Final Optical Coherence Tomography Results from the COBRA PzF SHIELD Trial

Long–Term Arterial Response to A Novel Coronary Stent System with Nano-Thin Surface Coating for Pro-Endothelialization

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Background

- The Polyzene-F™ NanoCoated Coronary Stent System (PzF stent) has shown reduced thrombogenicity and inflammation in preclinical studies, and favorable clinical and angiographic outcomes with very low stent thrombosis in initial clinical experience (1-4).
- The PzF SHIELD study was the first multicenter, prospective, single-arm, non-randomized trial, which included an optical coherence tomography (OCT) cohort to provide mechanistic and biological insights (5).

1) Satzl S et al. Invest Radiol, 2007;42:303-11. 2) Radeleff B et al. Cardiovasc Interv Radiol, 2008;31:971-80.
3) Tamburino C et al. JACC Cardiovasc Interv, 2009;2:197-204. 4) Tamburino et al. EuroIntervention, 2012;7:1062-8.
5) Cutlip DE et al. JACC Cardiovasc Interv, 2017;10:160-7.

Objective

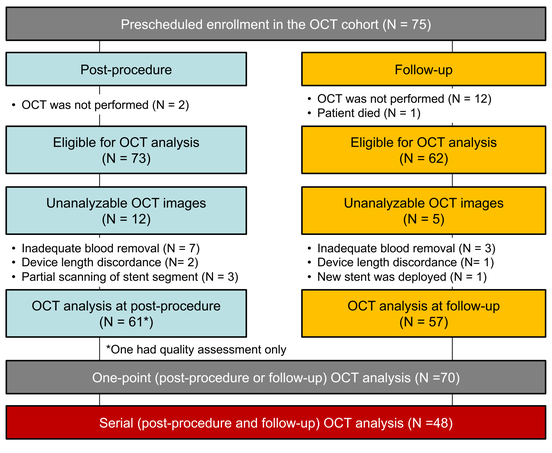
- This study aimed to characterize OCT findings in the PzF SHIELD study, focusing especially on acute device performance related to long-term outcomes.

Methods

1) Study design and population

- The PzF SHIELD study enrolled 296 patients undergoing percutaneous coronary intervention (PCI) from 35 investigational centers (including 23 centers in the United States).
- Among them, 75 patients were enrolled in the official OCT cohort of the study.
- The primary endpoints of this OCT analysis were binary in-segment restenosis (ISR) defined as a diameter stenosis ≥50% by quantitative coronary angiography (QCA), and clinically-driven or non-clinically driven target vessel revascularization (TVR).
- Key inclusion criteria:
  - >18 years old
  - Symptomatic ischemic heart disease (stable or unstable angina, positive functional study, or acute myocardial infarction > 72 hours)
  - Single *de novo* target lesions in a native coronary artery
  - Reference vessel diameter ≥ 2.50 mm and ≤ 4.00 mm
  - Lesion length ≤ 24 mm
- Key exclusion criteria:
  - Previous PCI within 30 days
  - Any previous stent within 15 mm of the target lesion
  - Previous drug-eluting stent (DES) anywhere within the target vessel
  - Left ventricular ejection fraction < 30%
  - Comorbid condition limiting participation or life expectancy < 12 months
  - Inability to comply with dual antiplatelet therapy (DAPT) for 1 month
  - Unprotected left main lesion
  - Non-target lesions > 50% within the target vessel
  - Excessive vessel tortuosity or severe calcification
  - Target vessel containing thrombus
  - Bifurcation lesion with side branch ≥ 2 mm in diameter

Patient flowchart



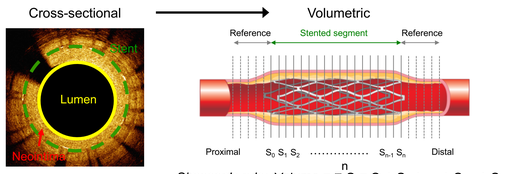
Methods

2) Core lab analysis

- QCA: Beth Israel Deaconess Medical Center
- OCT: Stanford Cardiovascular Core Analysis Laboratory

3) OCT measurements

- Standard imaging procedure with automated pullback at 20 mm/s.
- Lumen, stent, and neointimal (stent minus lumen) areas were measured at 1-mm intervals from proximal to distal reference segments (5 mm for each) throughout the target segment.
- Each volume was standardized as volume index (volume / length, mm^3/mm).



Simpson's rule: Volume = $\sum_{i=0}^{n} S_i = S_0 + S_1 + \cdots\cdots + S_{n-1} + S_n$

- Volumes: lumen, stent, and neointima
- Volume index = volume / length (mm^3/mm)

4) Definition of stent over-expansion by OCT

- **Stent over-expansion index** $_{volume}$ = $\frac{\textit{Stent volume index}}{\textit{Smaller reference* lumen volume index}}$
- **Stent over-expansion index** $_{area}$ = $\frac{\textit{Minimum stent area (MSA)}}{\textit{Smaller reference* lumen volume index}}$

*proximal or distal reference

Results

1) Baseline patient, lesion and procedural characteristics of the OCT cohort

Variables	Values
Patient characteristics	**N = 70**
Age (years)	66 ± 11
Male	48 (68.6%)
Body mass index (kg/mm^2)	28.9 ± 4.9
Current smoker	19 (27.9%)*
Hypertension	51 (75.0%)*
Hyperlipidemia	56 (82.4%)*
Diabetes mellitus	16 (23.5%)*
Prior PCI	18 (25.7%)
Prior myocardial infarction	13 (18.6%)
Clinical presentation	
Stable angina	42 (60.0%)
Positive functional study	10 (14.3%)
Unstable angina	17 (24.3%)
Acute myocardial infarction (>72 hours)	1 (1.4%)
Target lesion characteristics	**N = 70**
Target vessel	
Left anterior descending artery	28 (40.0%)
Left circumflex artery	11 (15.7%)
Right coronary artery	31 (44.3%)
Lesion location	
Proximal	31 (44.3%)
Mid	31 (44.3%)
Distal	8 (11.4%)
Calcification (moderate or severe)	31 (44.3%)
Lesion type (B2/C)	53 (75.7%)
Procedural characteristics	**N = 70**
Pre-dilation	
Pre-dilation performed	67 (95.7%)
Nominal balloon diameter (mm)	2.78 ± 0.41
Pre-dilation balloon pressure (atm)	13.2 ± 3.5
Stent deployment	
Nominal stent diameter (mm)	3.23 ± 0.42
Total stent length (mm)	18.7 ± 6.2
Deployment pressure (atm)	14.1 ± 2.9
Post-dilation	
Post-dilation performed	46 (65.7%)
Nominal balloon diameter (mm)	3.48 ± 0.56
Balloon pressure (atm)	16.9 ± 4.0

*Missing data in 2 cases

Results

2) QCA results of the OCT cohort

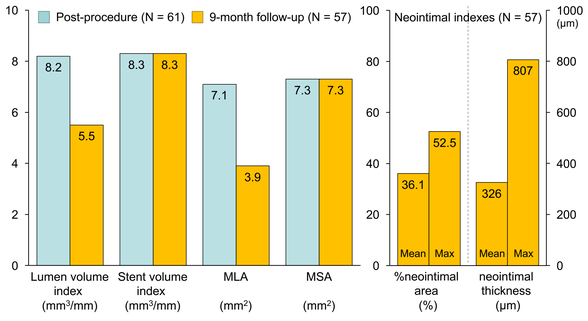
Variables	
Baseline	**N = 70**
Target lesion length (mm)	13.1 ± 5.4
Reference vessel diameter (mm)	2.86 ± 0.46
MLD (mm)	0.98 ± 0.34
Percent diameter stenosis (%)	65.5 ± 11.6
Post-procedure	**N = 68**
In-stent MLD (mm)	2.70 ± 0.40
In-stent diameter stenosis (%)	5.8 ± 8.3
In-segment MLD	2.32 ± 0.47
In-segment diameter stenosis (%)	19.8 ± 8.3
9-months follow-up	**N = 63**
In-stent MLD (mm)	1.91 ± 0.63
In-stent late lumen loss (mm)	0.77 ± 0.46
In-stent diameter stenosis (%)	32.4 ± 18.0
In-segment MLD	1.81 ± 0.60
In-segment late lumen loss (mm)	0.49 ± 0.49
In-segment diameter stenosis (%)	35.8 ± 16.7
In-stent binary restenosis*	10 (15.9%)
In-segment binary restenosis*	12 (19.0%)

3) OCT results at reference segment

Variables	Post-procedure	9-month follow-up
Proximal reference segment		
Number of segments analyzed	52	47
Mean lumen diameter (mm)	3.23 ± 0.58	2.99 ± 0.61
Lumen volume index (mm^3/mm)	8.5 ± 3.1	7.3 ± 3.0
Edge tear	18 (34.6%)	1 (2.1%)
Distal reference segment		
Number of segments analyzed	59	56
Mean lumen diameter (mm)	2.92 ± 0.60	2.76 ± 0.68
Lumen volume index (mm^3/mm)	7.0 ± 3.0	6.3 ± 2.9
Edge tear	13 (22.0%)	2 (3.6%)
Either reference segment		
Number of segments analyzed	61	57
Smaller mean lumen diameter (mm)	2.89 ± 0.56	2.66 ± 0.65
Smaller lumen volume index (mm^3/mm)	6.8 ± 2.7	5.9 ± 2.7
Edge tear	25 (41.0%)	3 (5.3%)

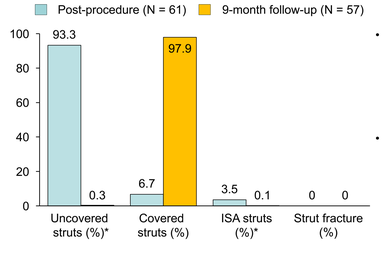
- Both reference lumen diameters and areas were well maintained at 9-month follow-up.
- Most of residual dissection seen at reference segment at post-procedure were resolved at follow-up.

4) OCT results at stented segment (stent-level analysis)



- Post-procedure OCT revealed well-expanded stents with mean MSA of 7.3 mm^2.
- At 9-month follow-up, mean neointimal thickness was 326 ± 148 μm, which resulted in %neointimal volume (or mean area) of 36.1 ± 15.9 % .

5) OCT results at stented segment (strut-level analysis)



- At 9-month follow-up, neointimal coverage was nearly completed, and uncovered struts and ISA (incomplete strut apposition) struts were only 0.3% and 0.1%, respectively.
- No late-acquired ISA, strut fracture, nor intra-stent thrombus was detected at 9-month follow-up.

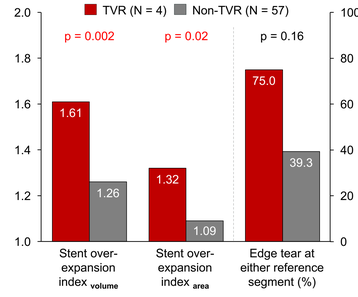
*Struts at side-branch orifice were excluded from analysis

6) Comparisons of baseline variables: patients with versus without binary ISR by angiography

Variables	ISR (N = 12)	Non-ISR (N = 51)	p value
Patient characteristics			*Missing data in 1 case
Age (years)	68 ± 12	65 ± 11	0.54
Hypertension	9 (81.8%)*	39 (76.5%)	0.69
Hyperlipidemia	8 (72.7%)*	43 (84.3%)	0.38
Diabetes mellitus	1 (9.1%)*	14 (27.5%)	0.16
Target lesion characteristics			
Target vessel			0.71
Left anterior descending artery	4 (33.3%)	22 (43.1%)	
Left circumflex artery	1 (8.3%)	6 (11.8%)	
Right coronary artery	7 (58.3%)	23 (45.1%)	
Lesion location			0.38
Proximal	5 (41.7%)	22 (43.1%)	
Mid	4 (33.3%)	24 (47.1%)	
Distal	3 (25.0%)	5 (9.8%)	
Calcification (moderate or severe)	3 (25.0%)	26 (51.0%)	0.10
Lesion type (B2/C)	9 (75.0%)	38 (74.5%)	0.97
Procedural characteristics			
Pre-dilation			
Pre-dilation performed	12 (100%)	48 (94.1%)	0.25
Nominal balloon diameter (mm)	2.77 ± 0.58	2.79 ± 0.36	1.00
Pre-dilation balloon pressure (atm)	13.8 ± 2.8	12.9 ± 3.7	0.35
Stent deployment			
Nominal stent diameter (mm)	3.13 ± 0.53	3.24 ± 0.41	0.49
Total stent length (mm)	18.4 ± 8.5	18.6 ± 5.5	0.65
Post-dilation			
Post-dilation performed	7 (58.3%)	34 (66.7%)	0.59
Nominal balloon diameter (mm)	3.18 ± 0.69	3.53 ± 0.55	0.20
Balloon pressure (atm)	17.7 ± 4.9	16.2 ± 3.0	0.62
OCT indices at post-procedure			
Stent volume index (mm^3/mm)	7.8 ± 3.0	8.4 ± 2.7	0.52
MSA (mm^2)	6.8 ± 3.1	7.5 ± 2.5	0.46
Stent over-expansion index $_{volume}$	1.45 ± 0.28	1.23 ± 0.21	0.007
Stent over-expansion index $_{area}$	1.22 ± 0.19	1.09 ± 0.18	0.03
% ISA struts	2.0 ± 5.6	4.1 ± 5.8	0.03

- Baseline clinical, lesion, and OCT variables were comparable between patients with and without binary ISR by QCA, except for higher stent over-expansion indices and lower % ISA struts in patients with binary ISR.
- After adjusting % ISA struts, stent over-expansion index $_{volume}$ remained associated with binary ISR by QCA (p = 0.02).

7) Stent over-expansion indices and residual edge tear at post-procedure: TVR versus non-TVR



- TVR at 9-month follow-up occurred only in 7.1% (N = 5) patients, which included 4 target lesion revascularization.
- Post-procedure OCT was available in 61 patients (4 TVR: 57 non-TVR)
- Patients with TVR showed significantly higher stent over-expansion indices compared with those without.
- Edge tear at reference segment (either proximal or distal) tended to be more frequent in patients with TVR compared with those without.

Limitations

- This was a retrospective analysis with small sample size and approximately 30 % of the patients did not complete serial OCT analysis; therefore further studies with larger sample size are warranted to confirm clinical significance of the present findings.
- Study population consisted of patients who fulfilled the inclusion/exclusion criteria of the PzF SHIELD study (i.e. patients with primarily stable coronary artery disease and single *de novo* relatively non-complex target lesions).

Conclusions

- The final OCT results of PzF SHIELD demonstrated excellent device performance with no adverse arterial response, achieving clinical outcomes comparable to current drug-eluting stents with antiproliferative agents.
- Appropriate optimization of procedures to avoid arterial injury at deployment may further improve the long-term clinical outcomes.

Disclosures

- Drs. D.E.C and S.S. are research advisors of CeloNova Biosciences; Dr. M.B. is an employee of CeloNova Biosciences; the other authors have nothing to disclose.