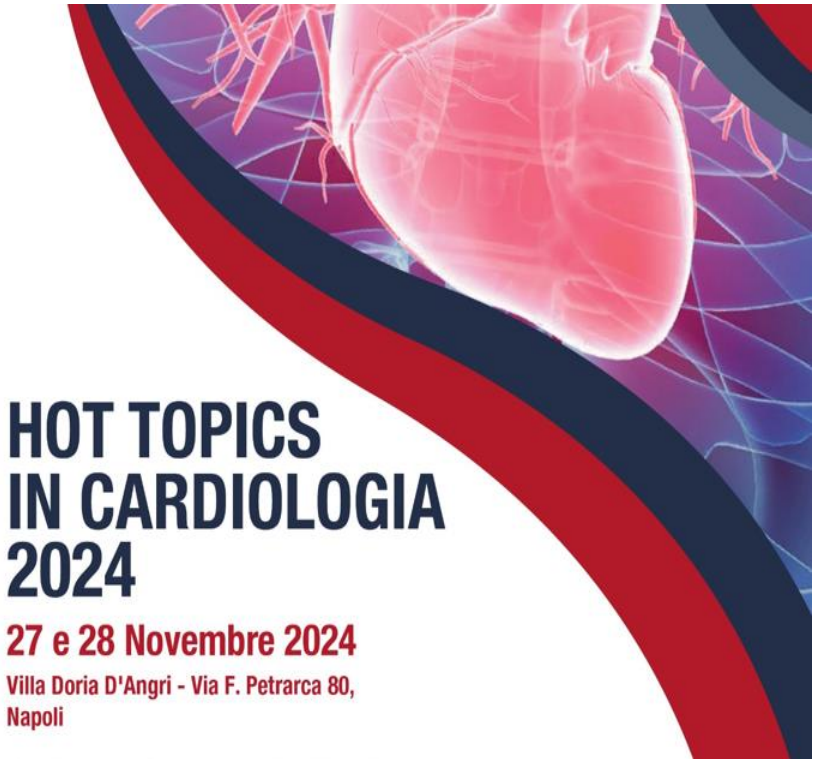


Il presente e il futuro dei "drug eluting balloon" nel distretto coronarico: sirolimus e farmaco-cinetica

Dott. Luigi Salemme
Clinica Montevergine
Mercogliano

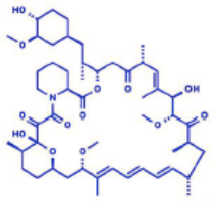
CASA DI CURA MONTEVERGINE

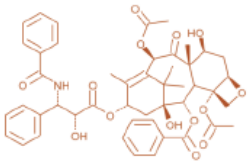
KLink profitable solutions

Do we need sirolimus?

Sirolimus and Paclitaxel

Sirolimus		Paclitaxel
ANTI-RESTENOTIC	Both are **antiproliferative agents**. They **inhibit smooth muscle cells** and **endothelial cells** proliferation and migration, *however* auxiliary pharmacological properties are considerably different	ANTI-RESTENOTIC
CYTOSTATIC		CYTOTOXIC
10'000 FOLD SAFETY MARGIN		100 FOLD SAFETY MARGIN
WIDE THERAPEUTIC RANGE		NARROW THERAPEUTIC RANGE
ANTI-INFLAMMATORY		X
LOW TISSUE ABSORPTION		FAST TISSUE ABSORPTION
SHORT TISSUE RETENTION		LONG TISSUE RETENTION

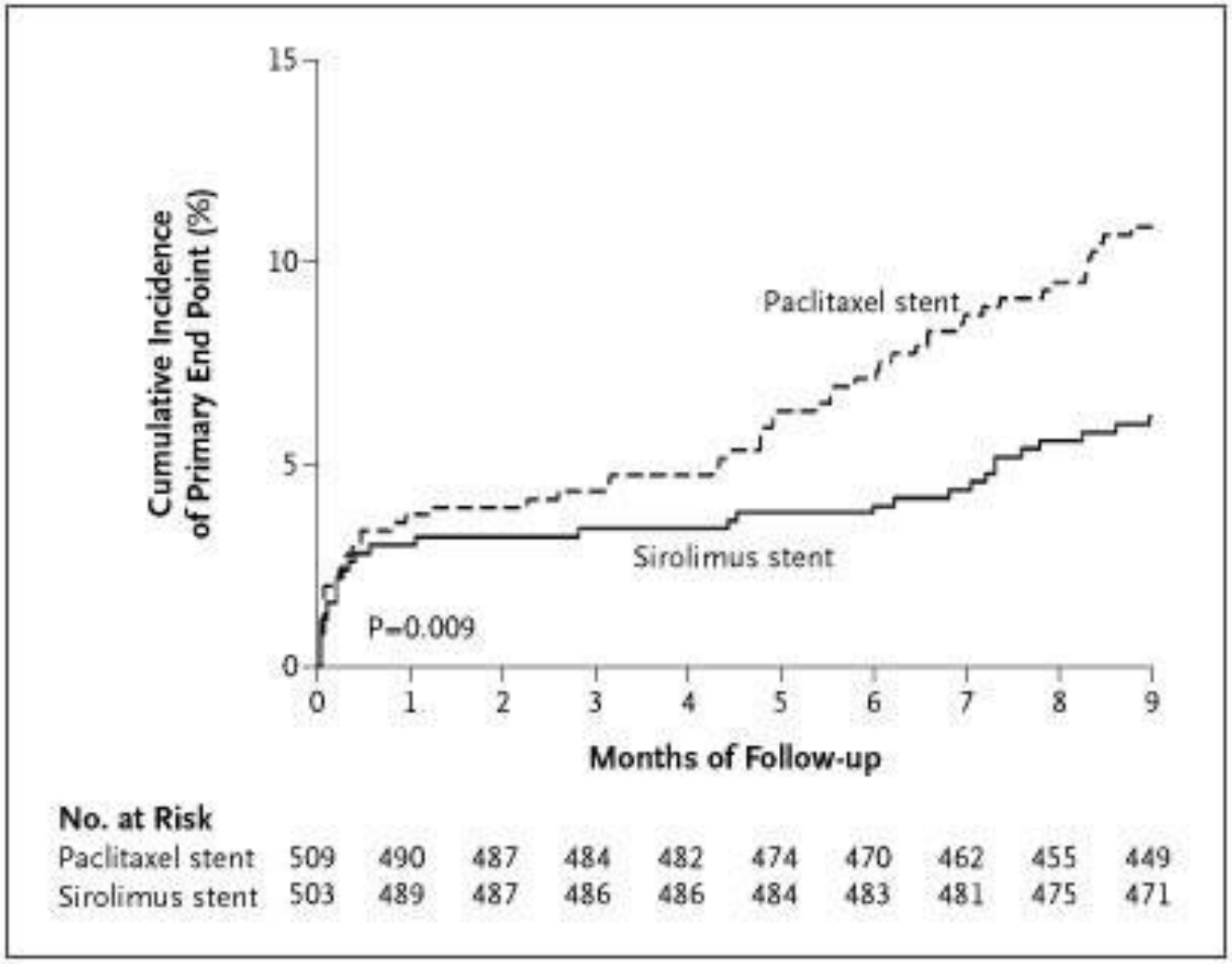




Do we need sirolimus?

- Rapalogs provide high level of safety – DES "drug of choice"
- PTX chosen for DEB because tissue transfer/absorption is far simpler

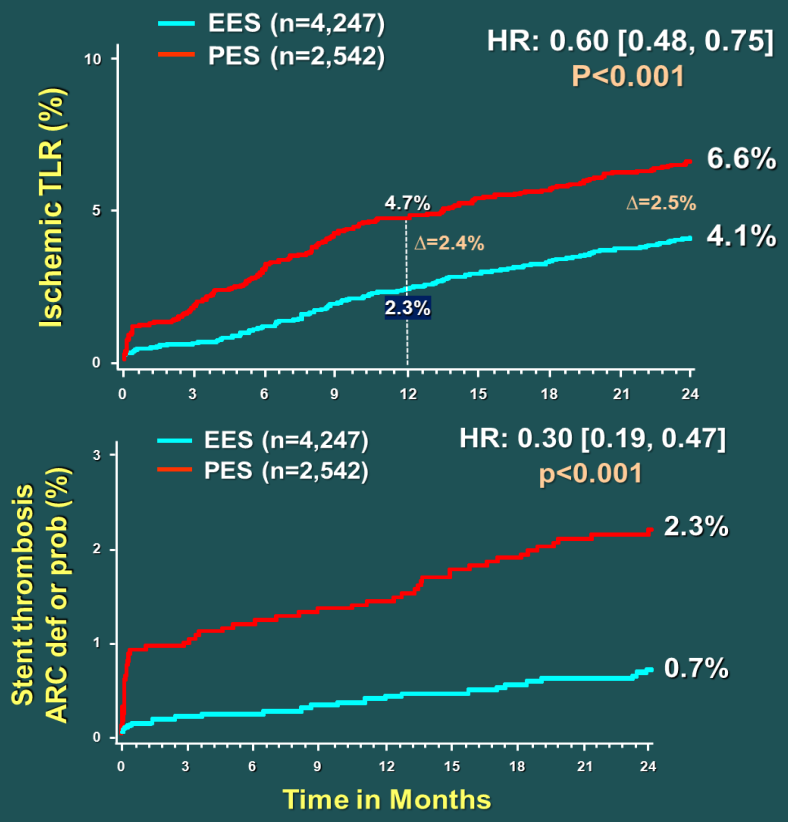
Attribute	Rapamycin (or Analogs)	Paclitaxel	Advantage
Mode of Action	Cytostatic	Cytotoxic	Rapamycin
Margin of Safety	10,000 fold	100 fold	Rapamycin
Anti-restenotic	YES – Lower Late Loss	YES	Rapamycin
Tissue Absorption	Longer	Shorter	Paclitaxel
Level of Competition	Low	Very high	Rapamycin
Physician Perception	Positive	Controversial	Rapamycin



Windecker et al. N Engl J Med 2005;353:653-662

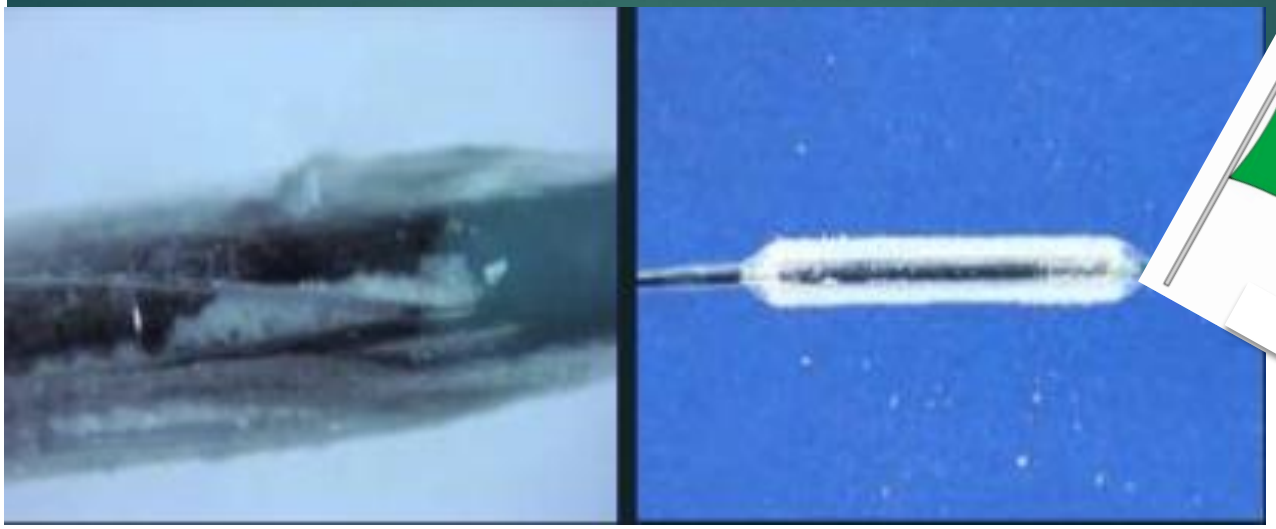
DES Efficacy and Safety
Lessons Learned From the Taxus™ Program

SPIRIT II, III, IV and COMPARE trials
Pooled Database Analysis (n=6,789)



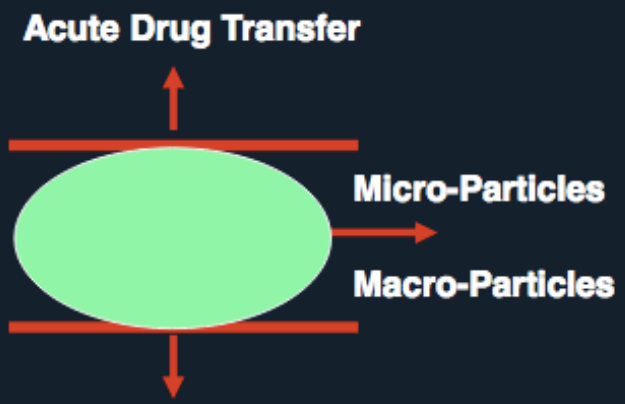
Kereiakes DJ et al. EuroIntervention 2011:7:74-83

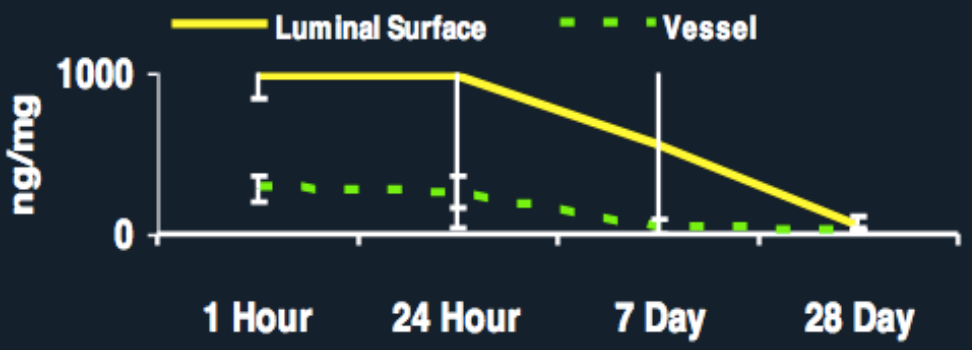
Drug Coated Balloon



First Generation Coating:

- Clinically effective formulation
- Manual “dip coating” technique
- Inconsistent drug coating concentration
- Significant drug loss at insertion
- High particulate formation



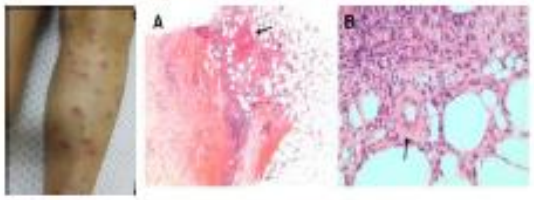


- Most of Paclitaxel remains on the vessel surface
- This "drug-reservoir" creates a gradient and serves as the source for sustained drug delivery
- Once the drug is transferred to the media of the vessel, tissue clearance depends on well described PK curves

Complications associated with Paclitaxel DCB downstream embolism

Panniculitis:
Downstream panniculitis secondary to Paclitaxel DEB
Ibrahim et al, JACC Cardiovasc Interv 2016;12:e177-9

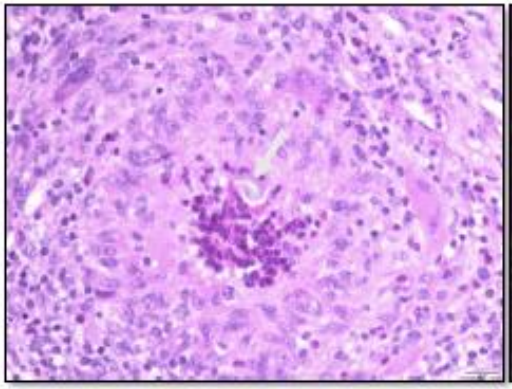
Vasculitis:
Vasculitis resulting from SFA angioplasty with a Paclitaxel DEB
Thomas et al, J Vasc Surg 2014; 59:520-3

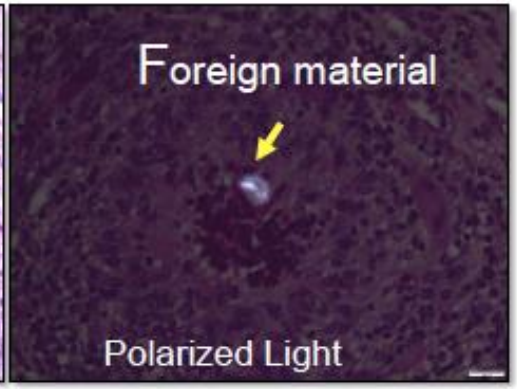


Hypersensitivity:
Acute hypersensitivity reaction to a Paclitaxel DEB
Lake et al, Vasa 2017; 46:223-5

Amputation Risk:
Amputation-free survival was significantly worse in CLI patients treated with paclitaxel versus plain angioplasty (Hazard ratio 1.52; 95% confidence interval: 1.12–2.07, p = .008)
Katsanos et al, JVIR 2020; 31:202-12

- ❑ Assessment for histologic findings
  - ✓ Infarction or microscopic scarring or necrosis
  - ✓ Emboli or foreign material





DEB technology: second generation

Device	Drug	Technology/Excipient	Dose (ug/mm^2)	Company	Approval
Selution	Sirolimus	Cell Adherent Technology (CAT™) Amphipathic Lipid Carrier	1	Med Alliance	CE certified IDE for small vessels and ISR ongoing
SeQuent Please SCB	Sirolimus	BHT (Butylated Hydroxy Toluol)	4	BBraun	CE certified
Magic Touch	Sirolimus	Nanolute technology (Phospholipid Based Excipient)	1.27	Concept	CE certified IDE for ISR ongoing
Mozec SEB	Sirolimus	Solid lipid nanospheres (SLN) consisting of Sirolimus + lipid	3	Meril	CE certified
Biolimus A9 BCB	Biolimus A9	Polyethylene oxide (PEO)	3	Biosensors International	-
Virtue	Liquid sirolimus	Submicron Sirolimus particles lyophilized with lyoprotectants	N.A.	Orchestra Biomed	-

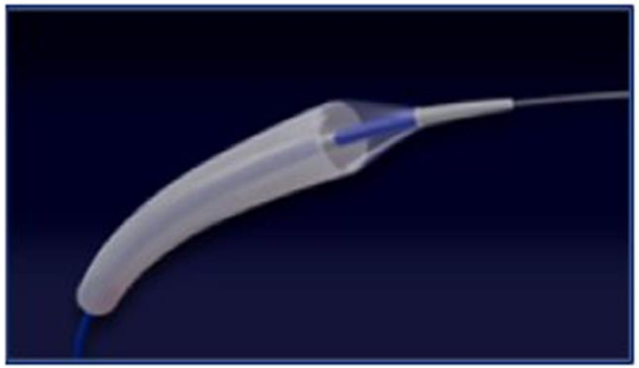
Technology

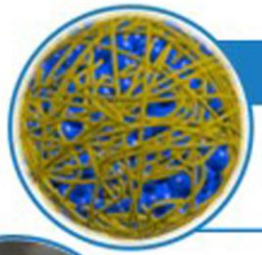
Drug coated balloon

Drug eluting balloon

SELUTION SLR™ DEB Technology

Sirolimus-Eluting Balloon with Sustained Release





Proprietary MicroReservoir Technology

- Creation of MicroReservoirs combining sirolimus & biodegradable polymer
- Sirolimus - a proven safe & effective cytostatic drug
- Offering a wider therapeutic range

MicroReservoirs: Miniature Drug-Delivery Systems

- Optimal size MicroReservoirs to achieve pharmaco- kinetic release profile comparable to best-in-class DES
- Consistent and predictable drug release
- Sustained therapeutic effect for up to 90 days[1]

Cell Adherent Technology (CAT™)

Proprietary amphipathic lipid technology which binds MicroReservoirs to the balloon surface

- Contains and protects micro-reservoirs during insertion and inflation
- Enhances drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1 µg/mm²)
- Optimizes transfer of MicroReservoirs to the tissue and maximizes the cellular uptake of sirolimus

1.Drug concentration evident in MicroReservoirs and tissue - Data on file at M.A. Med Alliance SA

SELUTION SLR & CAT are trademarks of M.A. Med Alliance SA.
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Cell Adherent Technology (CAT) acts as a "transfer membrane" that :

- **Contains and protects** MicroReservoirs during balloon insertion, lesion crossing and inflation.

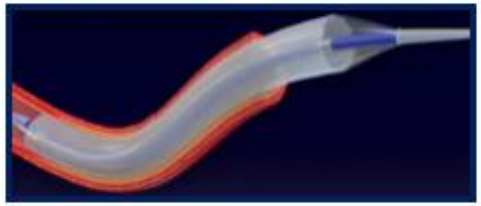
- **Enhances transfer** from balloon surface and **adheres** to vessel lumen during short balloon inflation.

- **Lowers** drug loss during transit to lesion and inflation.

- **Facilitates** absorption of MicroReservoirs into the vessel wall.

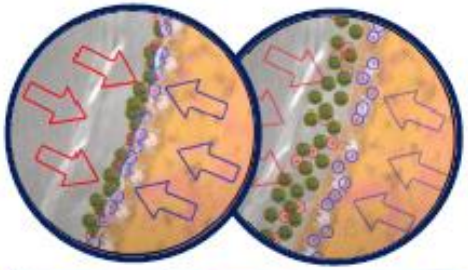
Proprietary Balloon Coating Technology - CAT™ 3 Mechanisms of Action

Utilizes **3 mechanisms of action** to bind coating to the cell membrane:



#1 Mechanical

→ Balloon compliance ensures optimal apposition of CAT coating to the vessel wall.

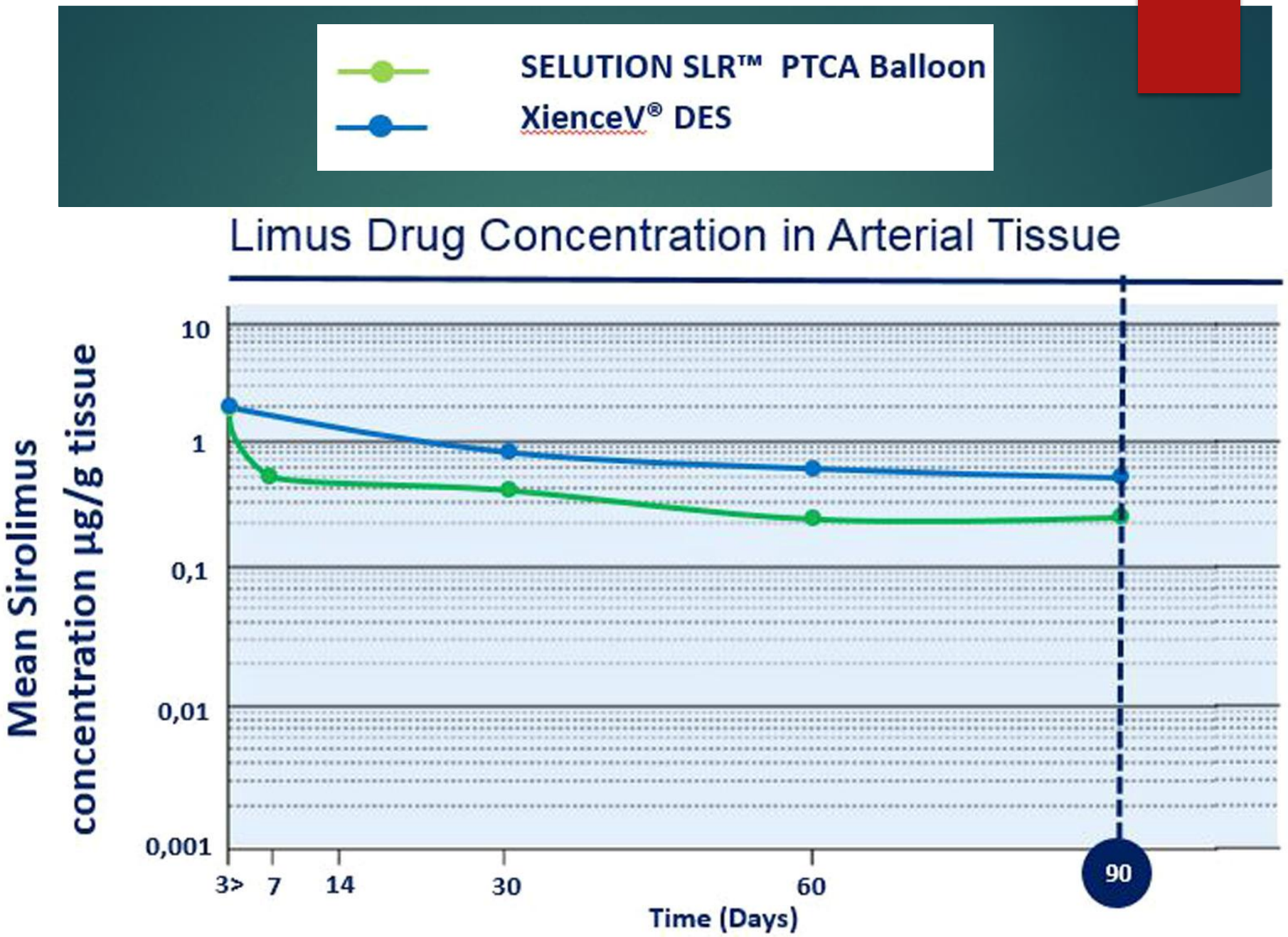


#2 Electrostatic

→ CAT coating is attracted to vessel wall through ionic interaction.

#3 Biological

→ Highly lipophilic CAT coating binds to fatty cells optimizing MicroReservoirs transfer into the vessel wall.

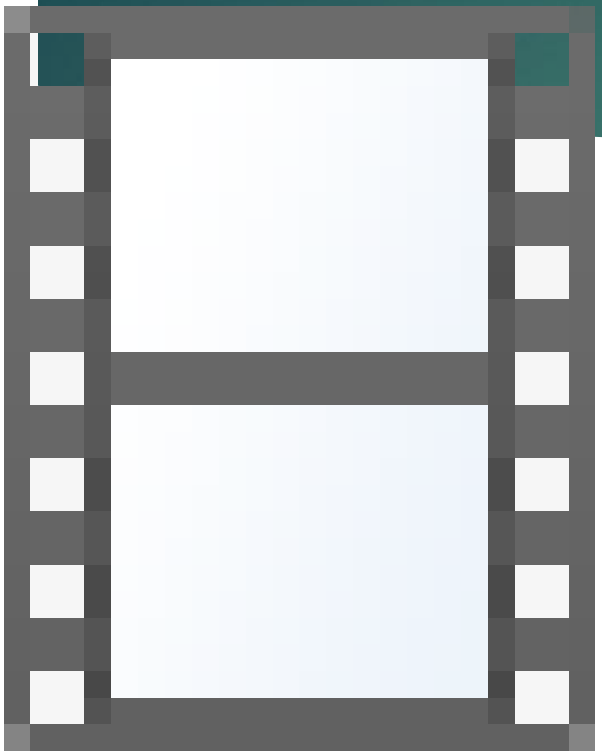

SELUTION SLR™ PTCA Balloon
XienceV® DES
Limus Drug Concentration in Arterial Tissue
Mean Sirolimus concentration µg/g tissue
10
1
0,1
0,01
0,001
3>
7
14
30
60
90
Time (Days)

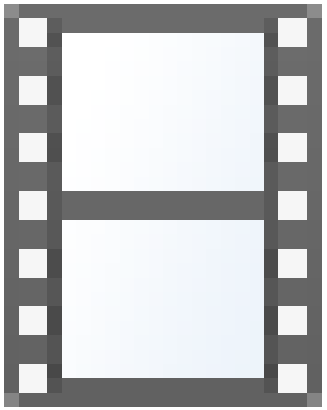
Restenosi intrastent
Piccoli vasi
Lesioni lunghe

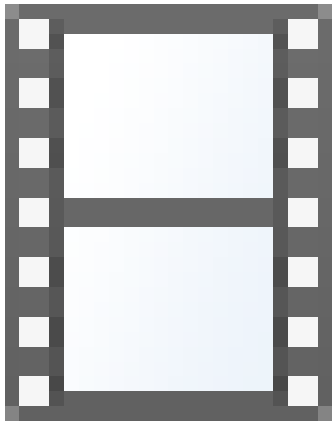
Restenosi occlusive intrastent
Multi vasali
Biforcazioni
Occlusioni
Calcificazioni
Lesioni prossimali
Lesioni complesse

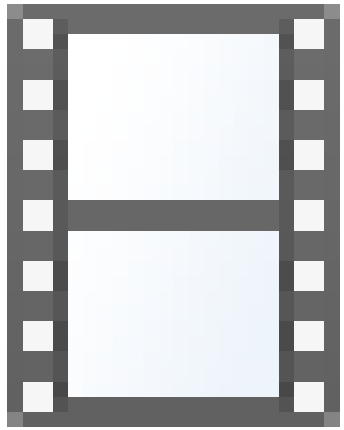
Caso #1, N.R., 69

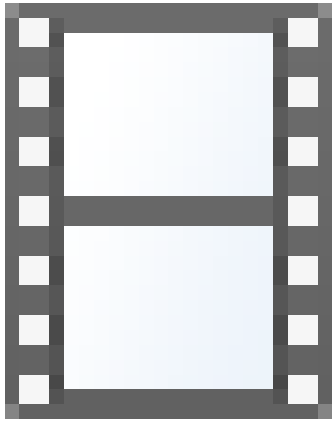
Angiography before PCI

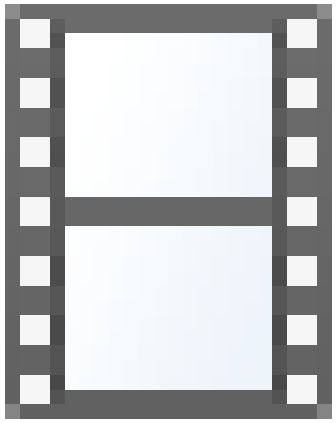


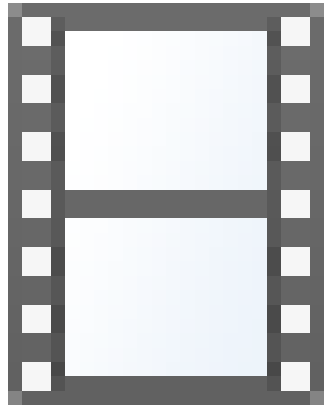






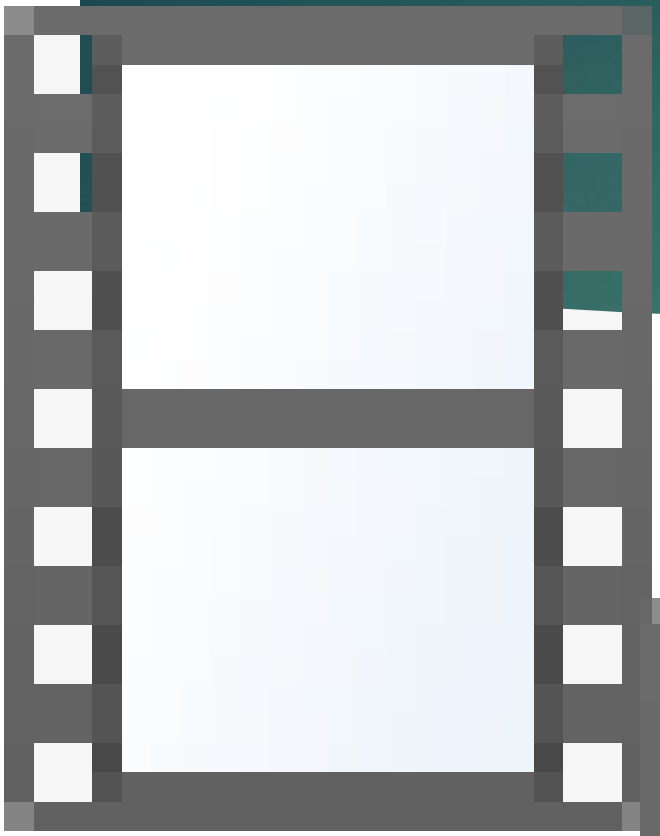




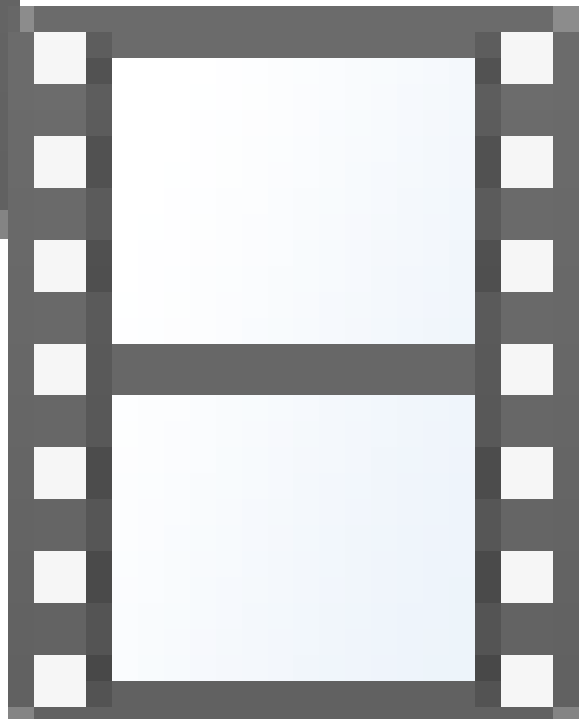


Images courtesy of Dr. Luigi Salemme; used with permission

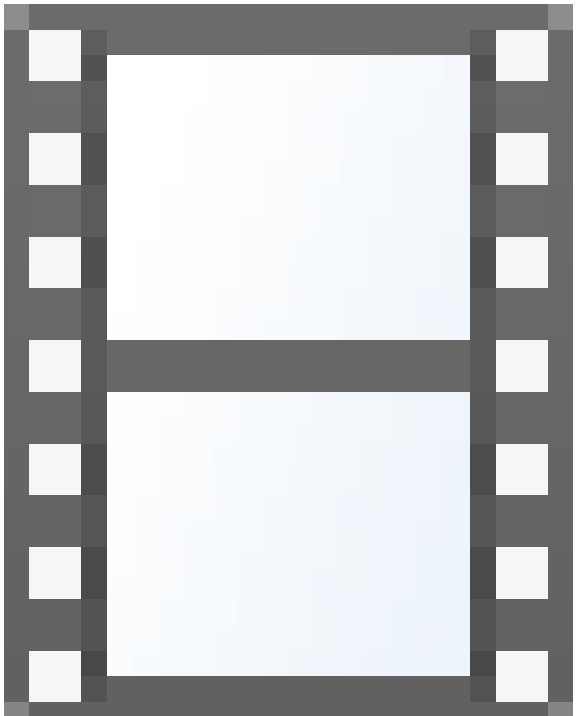
Post Pre-dilatation



SELUTION SLR™
2.5-40 distal LAD



SELUTION SLR™
3.0-40 mid LAD



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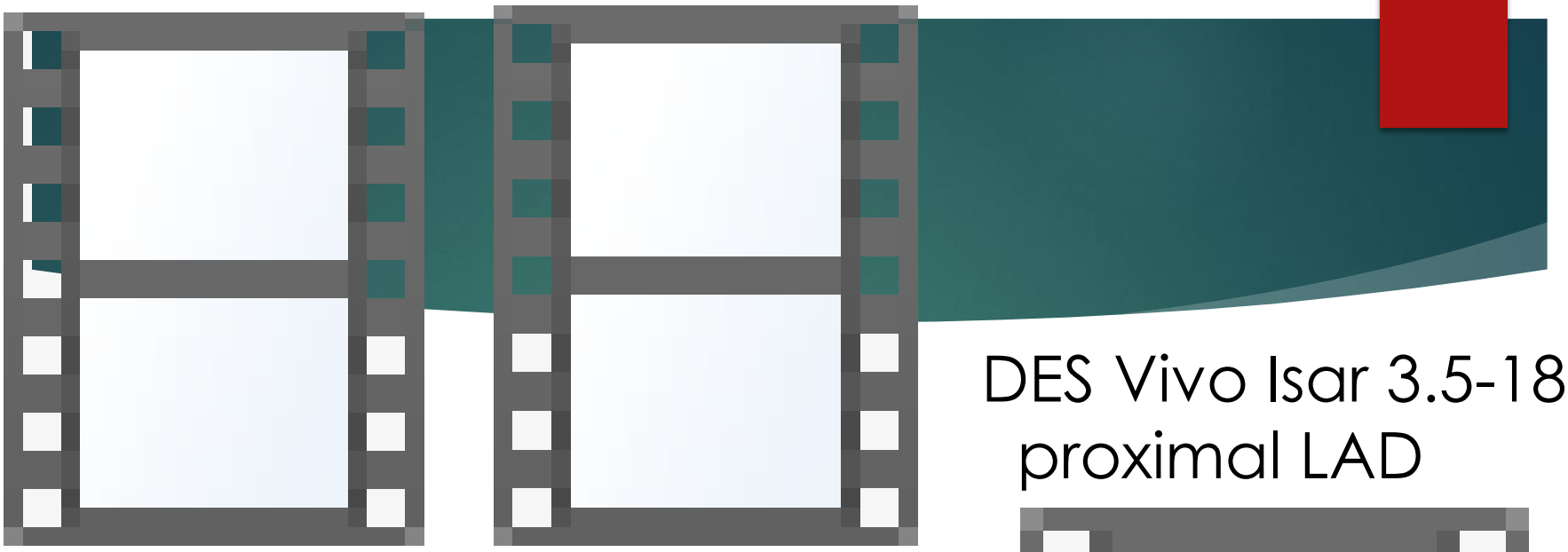
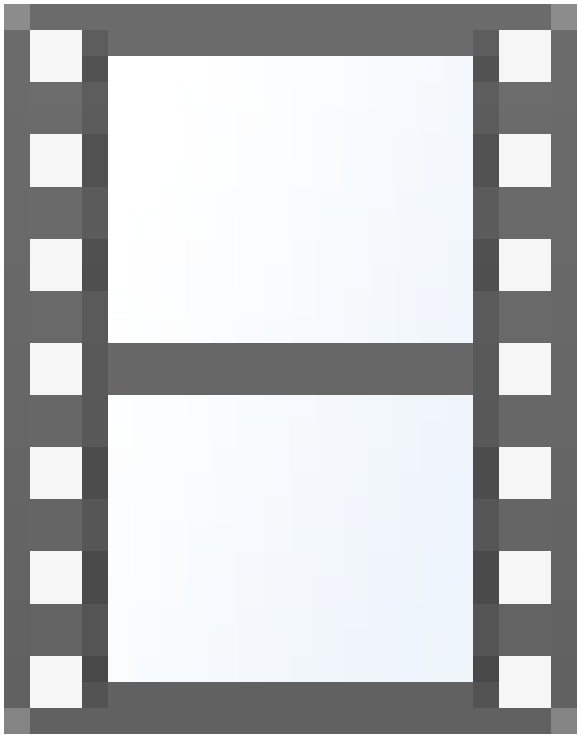
First Diag 2.5-30

SELUTION SLR™ 2.5-40



DES Vivo Isar 3.5-18
proximal LAD



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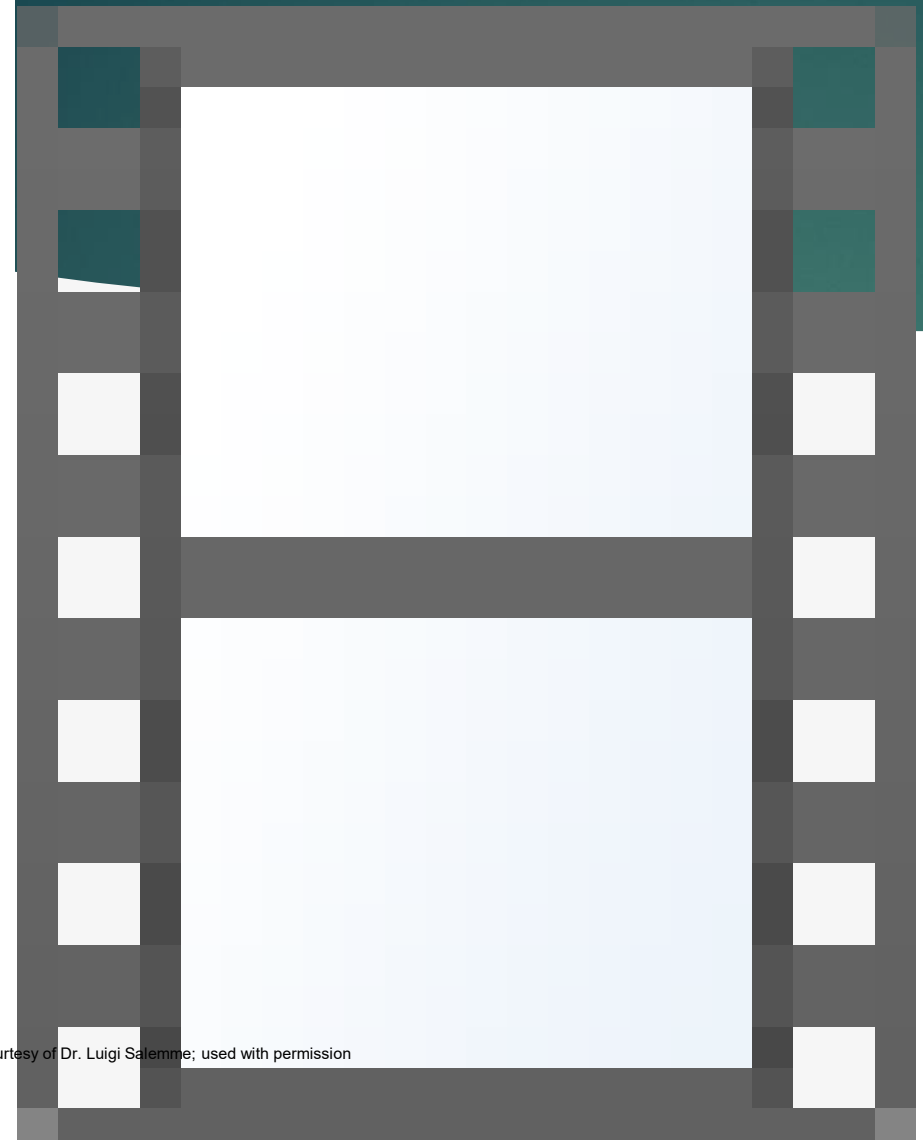
Final Angiography



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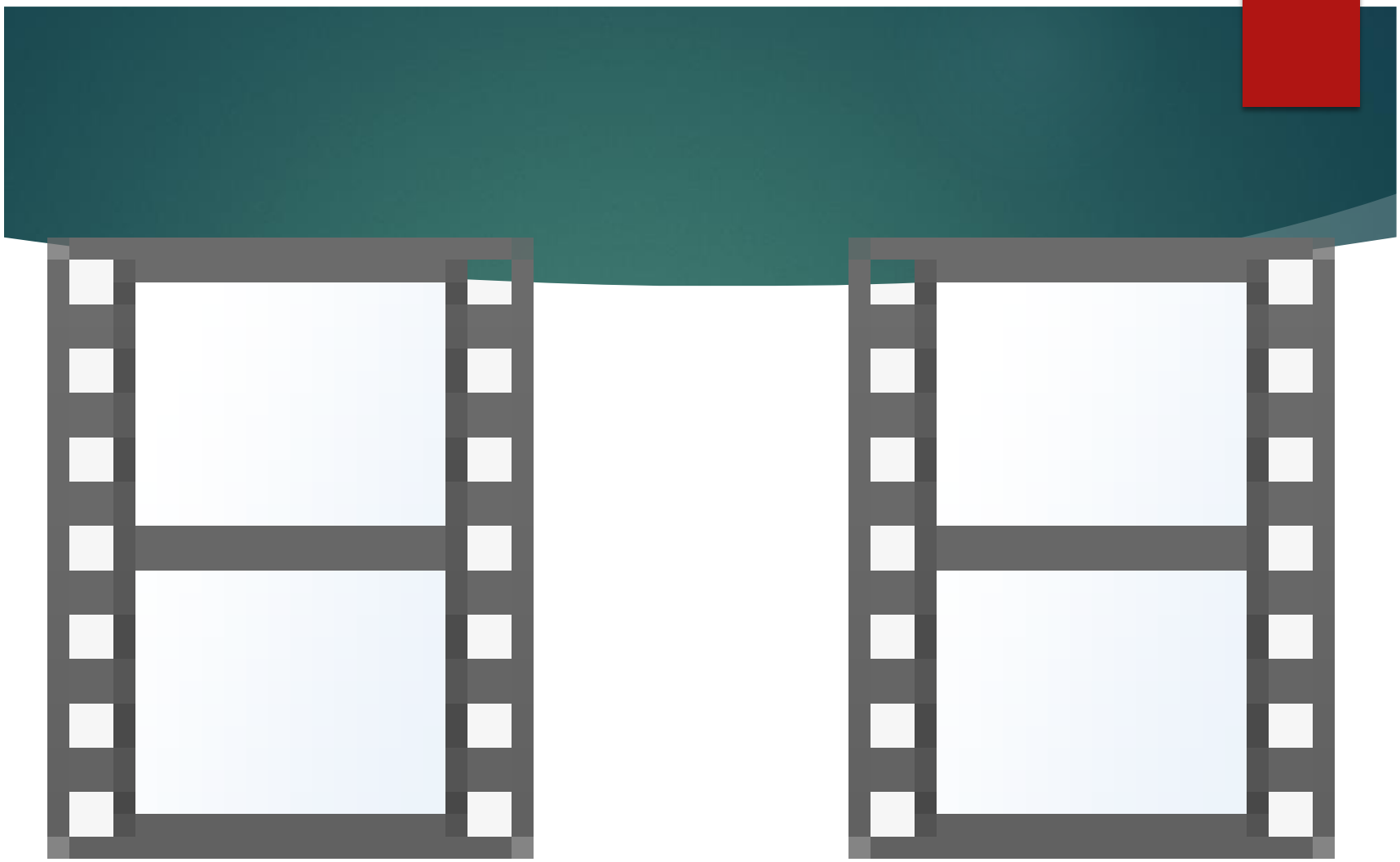
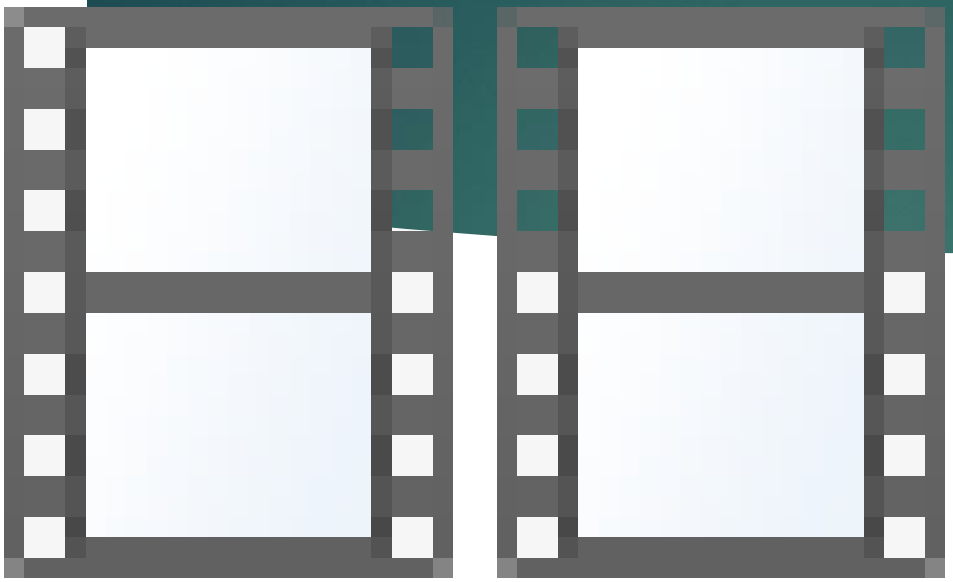
Hybrid procedure

DES prox LAD
DEB mid and distal LAD and first diagonal

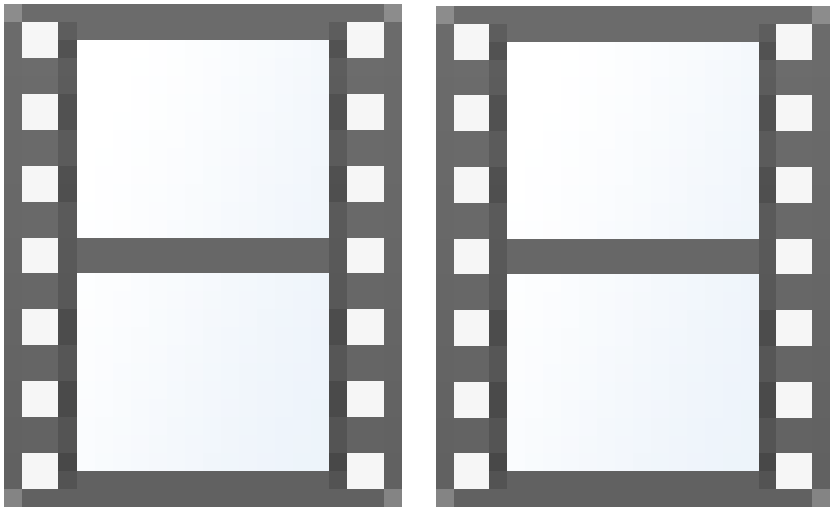
4 months LAD Follow-up and circumflex PCI





Pre-dilatation NC 2.5-30 e 3.0-30

Dilatation SELUTION SLR™ 3.0-30 and 3.5-30



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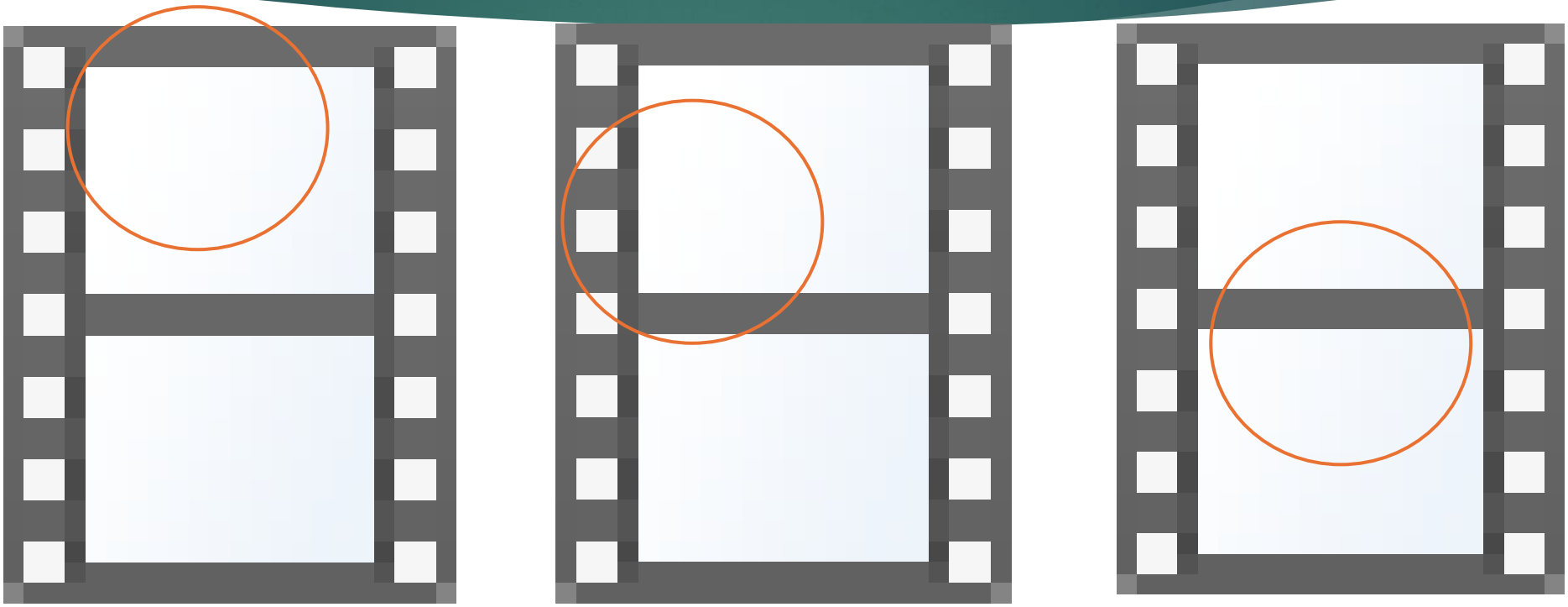
Post DEB angiography: prox dissection Vivo ISAR 3.5-13



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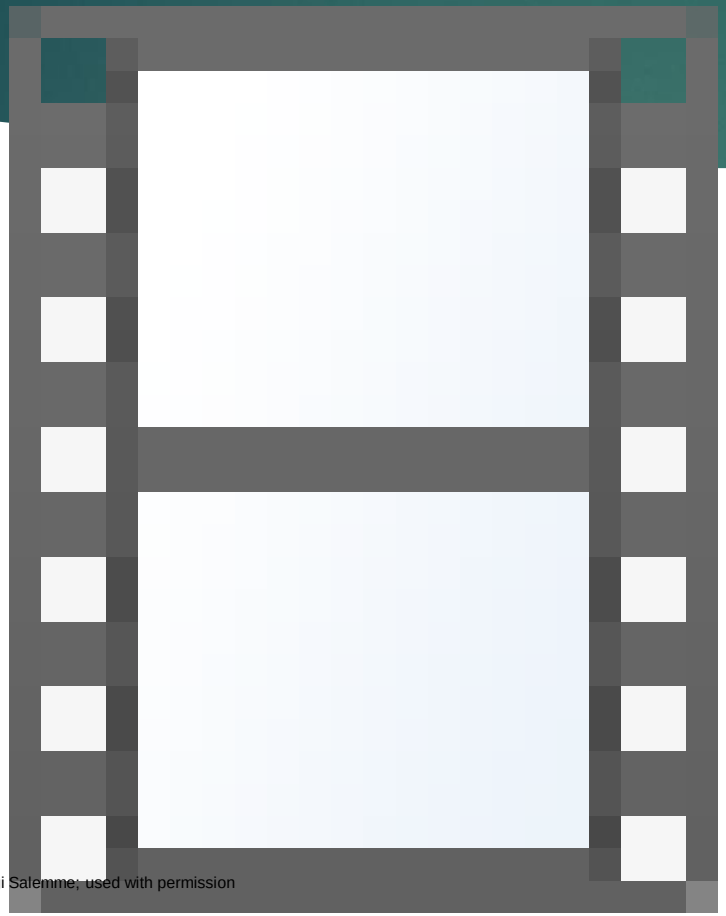
Final Angiography



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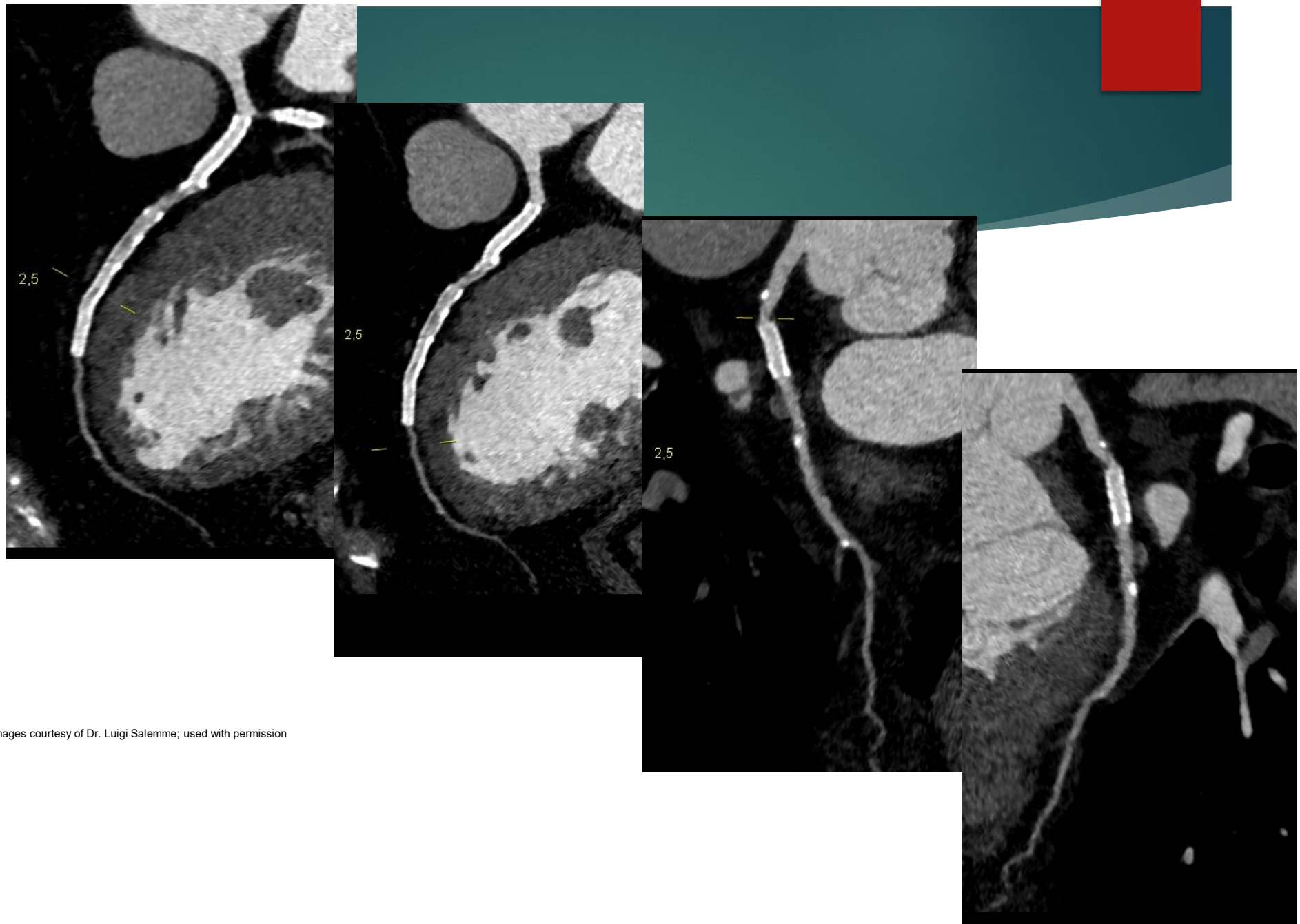
Hybrid procedure

DES ostium circumflex
DEB mid and mid distal circumflex

10 month Coronary CT scan



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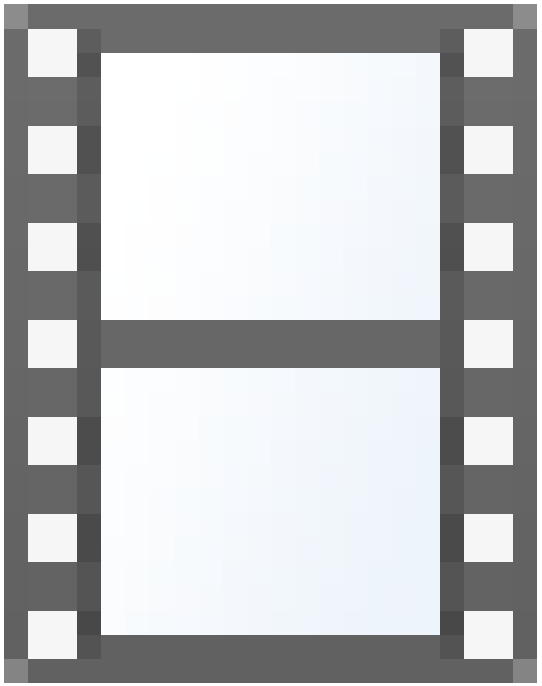
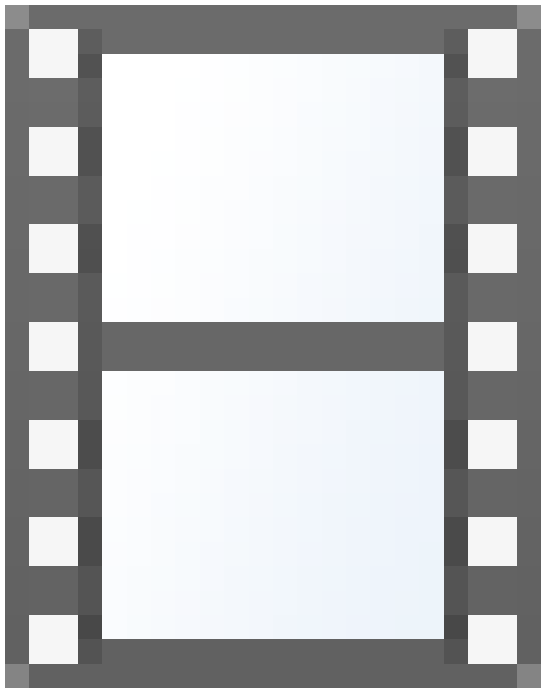
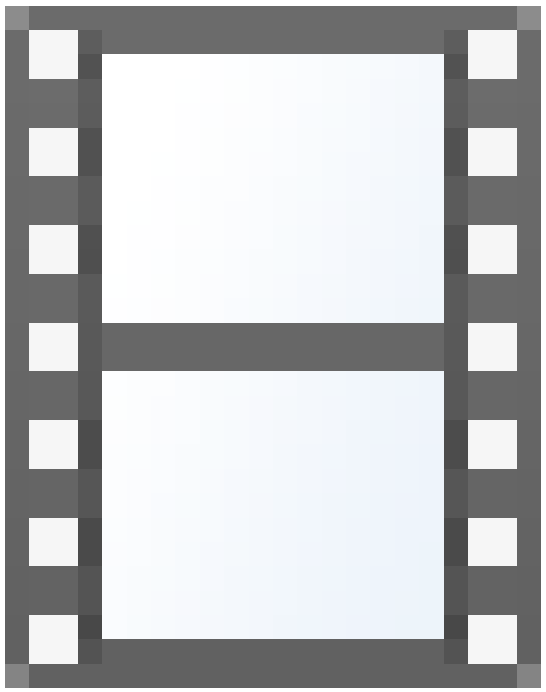
Caso #2, N.R., 88

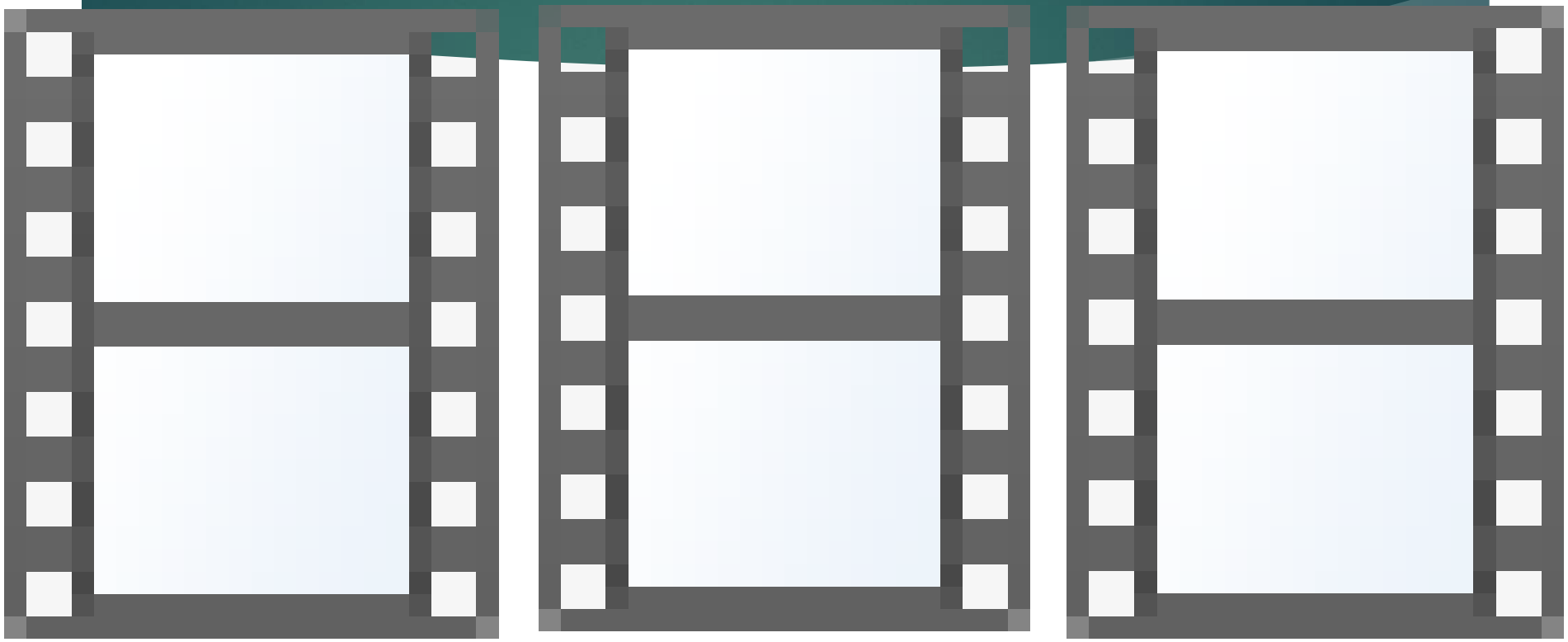
Angiography before PCI

Predil 1.0-10

Rotablator 1.5 mm

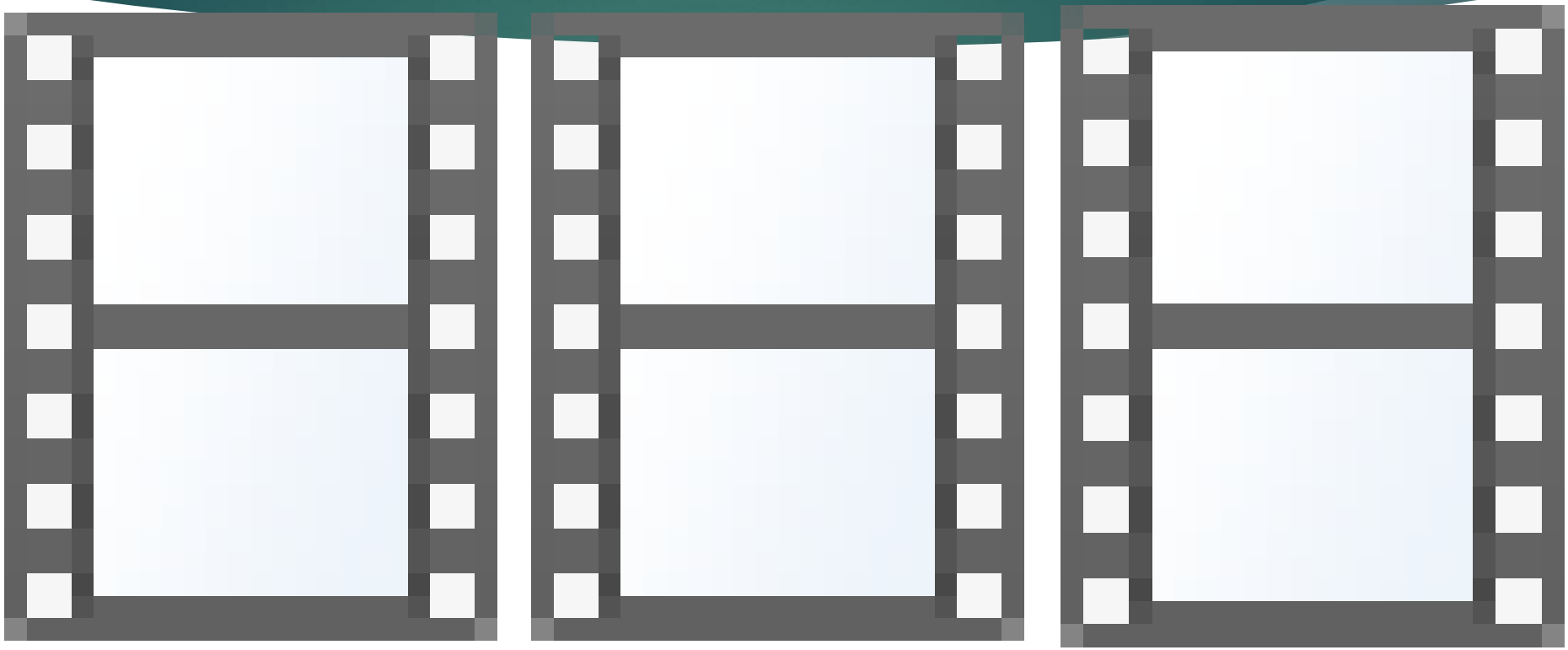
post Rotablator



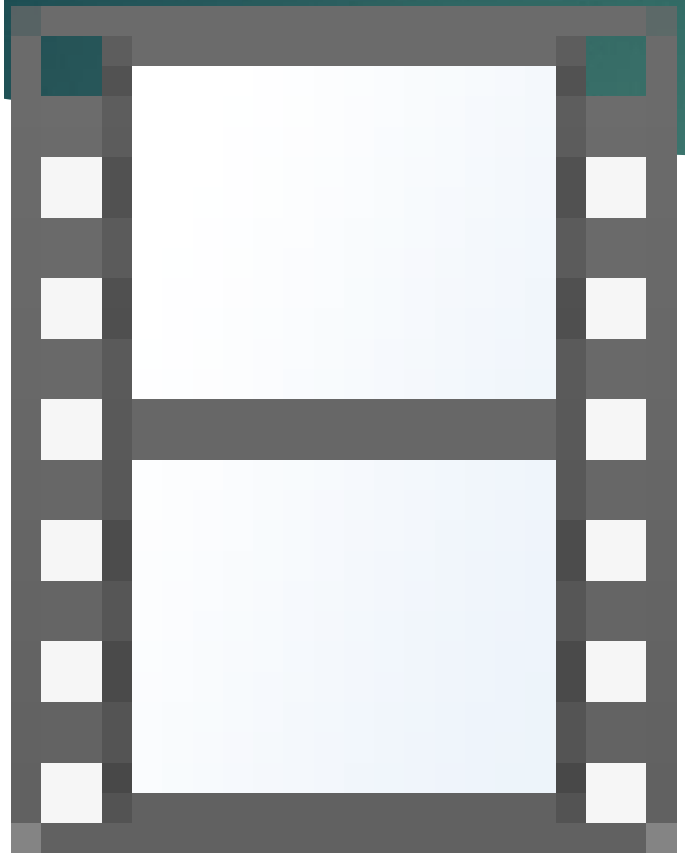
Predil 2.5-30 NC

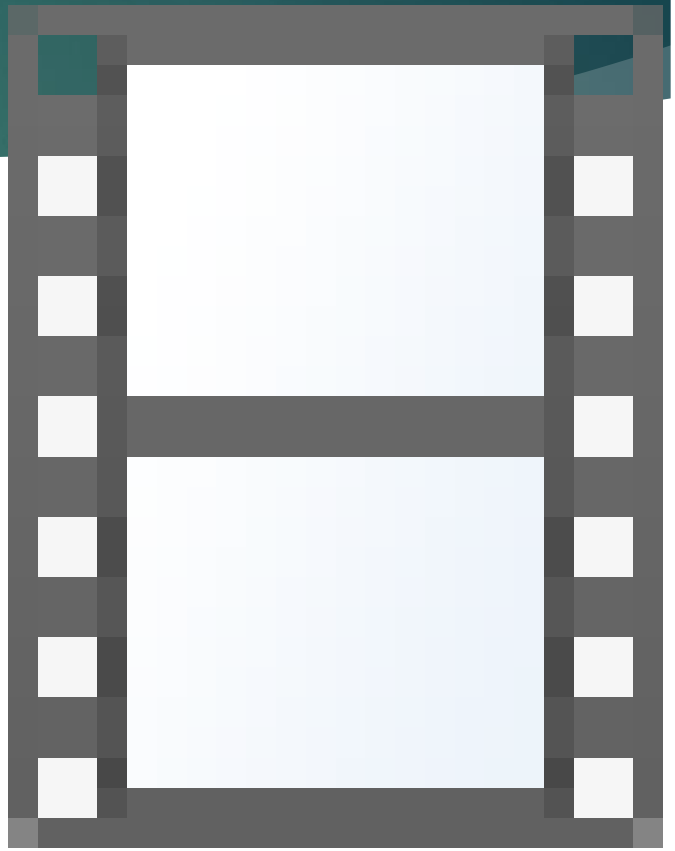
angio post

SELUTION SLR™ 2.5-40

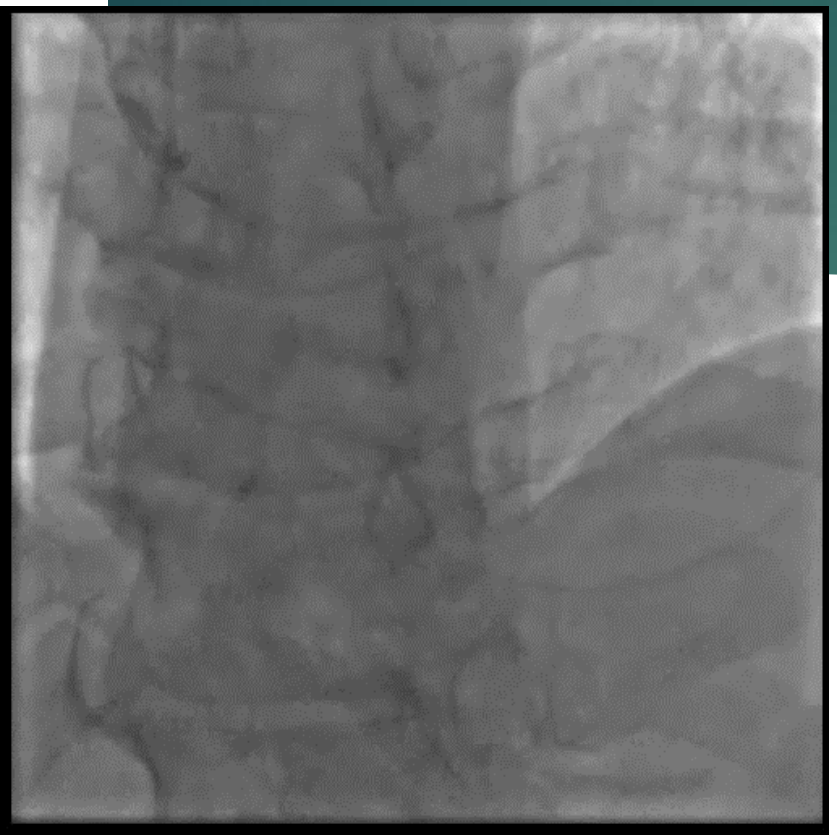


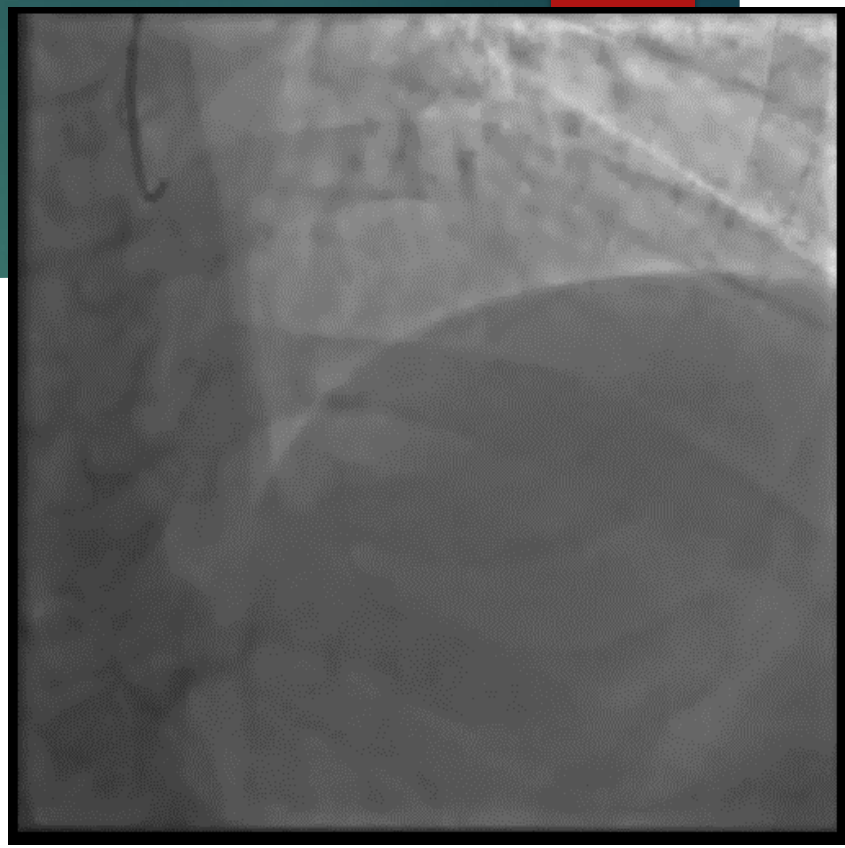
Final angiography



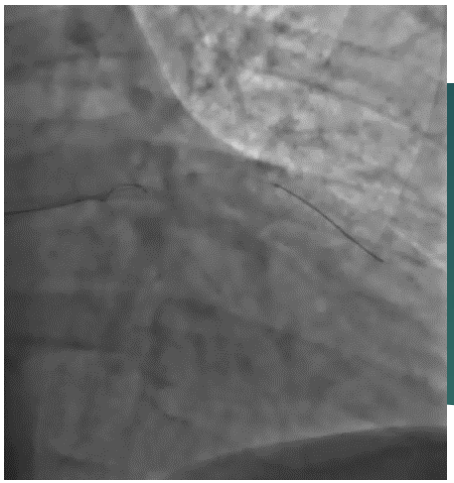


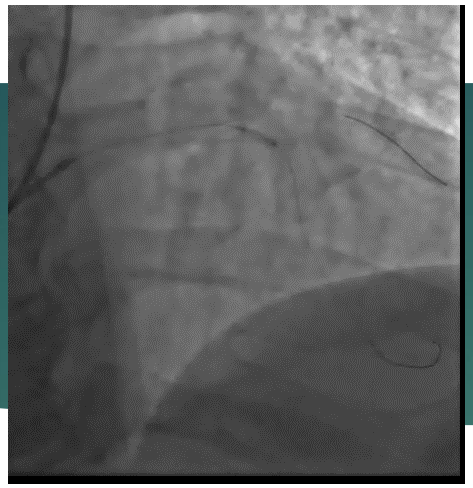
Case #3, R.R., 64 yo, male

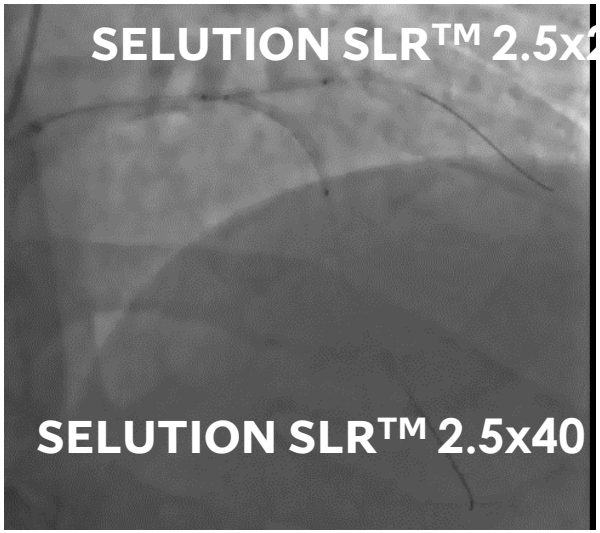


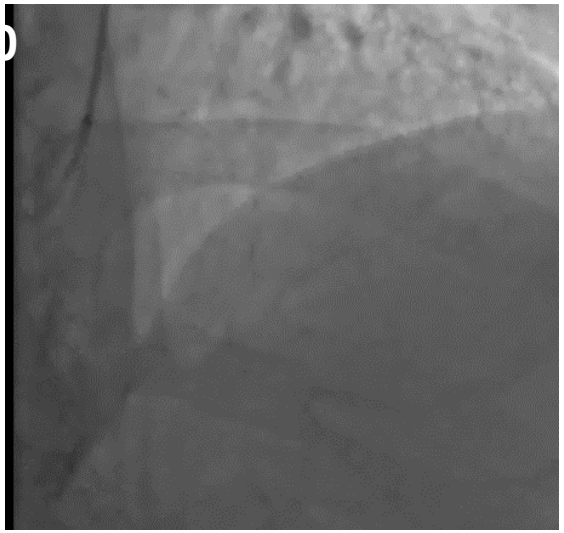


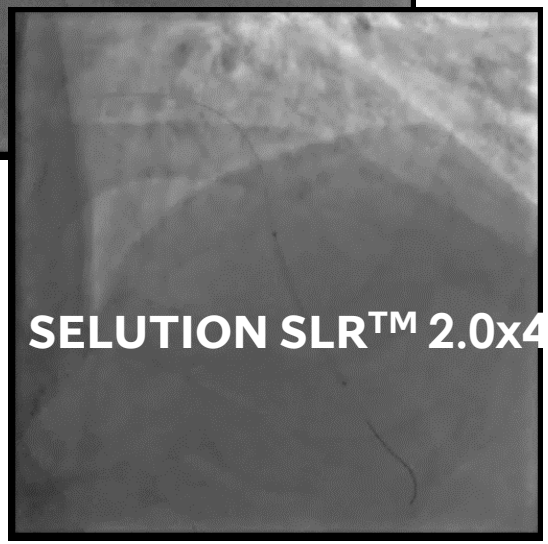
- LAD CTO, severe stenosis first diagonal
- Multiple severe stenosis on circumflex PCI-staged.



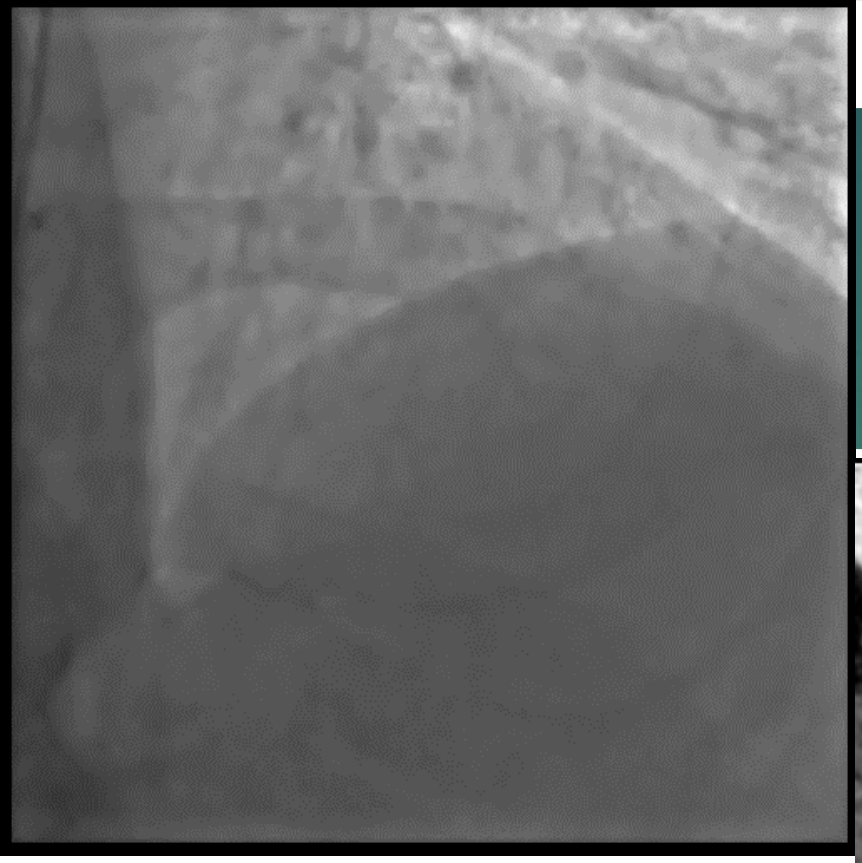



SELUTION SLR™ 2.5x40




SELUTION SLR™ 2.0x4

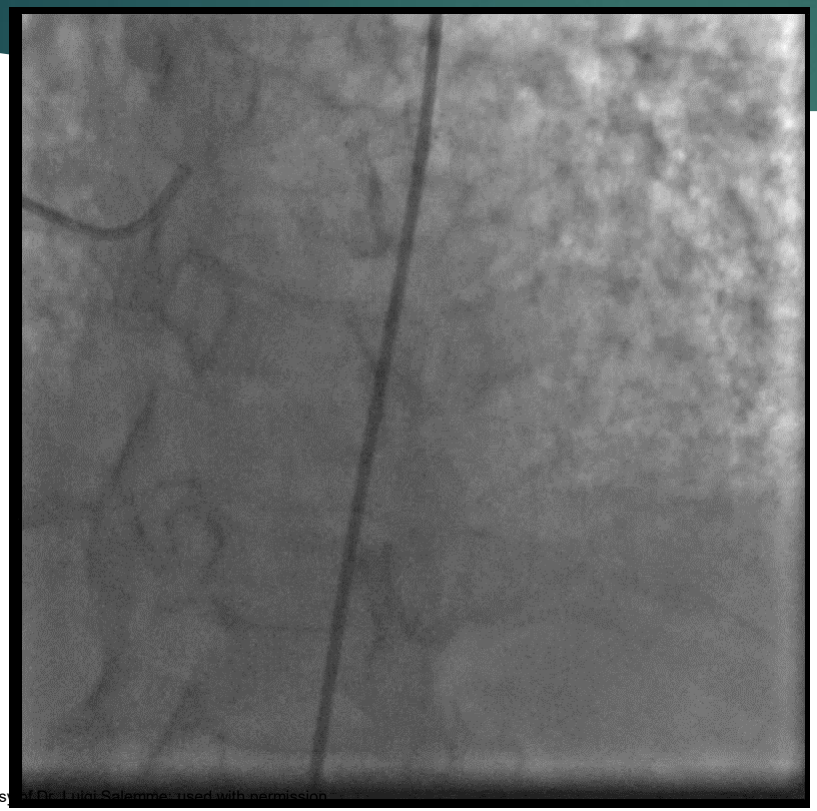
Final angiography



10 monyhs CT scan

Case #4, P.G., 79 yo

June 2023



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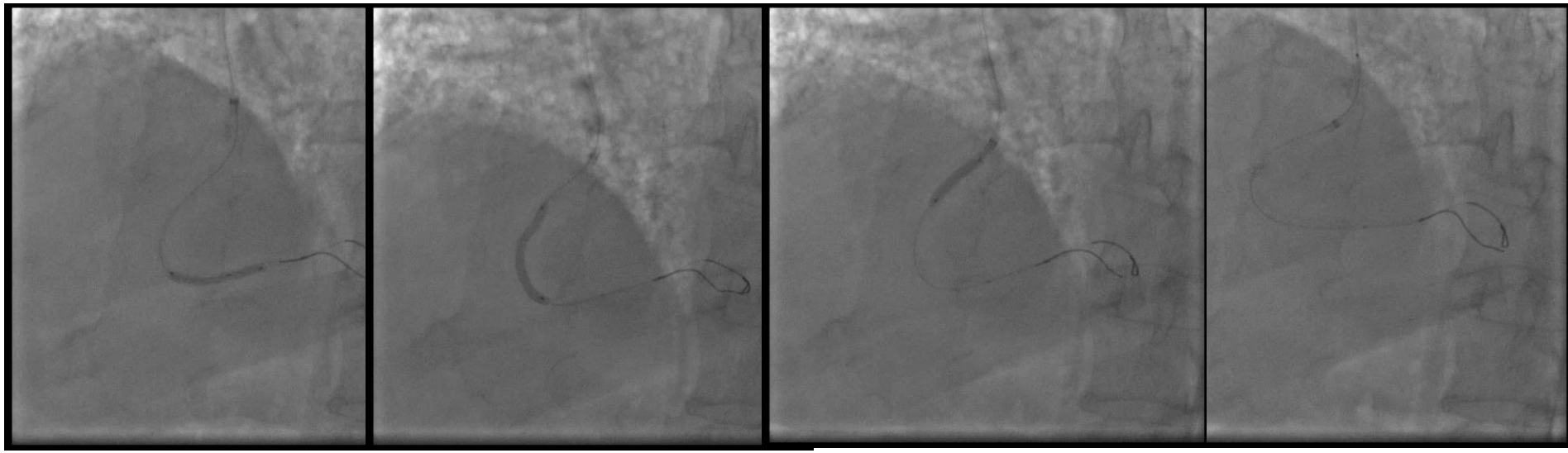
- 99% RCA, intermediate lesion LAD, CTO circumflex

Pre-dilatation SC 2.5x30 mm (20 atm) and 3.0x20 mm Preparation using Cutting 3.0x15 mm ostium, prox and mid



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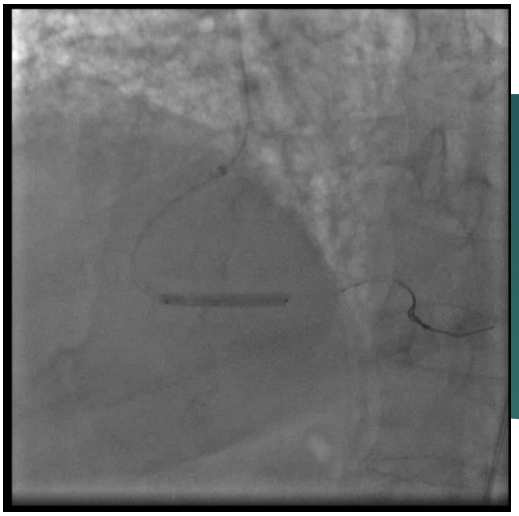
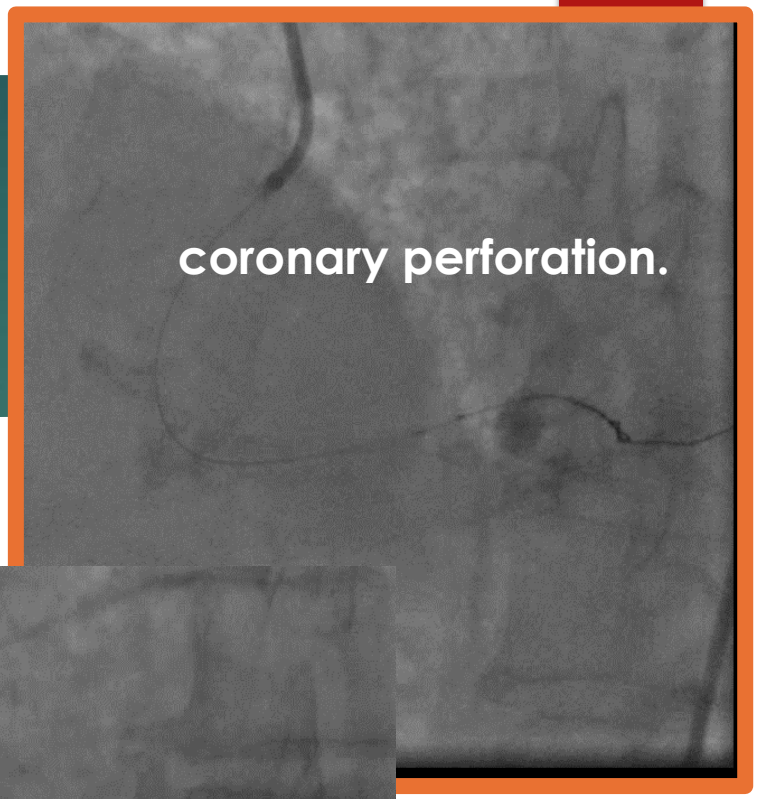
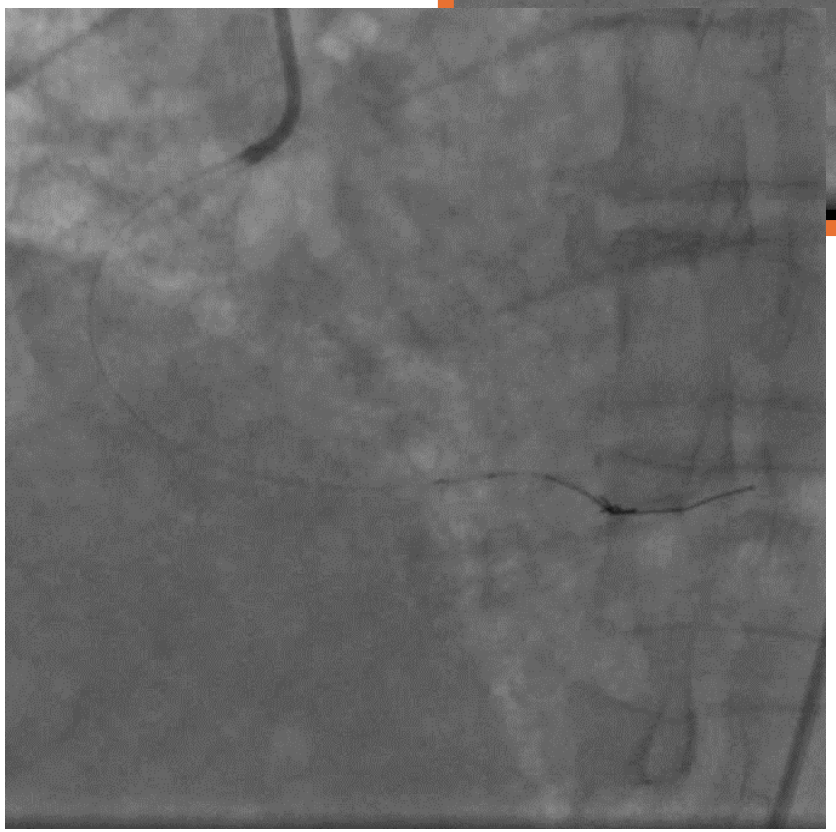
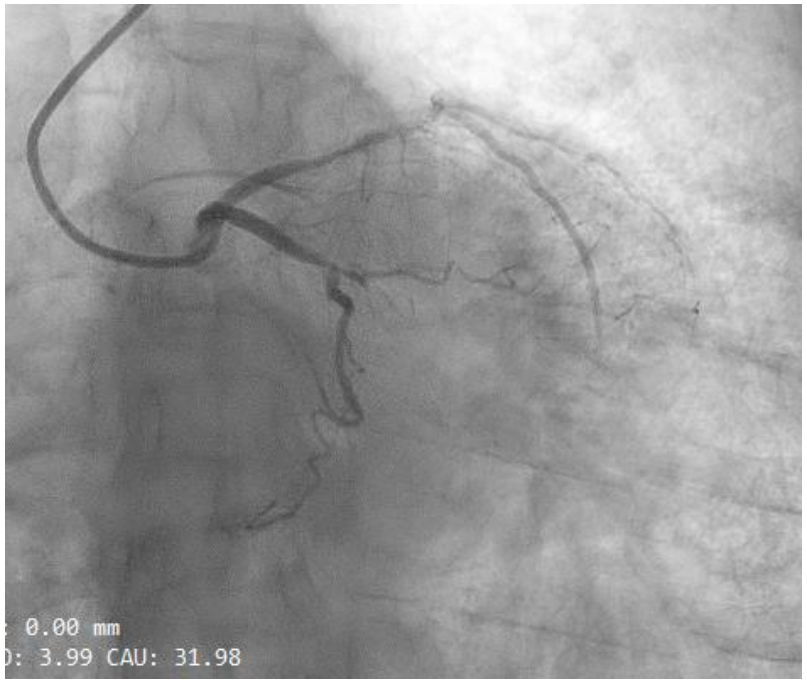


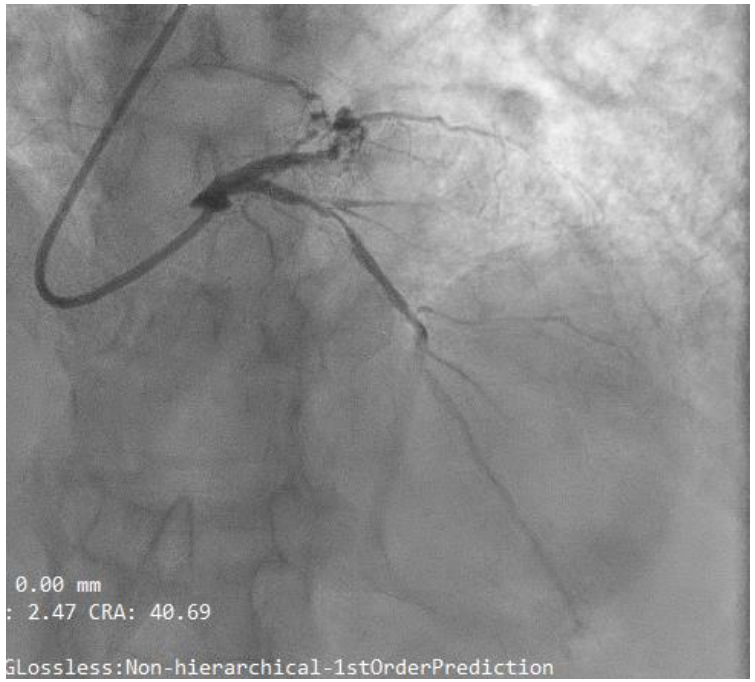


coronary perforation.



- August 2024 NSTEMI
- 90% proximal LAD stenosis treated with PCI and DES





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RCA angiography (14 months follow-up)

Images courtesy of Dr. Luigi Salemme; used with permission

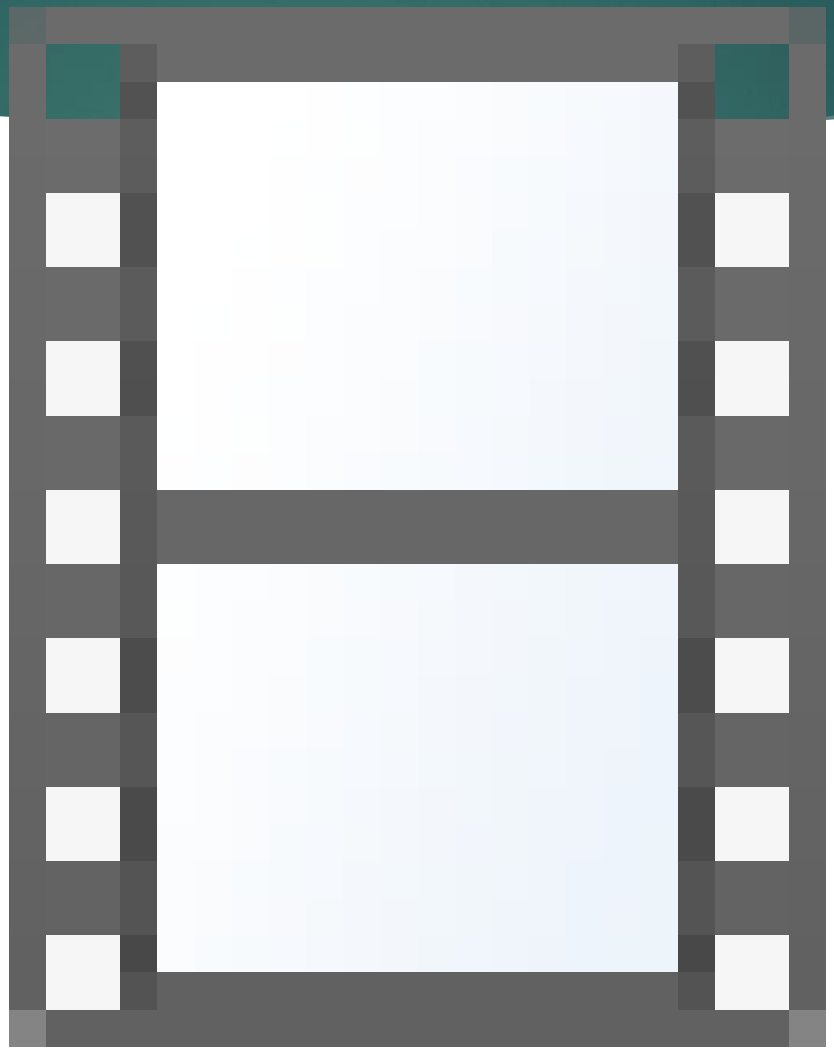
June 2023

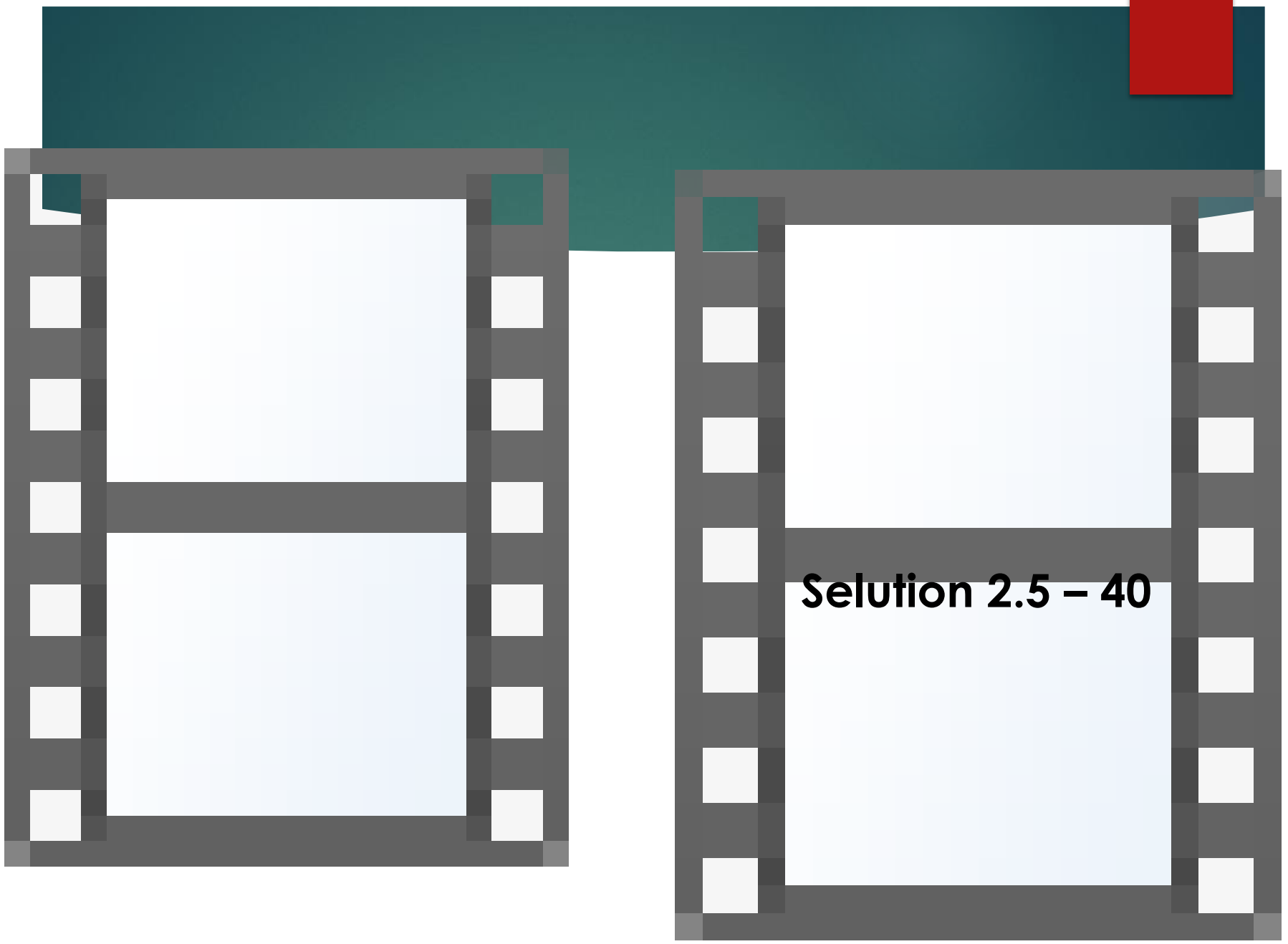
August 2024

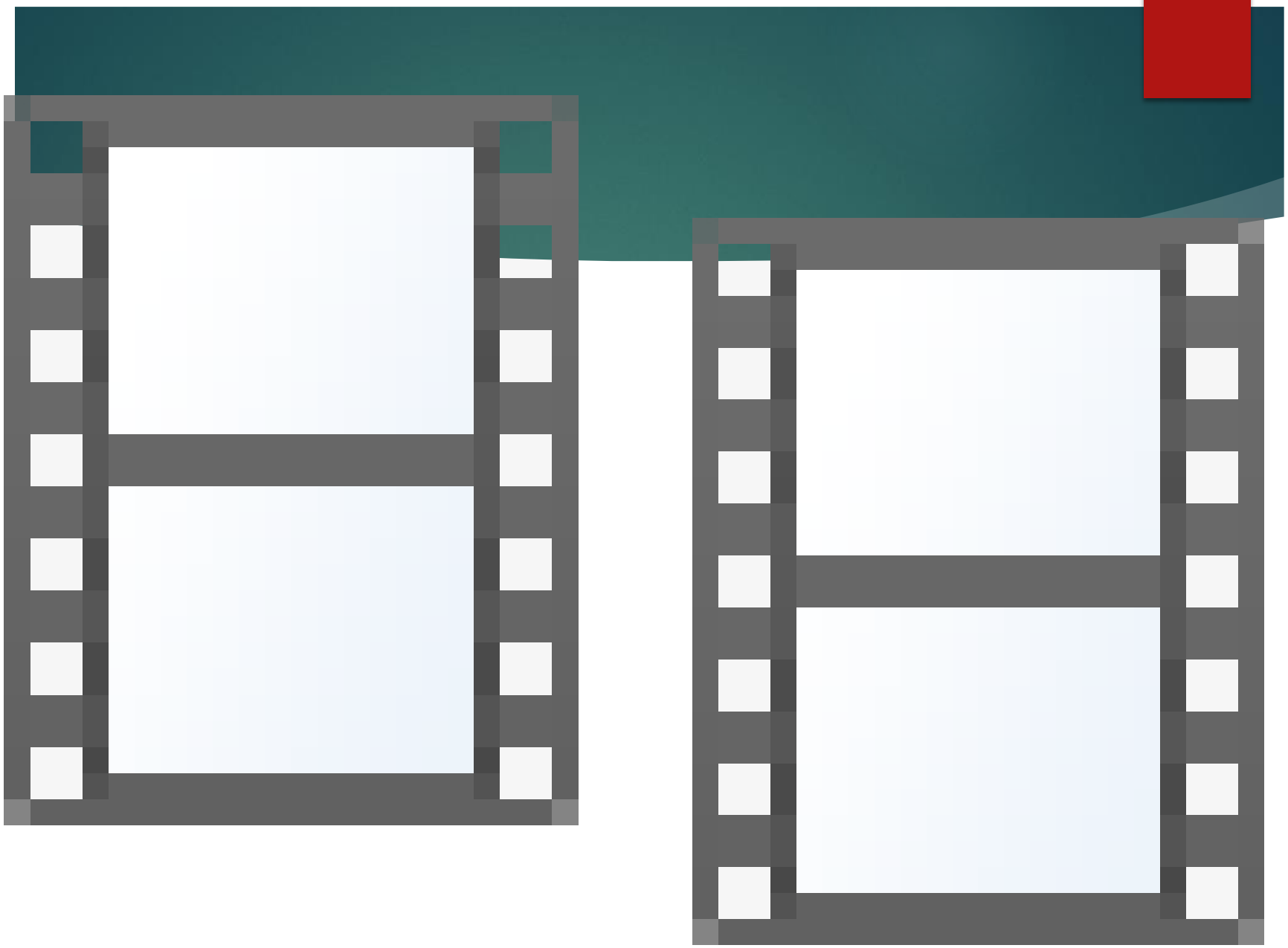
Images courtesy of Dr. Luigi Salemme; used with permission

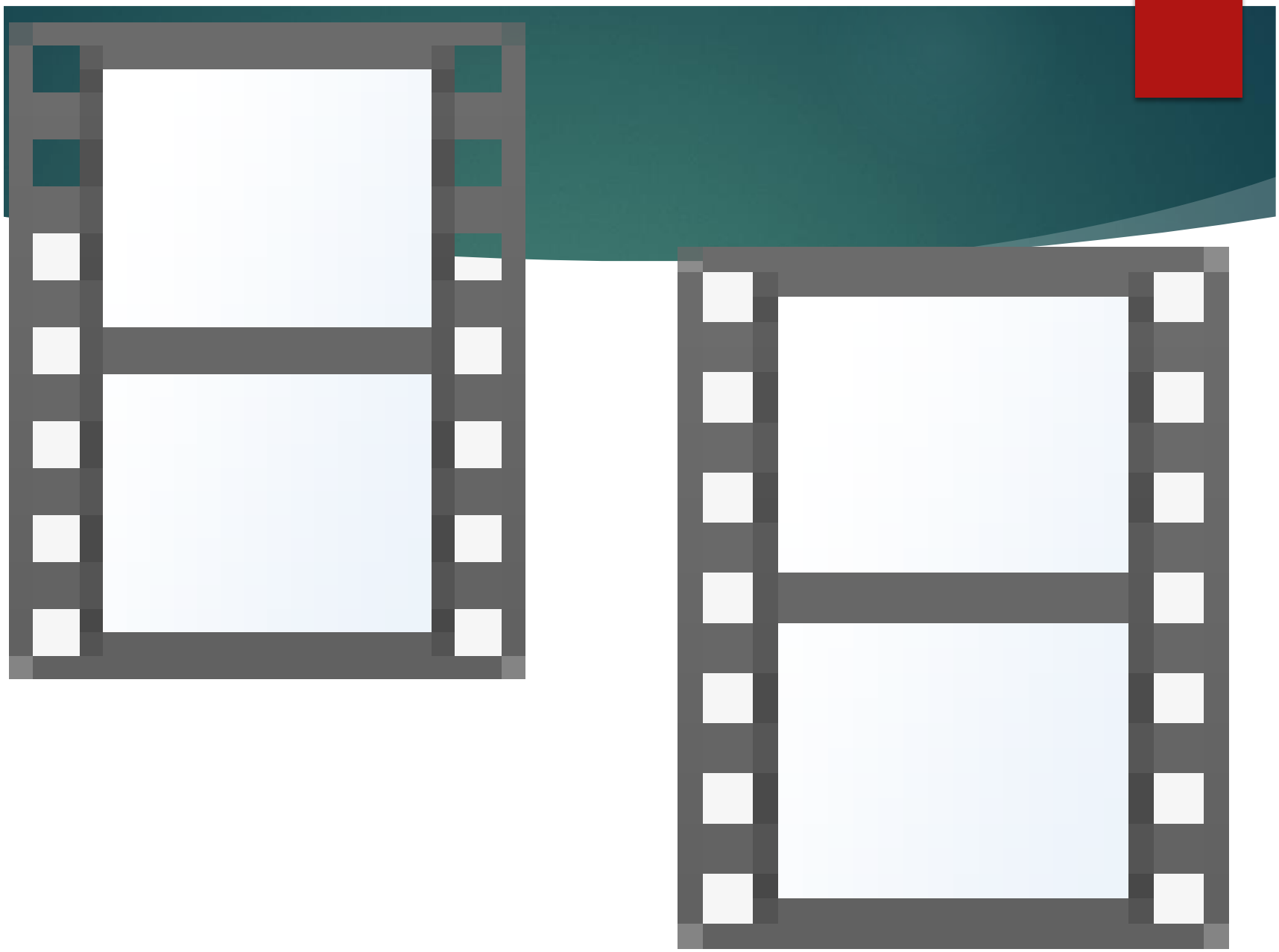
Case #5, C.L. 74 yo

pre PCI angio




Selution 2.5 – 40





24 months F-up