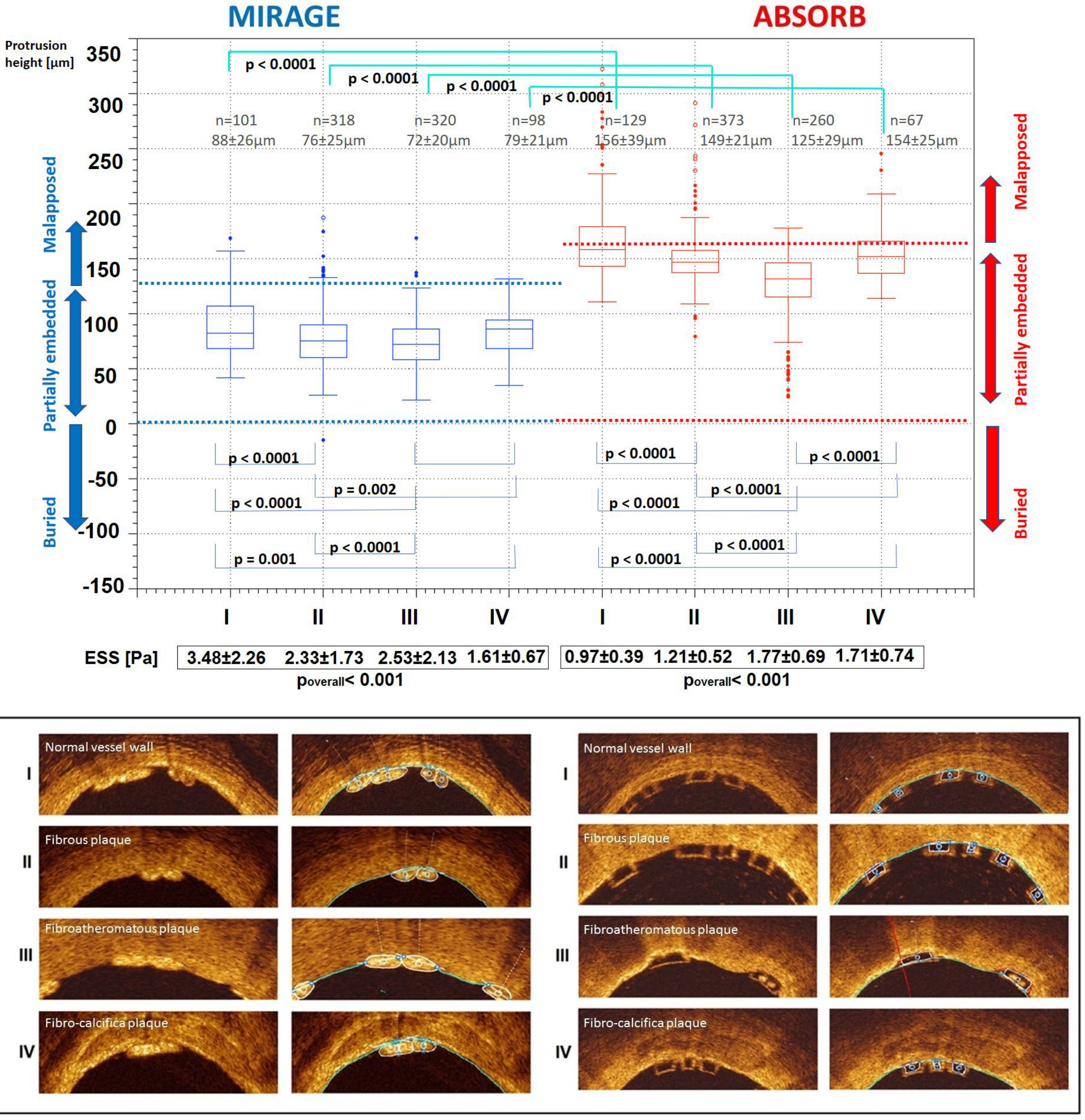
In the present analysis;1-Strut protrusion was lower in Mirage compared to Absorb;2-In both scaffold types,lower protrusion was noted in fibroatheromas compared to other plaque types; 3-Differences in protrusion affected local hemodynamics with higher ESS in Mirage than in Absorb; 4-ESS is higher in fibroatheromas when compared to other plaque types. Fibroatheromas are more compliant than fibrous and fibro-calcific plaques and provide deeper penetration resulting in less protrusion. In the present study, fibroatheromas revealed higher strut penetration than fibrous and fibro-calcific plaques in both scaffolds. Mirage struts embedded deeper than Absorb in all plaque types.The factor for higher embedment in Mirage should be sought in the principles of *contact mechanics*(4).The penetration distance(embedment depth) is in an inverse relation with strut contact-radius in which circular surface of strut in Mirage has shorter contact-radius than square-shaped struts of Absorb(4).When the same force is applied, device with a higher foot-print area would generate a lower pressure on the vessel wall according to the simple principle:Pressure=Force/Area. Circular geometries have also the advantage of enabling the flow acceleration crossing over convex strut surface with less disruption, that might also contribute to the improvement in shear stress not only on top-of-the struts but also in the inter-strut zones in Mirage(5). Absorb has lower vessel coverage ratio than Mirage(25% vs 46%). Due to this fact, higher vessel coverage in Mirage requires higher implantation pressures. With the advantage of higher tensile strength(300MPa Mirage vs 60-70MPa Absorb) and higher elongation-at-break in Mirage than Absorb,higher deployment pressures can be applied to embed circular struts of Mirage, deeper than Absorb with low disruption risk. Shear stress distribution seems to be related with scaffold design and strut penetration. Protrusion analysis may help to improve implantation process and hemodynamic performance of bioresorbable scaffolds. Poorly embedded scaffolds can create area with disturbed atheroprone low shear stress zones that may contribute the risk of acute scaffold thrombosis to late neo-atherosclerosis formation adjacent to the struts and later plaque rupture.

Figure Legend:

Figure: In both scaffold groups, due to higher strut penetration, fibro-atheromatous plaques demonstrated less protrusion distances compared to other plaque types.

References:

1. Jimenez JM, Davies PF. Hemodynamically driven stent strut design. Annals of biomedical engineering. 2009;37(8):1483-94.
2. Tenekecioglu E, Sotomi Y, Torii R, Bourantas C, Miyazaki Y, Collet C, et al. Strut protrusion and shape impact on endothelial shear stress: insights from pre-clinical study comparing Mirage and Absorb bioresorbable scaffolds. The international journal of cardiovascular imaging. 2017.
3. Sotomi Y, Tateishi H, Suwannasom P, Dijkstra J, Eggermont J, Liu S, et al. Quantitative assessment of the stent/scaffold strut embedment analysis by optical coherence tomography. The international journal of cardiovascular imaging. 2016;32(6):871-83.
4. Johnson KL, Johnson KL. Contact Mechanics: Cambridge University Press; 1987.
5. Anderson JD. Fundamentals of aerodynamics. Sixth edition. ed. New York, NY: McGraw-Hill Education; 2017. pages cm. p.


MIRAGE
ABSORB
Protrusion height [μm]
350
300
250
200
150
100
50
0
-50
-100
-150
p < 0.0001
p < 0.0001
p < 0.0001
p < 0.0001
n=101
88±26μm
n=318
76±25μm
n=320
72±20μm
n=98
79±21μm
n=129
156±39μm
n=373
149±21μm
n=260
125±29μm
n=67
154±25μm
Malapposed
Partially embedded
Buried
p < 0.0001
p = 0.002
p < 0.0001
p < 0.0001
p = 0.001
p < 0.0001
p < 0.0001
p < 0.0001
p < 0.0001
p < 0.0001
p < 0.0001
I
II
III
IV
I
II
III
IV
ESS [Pa]
3.48±2.26
2.33±1.73
2.53±2.13
1.61±0.67
0.97±0.39
1.21±0.52
1.77±0.69
1.71±0.74
$p_{overall}$ < 0.001
$p_{overall}$ < 0.001
Normal vessel wall
Fibrous plaque
Fibroatheromatous plaque
Fibro-calcifica plaque
Normal vessel wall
Fibrous plaque
Fibroatheromatous plaque
Fibro-calcifica plaque