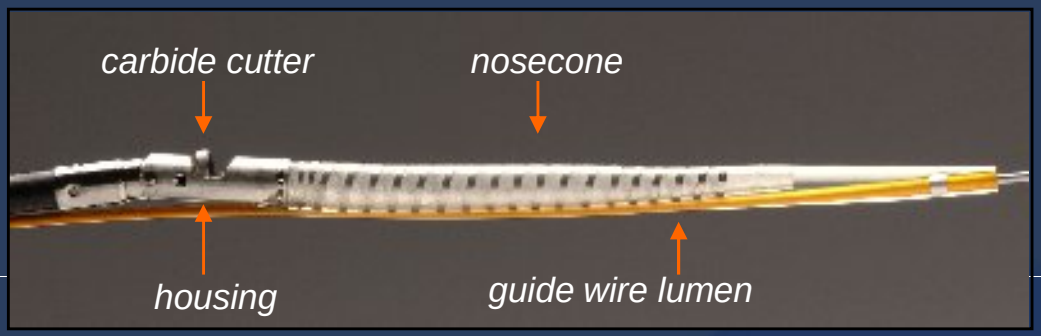
# Plaque Excision in Limb Salvage Beyond the SilverHawk in Treating Critical Limb Ischemia

Roger Gammon, MD

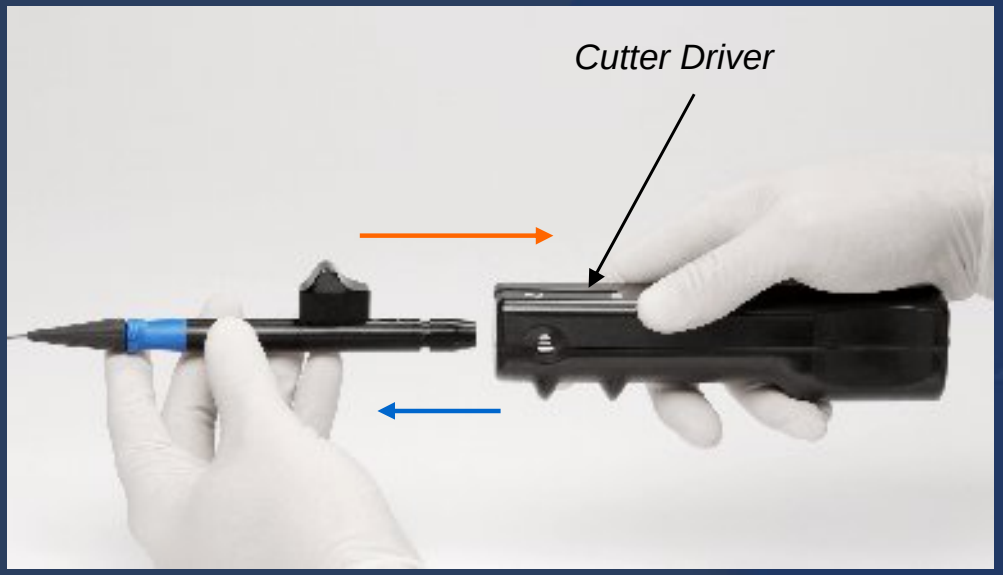
Austin Heart

# SilverHawk Device

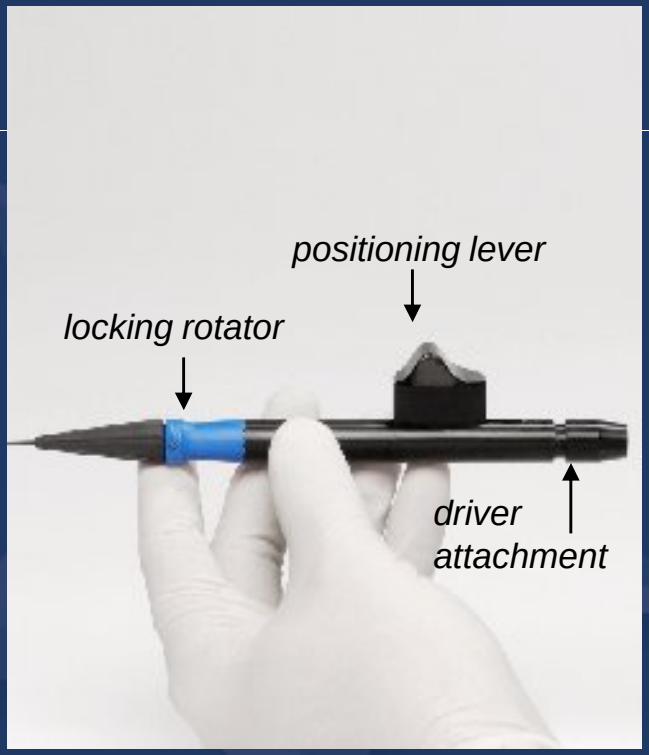
## Distal Tip: Cutter




## Driver Attachment




## Proximal End

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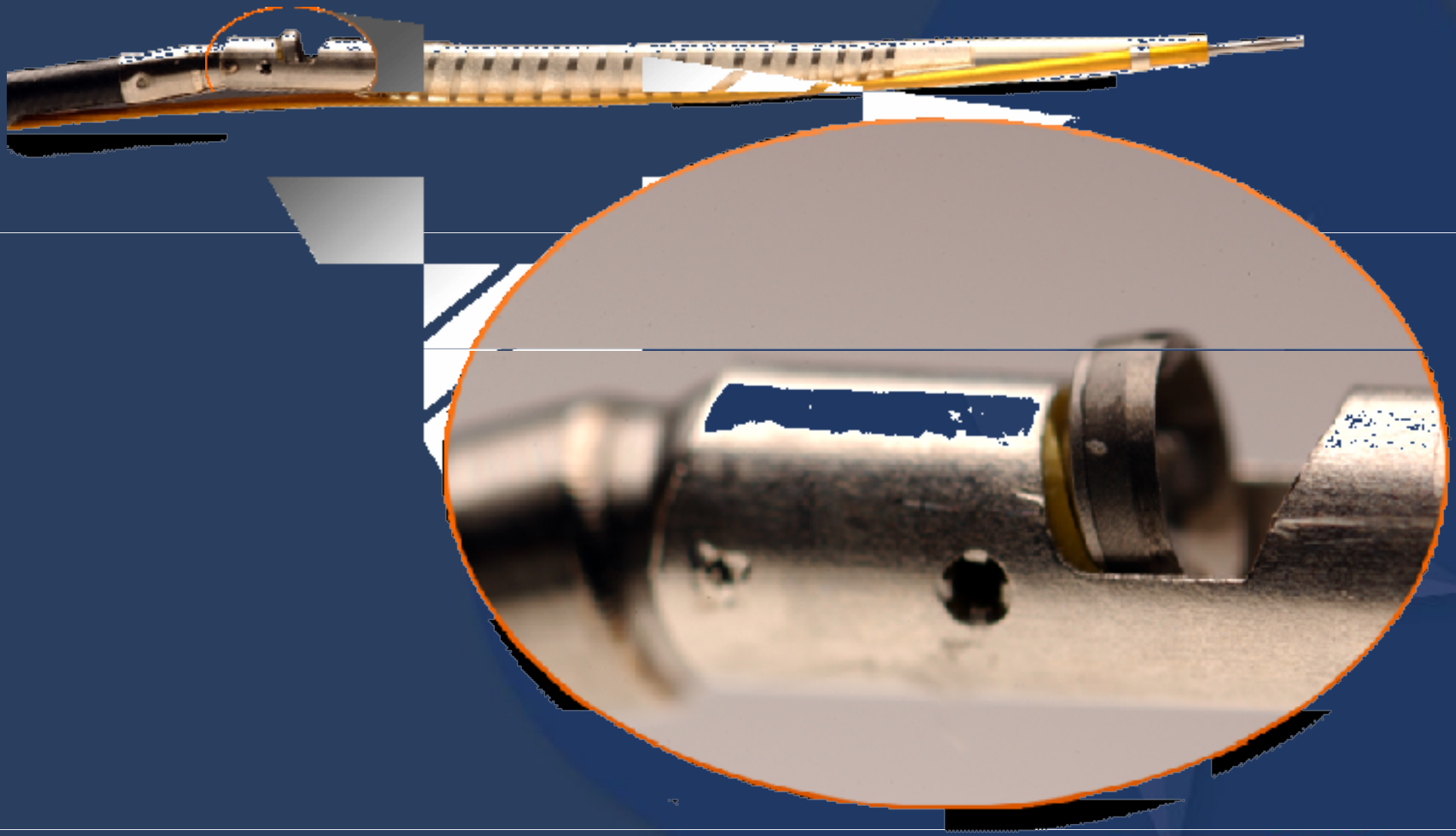
# Magnified View of Carbide Blade



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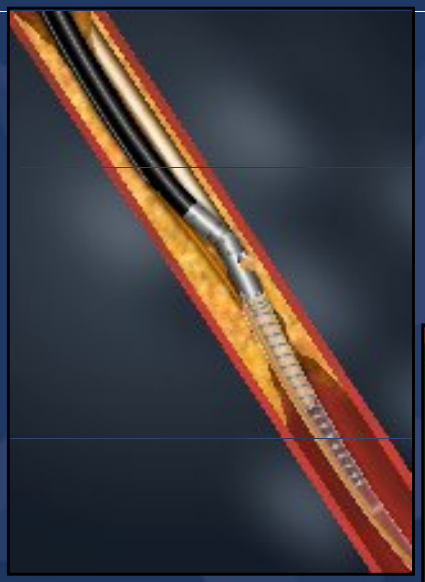
# Three-Step Procedure

1. Deliver the catheter to proximal end of target lesion, pull back thumb switch to activate cutter.

2. Advance the cutter through lesion, collecting tissue in the nosecone.

3. Push the thumb switchforward, and either torque the catheter to treat additional areas, or retract the catheter.



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# SilverHawk Catheters

Large Vessel, Ext. Length (LX)

Large Vessel, Standard (LS)

Small Vessel, Ext. Length (SX)

Small Vessel, Standard (SS)

Extra Small Vessel, (ES)

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# Plaque excision samples

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# The TALON Registry


Purpose:

- Web-based* outcomes tracking system designed to evaluate acute and long term outcomes of patients treated with the SilverHawk in the lower extremity peripheral vasculature
- Correlate patient outcomes, histology findings and genomic profiles

Endpoints:

- 6 and 12 month TLR

Registry population

- Consecutive SilverHawk patients; lower extremity peripheral vasculature

*Managed by Outcome Sciences

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# Baseline Clinical Characteristics


| | (N=728) |
|---|---|
| Age (average): | 70 ± 11 years |
| Male: | (57.2%) |
| DM%: | (50.2%) |
| Claudication history: | (96.5%) |
| Prior MI, CABG, PCI: | (54.9%) |
| Prior peripheral intervention: | (62.0%) |
| History of Smoking: | (65.9%) |
| History of Hypertension: | (85.3%) |

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# Baseline Clinical Characteristics


- Rutherford Becker (of SH treated limb):

| | N | % |
|---|---|---|
| 0 | 27 | 3.0% |
| 1 | 77 | 8.6% |
| 2 | 176 | 19.6% |
| 3 | 342 | 38.1% |
| 4 | 151 | 16.8% |
| 5 | 115 | 12.8% |
| 6 | 9 | 1.0% |

- Average ABI[1]: 0.71 (pre) – 0.86 (post)

[1]N=427- only patients with pre and post values included

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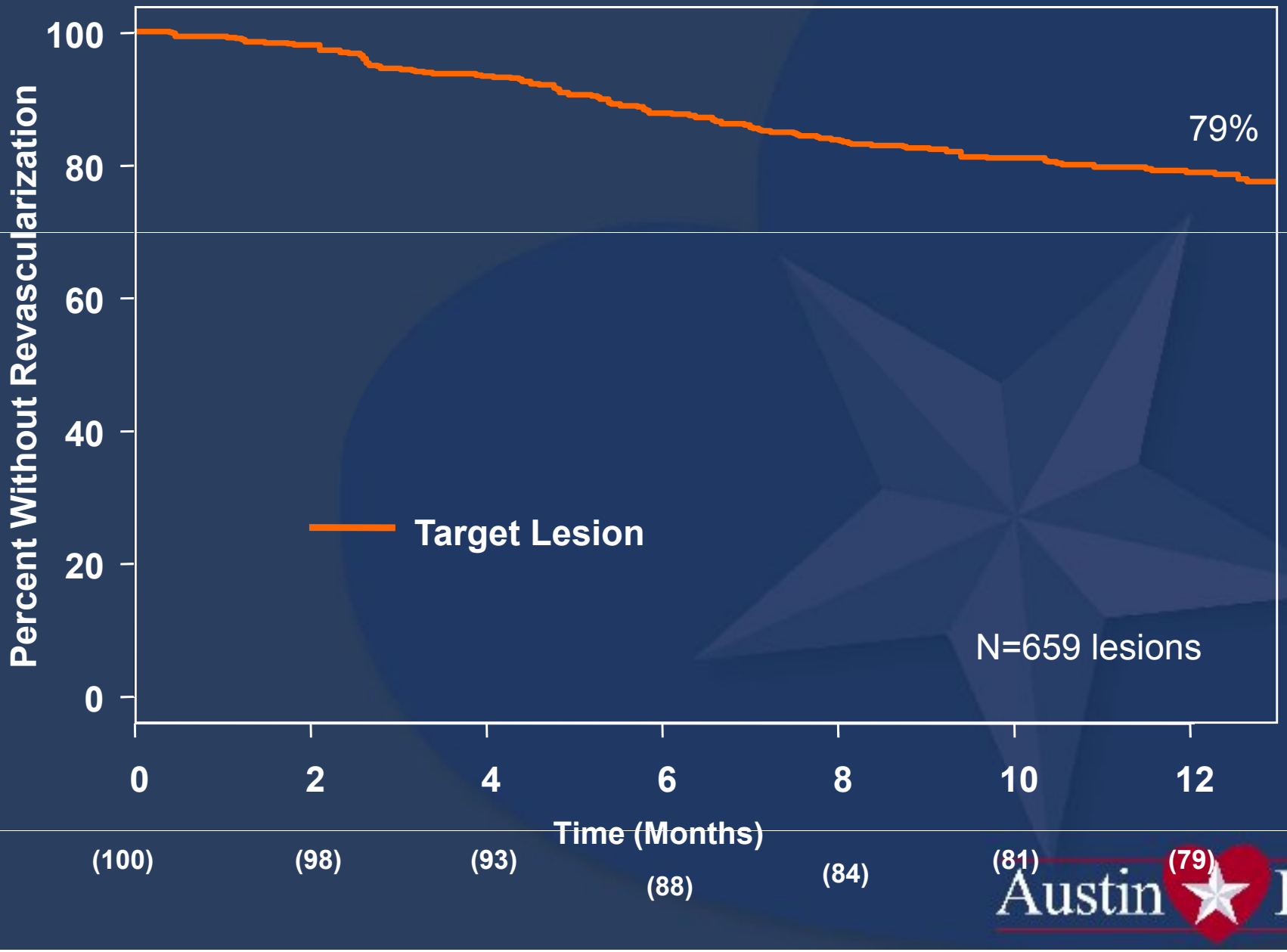
# 12 Month Outcomes Data

- Total Patients:  335
  - Limbs:  420
  - Lesions:  658
- Total Procedures:  427

# 12-month Freedom From Target Lesion Revascularization

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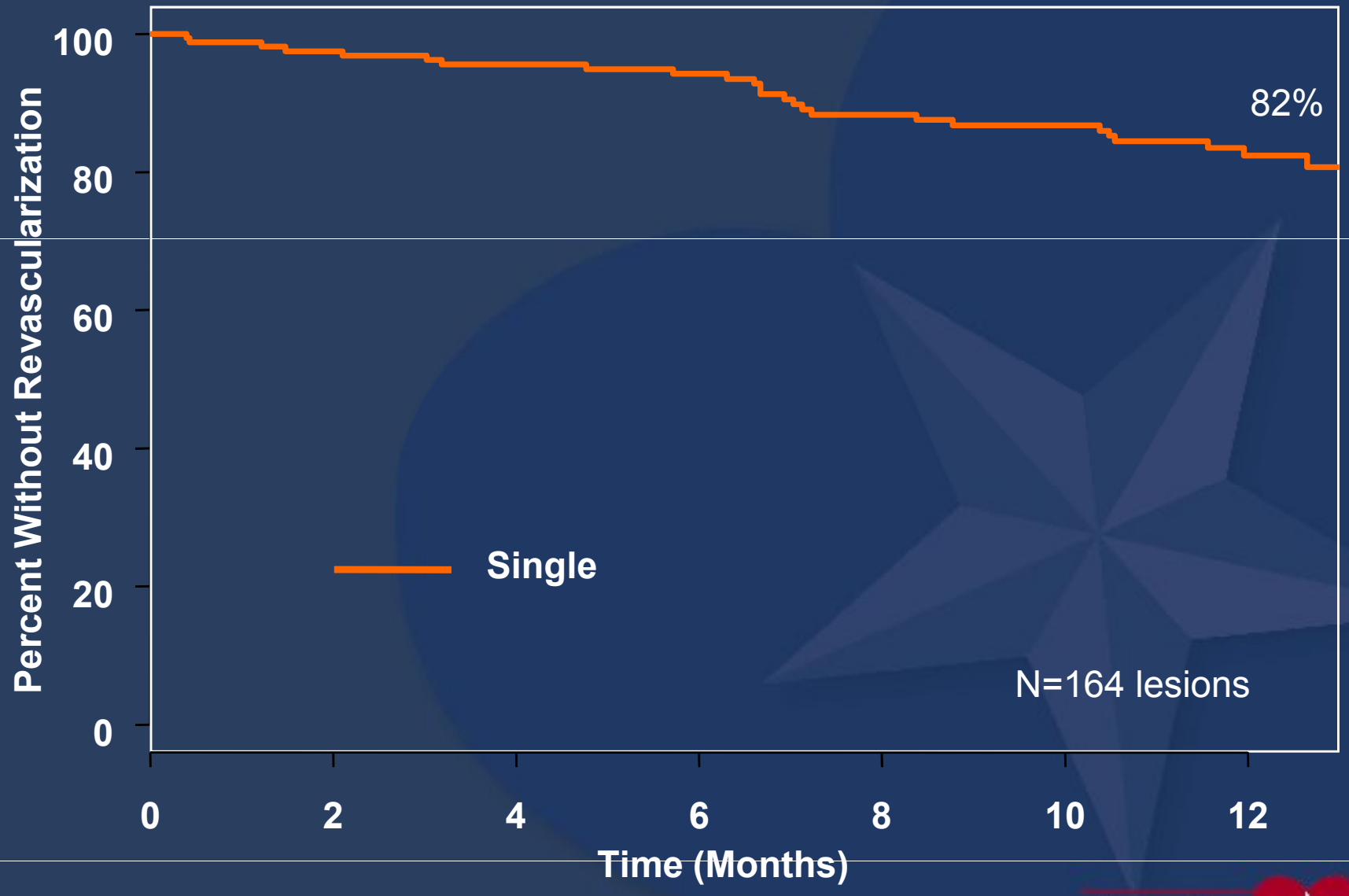
# 12-month Freedom From TLR – Single Lesions

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# Cardiovascular Institute of the South (CIS)

- Total Patients with 12-month CT angio follow-up: ***89***
- Number of Lesions Treated[1]: ***102***
- TASC B, C, or D lesions: ***71.8%***
- Rutherford-Becker 5 or 6: ***86.1%***
- Average Lesion Length: ***17.6 cm***
- Target Lesion Revascularization (TLR) Rate: ***13.4%***
- ***Angiographic Primary Patency Rate[2]: 80%***

1. SFA-Popliteal accounted for 88.1% of lesions treated
2. Using CT Angiography

Source: Allie, David. "CIS 12-Month Overall Experience." Presented at New Advances in Critical Limb Ischemia meeting. Chicago, IL, May 21, 2005.

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**Procedural and Clinical Outcomes with Catheter-based Plaque Excision in Critical Limb Ischemia**
**David Kandzari, et. al.**

***Journal of Endovascular Therapy, February 2006***

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# Multi-center CLI Study

PURPOSE:

To examine the safety and efficacy associated with plaque excision (PE) in patients with CLI undergoing percutaneous revascularization

METHOD:

- SilverHawk was performed in 69 patients (76 limbs, 159 lesions) with RB≥5 and clinical outcomes were prospectively followed for 6 months at 7 institutions.
- Primary endpoint was major adverse events at 30 days (death, MI, unplanned amputation, repeat TVR).
- Visible healing of ulcerated tissue, device success (<50% final residual diameter stenosis), avoidance of amputation, and performance of less extensive amputation than initially planned were also assessed.

David Kandzari, et. al. "Procedural and Clinical Outcomes with Catheter-Based Plaque Excision in Critical Limb Ischemia". Journal of Endovascular Therapy (JEVT), February 2006.

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# Multi-center CLI Study

RESULTS:

- TLR = 4% and no unplanned amputations.
- Amputation avoided or a less extensive amputation was performed in 92% of patients at 30 days and 82% at 6 months
- Procedural success = 99%
- Major adverse events occurred in 1% of patients at 30 days and 23% at 6 months

CONCLUSIONS:

- PE is a safe and effective method for patients with CLI

David Kandzari, et. al. "Procedural and Clinical Outcomes with Catheter-Based Plaque Excision in Critical Limb Ischemia". Journal of Endovascular Therapy (JEVT), February 2006.

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# SilverHawk Limb Salvage Data

| | Gammon[1] | Motarjame[2] | Turley[3] |
|---|---|---|---|
| Patients | 57 | 71 | 115 |
| Limbs | 57 | 83 | 134 |
| Lesions | 157 | | 411 |
| Limb Salvage* | 93% | 91% | 92% |

*Defined as freedom from amputation, or lesser part amputation than planned


1. Roger Gammon, MD, Austin Heart Hospital. "Long Term Lesion Patency And Freedom From Limb Amputation: A Unique Treatment Option For Critically Ischemic Lower Limbs." Presentation at TCT 2005.
2. Amir Motarjame, MD, Midwest Vascular Institutue. Presented to FoxHollow employees, August 26, 2005, Redwood City, CA.
3. Brian Turley, MD, Vascular & Interventional Specialists, Conroe Regional Medical Center. Presented to physicians at Texas Silverhawk Summit, November 12, 2005, Dallas, TX.


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# SilverHawk Plaque Excision in Diabetes

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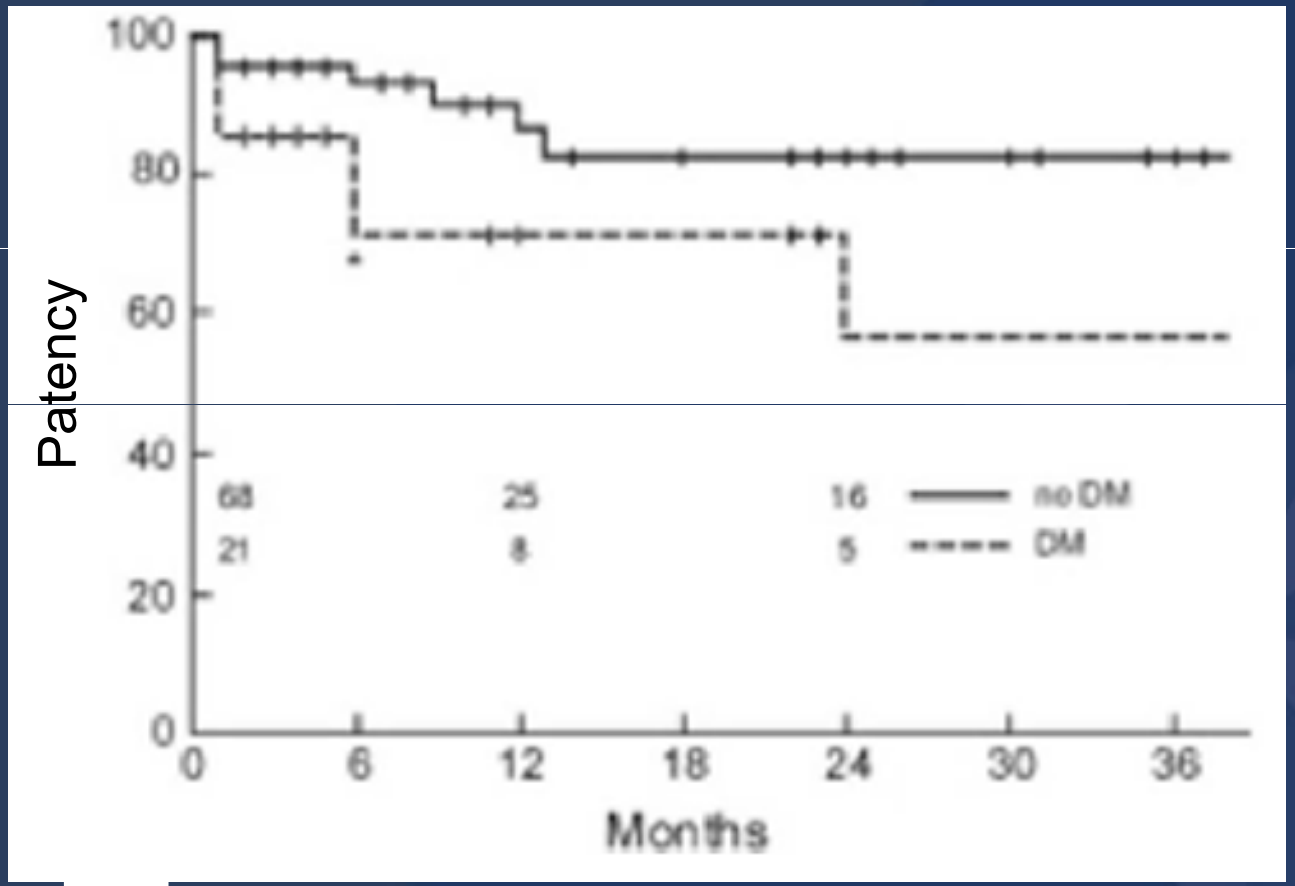
# ILIAC STENTING Restenosis is substantially increased in diabetics




Leville et al., J Vasc Surg 2006 43, 32

*retrospective study of 89 consecutive patients with symptomatic iliac occlusions (TASC-B,C,D), at Cleveland Clinic
** patency measured by Doppler, ABI decrease of >0.15, loss of palpable pulses

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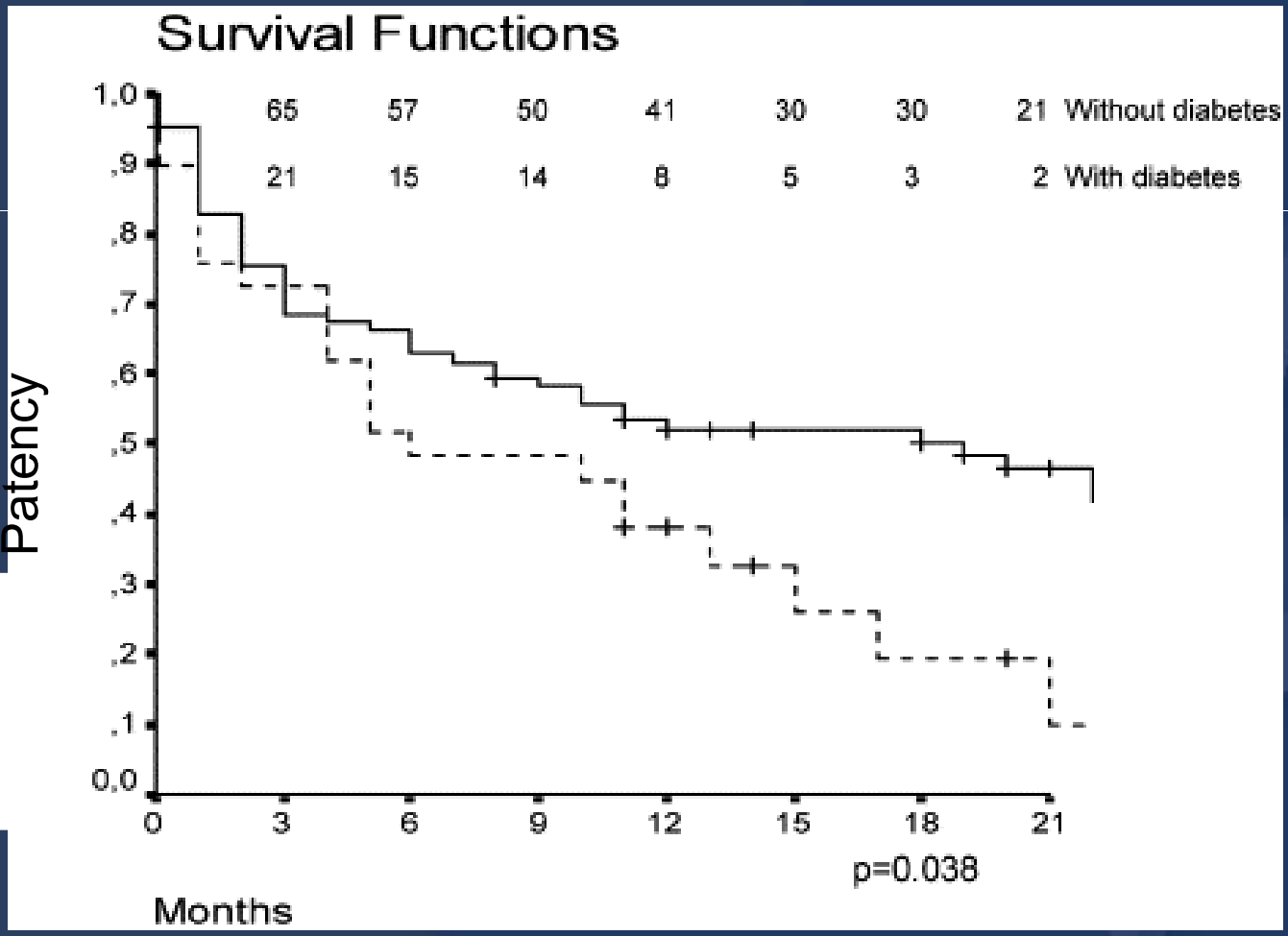
# ATK ANGIOPLASTY: Restenosis is substantially increased in diabetics




Eur J Vasc Endovasc Surgery 2004 28, 410

* Prospective study of 116 lesions treated with PTA or subintimal angioplasty, in Haukeland University Hospital, Norway

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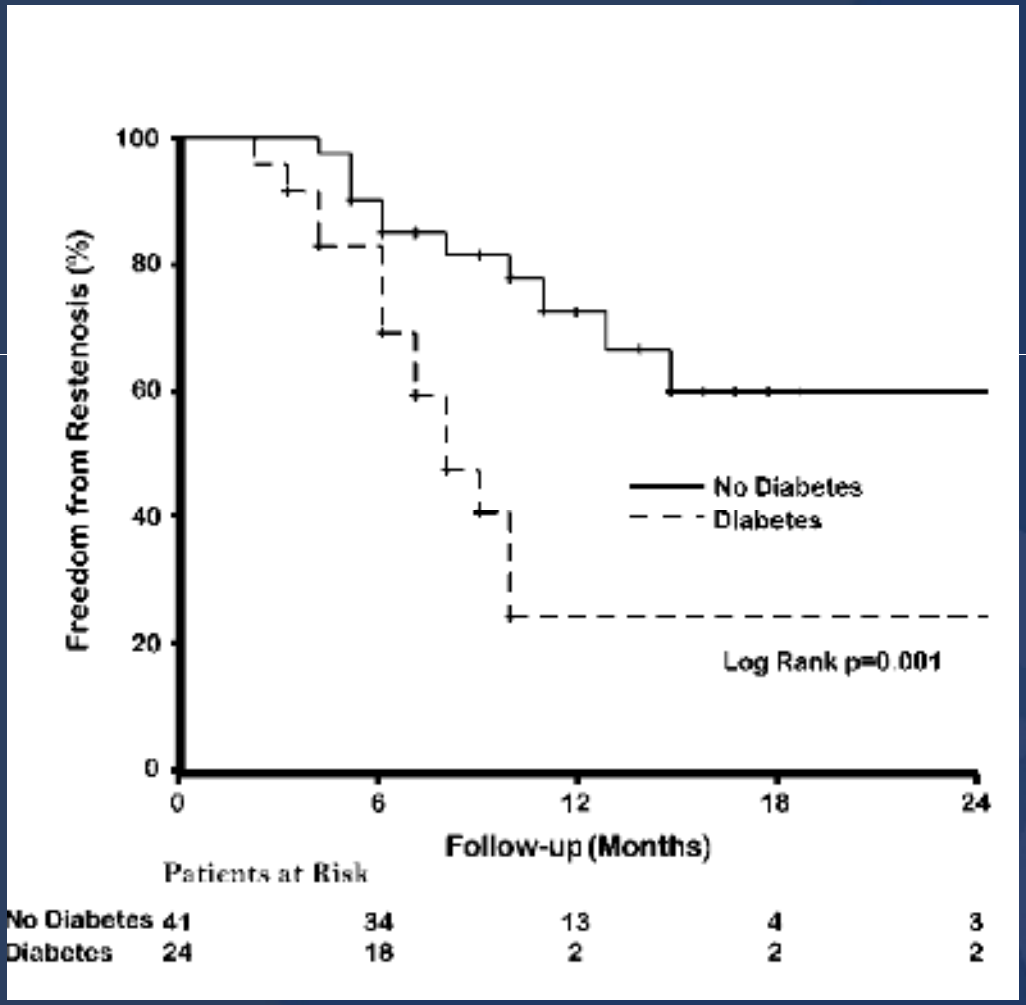
# ATK Nitinol Stenting: Restenosis is substantially increased in diabetics – lesions > 10cm




Sabeti et al. (Schillinger), JEVT (2005) 12, 6-12

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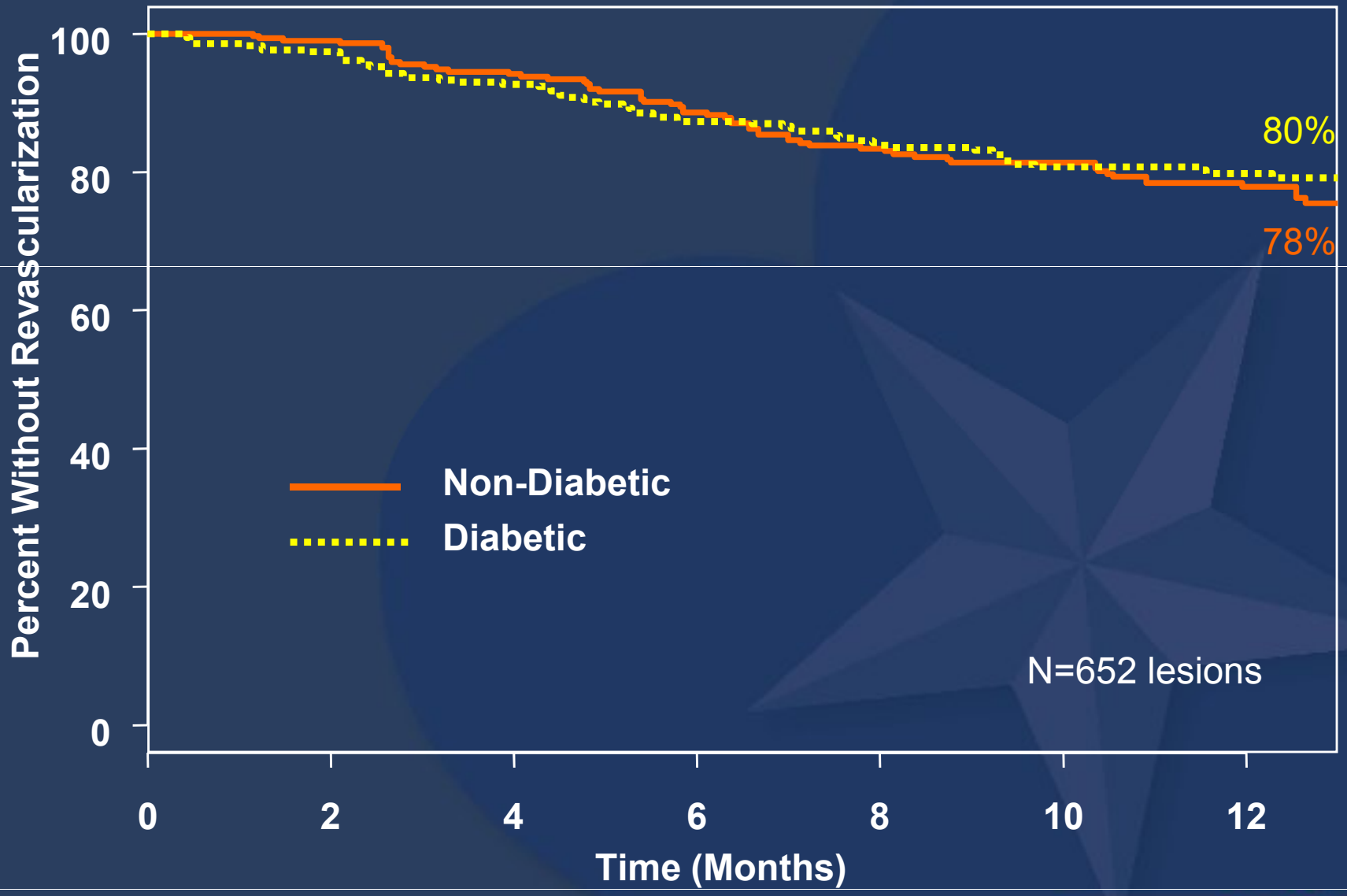
# SilverHawk (TALON)
# Diabetics vs Non-Diabetics




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Non-Diabetic : | (100) | (99) | (94) | (89) | (83) | (81) | (78) |
| Diabetic : | (100) | (97) | (93) | (87) | (84) | (84) | (80) |

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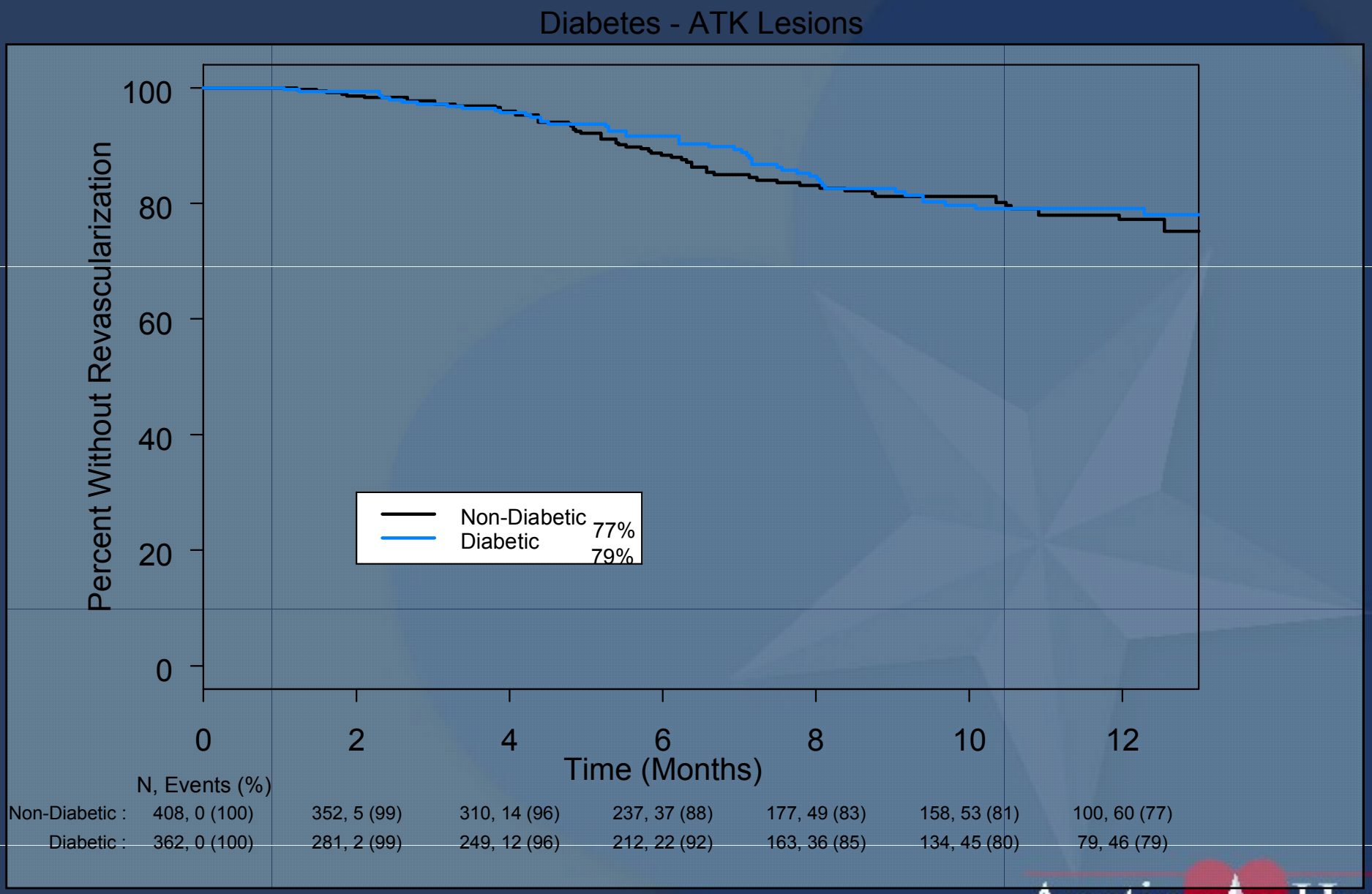
# TLR is similar for DM and non-DM after SH excision of *de novo* ATK lesions

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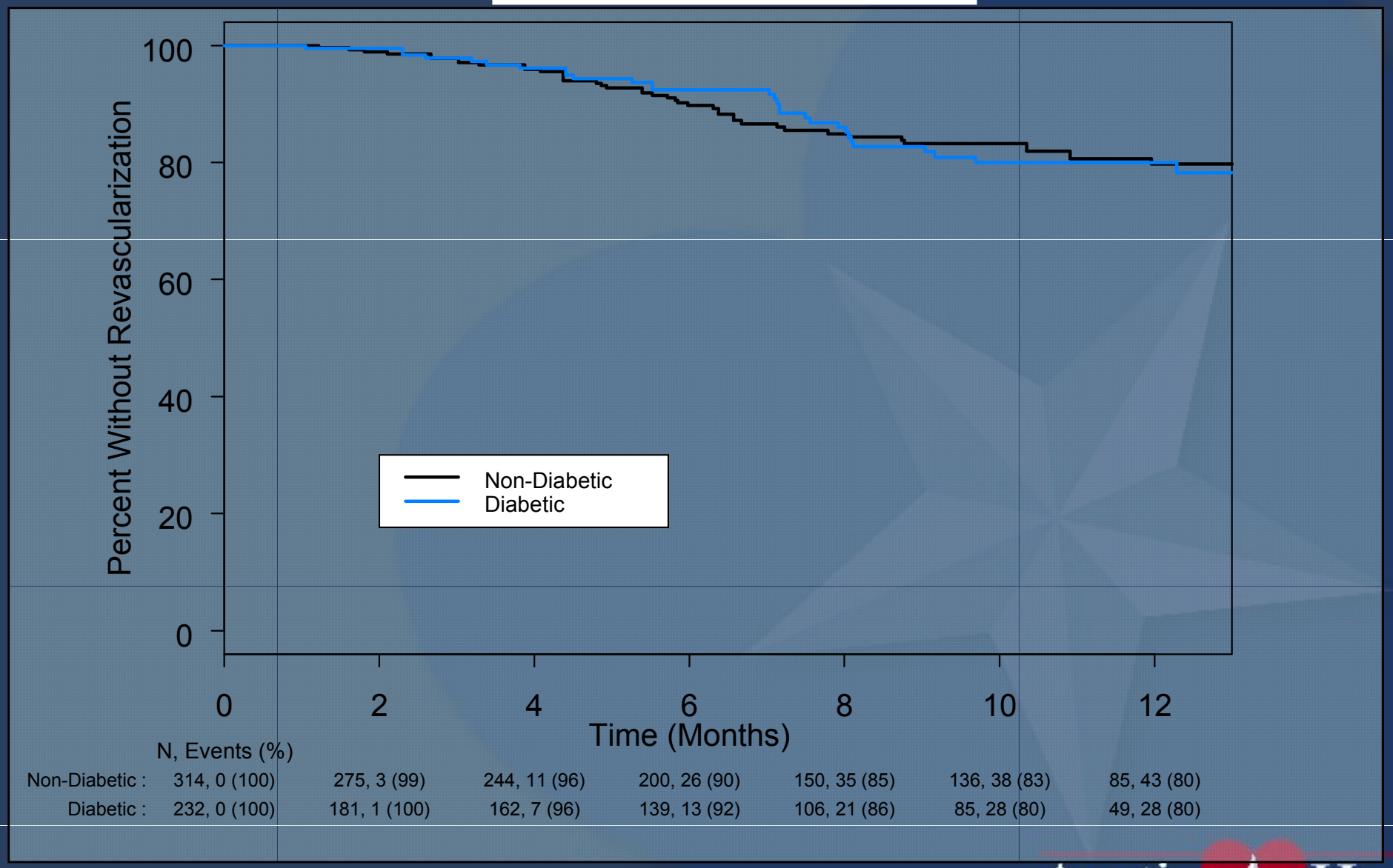
# CLAUDICANTS: TLR is similar for DM and non-DM after SH excision of *de novo* ATK lesions




| N, Events (%) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Non-Diabetic : | 314, 0 (100) | 275, 3 (99) | 244, 11 (96) | 200, 26 (90) | 150, 35 (85) | 136, 38 (83) | 85, 43 (80) |
| Diabetic : | 232, 0 (100) | 181, 1 (100) | 162, 7 (96) | 139, 13 (92) | 106, 21 (86) | 85, 28 (80) | 49, 28 (80) |

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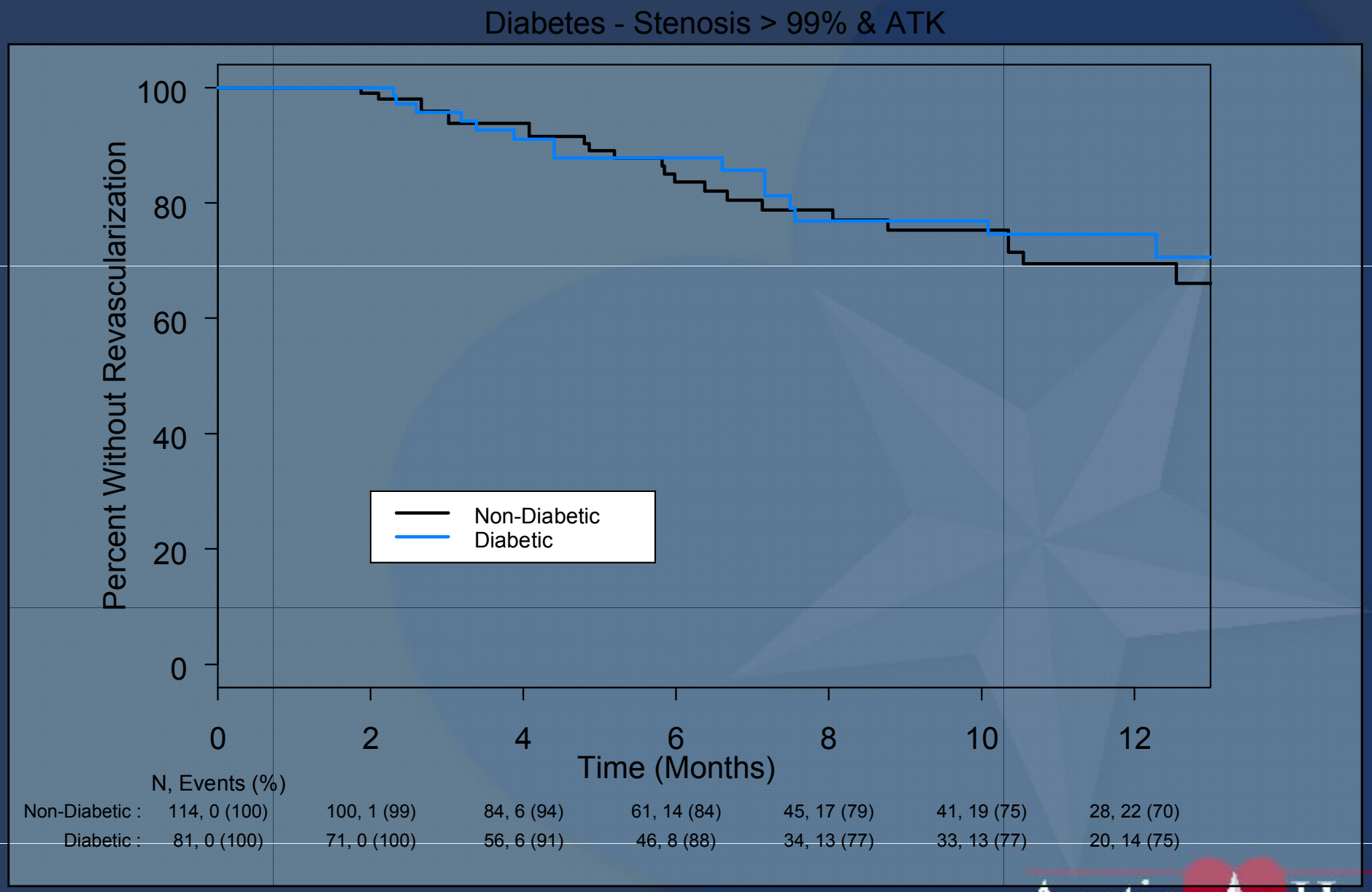
# CTOs: TLR is similar for DM and non-DM after SH excision of *de novo* ATK lesions




| N, Events (%) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Non-Diabetic : | 114, 0 (100) | 100, 1 (99) | 84, 6 (94) | 61, 14 (84) | 45, 17 (79) | 41, 19 (75) | 28, 22 (70) |
| Diabetic : | 81, 0 (100) | 71, 0 (100) | 56, 6 (91) | 46, 8 (88) | 34, 13 (77) | 33, 13 (77) | 20, 14 (75) |

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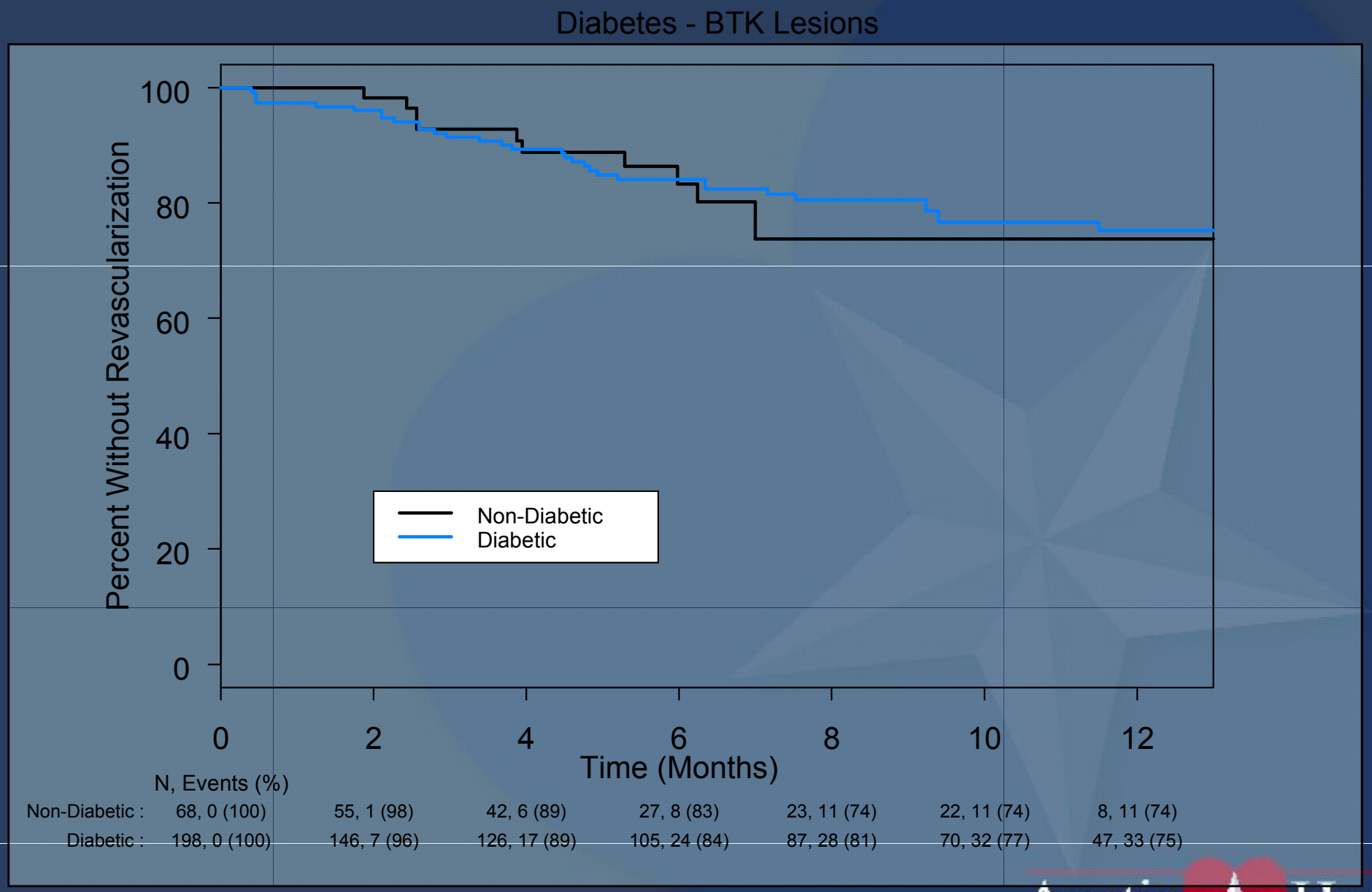
# TLR is similar for DM and non-DM after SH excision of *de novo* BTK lesions




| N, Events (%) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Non-Diabetic : | 68, 0 (100) | 55, 1 (98) | 42, 6 (89) | 27, 8 (83) | 23, 11 (74) | 22, 11 (74) | 8, 11 (74) |
| Diabetic : | 198, 0 (100) | 146, 7 (96) | 126, 17 (89) | 105, 24 (84) | 87, 28 (81) | 70, 32 (77) | 47, 33 (75) |

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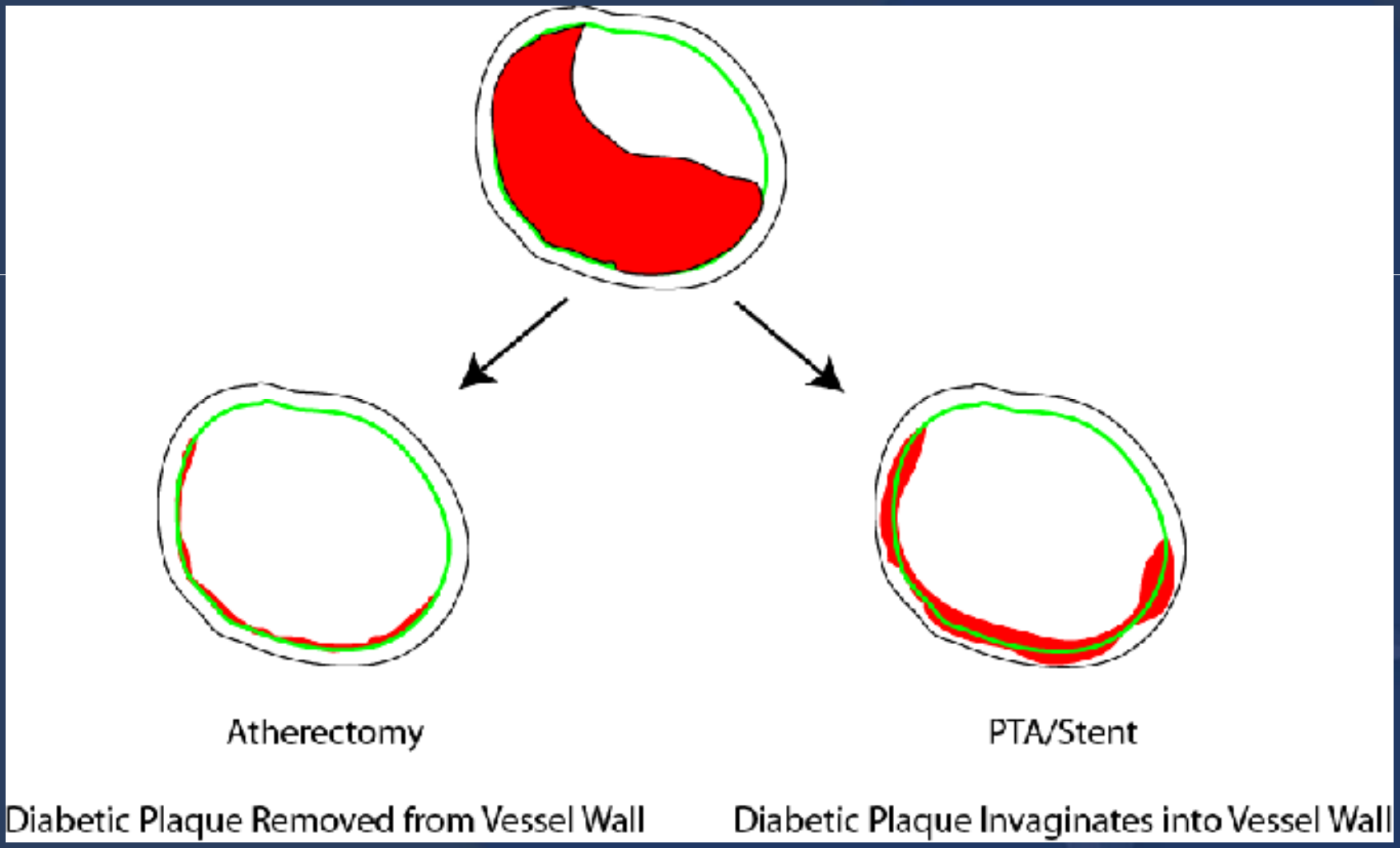
# PTA/Stenting Forces Plaque into the Injured Vessel Wall

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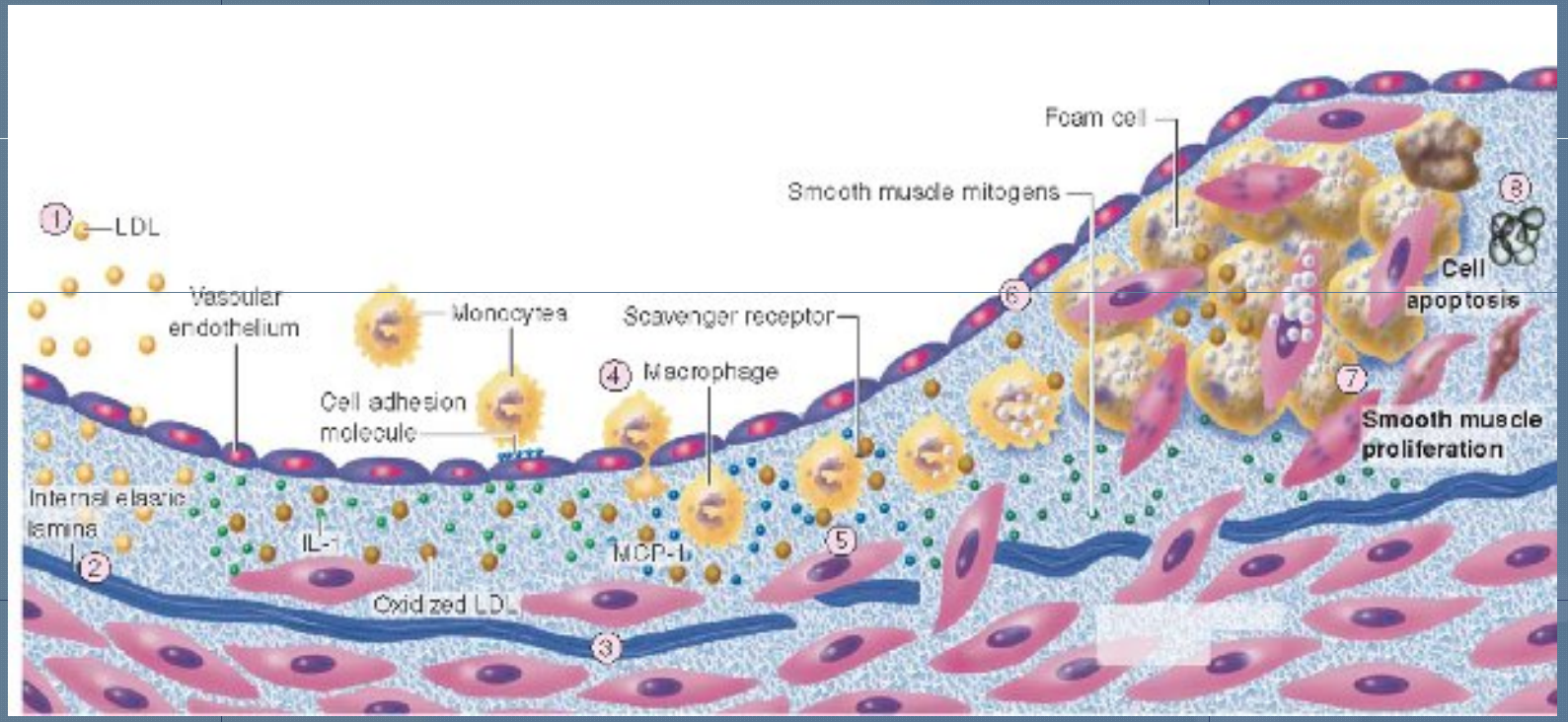
# Hypothesis: An accelerant for restenosis is present in diabetic plaque

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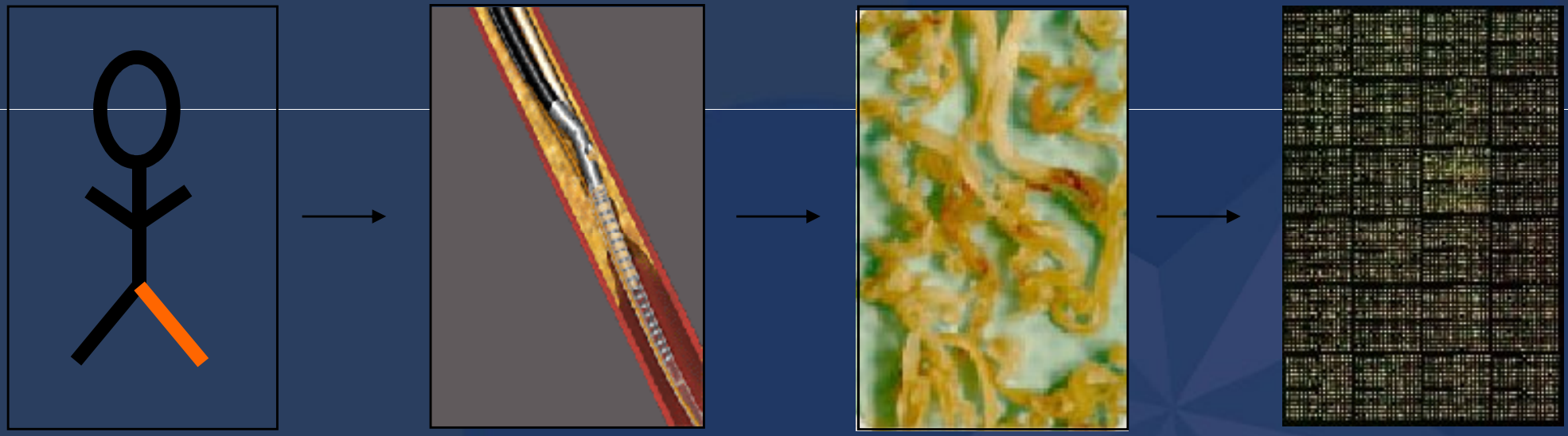
# Analysis of Plaque Gene Expression



Patient

Plaque Excision

Plaque

Microarray Analysis

Rosetta Inpharmatics
40K gene system (Affymetrix/Agilent)

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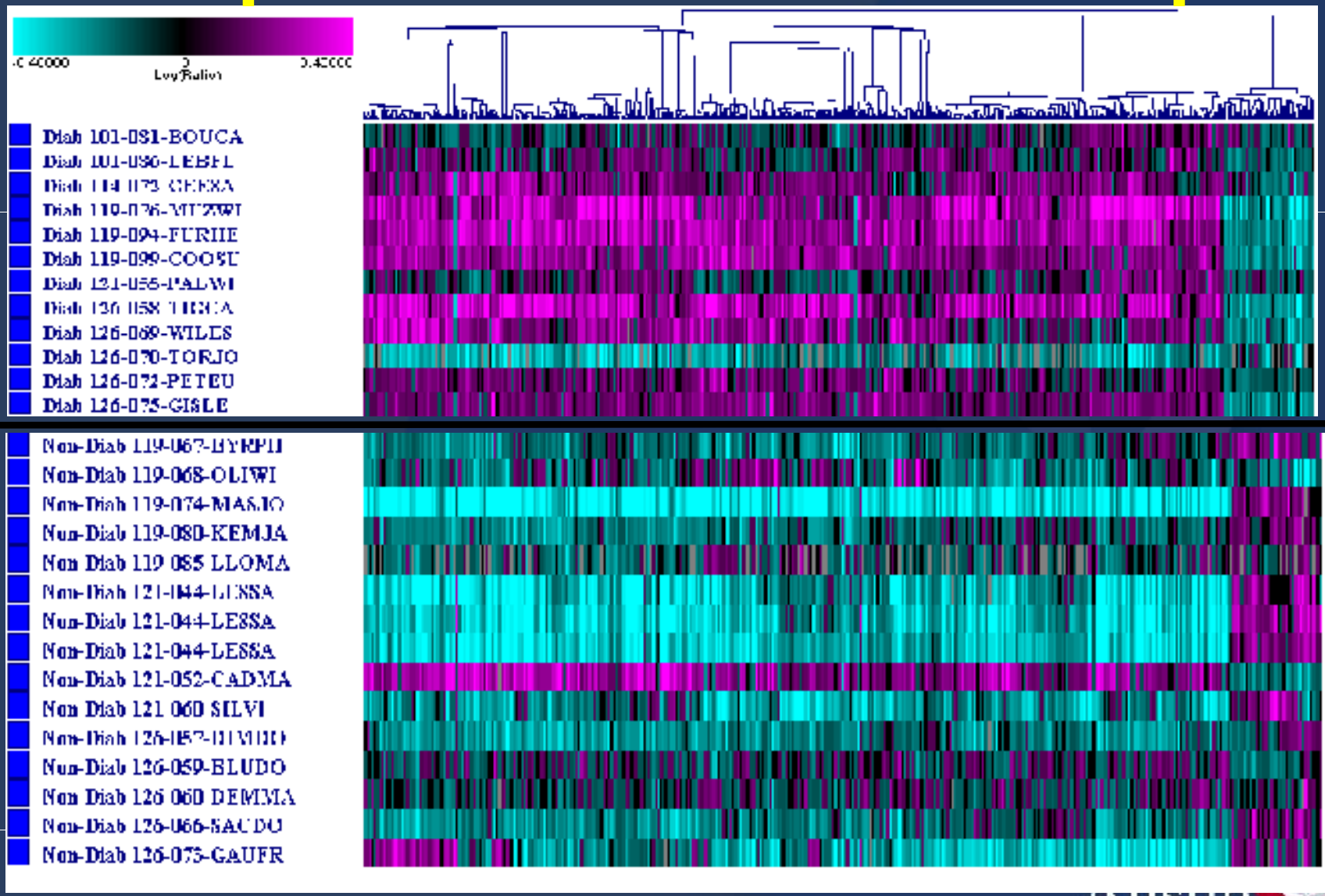
# FHT/Merck Plaque Analysis Is Identifying Genes Differentially Expressed in Diabetic Plaque

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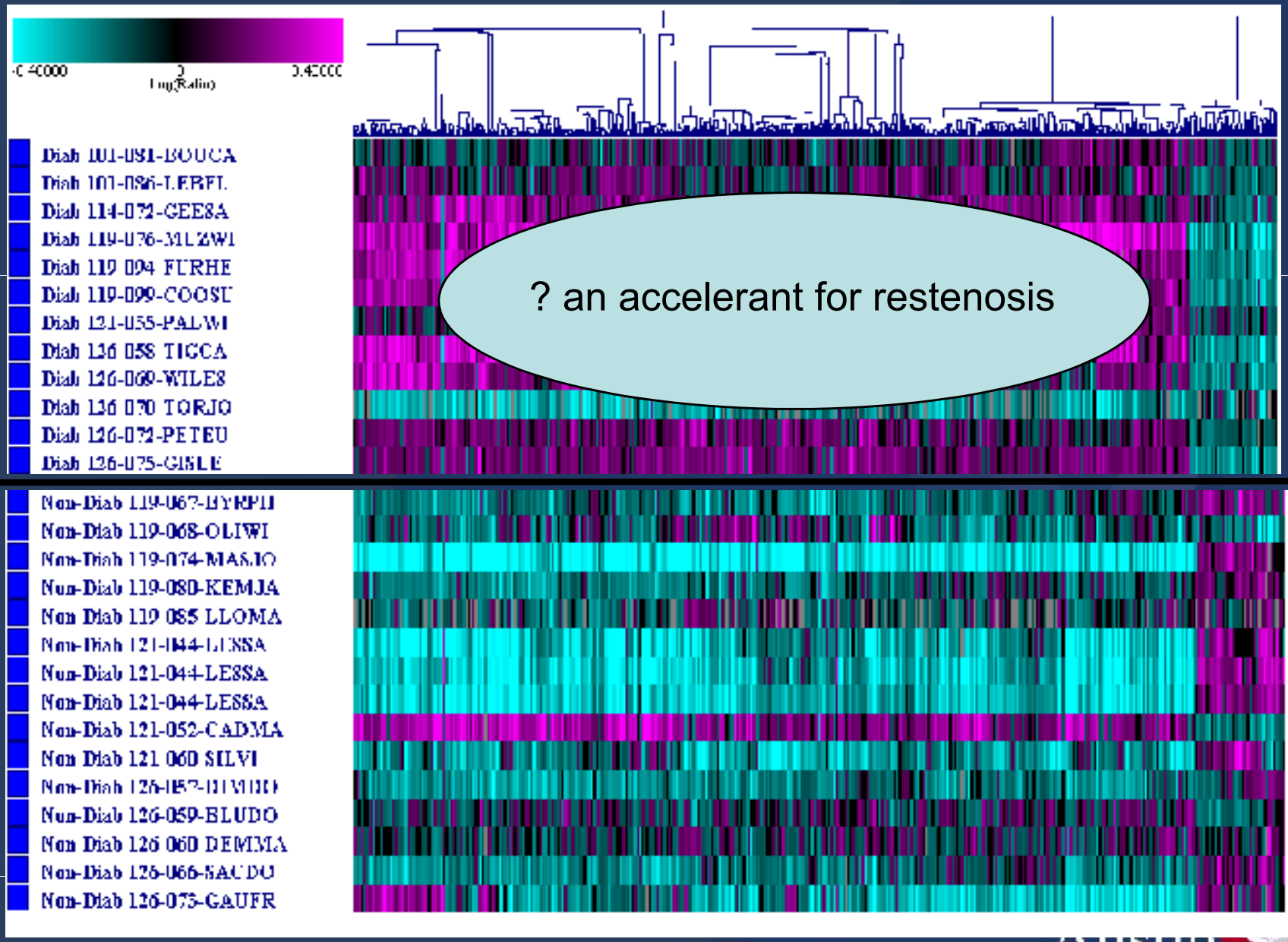
# Gene expression in diabetic plaque

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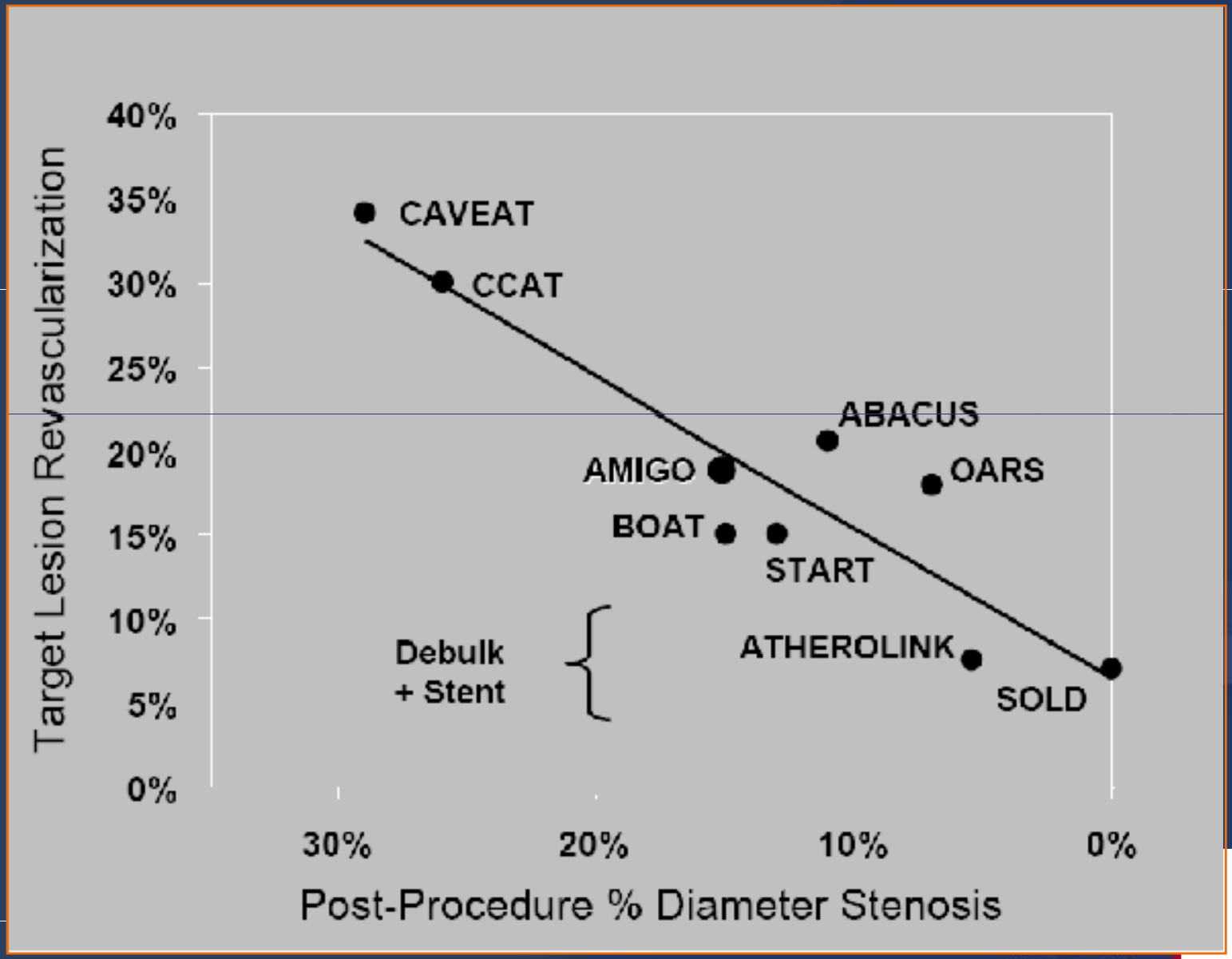
# Clinical Trial Evidence Supports Optimal Debulking

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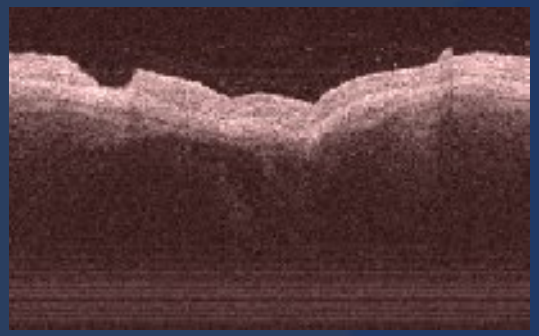
# Guided Plaque Excision

NIGHTHAWK

## CLINICAL NEED

- ***Optimal Plaque Removal***
  - ***Lower Restenosis***
- ***Precision and Guidance***
  - ***Cut Direction***
  - ***Cut Depth Estimation***



## TECHNOLOGICAL SOLUTION

- ***Integrated Optical Coherence Imaging***

## TEAM EXECUTION

- ***OUS Peripheral Feasibility September, 2006***
  - ***(< 1 year Concept to Clinical Use)***



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# Vascular Imaging

## Fluoroscopy

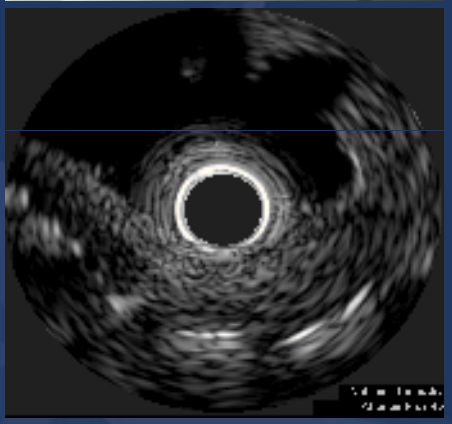
- Standard of Practice
- Identifies Vessel Narrowing
- Longitudinal Positioning
- Single Plane Rotational Orientation

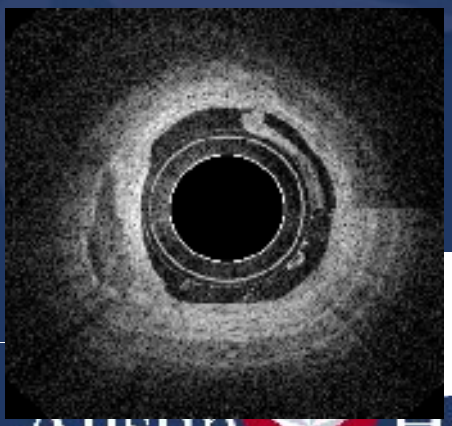
## Intravascular Imaging

- Identify characteristics of plaque hidden in the vessel wall
- Precise rotational orientation of the disease and device

- Intravascular Ultrasound (IVUS)
  - Good visualization through blood
  - Resolution (~100 – 300 $\mu$m)
  - Depth penetration (~5 – 7 mm)

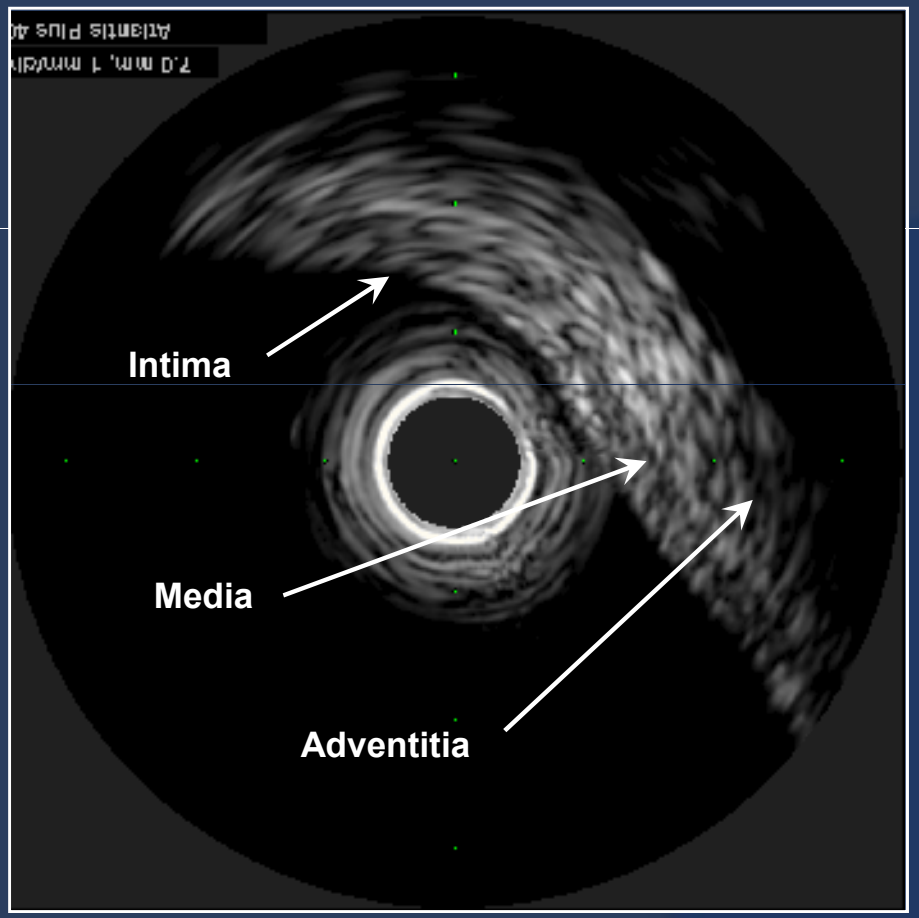
- Optical Coherence Tomography (OCT)
  - Very limited visualization through blood
  - Resolution (~10 – 20 µm)
  - Depth penetration (~2 – 3 mm)



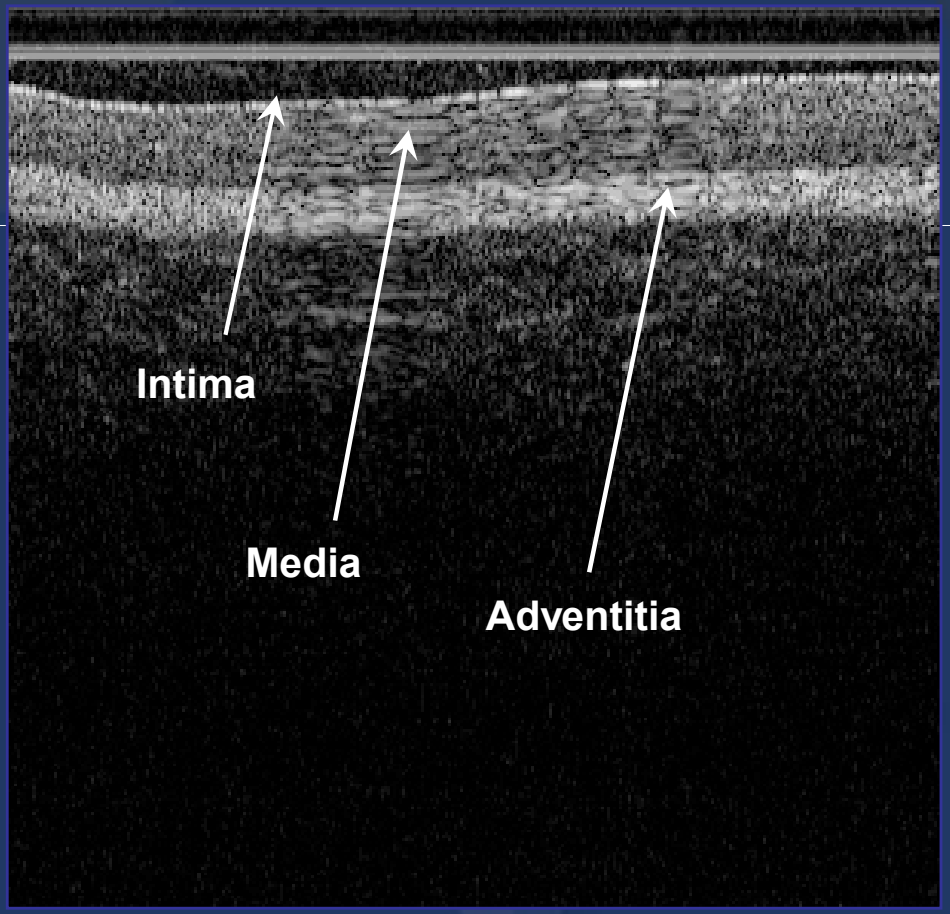


# *In Vitro* Imaging Comparison

## Same Porcine Coronary Wall: Visualized with Both IVUS and OCT




IVUS – 40 MHz




FoxHollow OCT Gen I



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# Catheter Design

## NIGHTHAWK

- LS, SS, and SX Nighthawk Devices
  - Nighthawk SX is a non-packing device
- 0.1 mm Torque Shaft Embedded Fiber Optics
  - Crossing Profile or Torque Transmission Maintained
  - Telecom Single Mode Fiber, 155 micron OD
- Image in cutting plane
  - ~ 3 mm proximal to cutter

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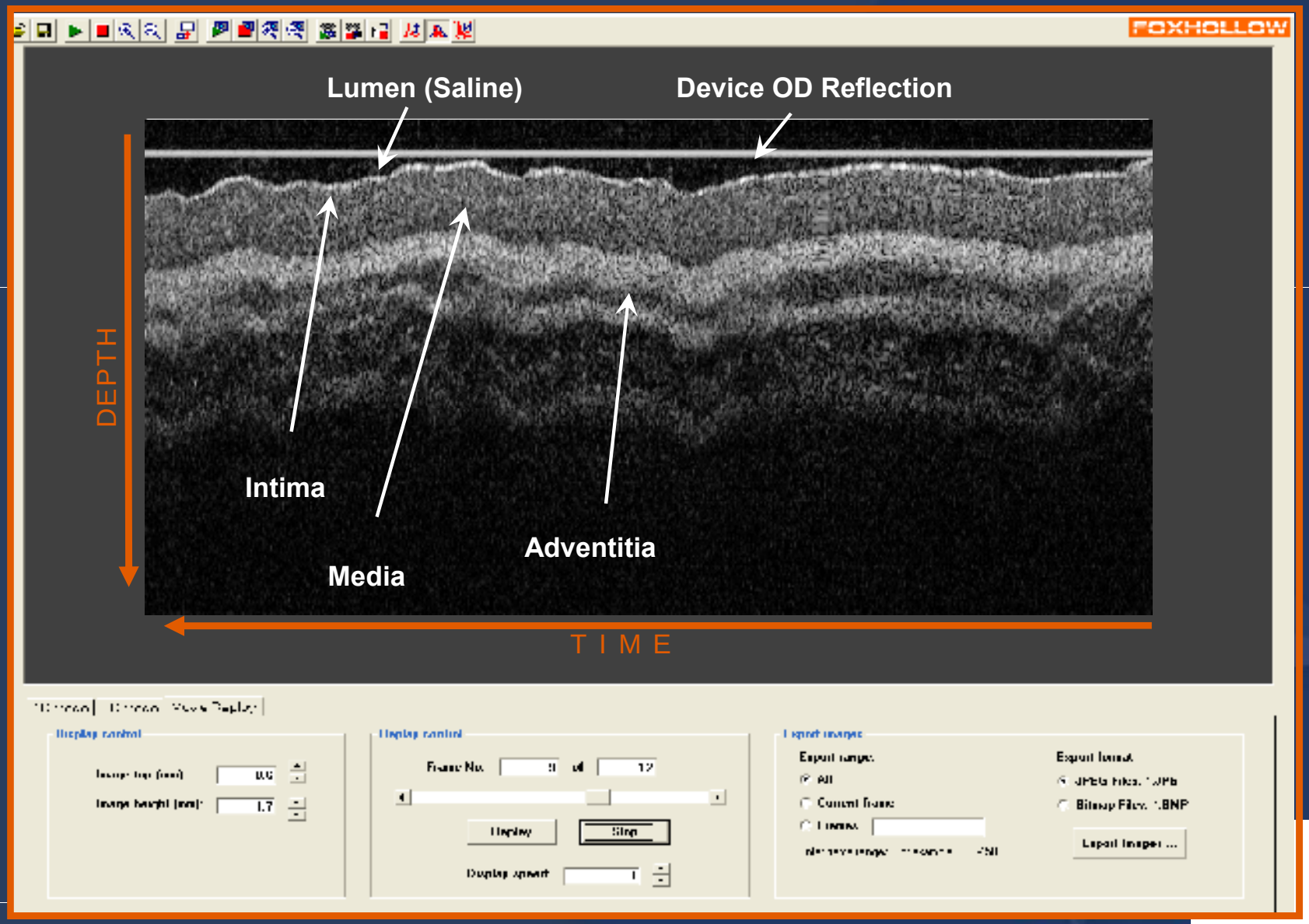
# NightHawk Image: M-Mode Waterfall



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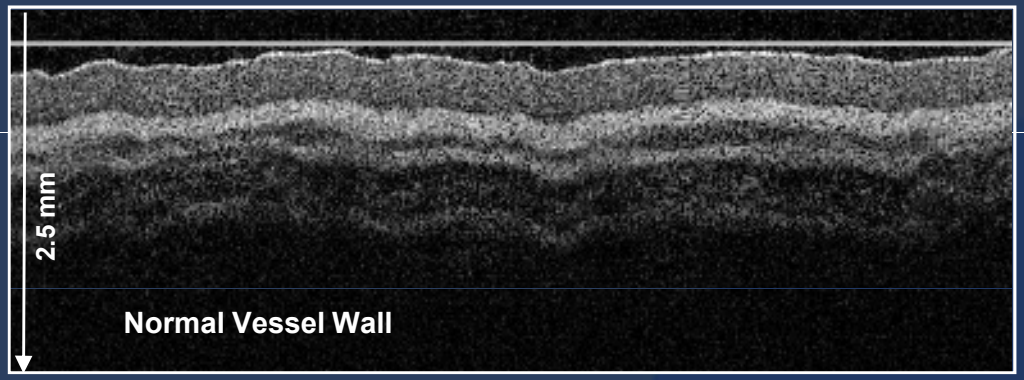
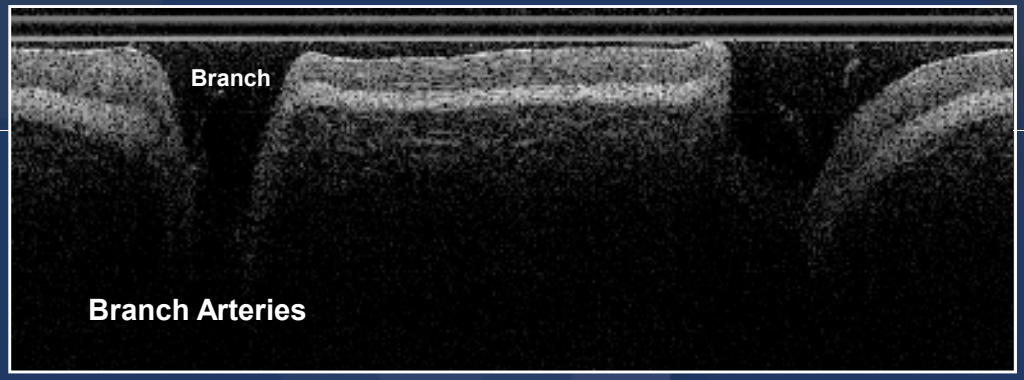
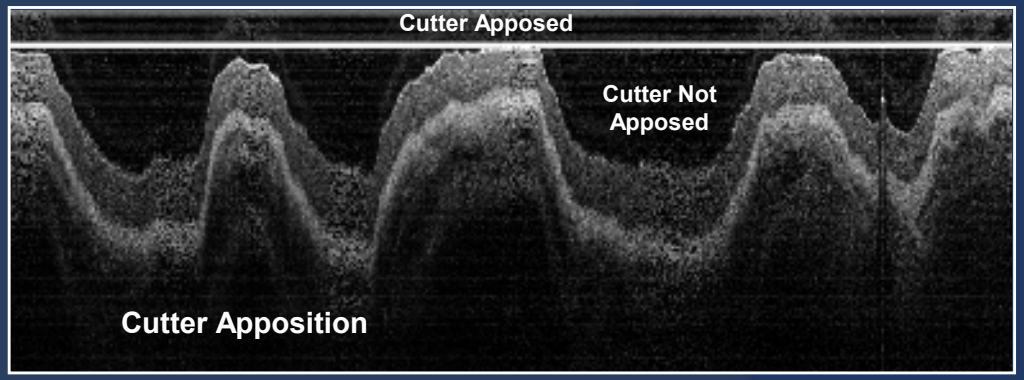
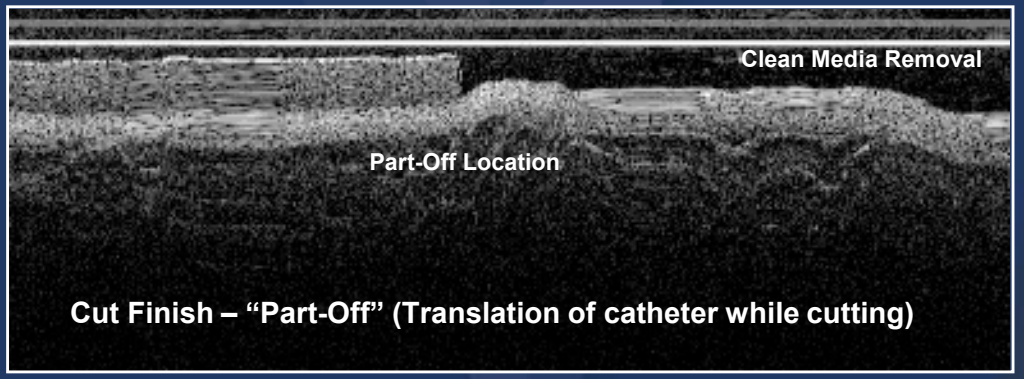
# In Vitro Images

## *In Vitro* Porcine Coronary Wall: Single Frame



# Integrated Optical Coherence Tomography (OCT)

## … A Deeper Look

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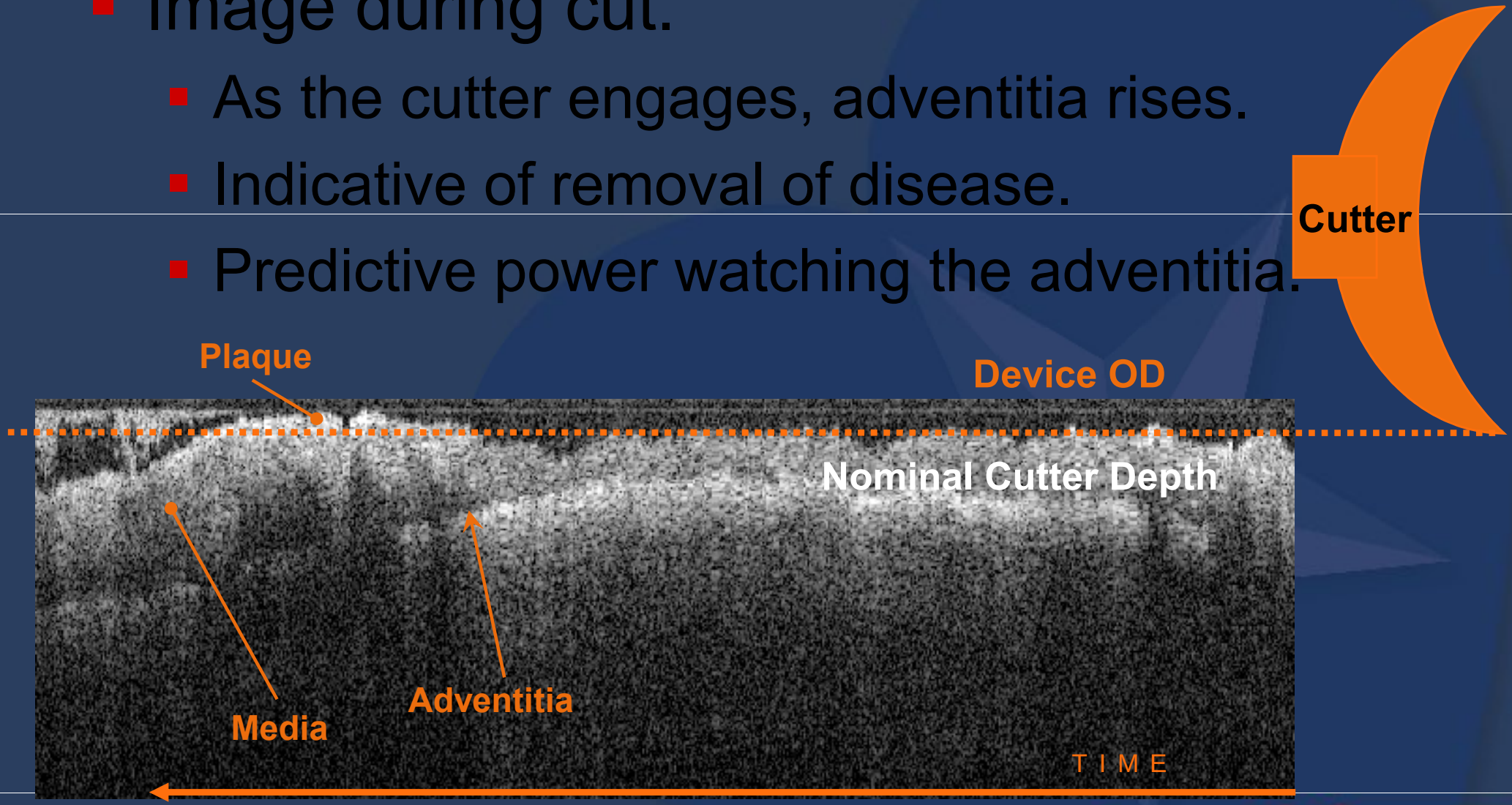
# Imaging and Cutting

- Image during cut.
  - As the cutter engages, adventitia rises.
  - Indicative of removal of disease.
  - Predictive power watching the adventitia.

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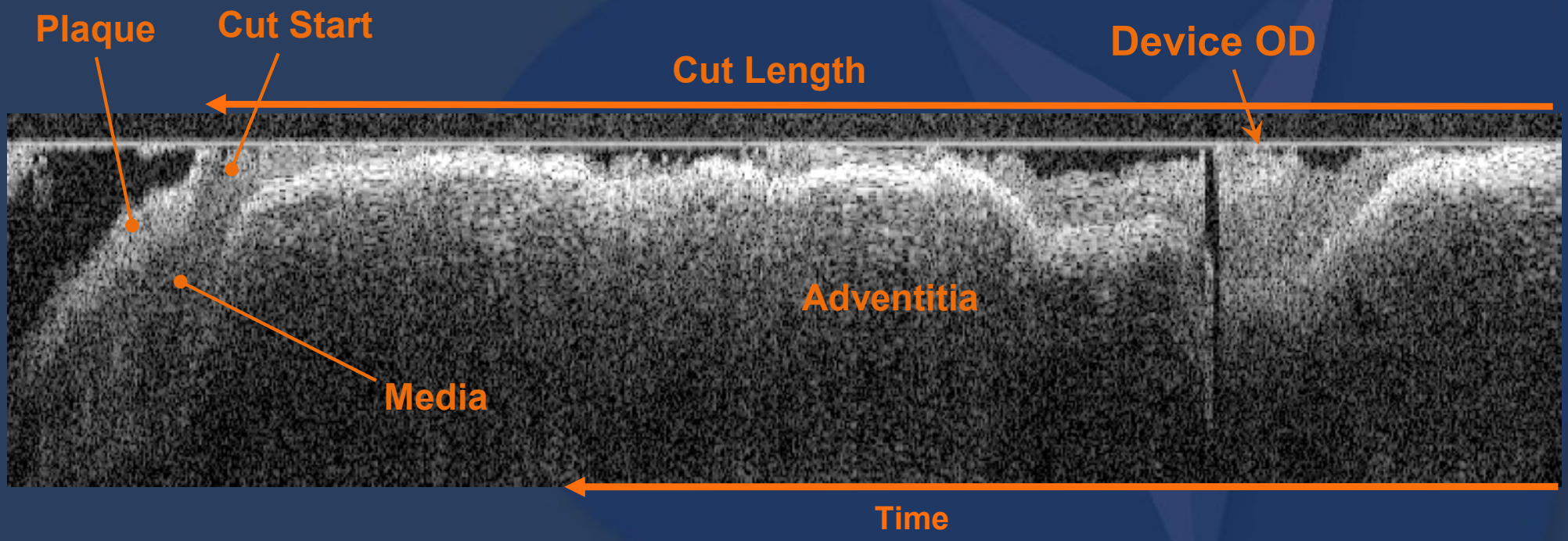
# Post-Cut Device Retraction

- A post cut survey pass reveals plaque removal
  - Small thickness of media.
  - No exposed adventitia

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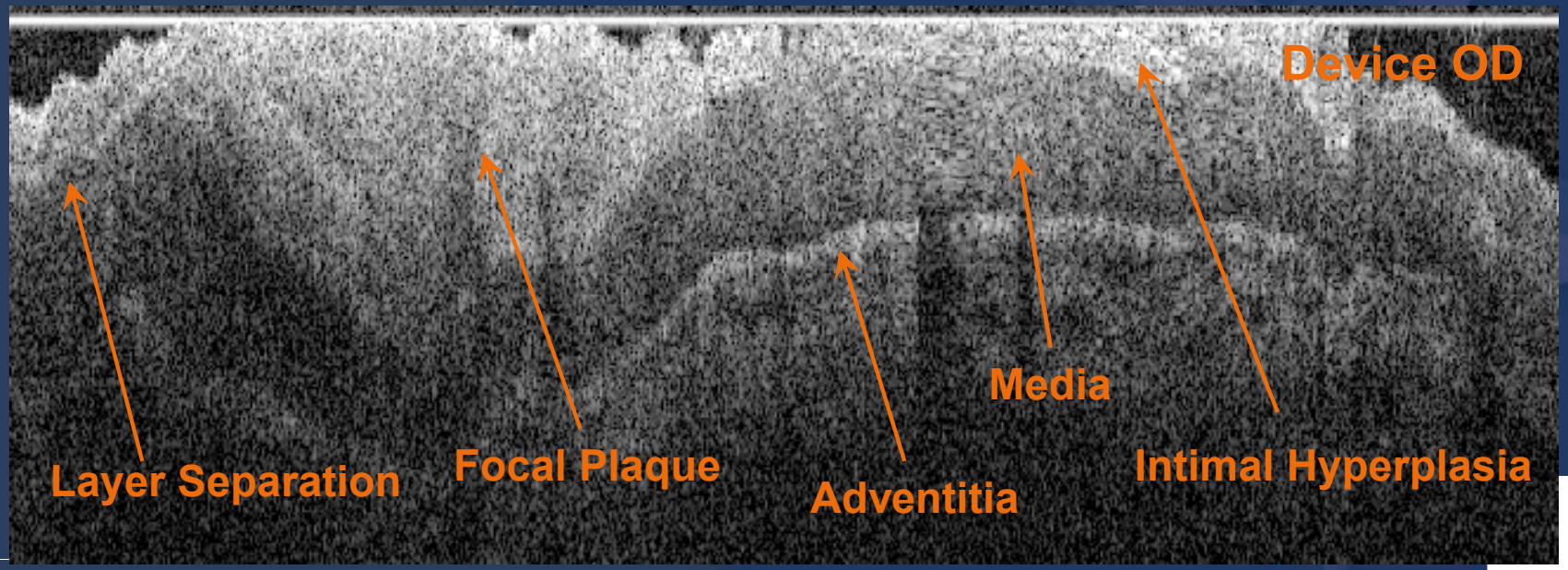
# Plaque Identification

- Plaque development
  - Intimal Hyperplasia
  - Separation of endothelium and IEL.
  - Media largely unaffected at this stage.

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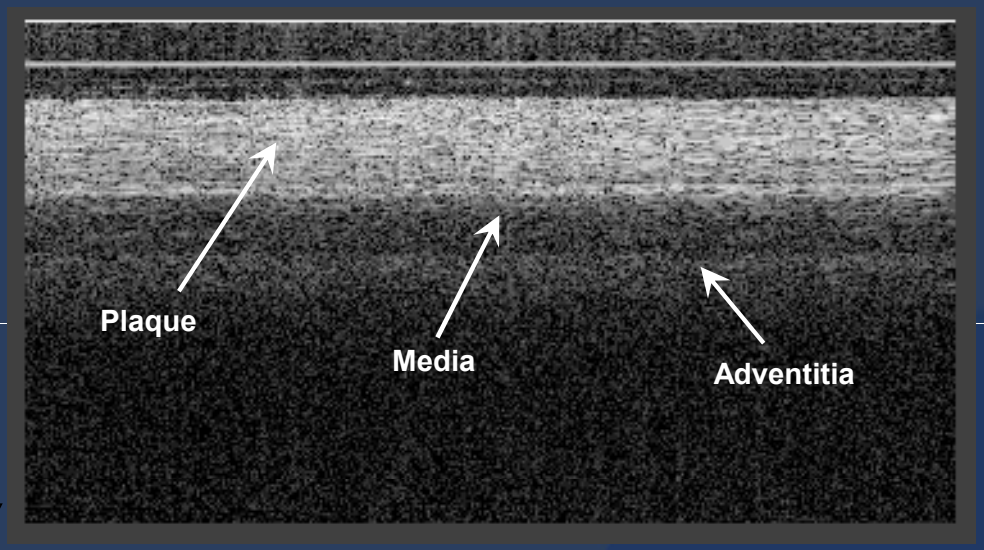
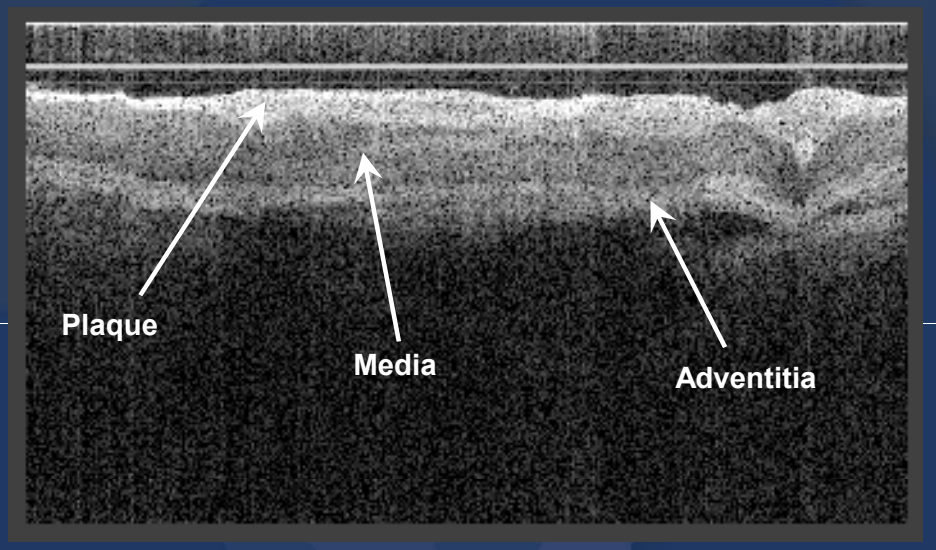
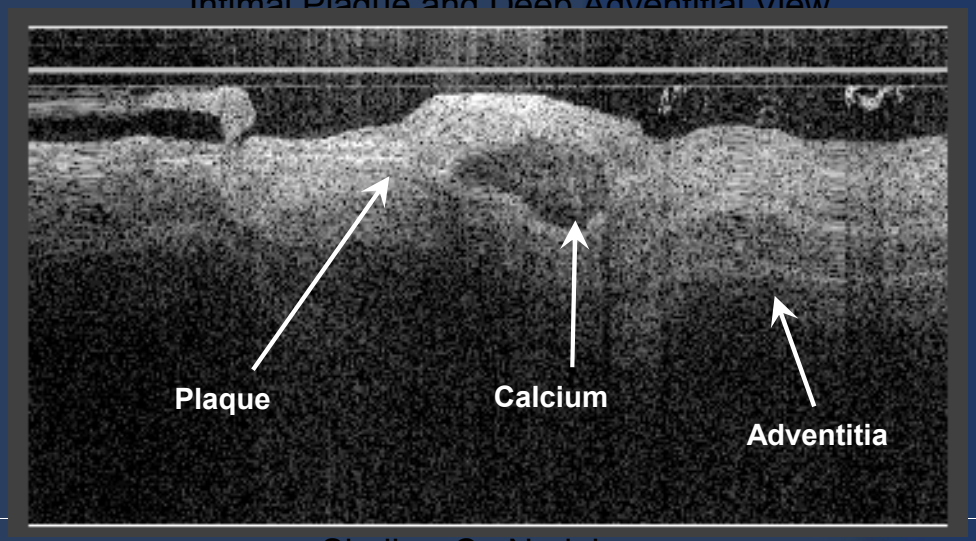
# Example Images: Poland Feasibility



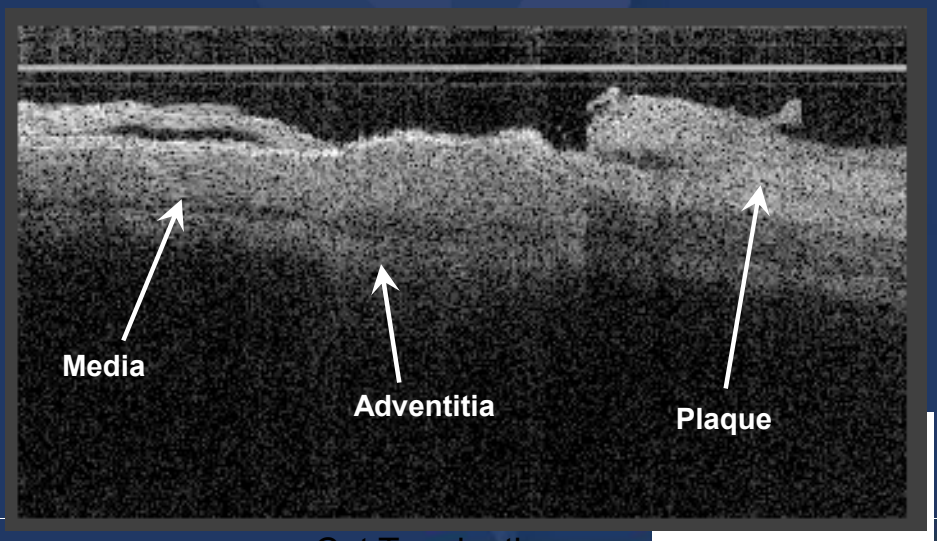

Intimal Plaque and Deep Adventitial View




Intimal/Medial Plaque and Deep Wall Ca




Shallow Ca Nodule




Cut Termination



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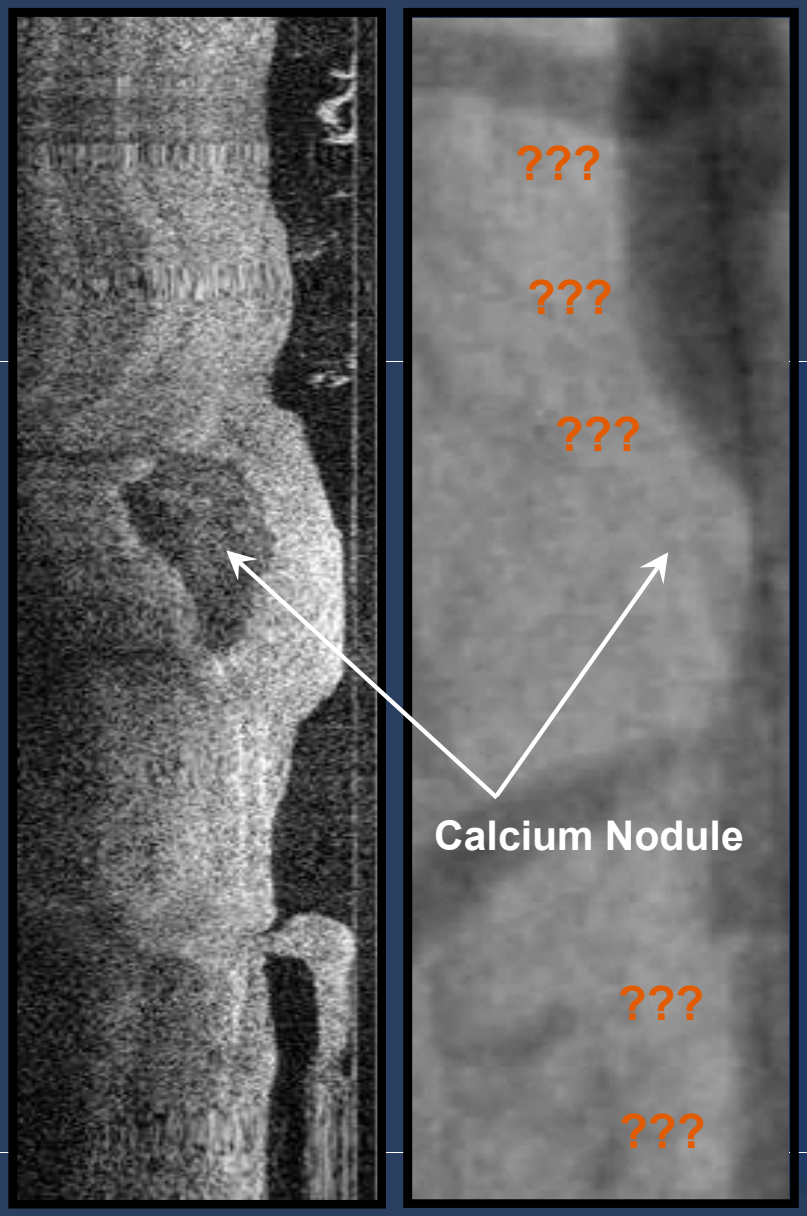
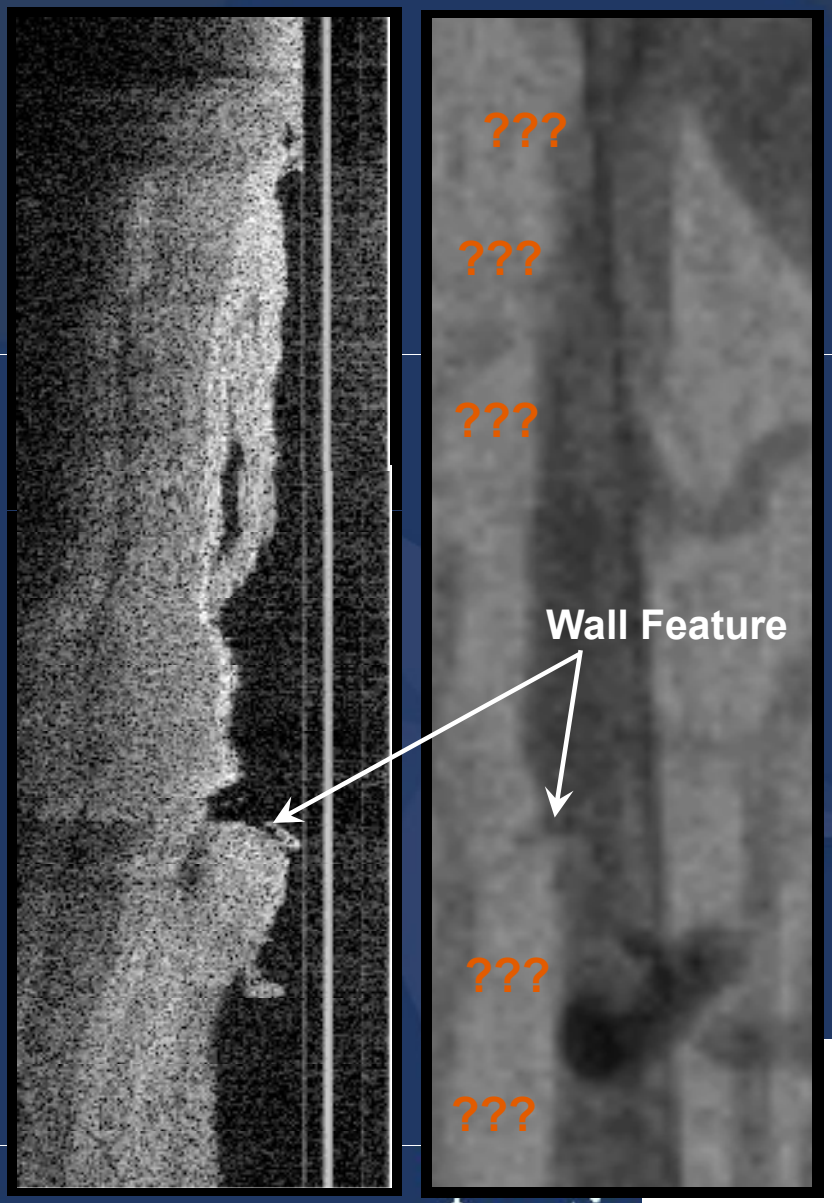
# OCT v. Fluoro: Poland Feasibility



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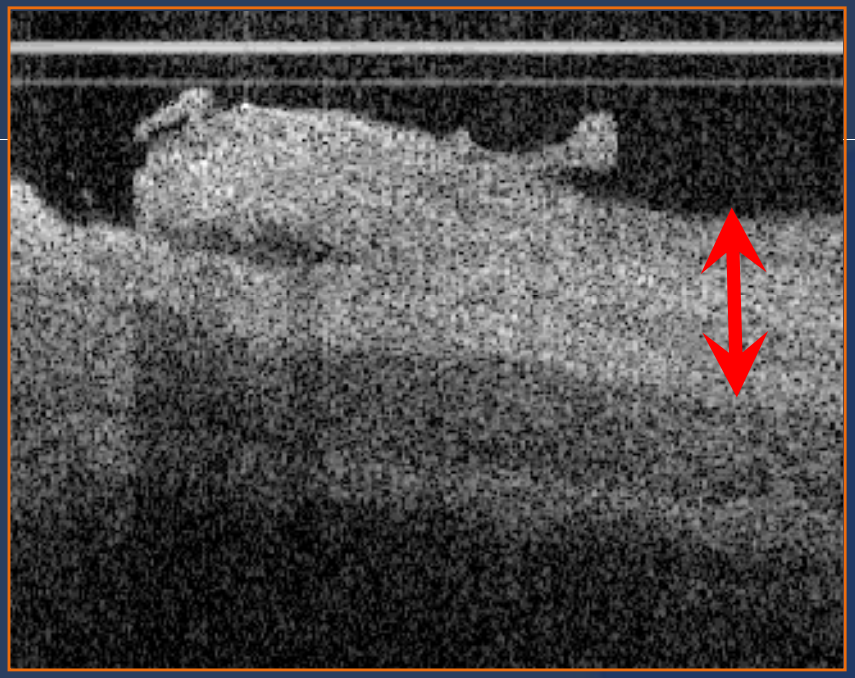
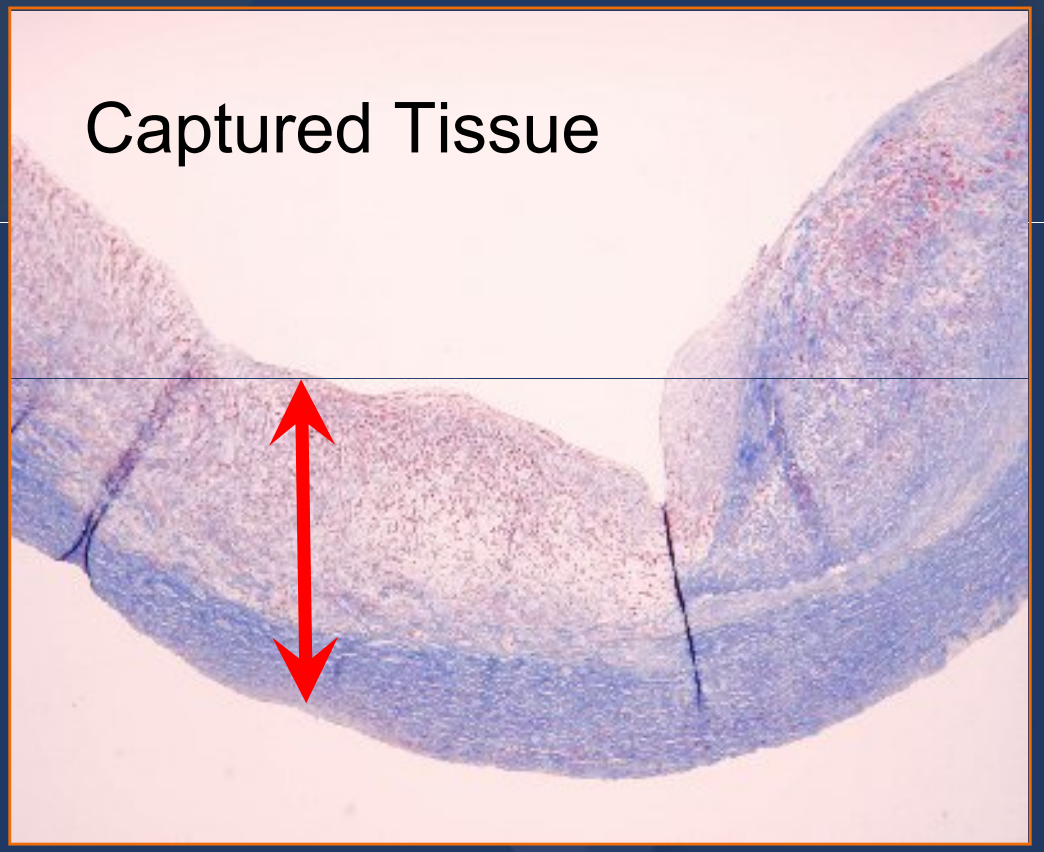
# OCT vs. Histology

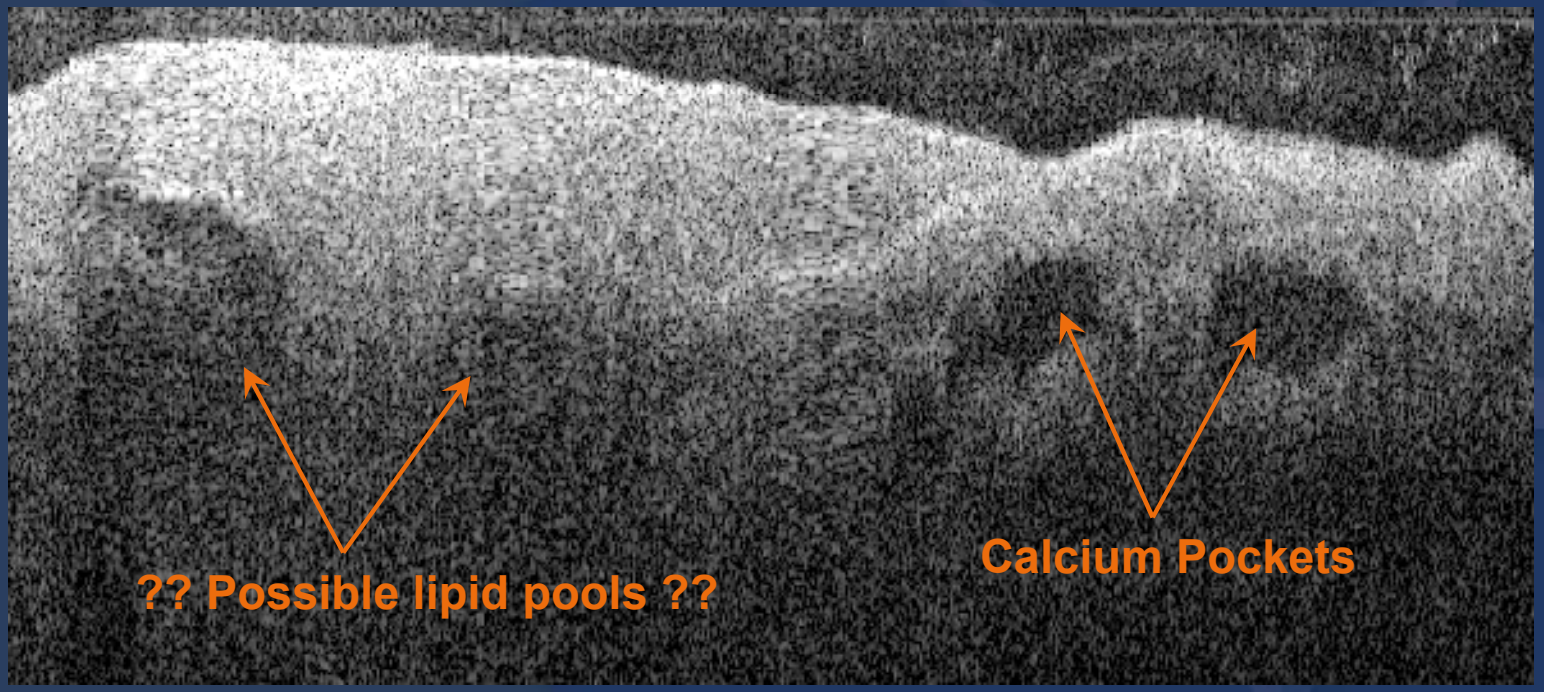





OCT image displays complex structure of disease

# Calcium and Lipid Pools?

- Thin cap fibroatheroma (TCFA)
  - Lipid filled pocket with thin fibrotic cap.
  - “Vulnerable plaque”

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# Current Trials

- NightHawk IDE Trial
- PROOF
- STEP-UP & BTK Trial
- PATENT-SFA
- Merck Collaboration Trials

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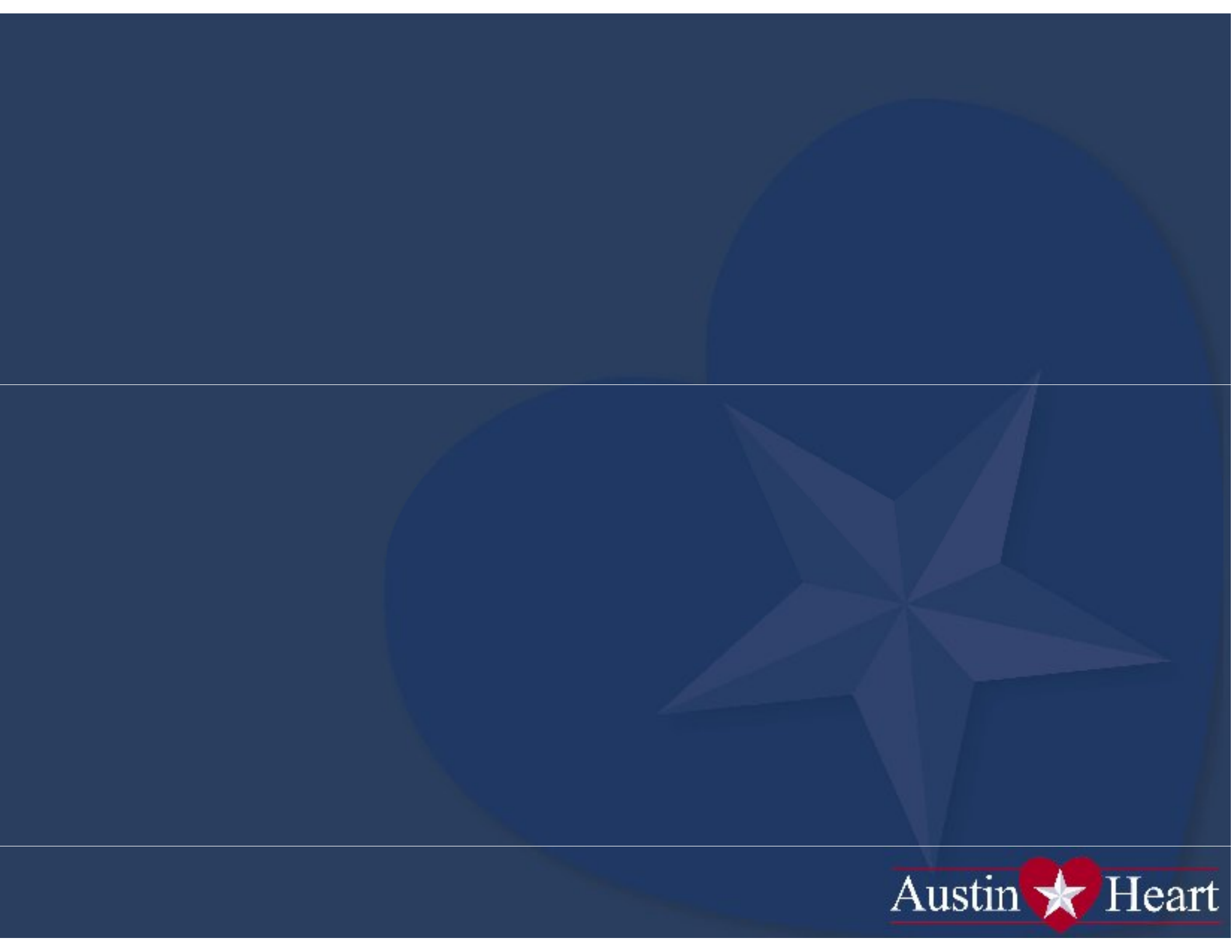
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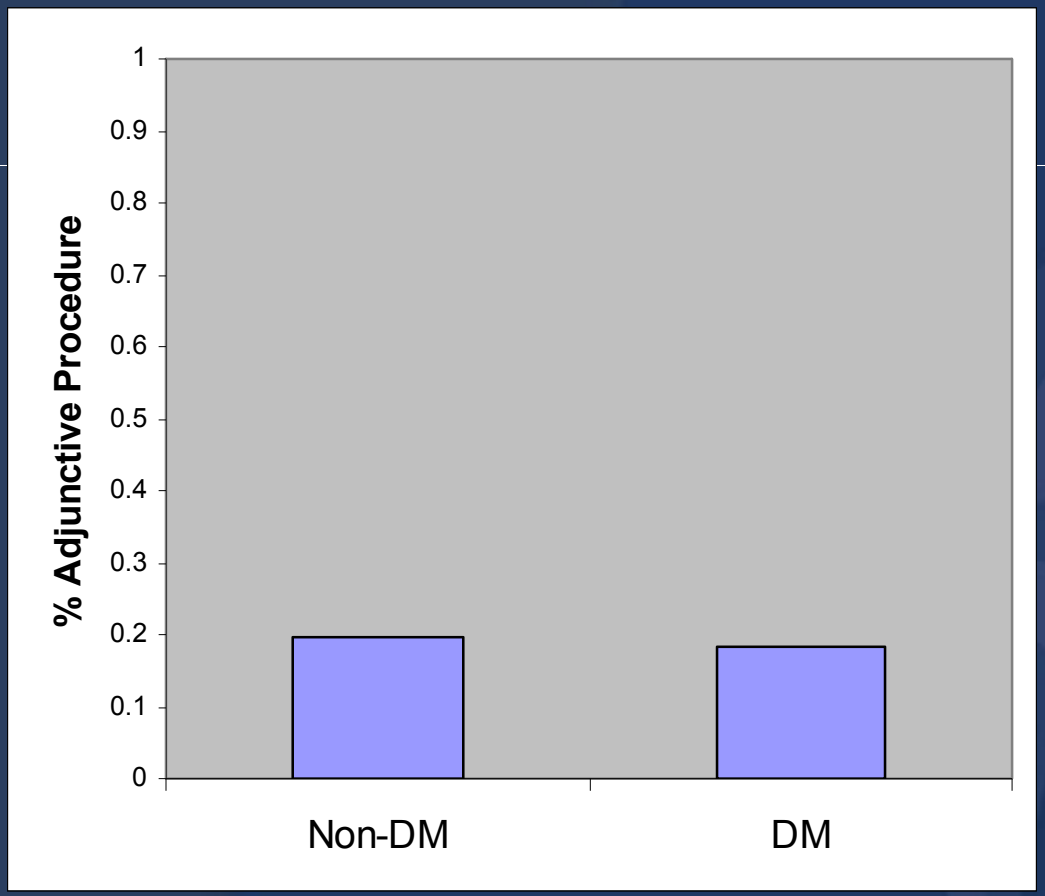
# SFJ excision of *de novo* BTK lesions required similar rates of adjunctive therapy in DM and non-DM

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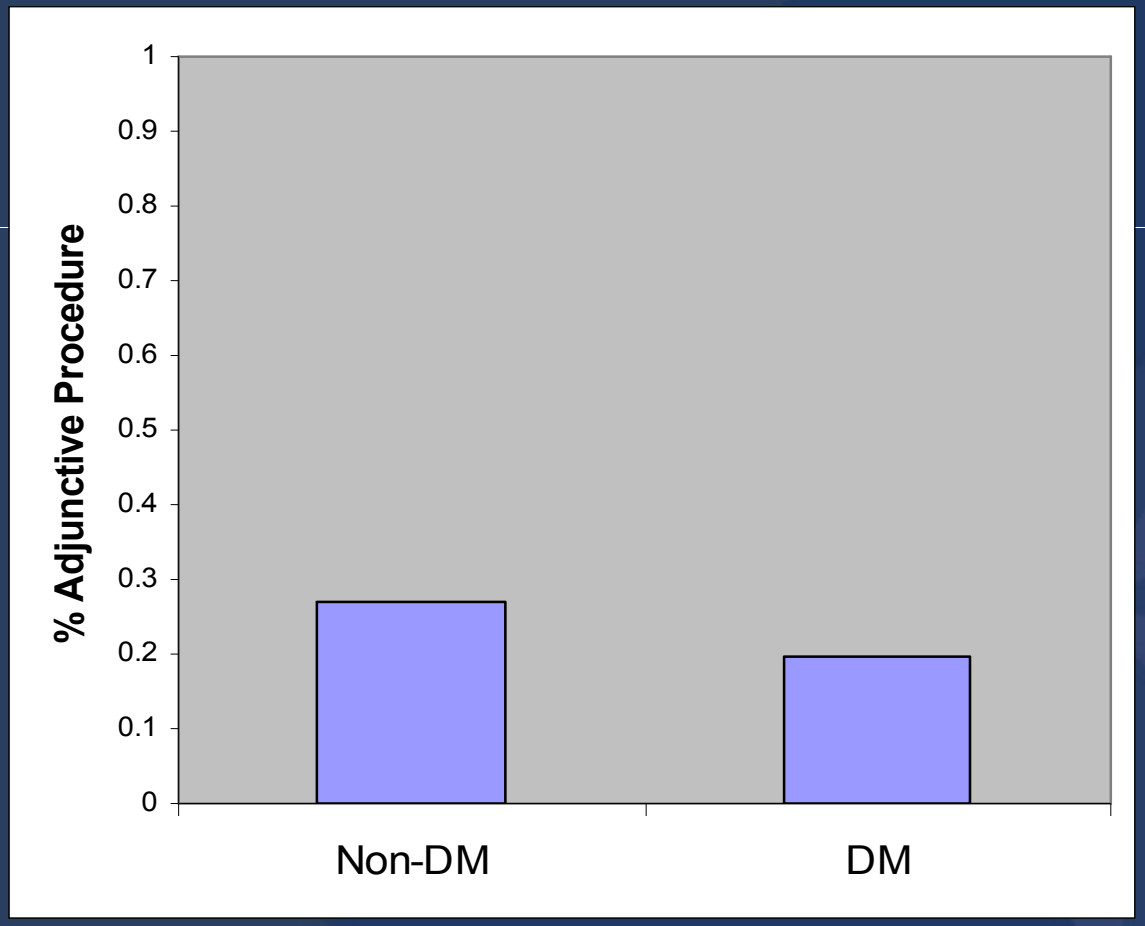
# SH excision of *de novo* ATK lesions required similar rates of adjunctive therapy in DM and non-DM

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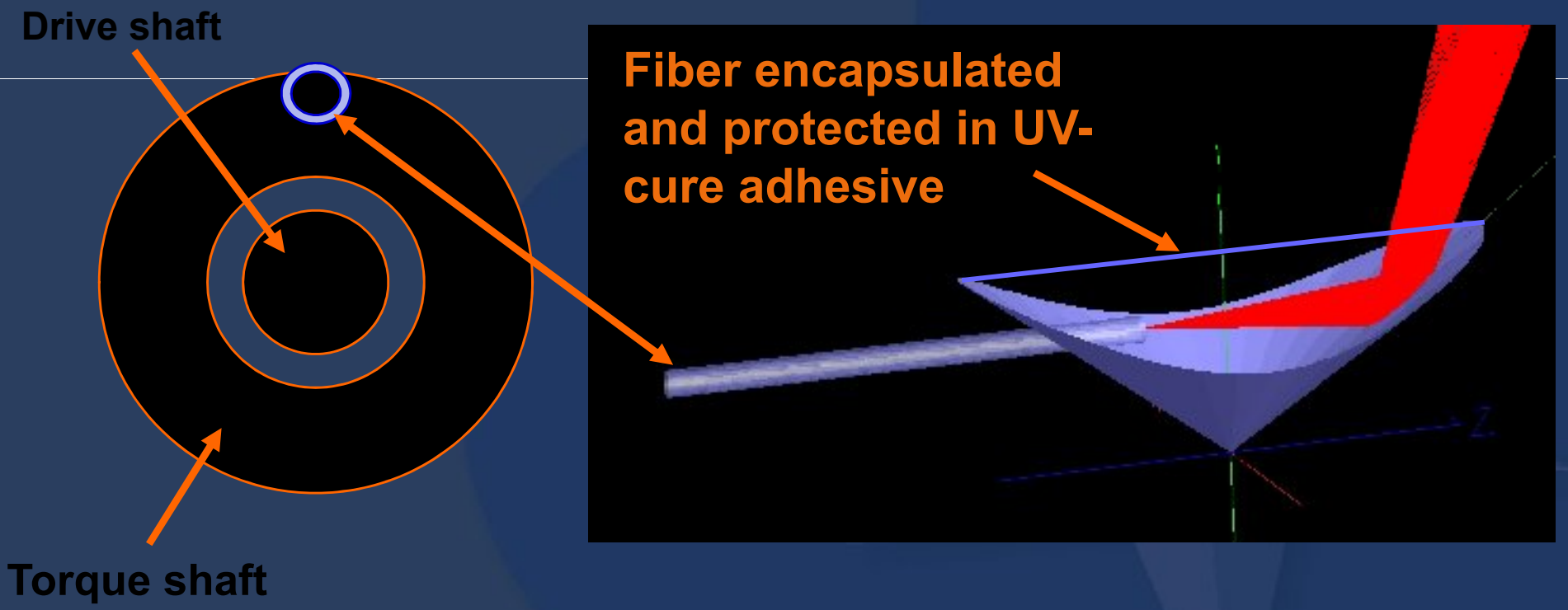
# Catheter Optical Design

## Fiber runs in a small lumen on the torque shaft

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# Optical Coherence Tomography

- Optical analog to Ultrasound
  - Send out a pulse of light
  - Listen for the return.
- Difference is the speed in tissue.
  - Ultrasound – 1500 m/s.
  - Light – $2x10^{8}$ m/s
- 2 mm propagation
  - Sound – 2.7 microseconds ($10^{-6}$)
  - 20 picoseconds ($10^{-12}$)

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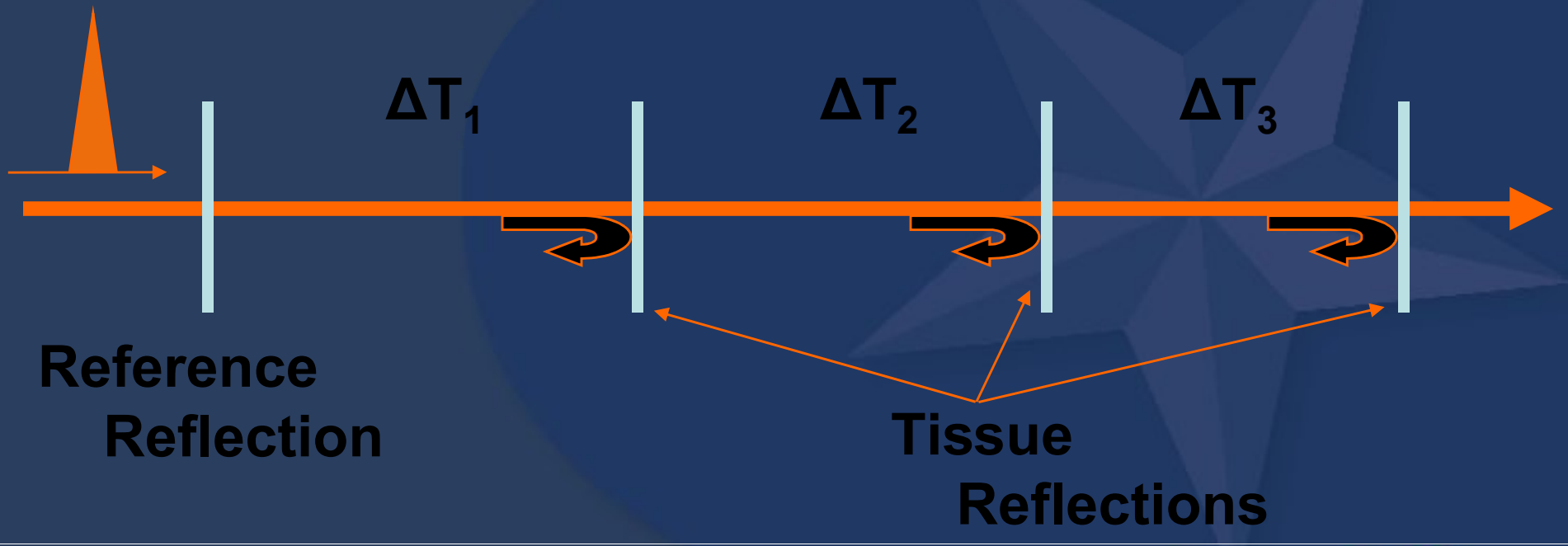
# Principles of Operation

- Cannot measure time-of-flight directly.
- Can measure the beat frequency between two waves.

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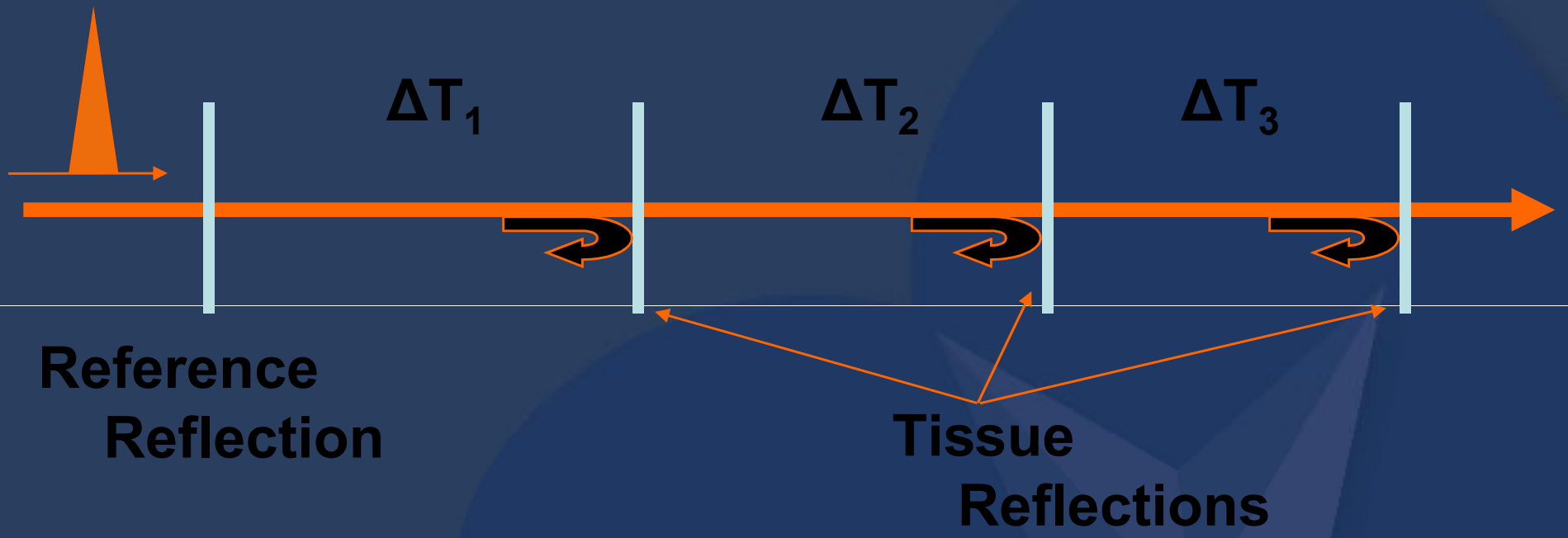
# Principles of Operation




- Source sweeps in frequency rapidly ($5x10^{17}$ $Hz^2$)
  - $t = 0$ ➢ frequency $\omega_0$
  - $t = \mathbf{\Delta T_1}$ ➢ $\omega_1$ : $t = \mathbf{\Delta T_2}$ ➢ $\omega_2$ : $t = \mathbf{\Delta T_3}$ ➢ $\omega_3$
  - Beat Frequency = $\omega_0 - \omega_1$ : $\omega_0 - \omega_2$ : $\omega_0 - \omega_3$
    - $20x10^{-12}$ seconds x $5x10^{17}$ $Hz^2$ = 10MHz

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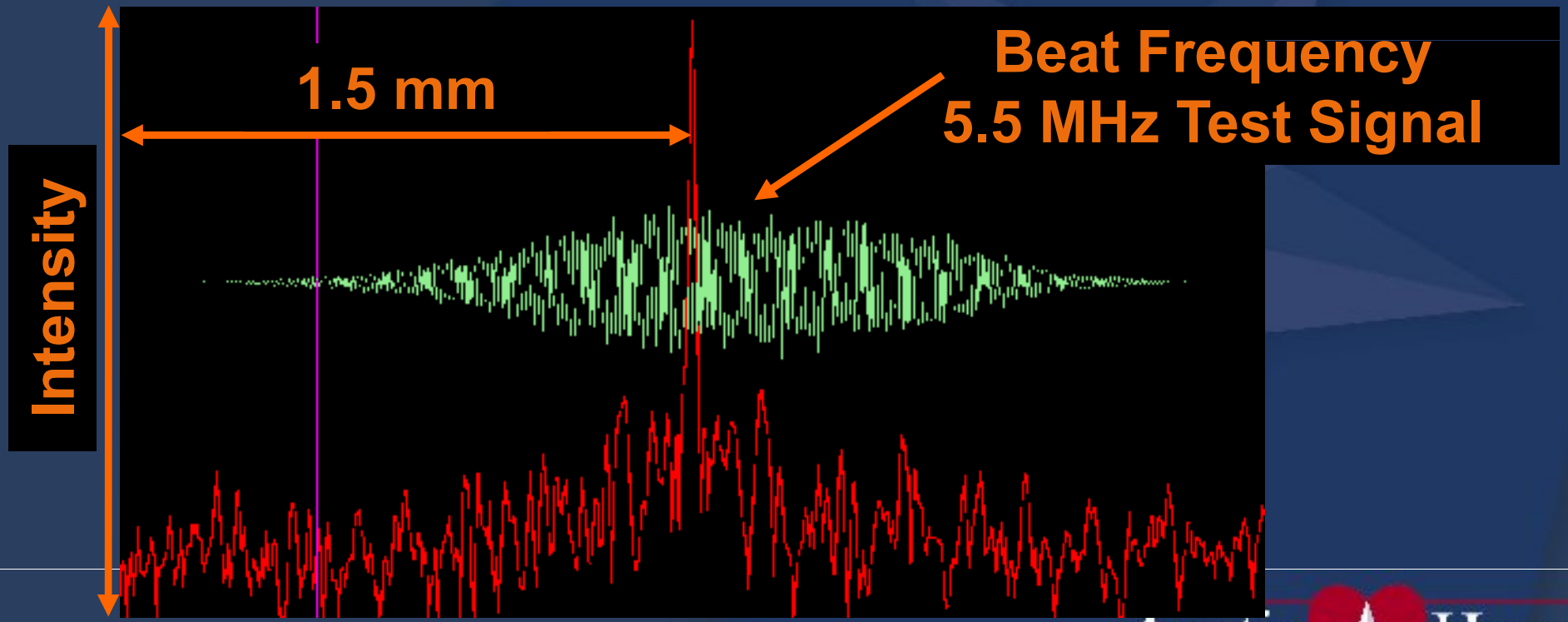
# Effect of Frame Transformation

- As $\Delta T_i$ increases so does the beat frequency.
  - 0 – 3 mm propagation (in air)
  - ➢ DC – ~12 MHz beat frequency
  - Well with range of contemporary electronics.

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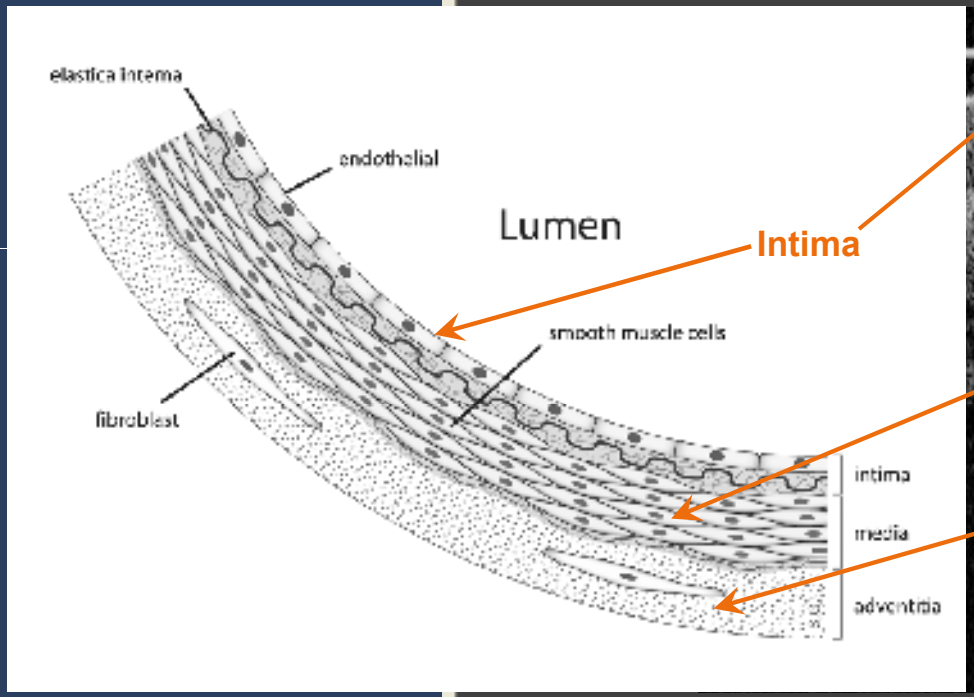
# NightHawk Image Review
## *In Vitro* Pig Coronary









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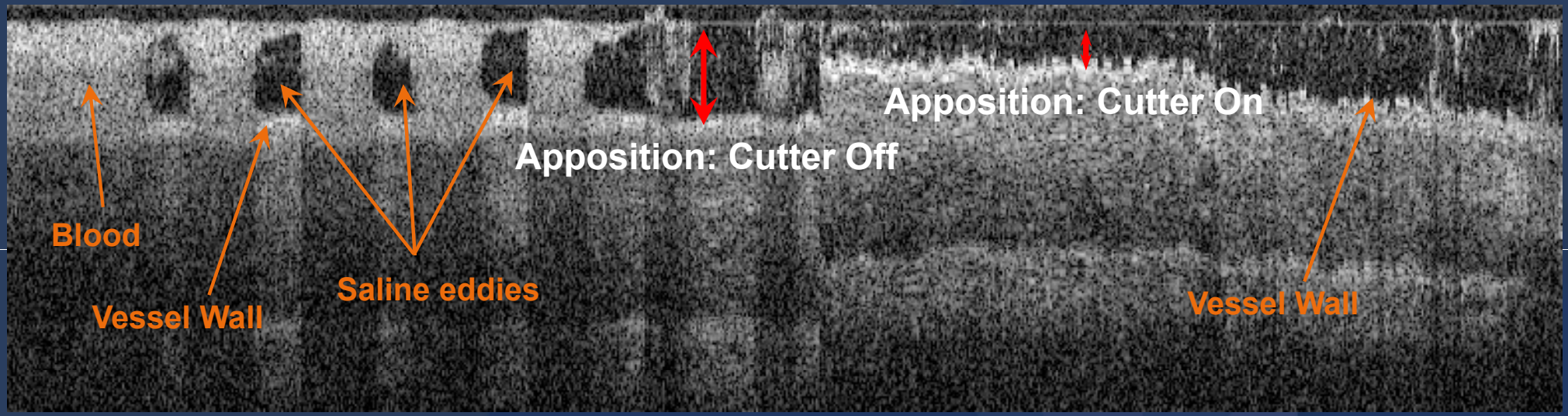
# Apposition Assessment




- Phasic blood-related image loss
  - Mixture of blood and saline
- Cutter opens
  - Device is “urged” up against the vessel wall.

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