Prevail Introduction & Case Sharing

Right Case, Right Time : Prevail

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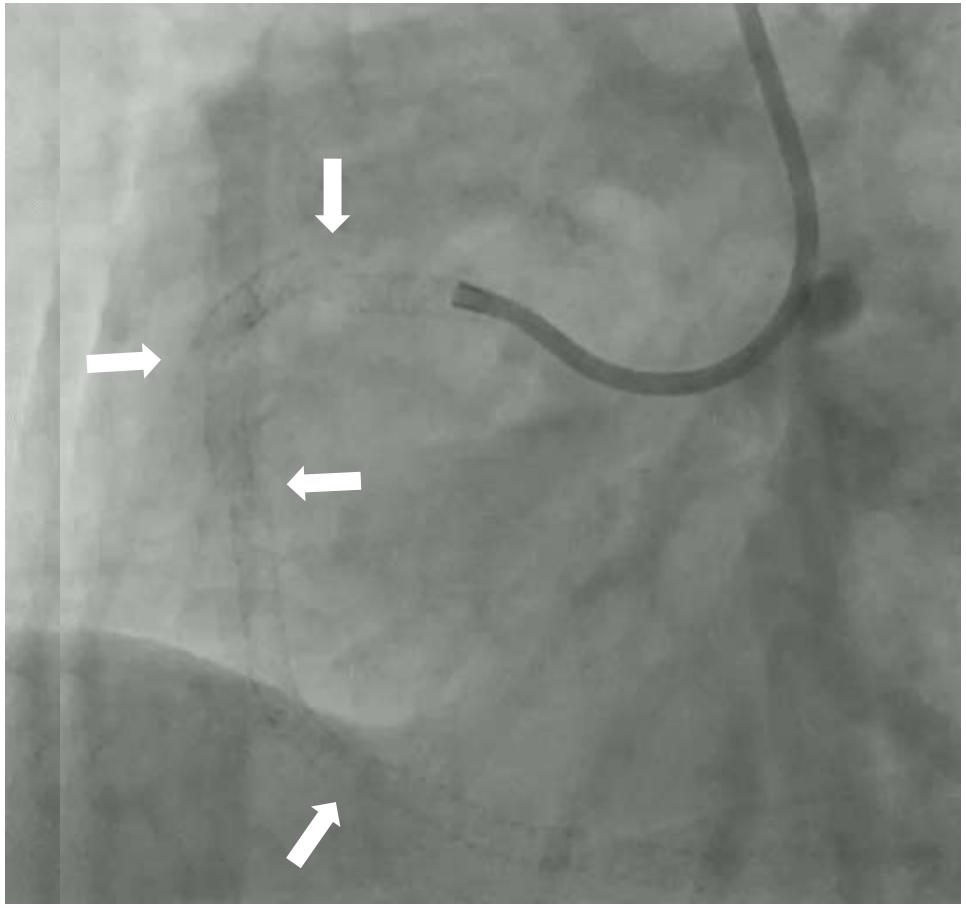
Disclosure

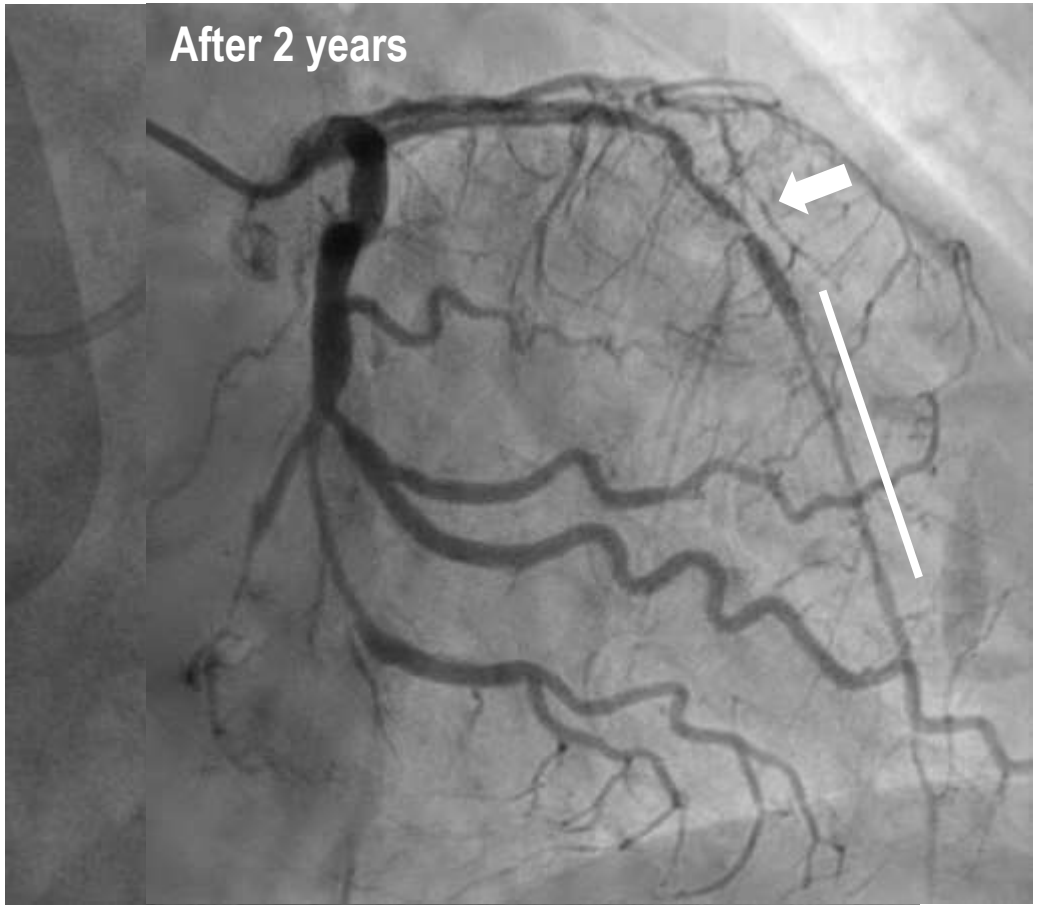
- Relationships with commercial interests:
- Grants/Research Support: Abbott Korea, Abbott Vascular, Korean Cardiac Research Foundation
- Speakers Bureau/Honoraria: Abbott Vascular
- Consulting Fees: None
- Other: None

Problems Arising from Leaving Metals and Polymers

Full metal jacket at p-dRCA → Multiple stent fractures



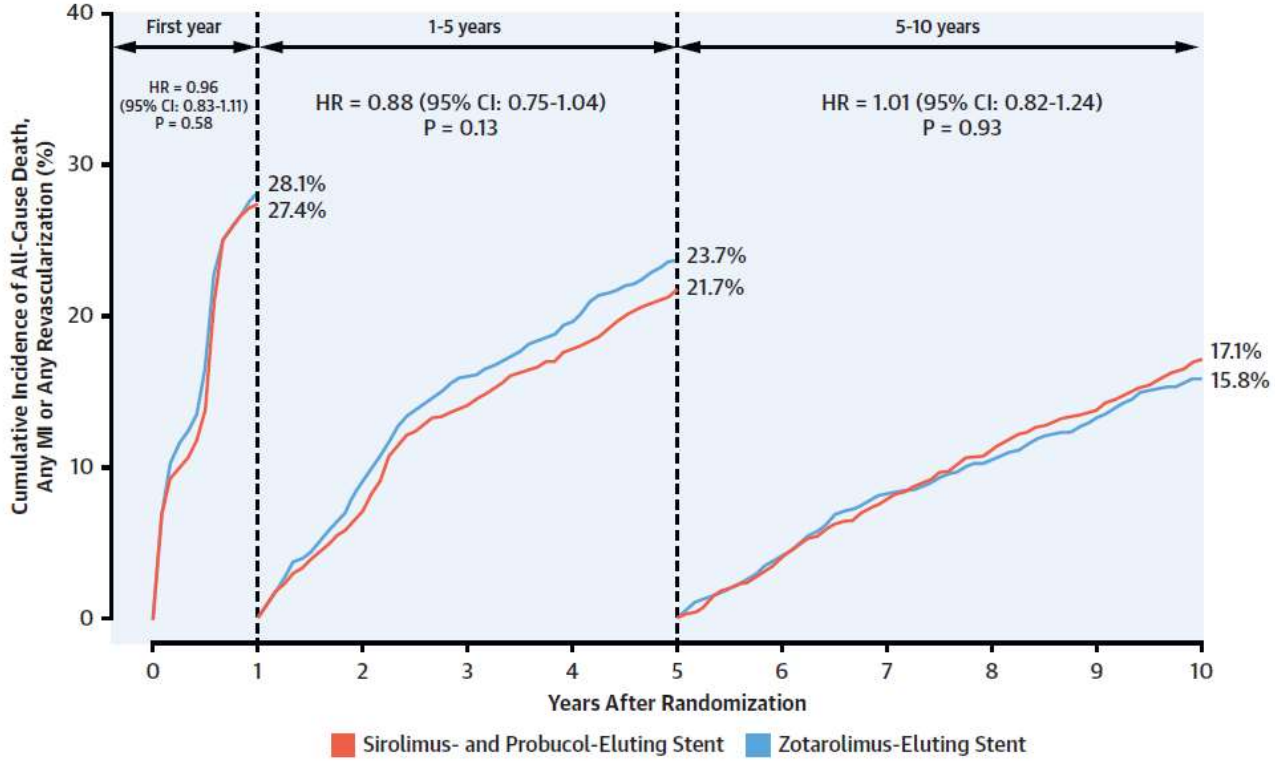
Multiple and long stenting → Recurrent ISR



Very Long Term Clinical Outcome after Drug-Eluting Stent Implantation

ISAR-TEST 5 Trials, Patient N=3,002
Coroflex ISAR vs. Resolute

CENTRAL ILLUSTRATION Landmark Analysis, Patient-Oriented Outcomes According to Treatment Groups

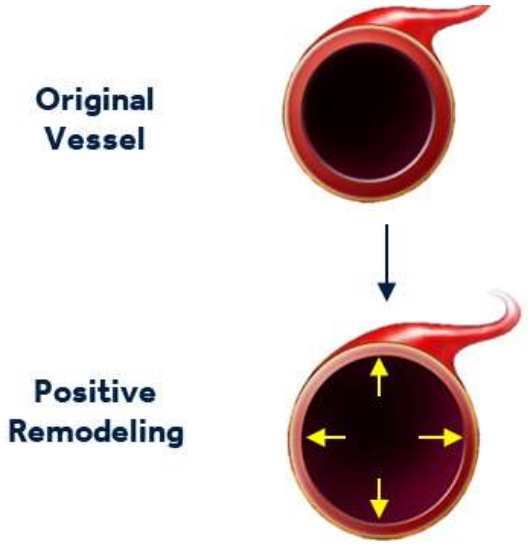


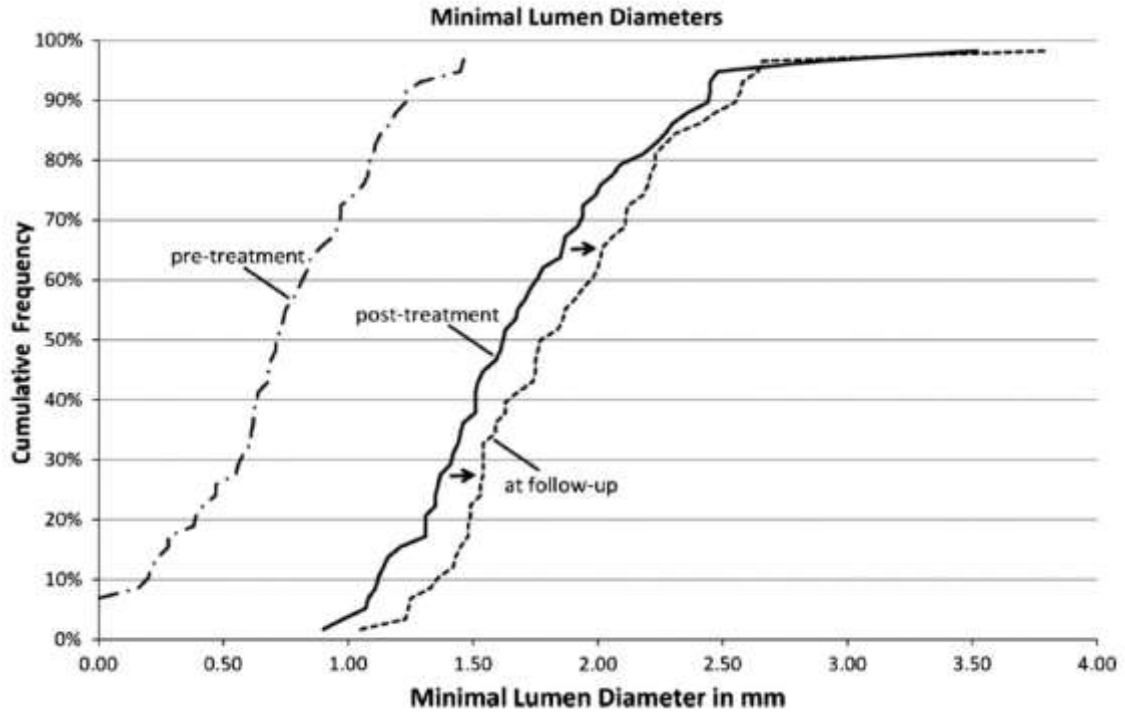
Regardless of stent type,
Death, MI, revascularization occur in linear fashion along with the time.

J Am Coll Cardiol. 2020;76(2):146–58.

Advantages of DCB Treatment – “Leave Nothing Behind”

- Up to 10% of positive remodelling of the treated vessel segment might occur after DCB treatment because no metallic material is left in the vessel to prevent later enlargement.
- The recommended duration of dual antiplatelet therapy is short (1 month for stable coronary artery disease) after PCI using DCB.



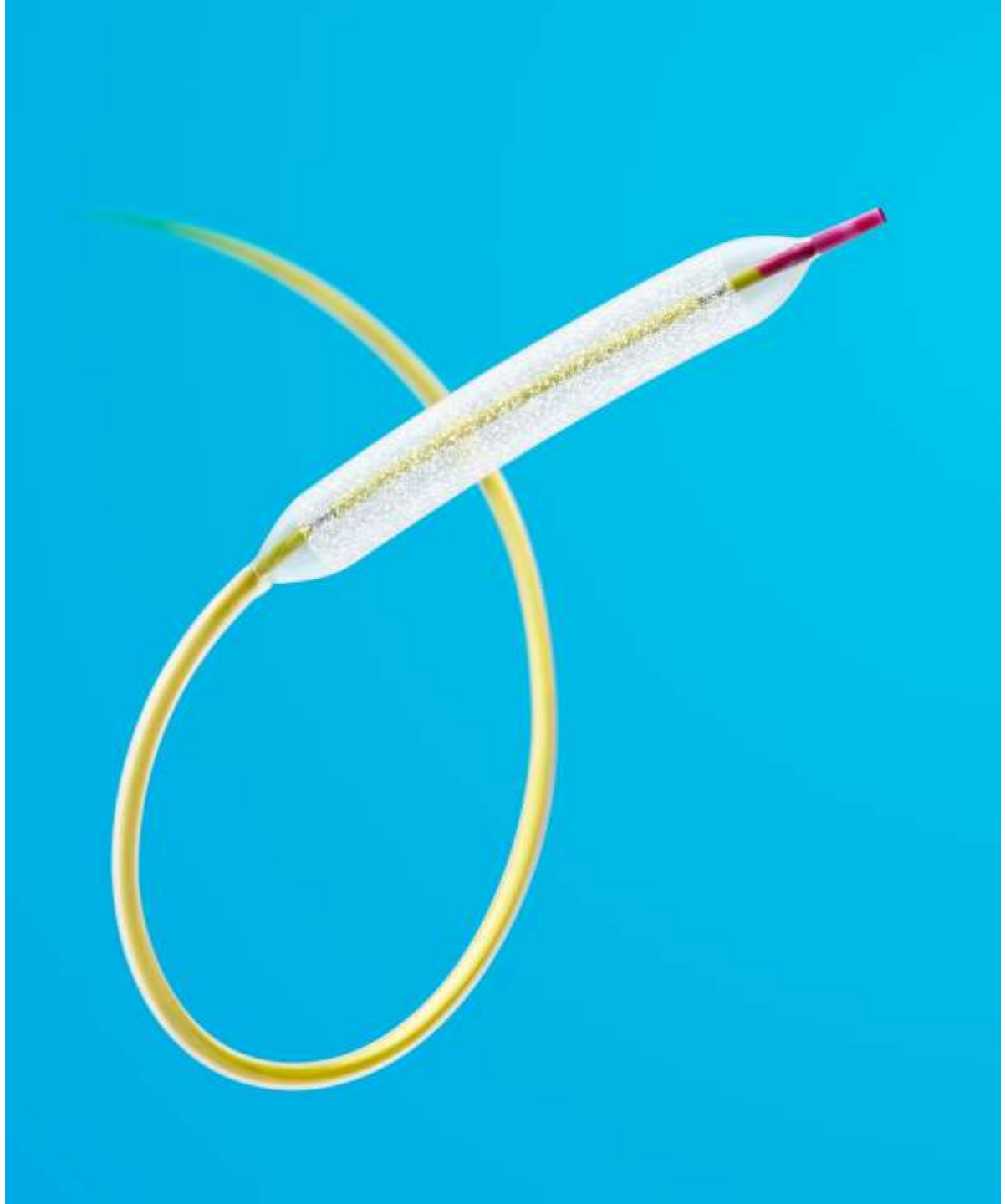


Kleber FX et al. Clin Res Cardiol 2015;104:217–25; Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239
Jeger et al. J Am Coll Cardiol Intv. 2020;13(12):1391-1402; Kleber et al. Clin Res Cardiol 2015;104:217–25; Cortese et al. J Am Coll Cardiol Intv 2015;8:2003–9.

PREVAIL™ DRUG COATED BALLOON

Prevail™

Paclitaxel Coated PTCA
Balloon Catheter



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PREVAIL™ DRUG COATED BALLOON
CHARACTERISTICS

Prevail DCB

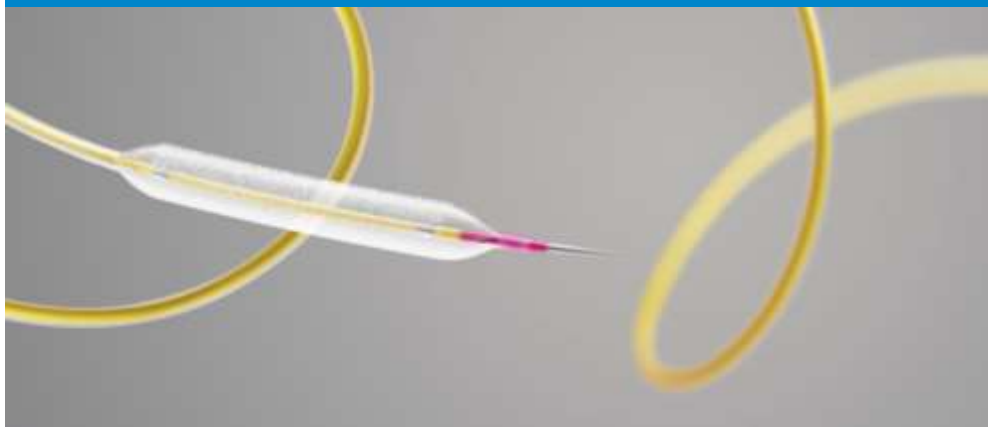
IN.PACT™ Falcon DCB

FreePac™ coating

Paclitaxel drug — potent antiproliferative drug persists in the tissue throughout the healing process.[1,2]

Urea excipient — highly biocompatible excipient enables rapid drug transfer to the vessel wall within 30–60 seconds.[3,4]

Enhanced delivery system† and hydrophilic coating



PowerTrac™ technology combined with a hydrophilic coating facilitates superior deliverability and device performance.[5]

Third-party brands are trademarks of their respective owners.
† Based on bench test data, 2020. Bench test data may not be indicative of clinical performance.
[1] PS762 preclinical study report: An Evaluation of the Medtronic Drug Coated Coronary Balloon Catheter in a Porcine Artery Model, 2016. On file at Medtronic.
[2] Cremers B, et al. *Minerva Cardioangiol* 2010: Oct;58(5):583–8.
[3] Cremers B, et al. *Thromb Haemost*
[4] Prevail Instructions for Use
5 Compared with IN.PACT Falcon DCB, Deliverability defined as pushability. Based on bench test data, 2020. Bench test data may not be indicative of clinical performance

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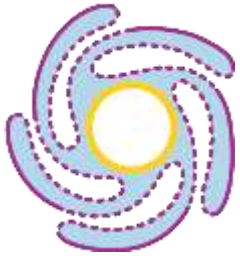
DRUG AND EXCIPIENT
AN OPTIMISED PARTNERSHIP

Protected FreePac coating

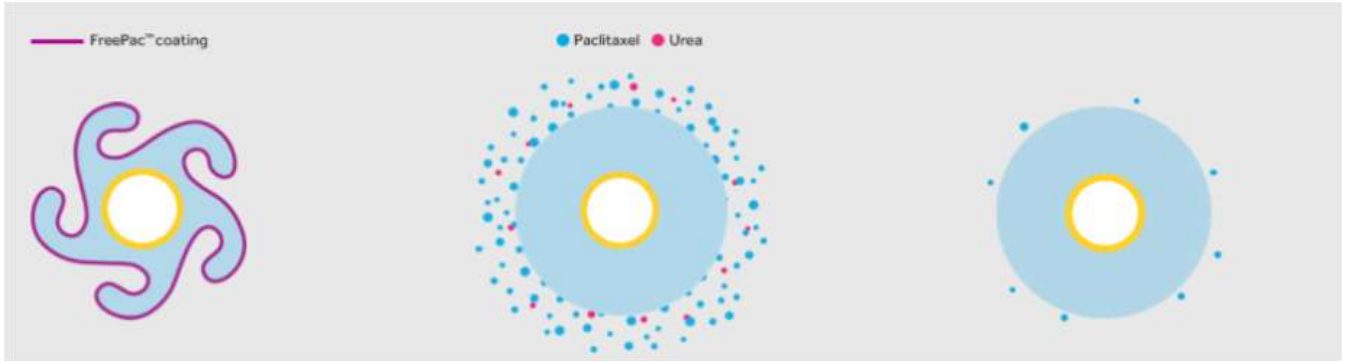


Up to 65% of drug is protected within the folds

FreePac Coating

FreePac™ coating combines two proven[1] components that work together:

- **Paclitaxel** — potent antirestenotic drug[2]
- **Urea** — biocompatible excipient that enables rapid drug delivery[3,4]



Inflation begins at the target lesion

0–30 sec

Balloon expands, releasing majority of the drug. FreePac coating is fully exposed to the artery and urea allows paclitaxel to absorb into the vessel wall

30–60 sec

Optimal release completed

[1] Virmani R. Arterial wall response to drug-coated balloons Confluence September 2016: 13: 15–19.
[2] Cremers B, et al. *Minerva Cardioangiol* 2010: Oct;58(5):583–538.
[3] Prevail Instructions for Use.
[4] Barrett BJ. *J Am Soc Nephrol.* 1994;5:125-137.

WHICH DRUG FOR DCB?
PACLITAXEL HAS UNIQUE CHARACTERISTICS MAKING IT SUITABLE FOR A DCB

A DCB drug must achieve:

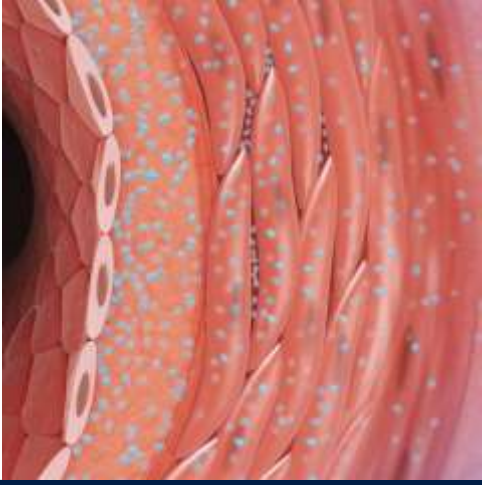
- **Limited drug loss during delivery** (i.e. it must be **hydrophobic**)
- **Quick and deep tissue penetration** (i.e. it must be **lipophilic**)
- **Sustained and potent** antiproliferative action (i.e. **potent** inhibitor of cell proliferation)

So far, paclitaxel has been considered as the drug of choice for DCB because of its rapid tissue uptake.

	Limus	Paclitaxel
History	Discovered in 1970's (Easter Island soil) Immunosuppressive and antiproliferative drug	Discovered 1960's (Pacific yew tree bark) Antiproliferative chemotherapy drug
Mechanism of Action	mTOR inhibitor TEMPORARY – puts cells in a resting state, once the drug is gone, proliferation resumes	Disrupts microtubules LONG LASTING – durable effect, induces cell death, more potent inhibitor of cell proliferation than limus drugs
Key Features	Less lipophilic – slower transfer and limited tissue penetration	More lipophilic – attracted to lipids and proteins in the tissue/cells, which leads to rapid transfer and deep penetration into tissue
PCI Device Application	**Ideal for DES applications**, where controlled elution allows sustained delivery; especially beneficial when foreign material is left behind in the vessel (i.e. polymer or stent)	**Ideal for DCB applications**, where short delivery time requires rapid uptake and prolonged retention of drug; especially beneficial when there is no implant left behind and elution cannot be moderated

Habib and Finn. Intervent Cardiol Clin 5 (2016) 321–329. Ramakrishna et al. Journal of Clinical and Diagnostic Research. 2017;11(6).Rowinsky EK, Donehower RC. Paclitaxel (Taxol).N engl J Med 1995;332:1004-1014
Wild et al. Circulation. 1997;96:636–645; Schnorr B et al. Minerva Cardioangiol. 2010;58(5):567–582.; Margolis et al. Clin Cardiol 2007;30:165-170. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3561035/

PACLITAXEL HAS SUSTAINED TISSUE RESPONSE[1]



RAPID DRUG ABSORPTION

Urea excipient enables rapid and reliable drug transfer to vessel wall within **30–60 seconds.**[2,3]

93% of delivered paclitaxel is retained in solid phase at **24 hours,** critical to ensuring prolonged tissue response.[1]

SUSTAINED BENEFIT

Solid-phase paclitaxel remains in tissue throughout the healing process.[1]

CLINICAL BENEFITS

The PREVAIL Study showed[5]:

- **Very low late loss** at 6 months **(0.05 ±0.44 mm)**[5]
- 4.0% TLR at 6 months[5]
- 0% stent thrombosis, TVMI, and cardiac death through 12 months[5]

[1] PS762 preclinical study report: An Evaluation of the Medtronic Drug Coated Coronary Balloon Catheter in a Porcine Artery Model. 2016. On file at Medtronic.
[2] Cremers B, et al. *Thromb Haemost*. 2009:101 (201-6)
[3] Prevail Instructions for Use.
[4] 10582513DOC_A1 report on file at Medtronic.
[5] Latib A, et al. *J Invasive Cardiol*. Published online August 19, 2021. PREVAIL study did not have powered endpoints.
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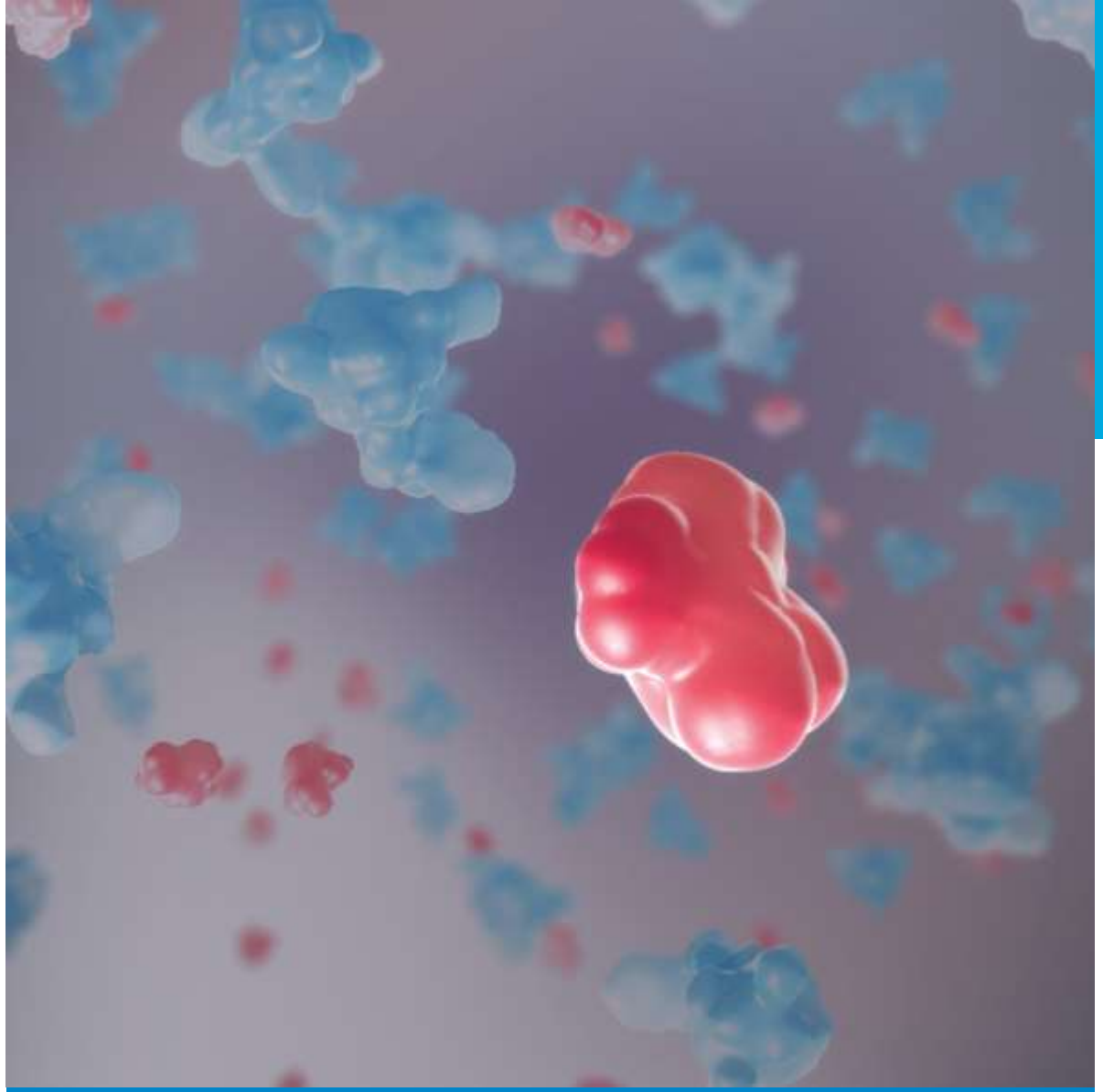
THE ONLY DCB WITH UREA*[1]

Urea excipient:

- Is a biocompatible naturally occurring molecule[2]
- Plays a critical role in delivering solid-phase drug to the tissue
- Enables rapid drug transfer to the vessel wall within 30–60 seconds[3]



Urea Excipient

* Refers to the Medtronic DCB family.

[1] Granada, *J. Cardiac Interventions Today. May*/June 2010: 35-40.
[2] Chang GH et al. *Scientific Reports.* May 2, 2019;9(1):6839.
[3] Prevail Instructions for Use.

UC202014514b ML

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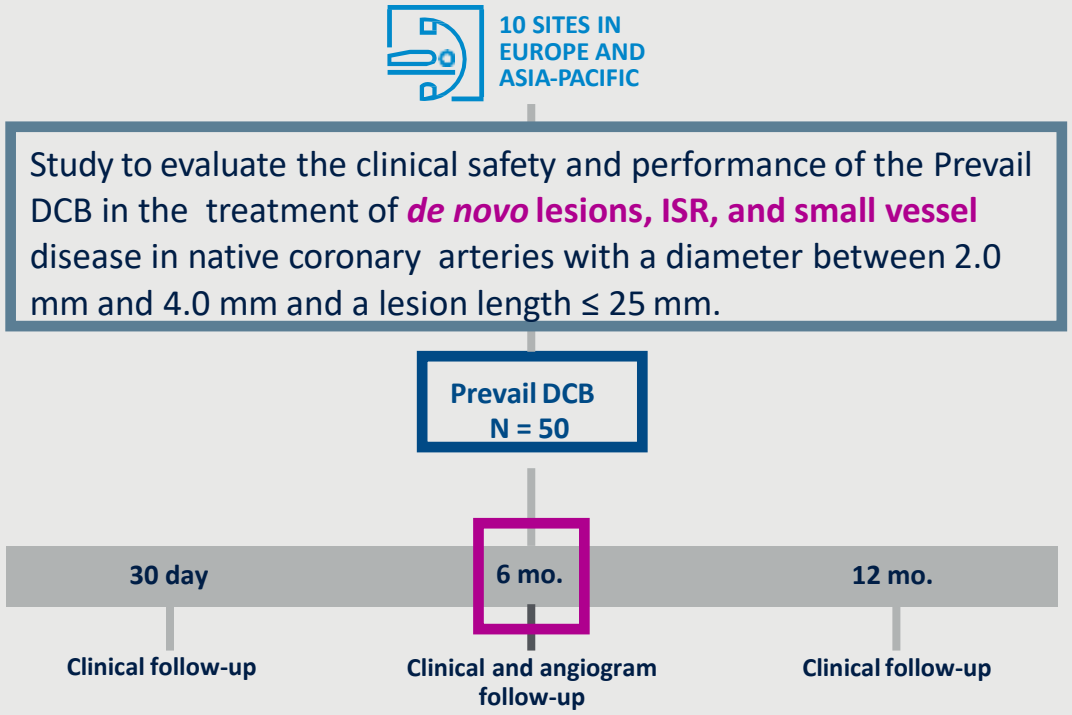
PREVAIL STUDY DESIGN
PROSPECTIVE, MULTICENTRE, SINGLE-ARM STUDY



PRIMARY ENDPOINT

In-stent (in-balloon) Late Lumen Loss (LLL) measured by QCA at 6 months

SECONDARY ENDPOINTS

- Clinical endpoints assessed at 30 days, 6 months, and 1 year: death, TVMI, MACE, TVF, TLF, all revascularisations, stent thrombosis, acute success (device, lesion, and procedure success).
- Angiographic endpoints assessed at 6 months: In-stent (in-balloon) and in-segment LLL, % DS, BAR, and MLD.

CLINICAL TRIAL DAPT RECOMMENDATIONS POSTPROCEDURE

Minimum of 4 weeks, or longer upon investigator's discretion.

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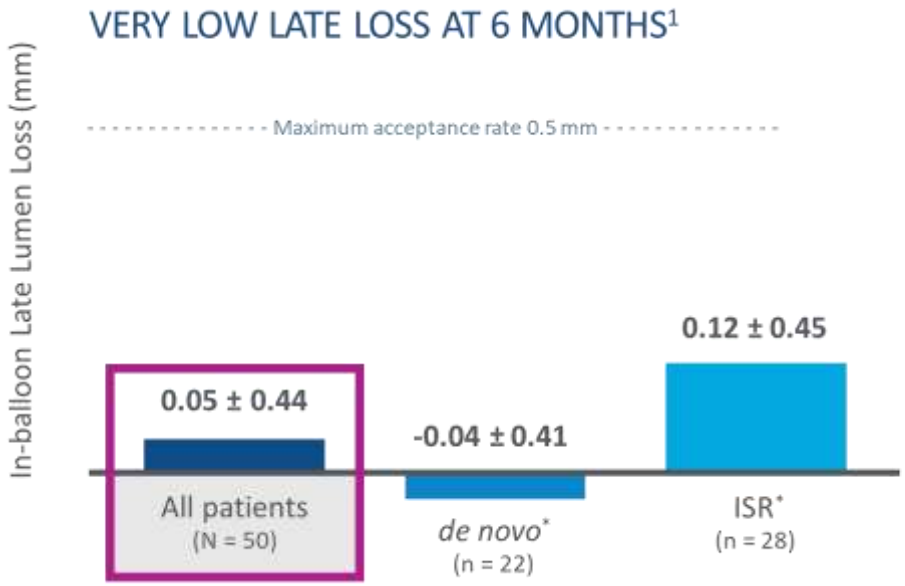
EXCELLENT RESULTS WITH PREVAIL STUDY[1] THROUGH 12 MONTHS



INCLUDES COMPLEX LESIONS

Complex lesion characteristics included:

- 54.7% ISR
- 79.2% small vessel in *de novo* lesions

POSITIVE ANGIOGRAPHIC RESULTS

6-month results showed **very low late loss**[1] of 0.05 ± 0.44 mm,* meeting the primary endpoint.

DEMONSTRATED SAFETY

0% stent thrombosis, TVMI, and cardiac death at 6 and 12 months for all patients.

*Lower than the prespecificed maximum acceptance rate of 0.5 mm.

[1] Latib A, et al. *J Invasive Cardiol*. Published online August 19, 2021. PREVAIL study did not have powered endpoints.

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What Does the Guideline Say on Drug-coated Balloons (DCBs)?

2018 ESC/EACTS Guidelines on myocardial revascularization

Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

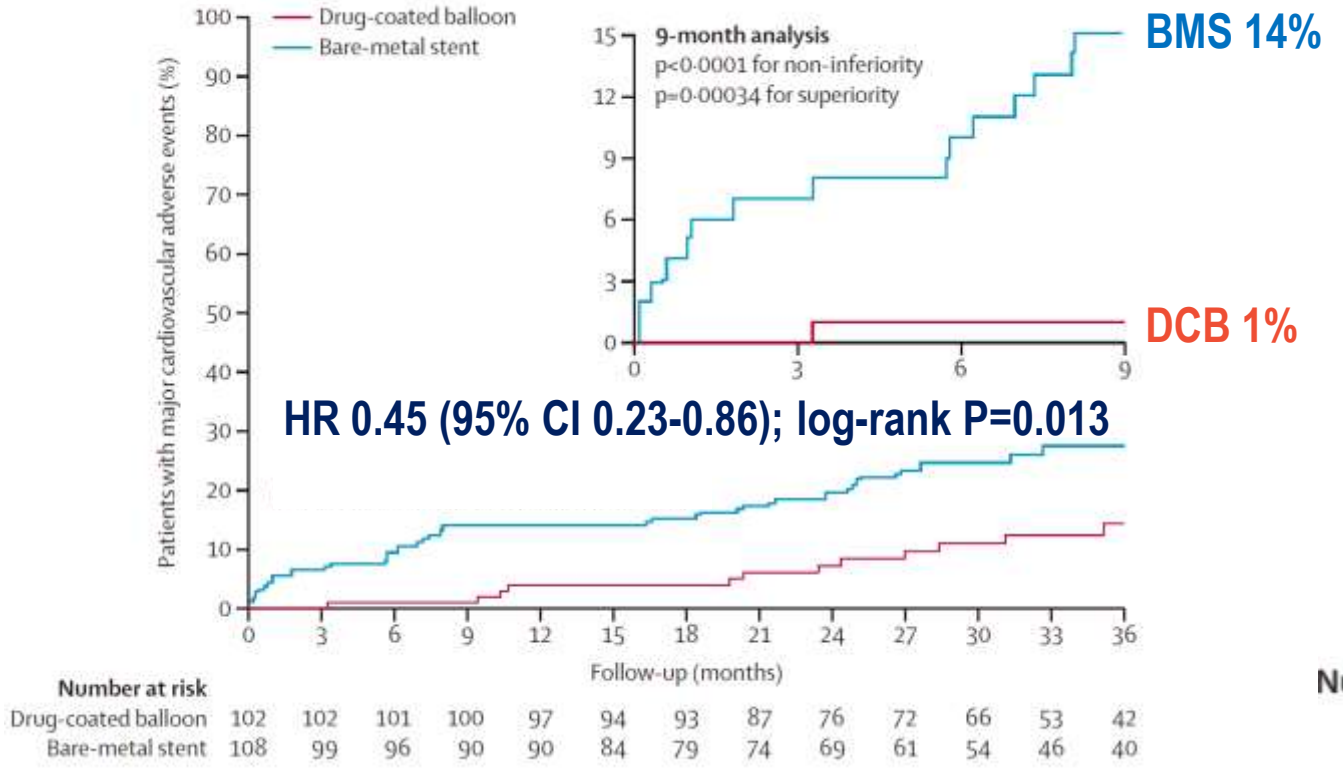
DCBs are recommended for treatment of ISR of BMS or DES (Class I, LOE A)
How about DCBs for de novo lesions?

Neumann FJ et al. EHJ 2019;40:87–165

Evidence Supporting DCBs for De-novo Lesions

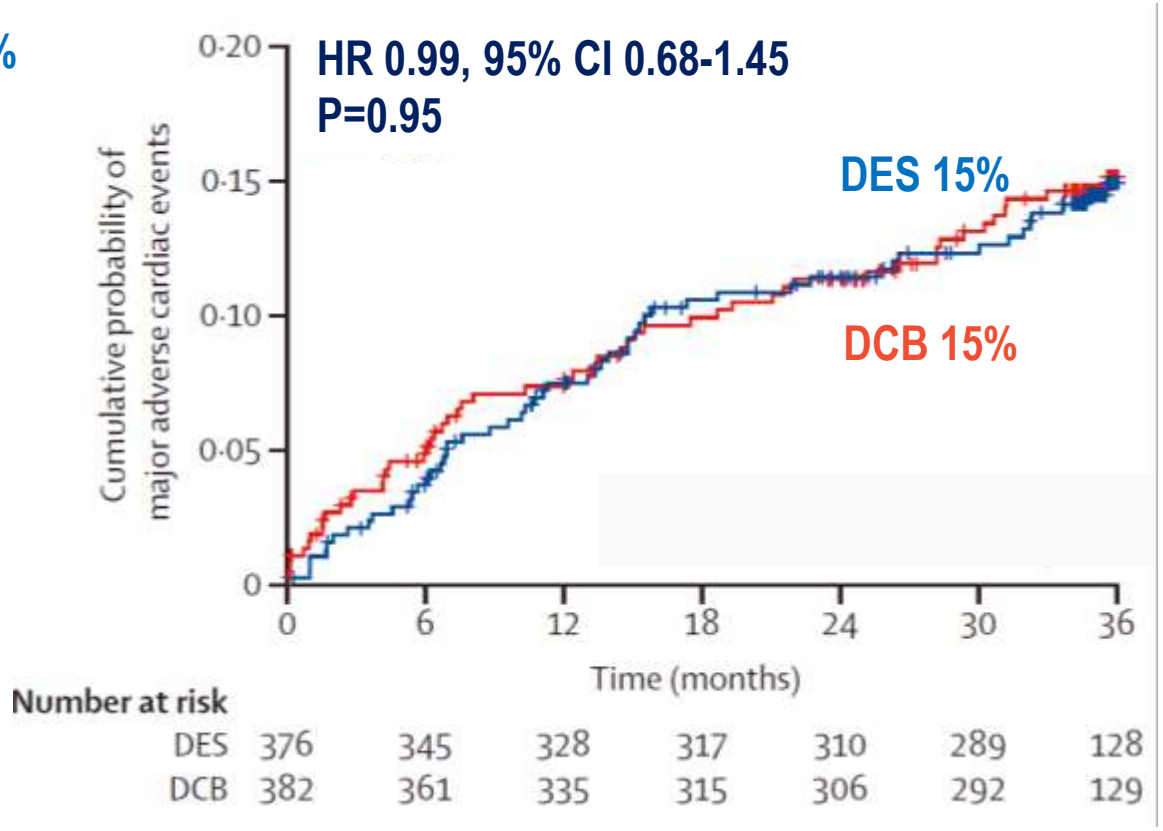
DEBUT (DCB vs. BMS in HBR)

Main Results – 9M MACE
(CV death, non-fatal MI, or ischemia-driven TLR)



BASKET-SMALL2 (DCB vs. DES)

Main Results – 3Y MACE
(Cardiac death, non-fatal MI, TVR)



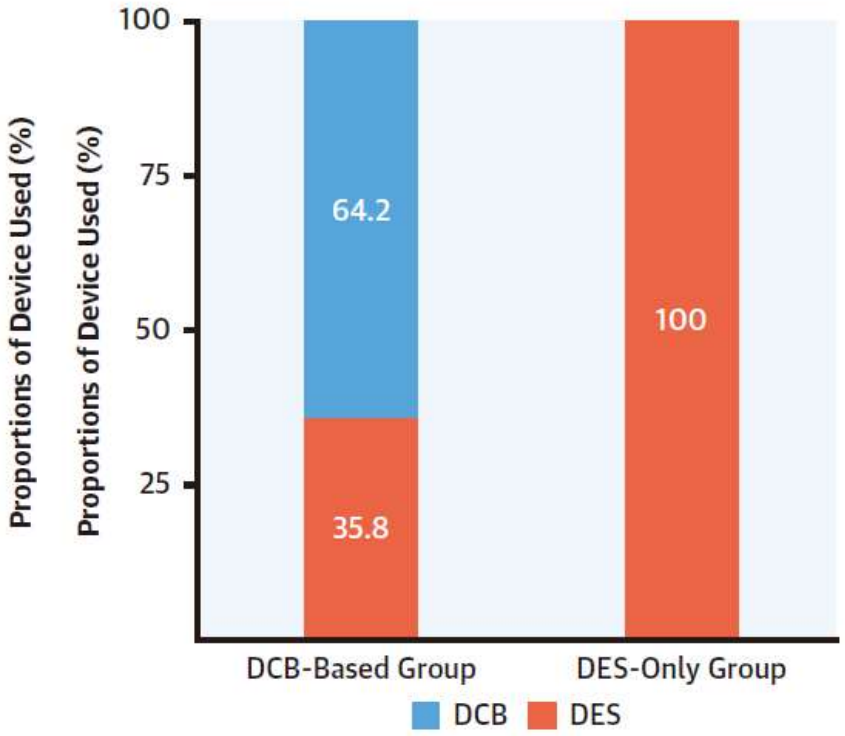
Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856; Lancet 2020;396:1504-1510

Evidence Supporting DCBs for De-novo Lesions

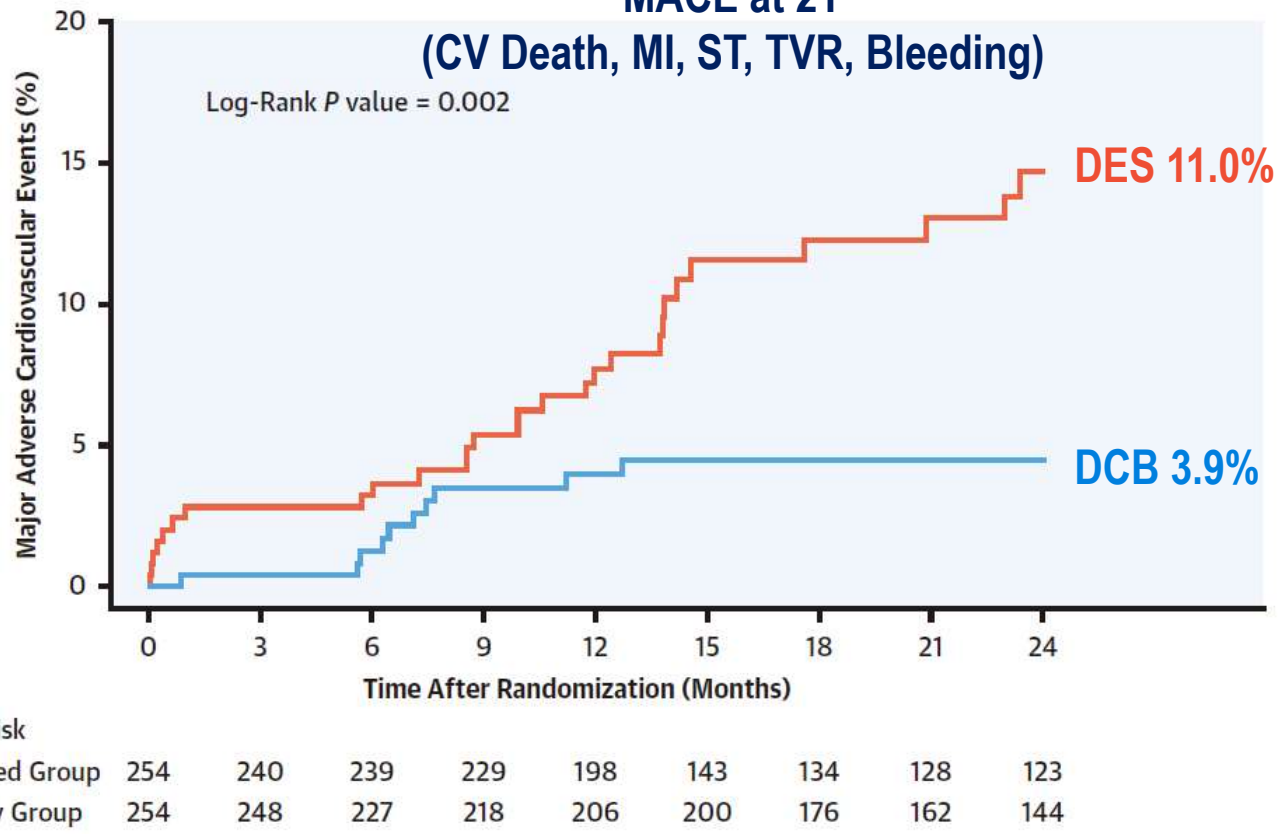
DCB-Based vs. DES for Multivessel Disease (NCT04619277)

254 Patients Matched with PTRG-DES Registry

Proportions of Device Used



MACE at 2Y
(CV Death, MI, ST, TVR, Bleeding)



DCB-based treatment approach showed a significantly reduced stent burden for MVD, which related to lower rate of MACE than DES-only treatment.

Shin ES et al. JACC Intervention. 2023 Feb, 16 (3) 292–299

Right Case and Right Time of DCB

Candidates for DCB

ISR of BMS or DES (Class IA)

De Novo Lesions
with Small vessel (2.5±0.25 mm)
in Patients with HBR
in Patients with MVD

Proven Safety for De Novo Lesions

Abrupt vessel closure after DCB: about 0~1%

Bail-out stenting

DEBUT	2/102 (2%)
BASKET-SMALL 2	19/349 (5%)

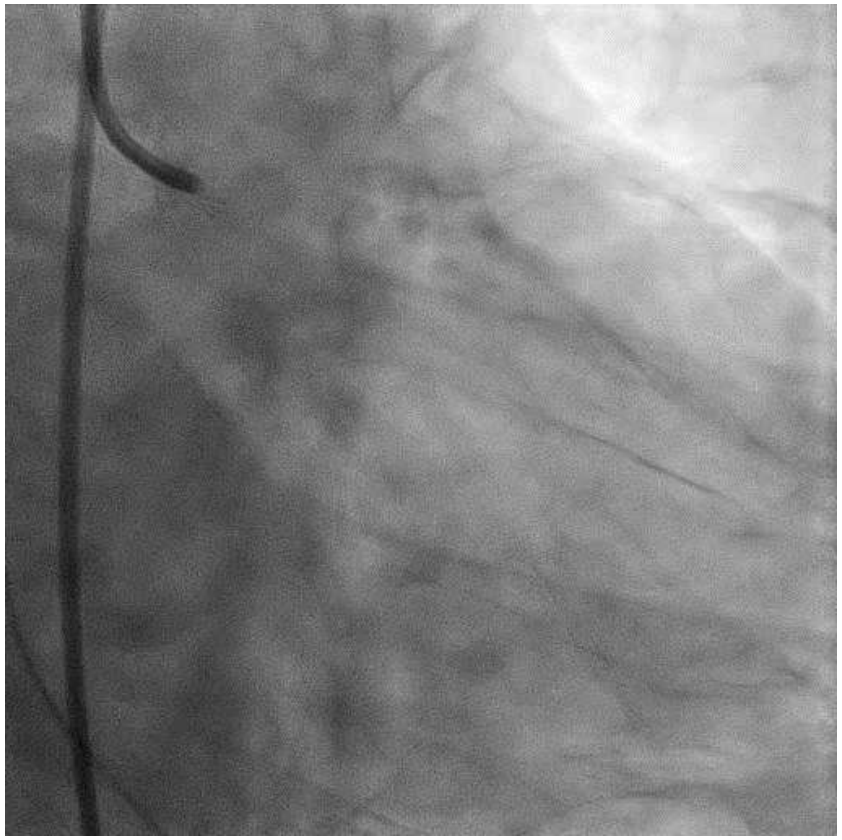
Myocardial Infarction

DEBUT(9M)	DCB 0% vs. BMS 6%
BASKET-SMALL 2(1Y)	DCB 2% vs. DES 4%
BASKET-SMALL 2(3Y)	DCB 6% vs. DES 6%

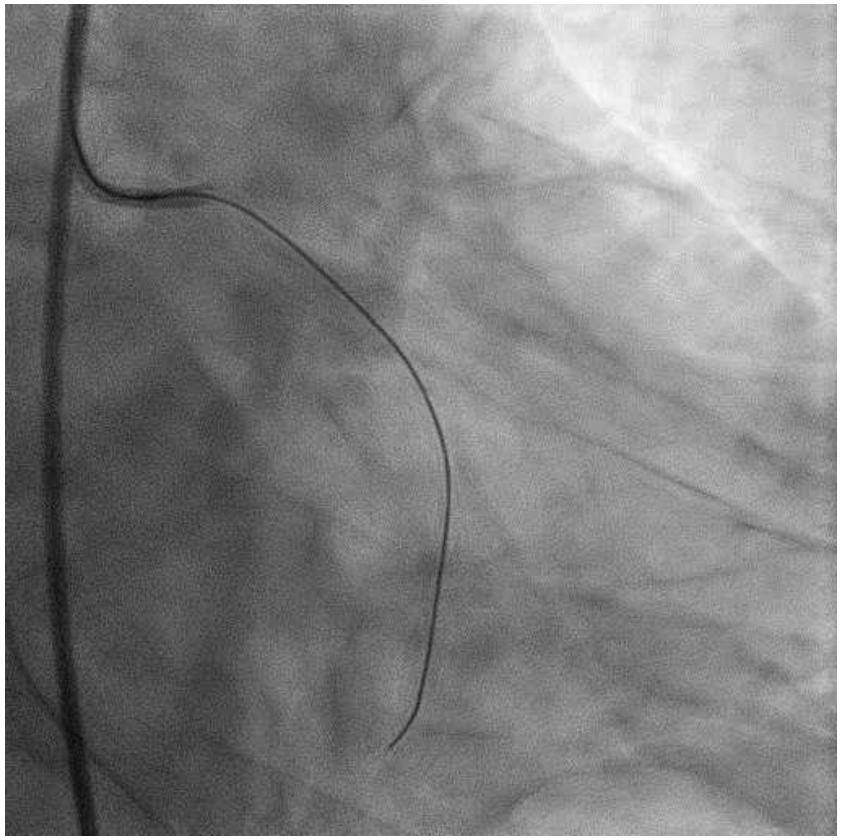
Jeger RV et al. Lancet. 2018 Sep 8;392(10150):849-856; Lancet 2020;396:1504-1510
Rissanen TT et al. Lancet. 2019 Jul 20;394(10194):230-239; Shin ES et al. JACC Intervention. 2023 Feb, 16 (3) 292–299

Case #1 - 67 YO Male

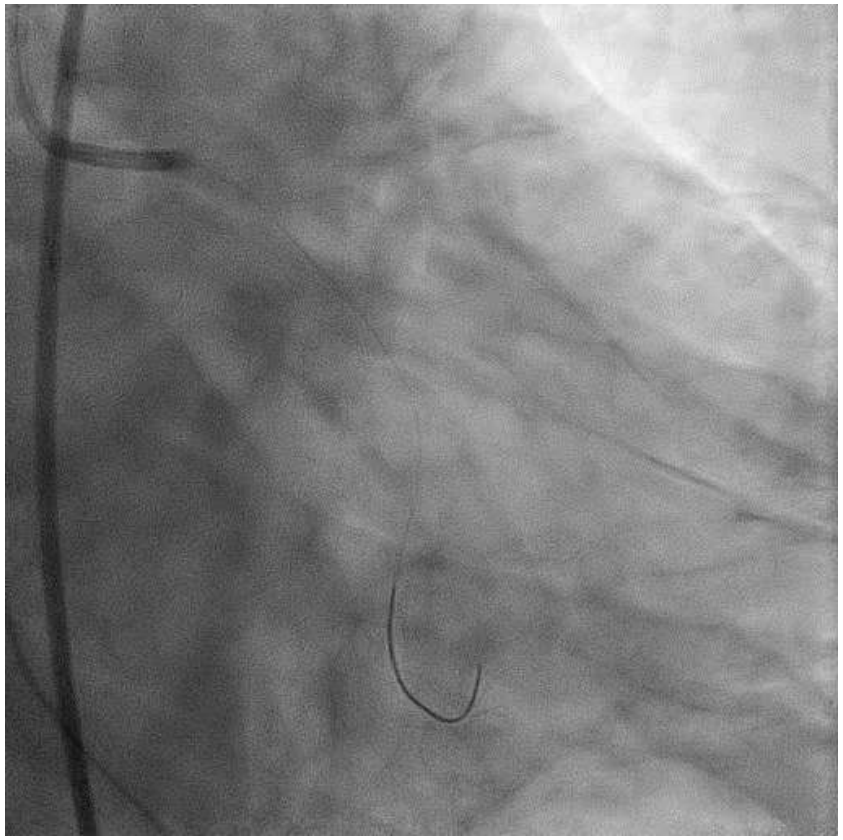
CTO at dLCX with collateral flow from interarterial branch (Gr. II)



6F EBU3.75 guiding catheter



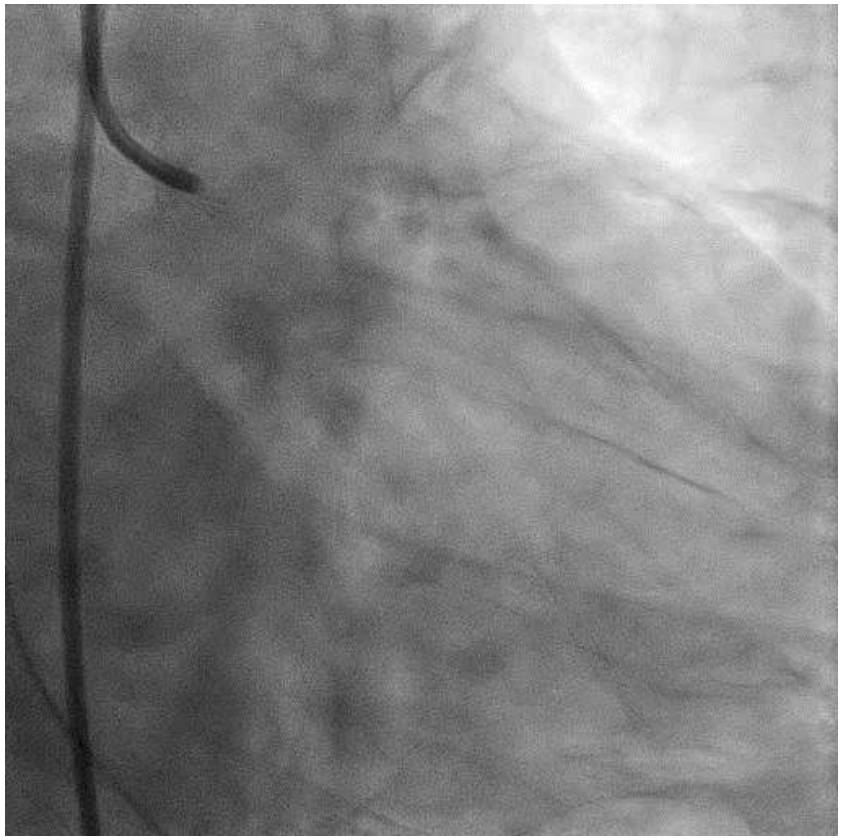
UB3 guidewire + Corsair Pro XS



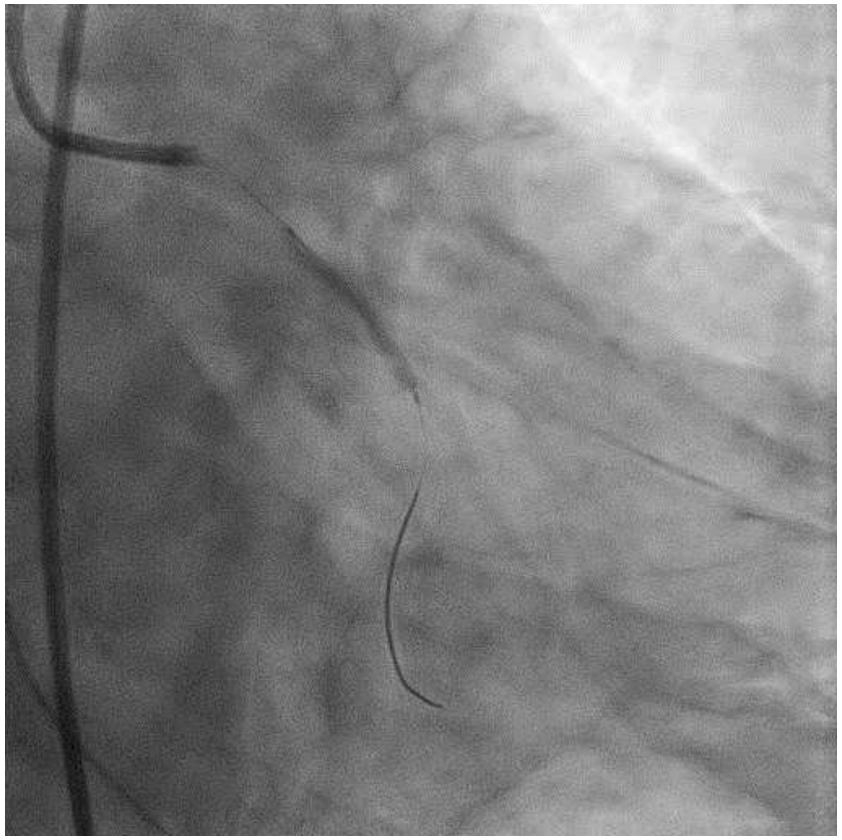
Lesion preparation with 1.5mm
→ 2.0mm balloon

Case #1 - 67 YO Male

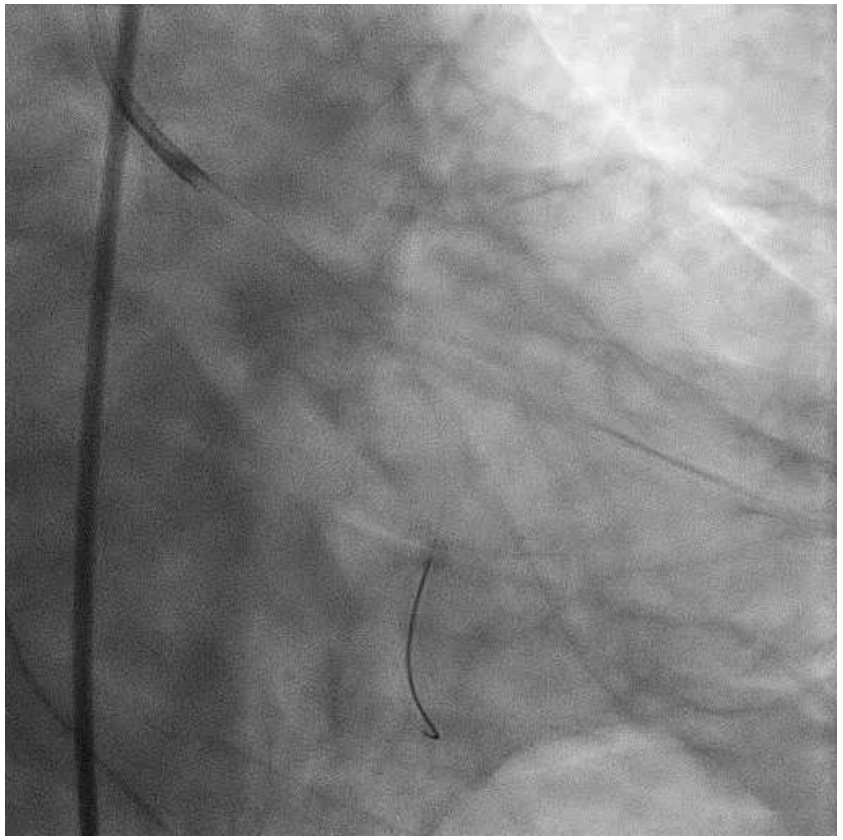
CTO at dLCX with collateral flow from interarterial branch (Gr. II)



Initial CAG



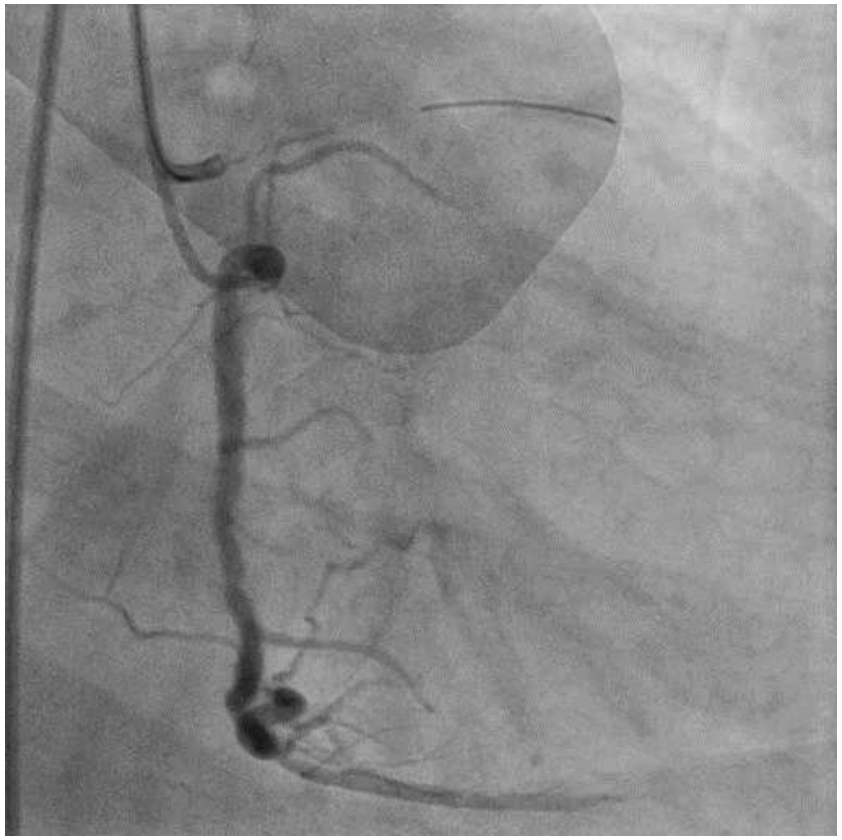
2.25x25mm Prevail
delivery time=15sec, total inflation time=60sec



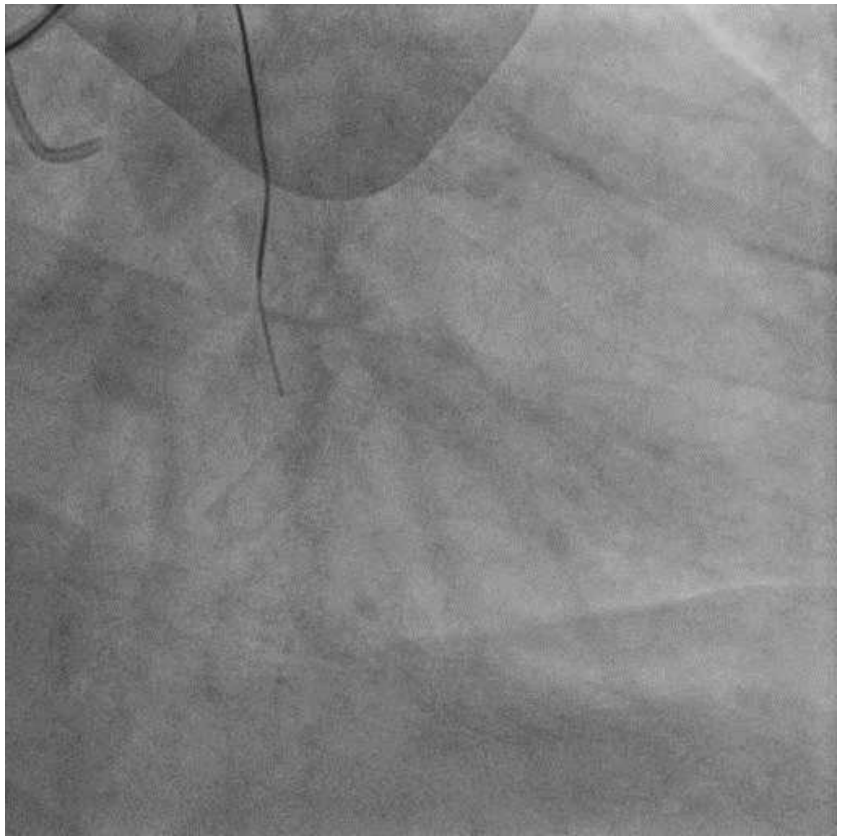
Final CAG

Case #2 - 60 YO Male

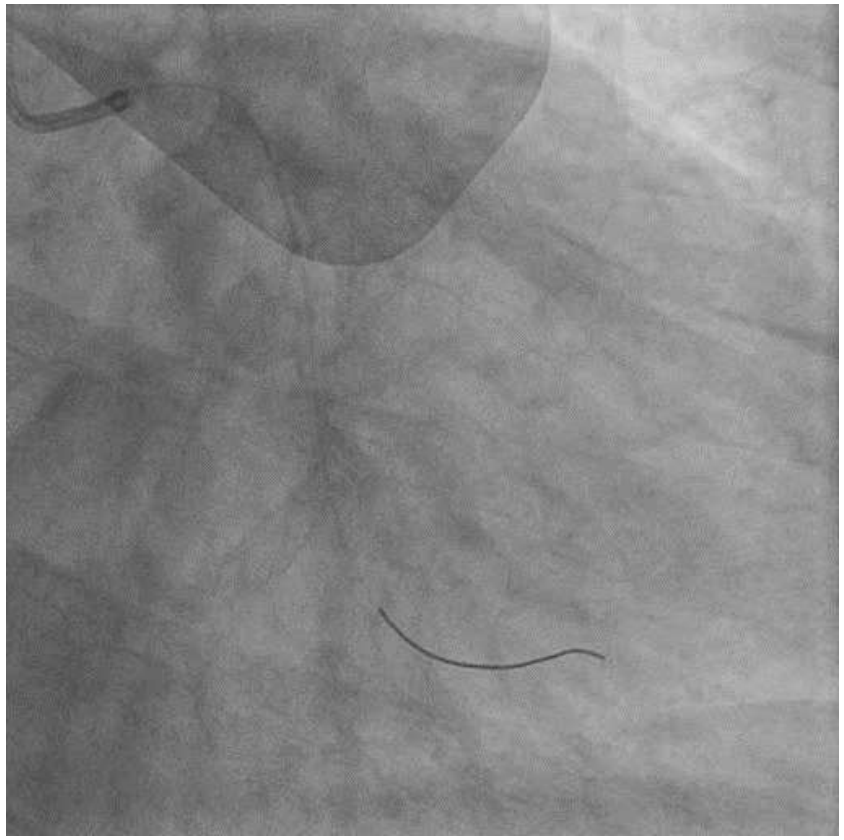
CTO at dLCX with collateral flow from RCA (Gr. III)



6F EBU3.75 guiding catheter



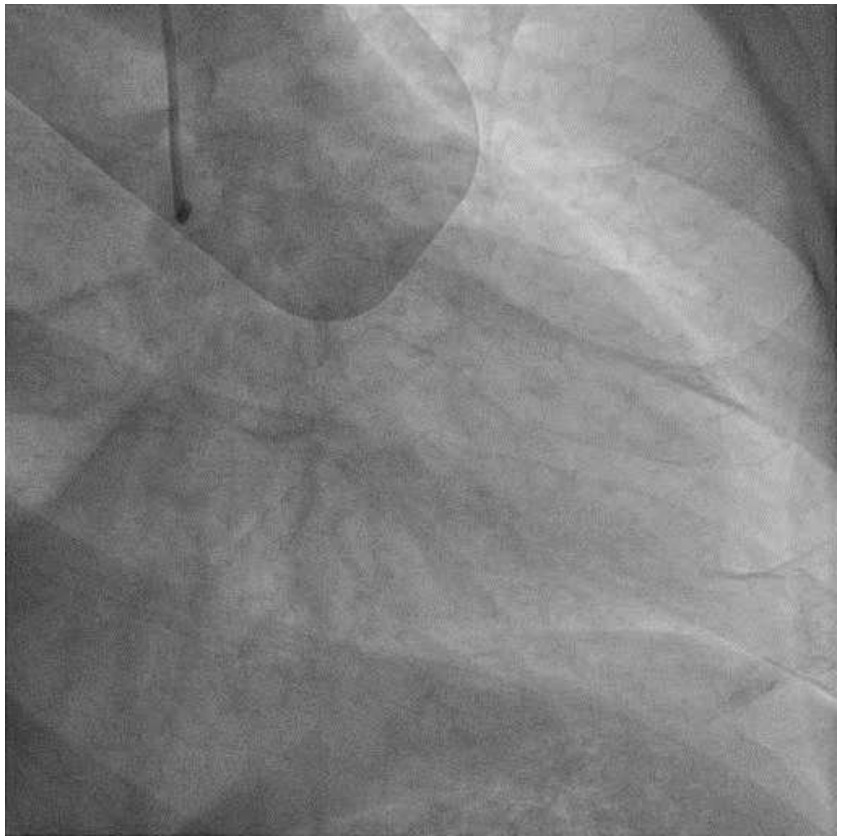
Gaia2 guidewire + Corsair Pro XS



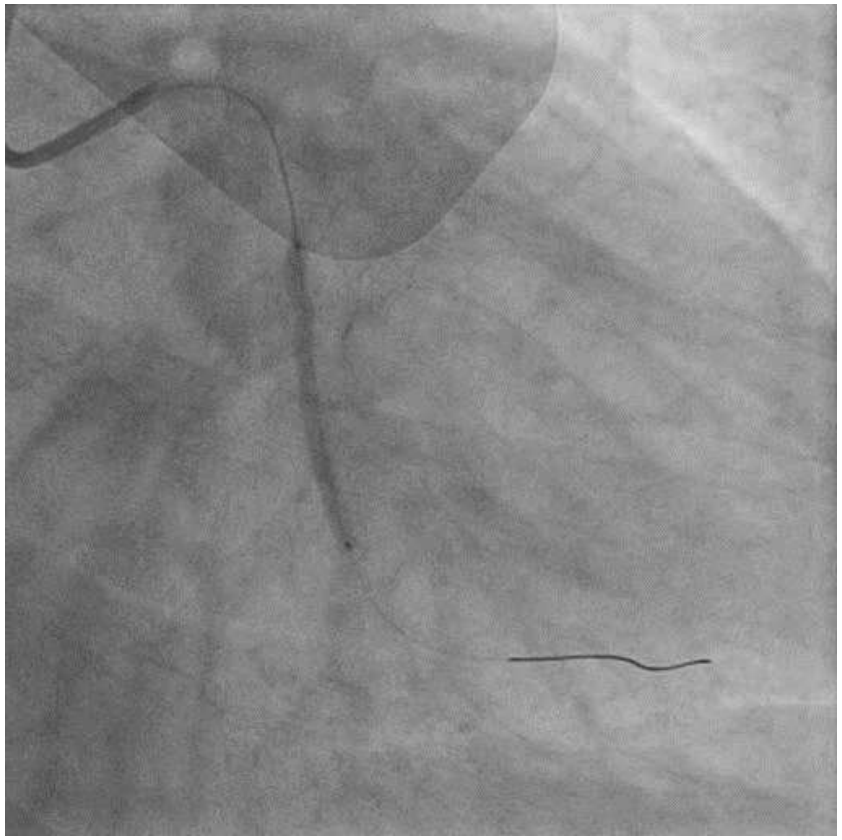
Lesion preparation with 1.5mm
→ 2.5mm balloon

Case #2 - 60 YO Male

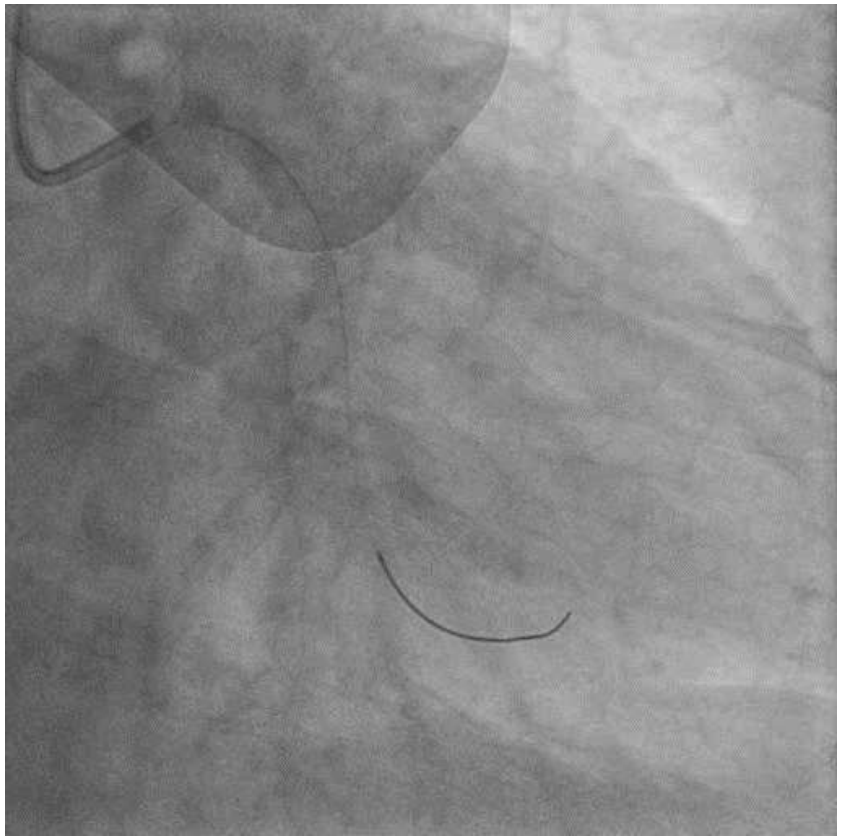
CTO at dLCX with collateral flow from RCA (Gr. III)



Initial CAG



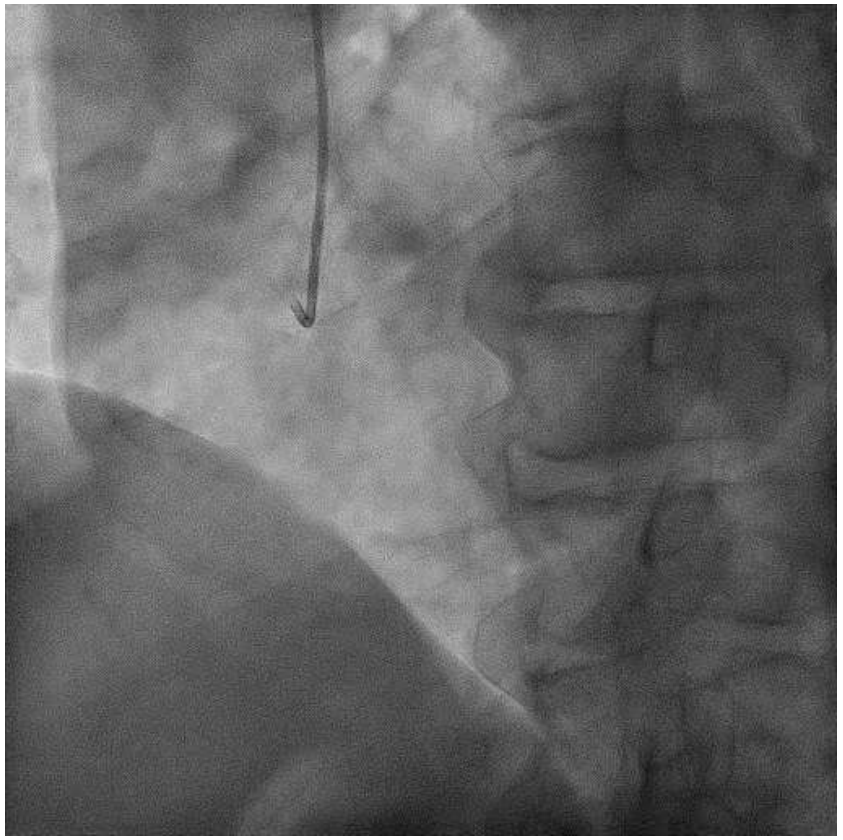
2.5x30mm Prevail
delivery time=10sec, total inflation time=60sec



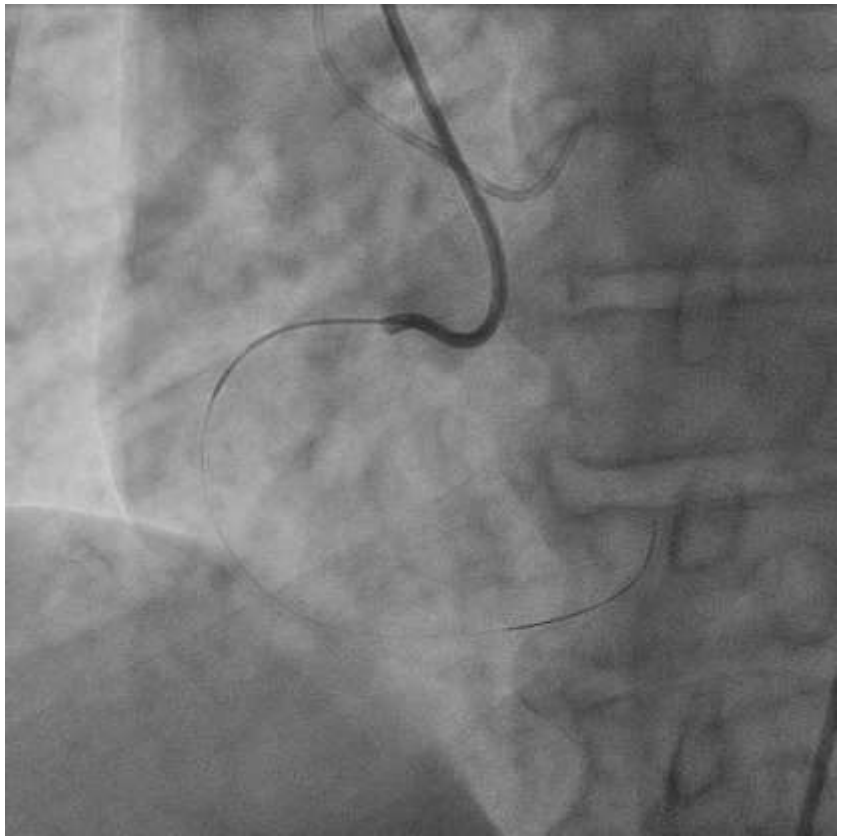
Final CAG

Case #3 - 67 YO Male

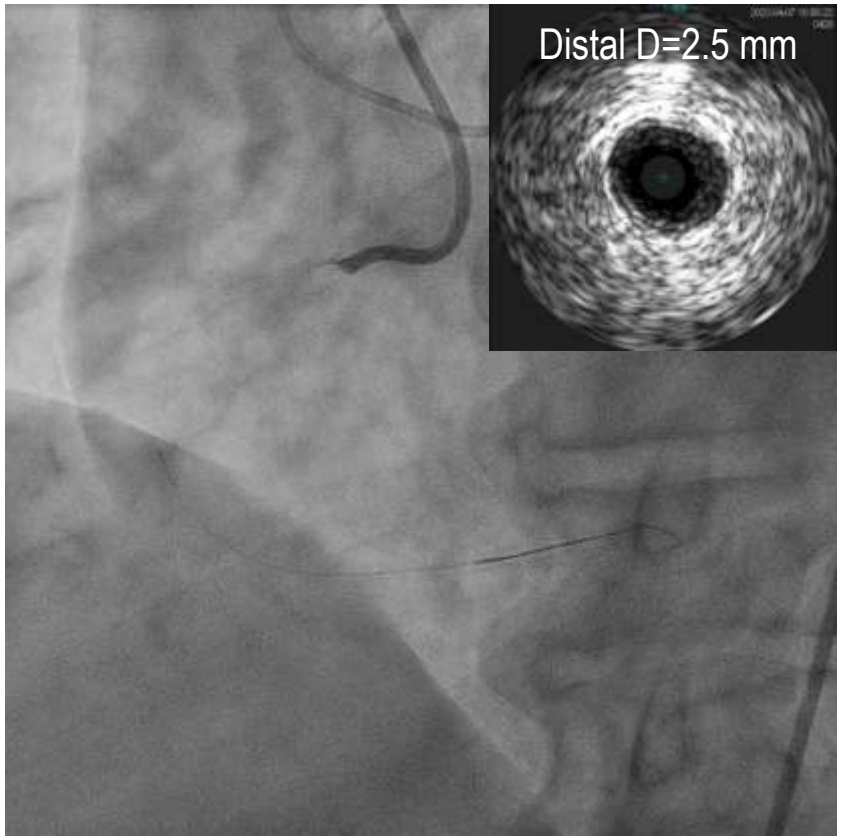
CTO at mRCA with collateral flow from bridging a. and LAD (Gr. II)



7F AL1 guiding catheter



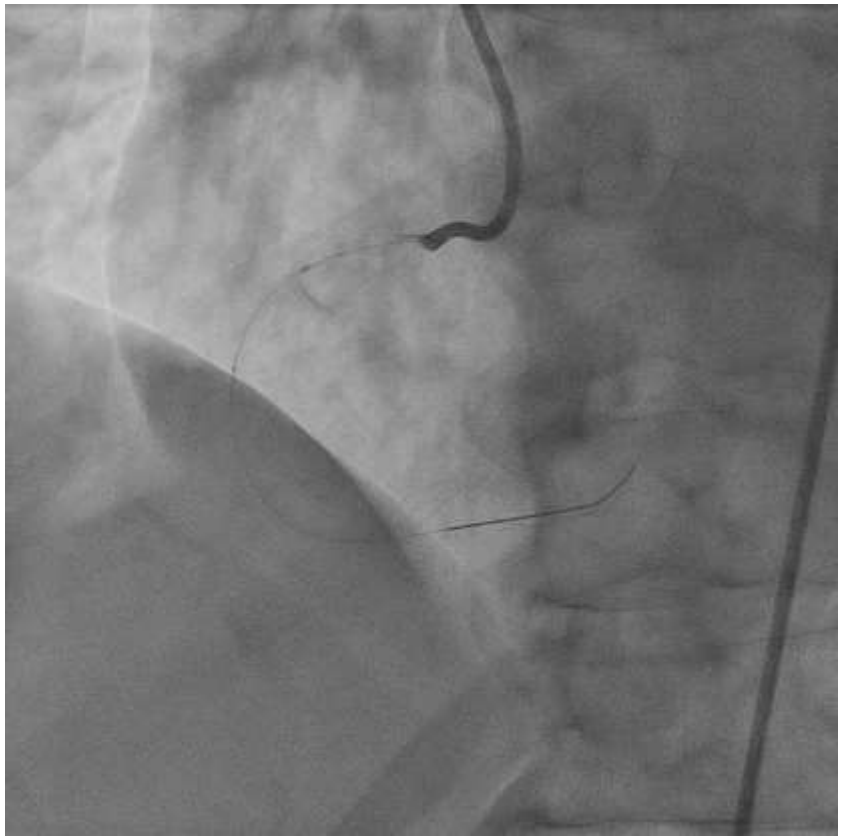
UB3 + Corsair Pro



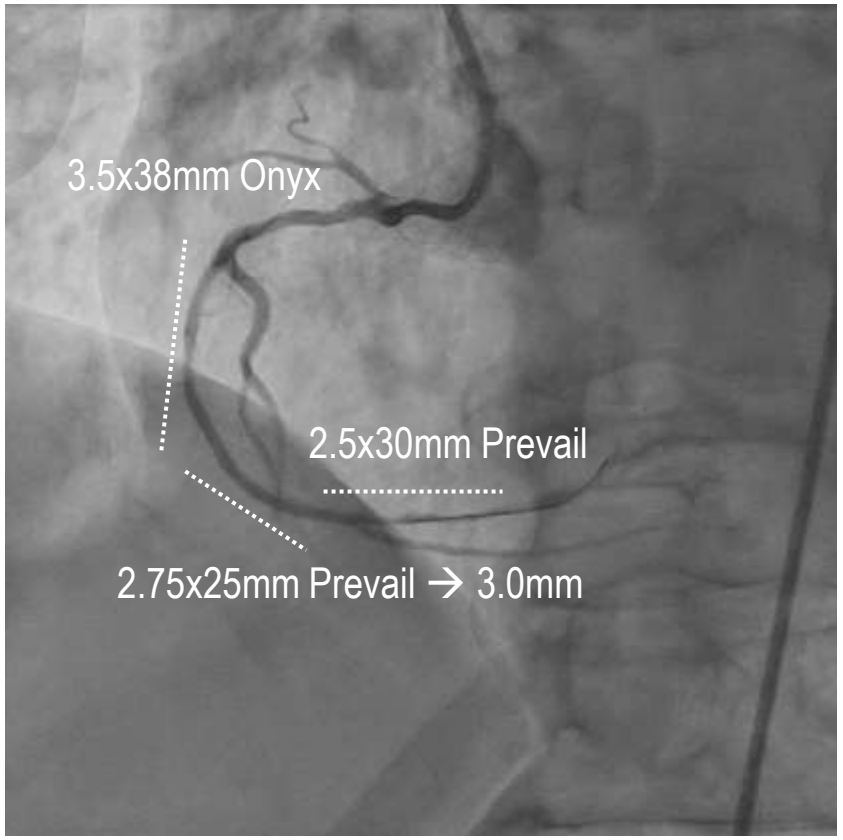
2.0x20mm balloon at CTO site → IVUS(+)

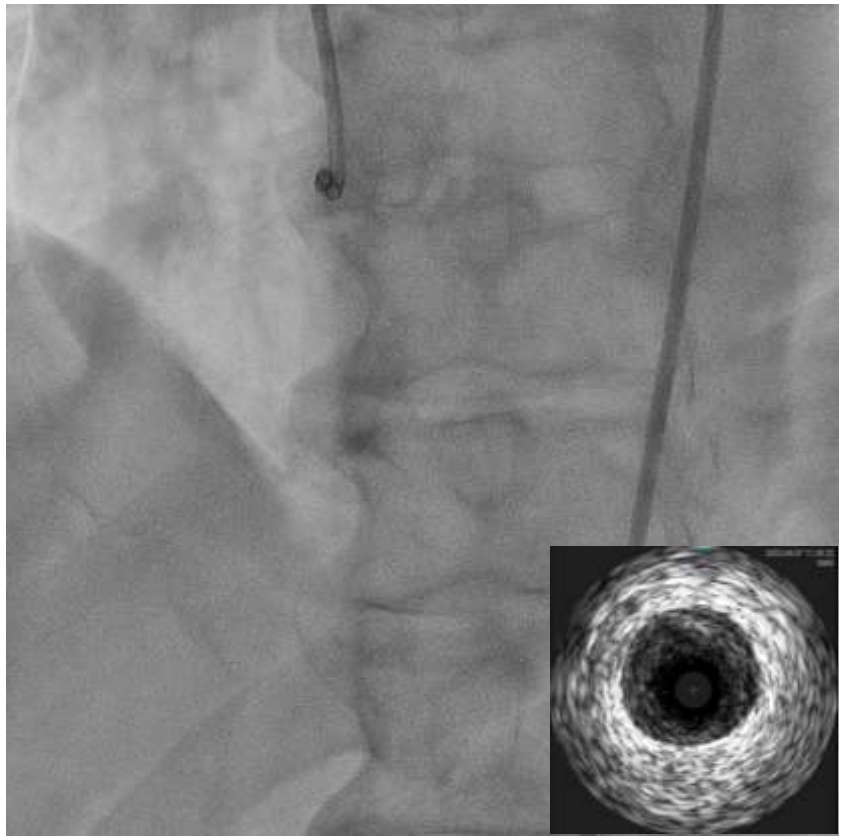
Case #3 - 67 YO Male

CTO at mRCA with collateral flow from bridging a. and LAD (Gr. II)



Lesion preparation with
2.5x20mm scoring balloon for mRCA-PL

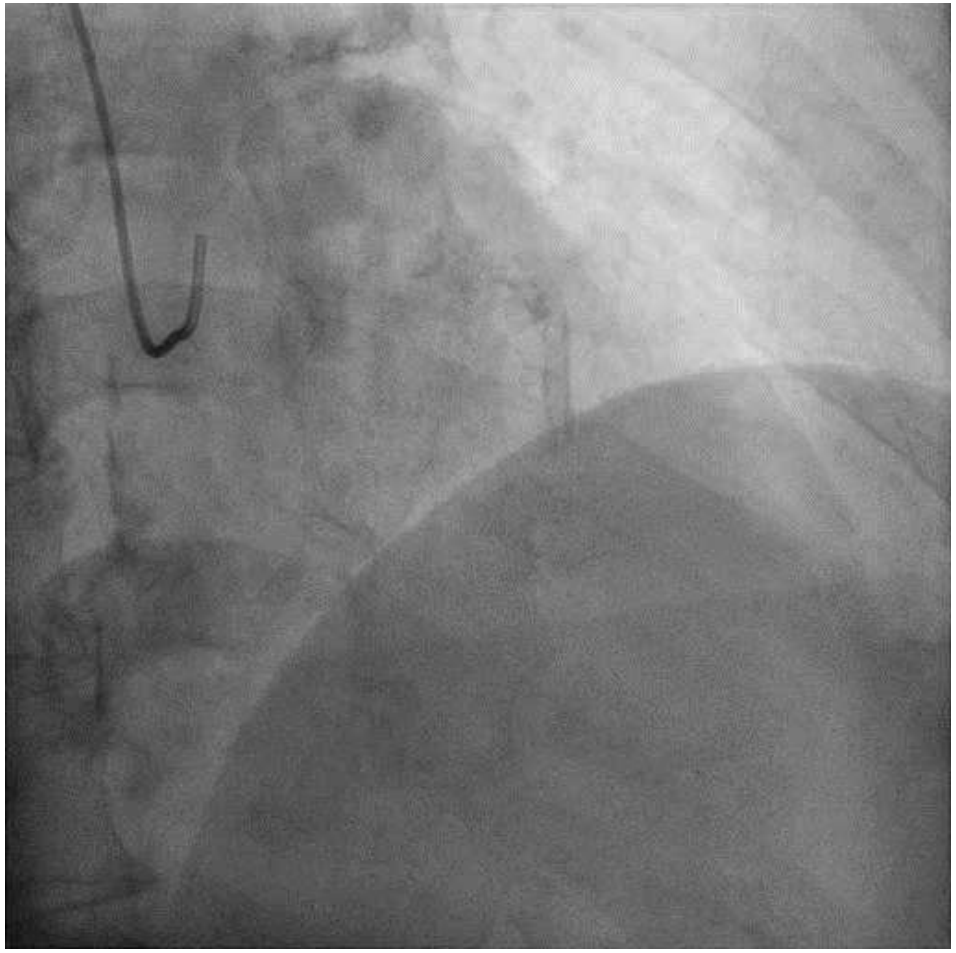


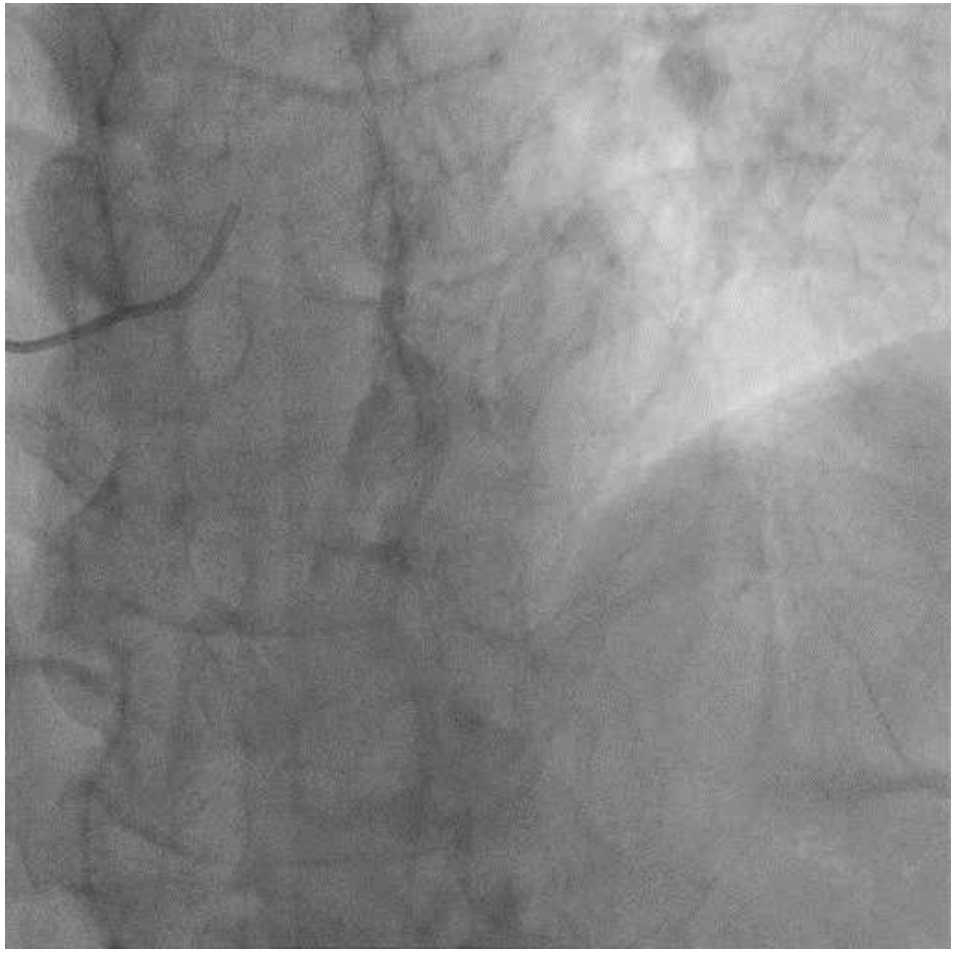


Final CAG
MLA(DCB site)=5.5 mm^2

Case #4 - 82/M, NSTEMI, Anemia, Plt 98K, ESRD on HD

Diffuse calcified lesion at mLAD

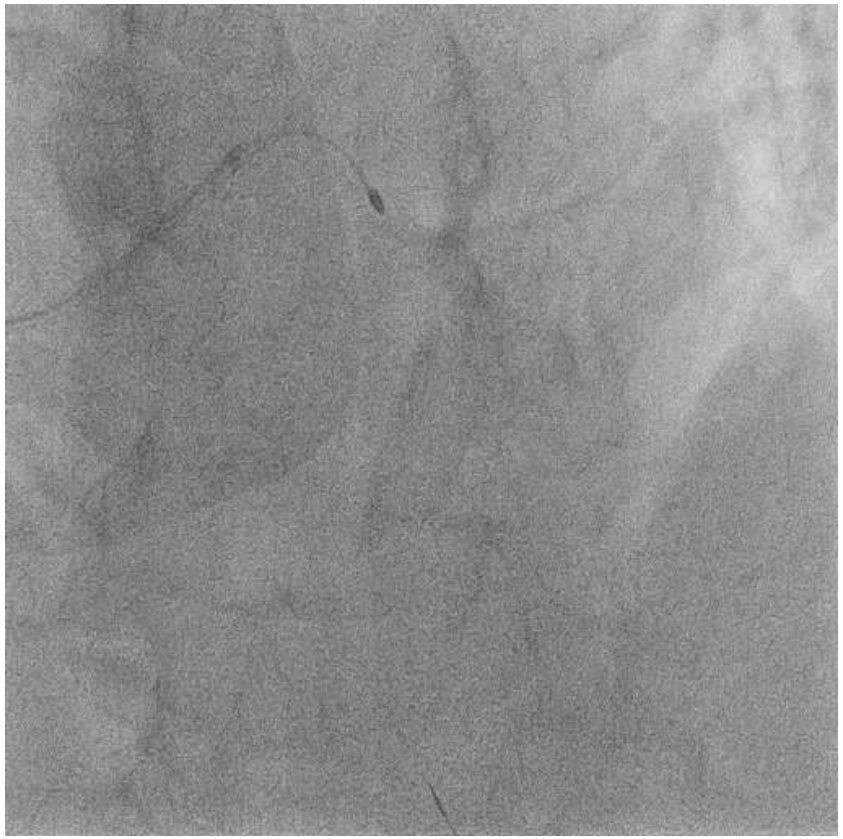


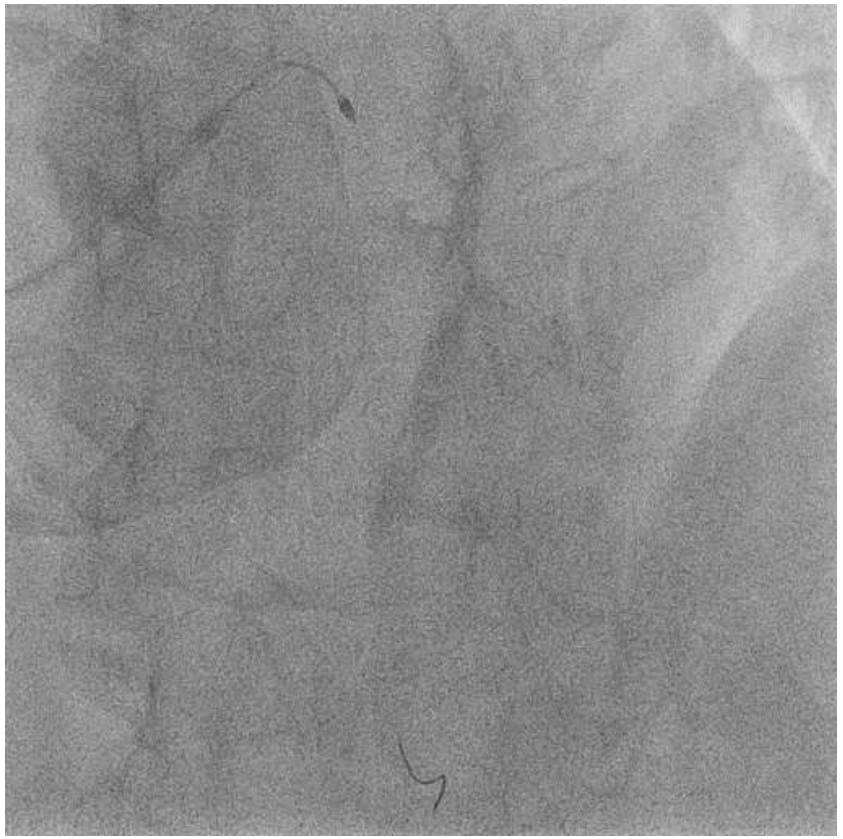


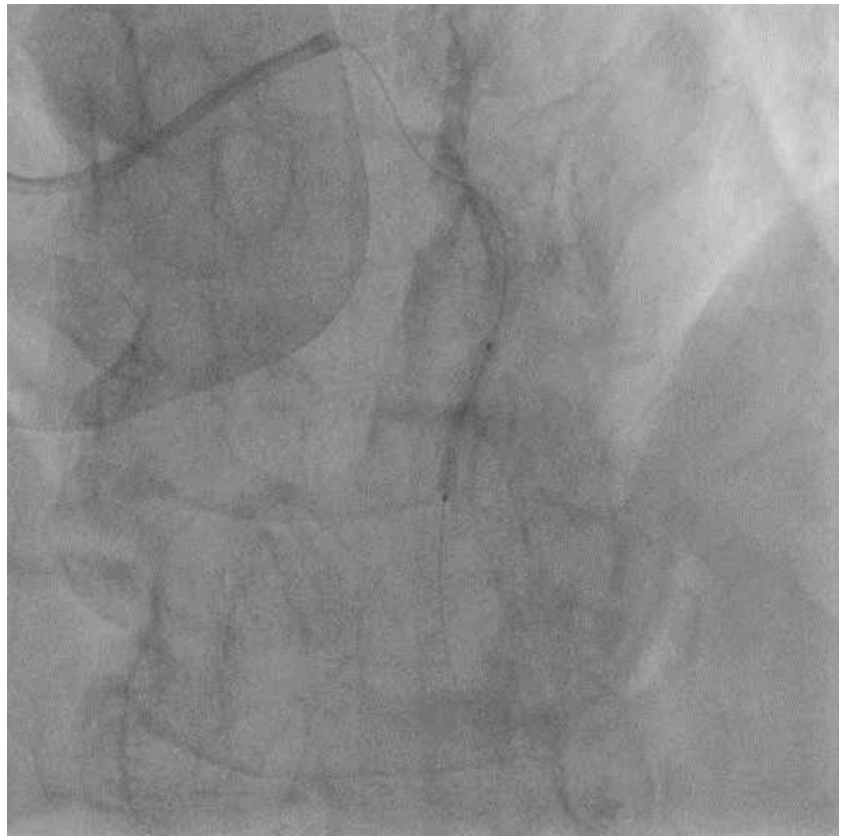
Imaging catheter and small balloon catheters were not crossed.

Case #4 - 82/M, NSTEMI, Anemia, Plt 98K, ESRD on HD

Diffuse calcified lesion at mLAD





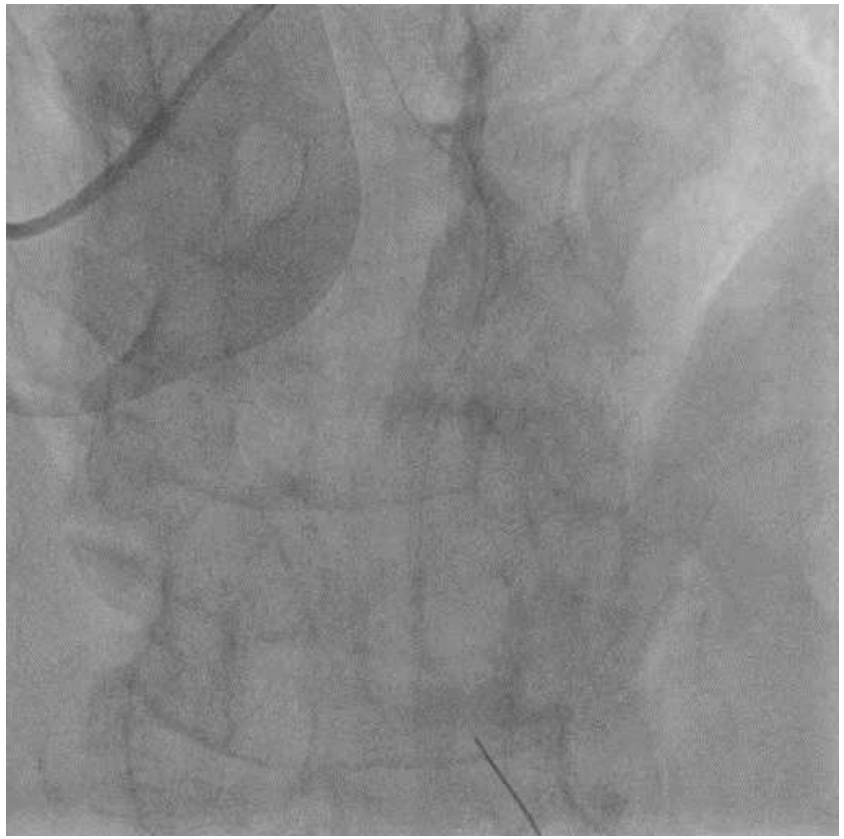


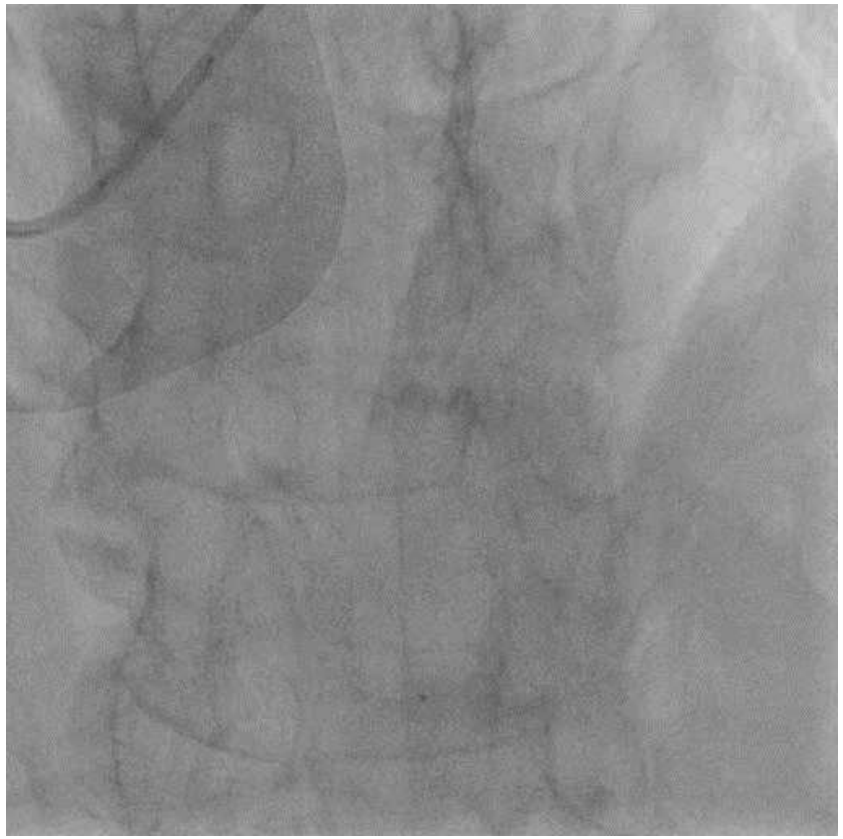
Rotational atherectomy was done. (1.5mm burr, 190K)

2.5x20mm balloon

Case #4 - 82/M, NSTEMI, Anemia, Plt 98K, ESRD on HD

Diffuse calcified lesion at mLAD

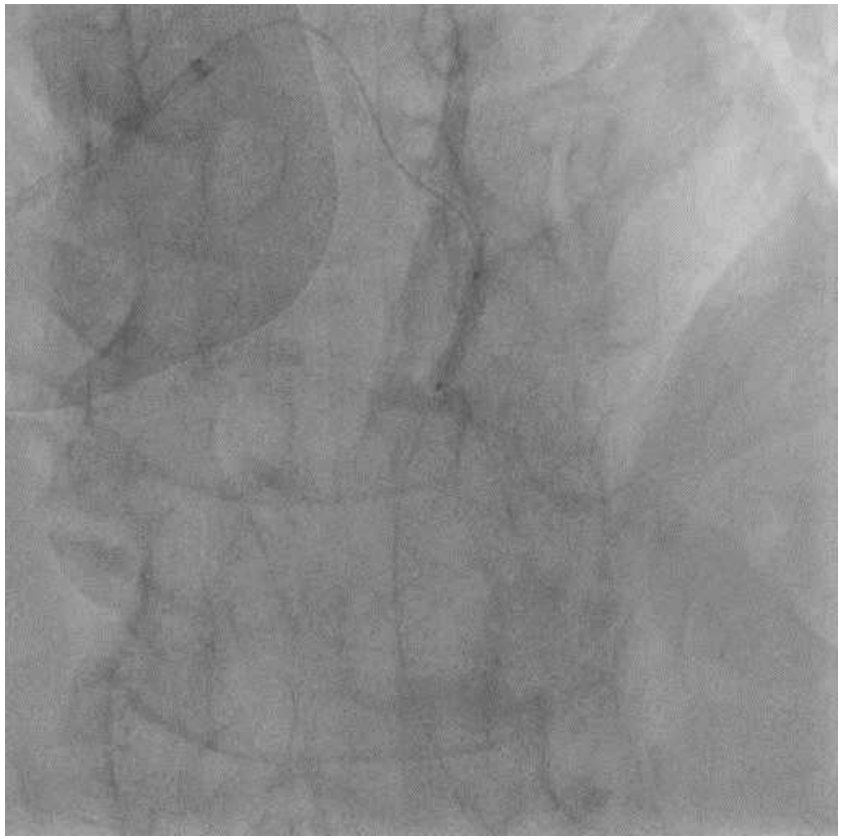
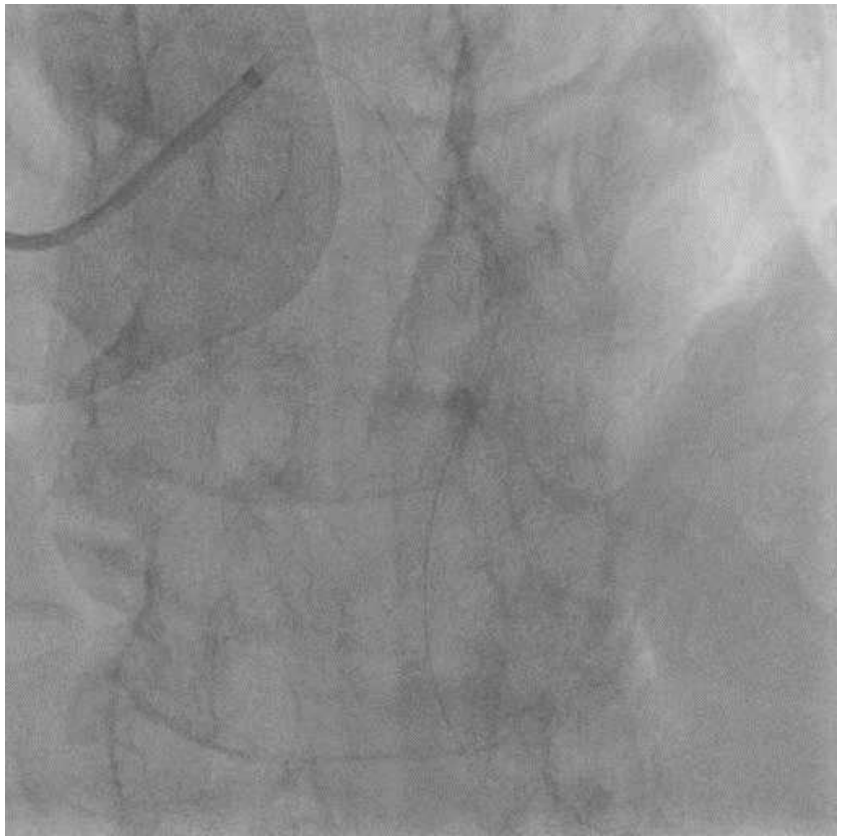
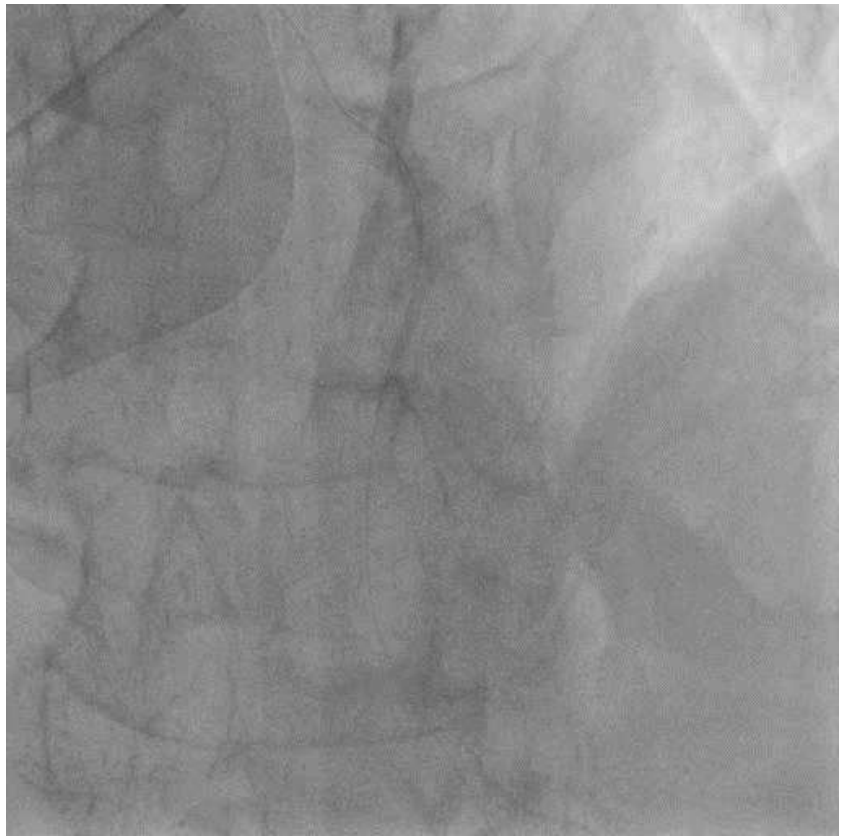




No-reflow → IC Nicorandil, Nitroprusside via Microcatheter → TIMI 2 flow

Case #4 - 82/M, NSTEMI, Anemia, Plt 98K, ESRD on HD

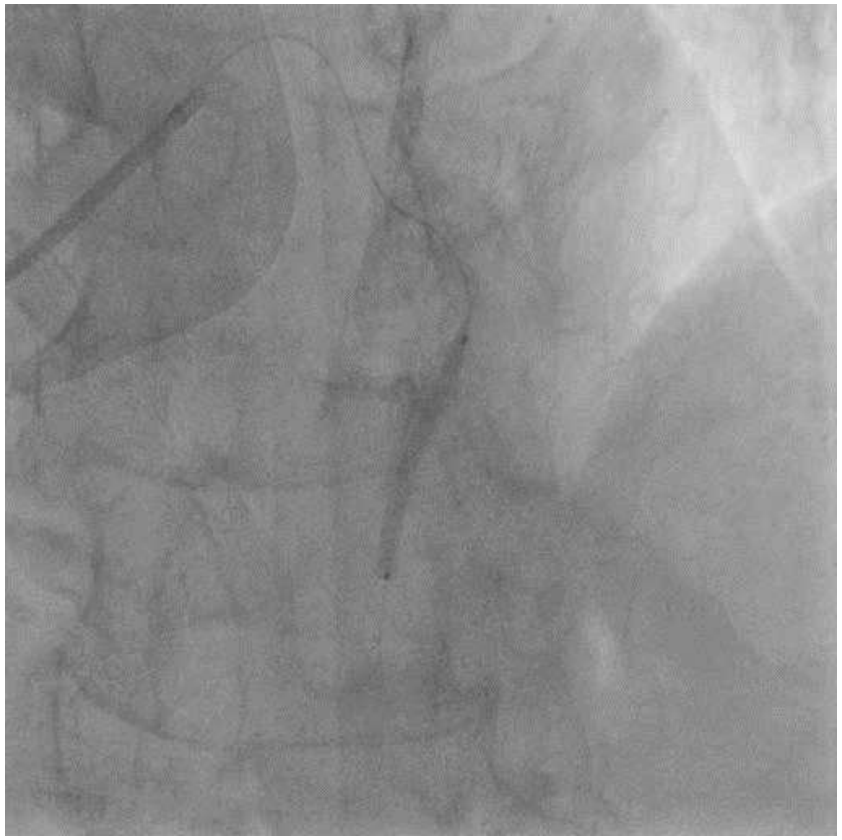
Diffuse calcified lesion at mLAD

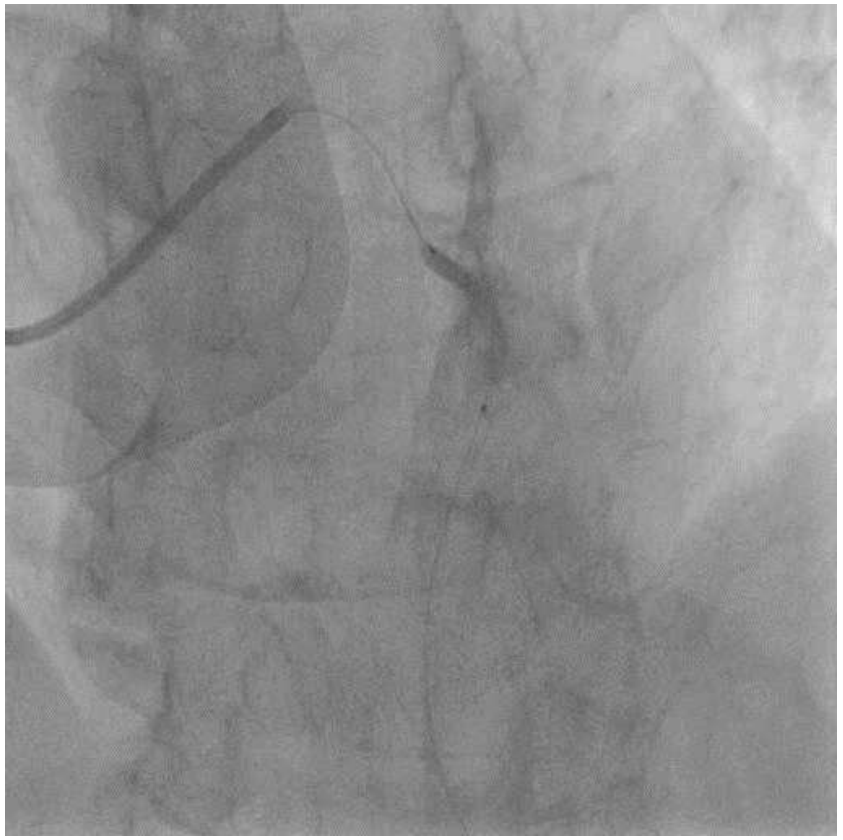




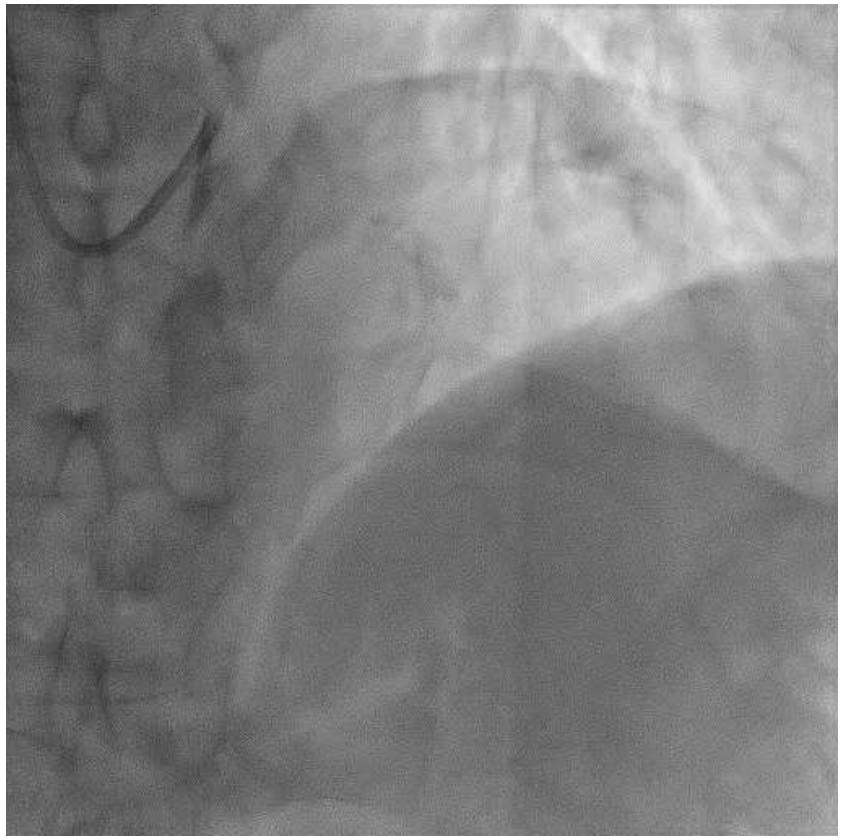
3.0x15mm NC balloon → No-reflow again! → IC nicorandil

Case #4 - 82/M, NSTEMI, Anemia, Plt 98K, ESRD on HD

Diffuse calcified lesion at mLAD







3.0x30mm Prevail
delivery time=20sec
total inflation time=70sec

3.0x25mm Prevail
delivery time=10sec
total inflation time=70sec

DCB-HBR

Ongoing Studies for De-novo Lesions

DCB-HBR Trial (NCT05221931)

Study Flow

1350 Patients with High Bleeding Risk
Undergoing Percutaneous Coronary Intervention and
1-3 months Dual Antiplatelet Agents

↓

Randomization (1:1) into DCB versus DES
(Stratified by Participating Centers and Clinical Presentation)

↓

Optimal Lesion Preparation
(Balloon with vessel ratio >0.90, residual stenosis≤35%, TIMI flow grade 3)

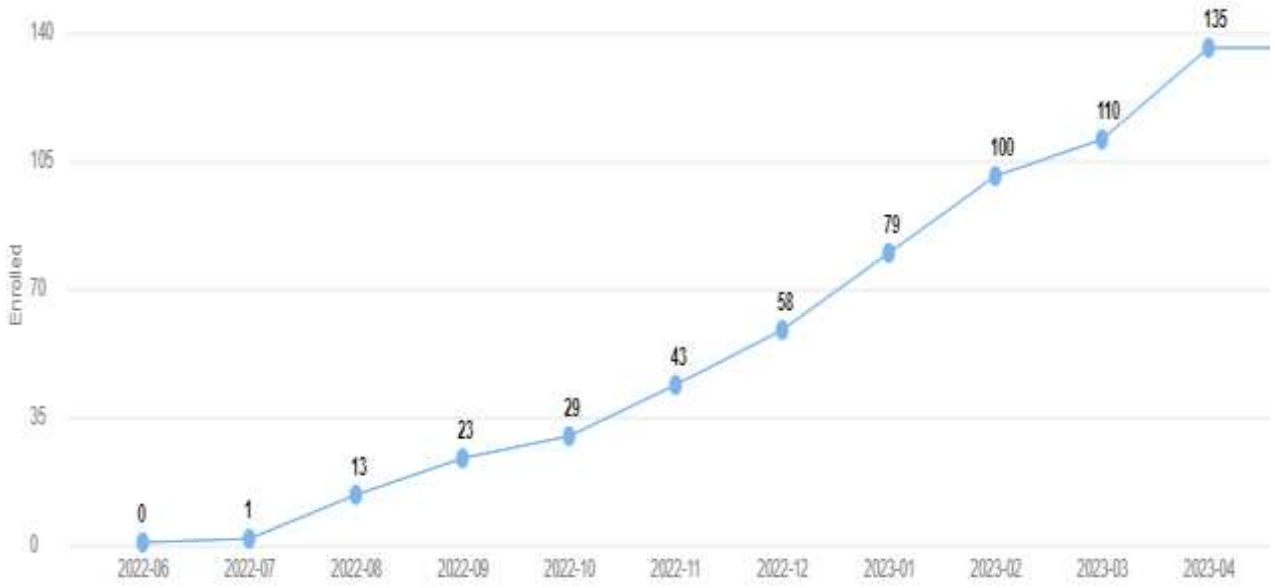
↓

DCB	DES
N = 675	N = 675

Primary Endpoint

TVF (a composite of CV death, target-vessel MI, TVR)

10 Centers in Korea (10% Enrolled)



We will test that DCB would be noninferior to DES for target-vessel failure (TVF) in de-novo coronary lesions in patients with HBR.

CHOOSE THE RIGHT **TREATMENT OPTION**

Resolute Onyx™
Zotarolimus-eluting Coronary Stent

Prevail™
Paclitaxel-coated PTCA Balloon

Medtronic

UC202014514b ML