A new classification system for femoropopliteal artery patterns of restenosis: introduction and application

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott, Covidien/Medtronic
• Consulting (non-compensated)	• Covidien/Medtronic, Boston Scientific, Abbott
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical
• Royalty Income	• None
• Ownership/Founder	• None
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

The Challenge of Femoropopliteal Artery Disease

- **Peripheral Artery Disease (PAD) affects up to 200 million people worldwide[1] and prevalence of PAD is increasing with an aging population and increasing prevalence of diabetes[2-3] and increasingly more endovascular therapy**

- **No single endovascular therapy has emerged as a "*gold standard*"**

- **Multiple factors influence operator selection of device treatment to include morphology, lesion length, calcification**

- **All devices have primary patency, CD-TLR rates that on average seem similar from device to device**

- **However, to date we still do not understand the failure mode and restenotic pattern on any one device**

- **Therefore, characterizing "the restenotic pattern" remains a critical component in advancing PAD standard of care and device specific treatment choices and may impact healthcare economics**

1. *Fowkes FGR, et al. Lancet 2013;382:1329-40.*
2. *Dua A, Lee CJ. Tech Vasc Interv Rad 2016;19:91-5.*
3. *Criqui MH, Aboyans V. Circ Res 2015;116:1509-26.*

Motivation

- **Benefits of existing scoring systems**
  - **Mehran, et al., developed a pragmatic and easily-applied system for stent-based restenosis classification1**
  - **Tosaka, et al., applied a similar system to the periphery2**
  - **Both systems have demonstrated associations of restenosis type or class to outcomes**
- **Limitations of existing scoring systems**
  - **Limited to in-stent restenosis (ISR) classification, thus not applicable to PTA-, DCB- and Atherectomy-based approaches**
  - **May lack descriptive value in long, complex femoropopliteal artery (FPA) lesions commonly confronting operators**
- **We have developed a scoring system agnostic to treatment modality and applicable by both operators and core labs**

1. *Mehran R, et al. Circ 1999;100:1872-8.*
2. *Tosaka A, et al. J Am Coll Cardiol 2012;59:16-23.*

Multidisciplinary Team

Oversight and Steering Board

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Mark Turco, MD   ▪ *Chris Tieché, PhD*   ▪ *Lynn Oster, RN*   ▪ *Simona Zannetti,MD*

Core Labs

SynvaCor, Springfield, IL, USA   ▪ *Beth Israel Deaconess Medical Center, Boston, MA, USA*

1. *Mehran R, et al. Circ 1999;100:1872-8.*
2. *Tosaka A, et al. J Am Coll Cardiol 2012;59:16-23.*

Methods: Study Scope

- **Inclusion Criteria**
  - **Medtronic Peripheral trials and registries**
  - **First TLRs ≤12mo of index procedure**
- **Exclusion Criteria**
  - **Unevaluable or absent angiographic studies**
  - **Below-knee TLRs (as part of DEFINITIVE LE)**

Study	Treatment Cohort	Total Subjects	Target Lesion Revascularizations
IN.PACT SFA	PTA	111	22
IN.PACT SFA	DCB	220	6
IN.PACT Global - Interim Analysis	DCB	655	54
DEFINITIVE LE - Above-knee	Atherectomy	655	139
DEFINITIVE AR	Atherectomy+DCB	121	22
DURABILITY II	BMS	287	33
Complete SE SFA	BMS	196	18
IN.PACT Global ISR - Baseline ISR	BMS	131	169
IN.PACT Global ISR - DCB treatment	BMS+DCB		23
		2376	*486*

Methods: Index Treated Length

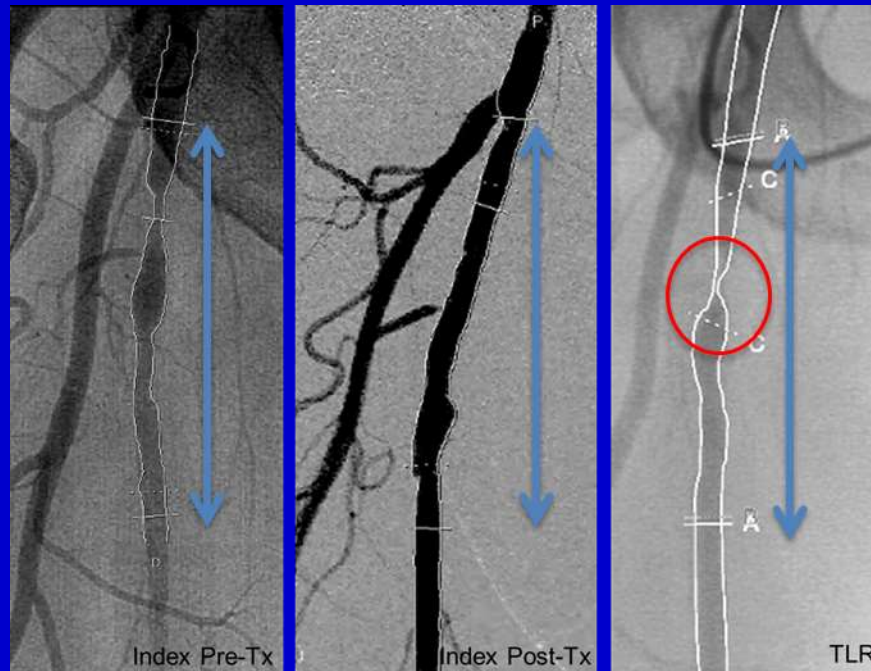**The index treated length (ITL) for non-stent cases, was determined by the angiographic core lab**
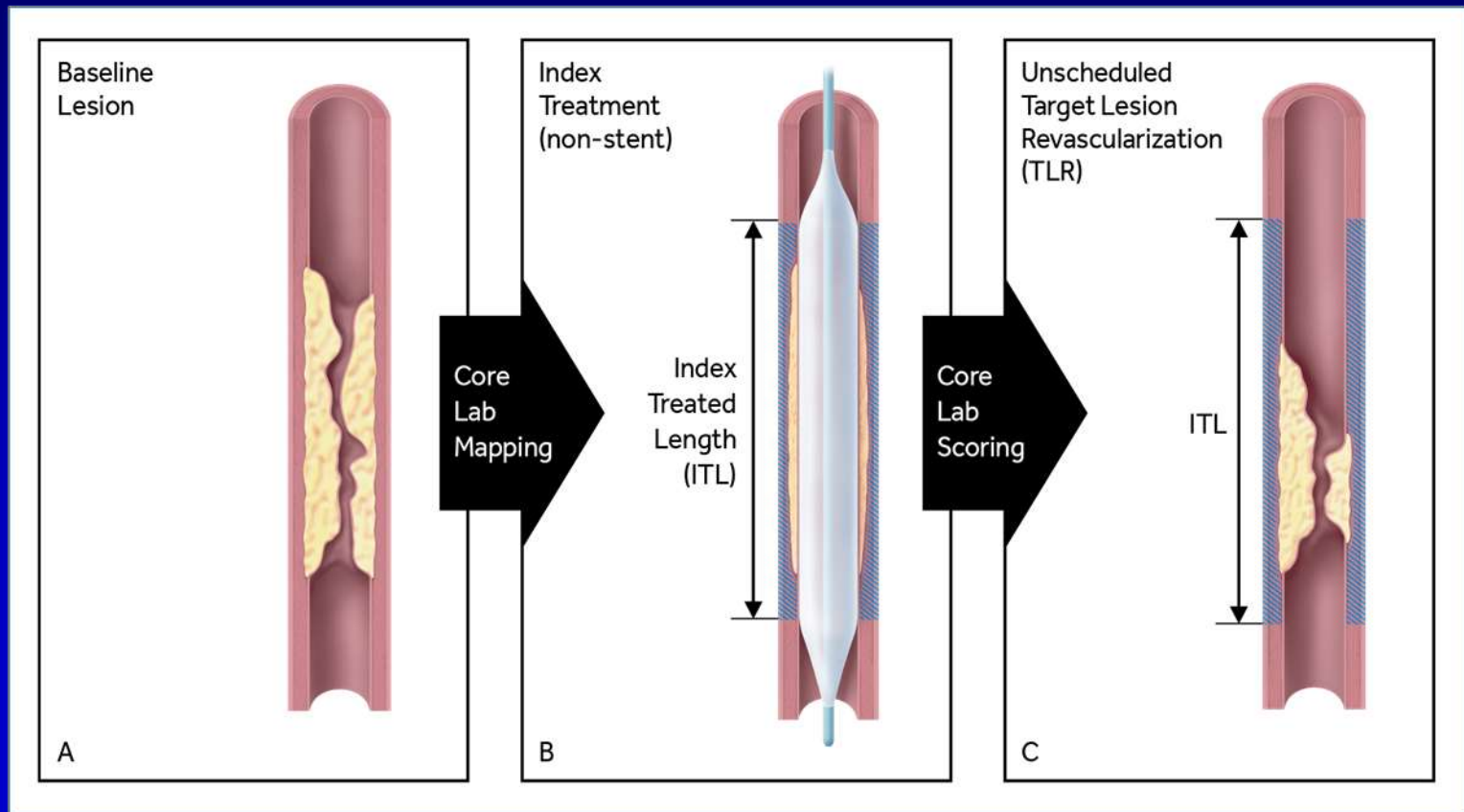
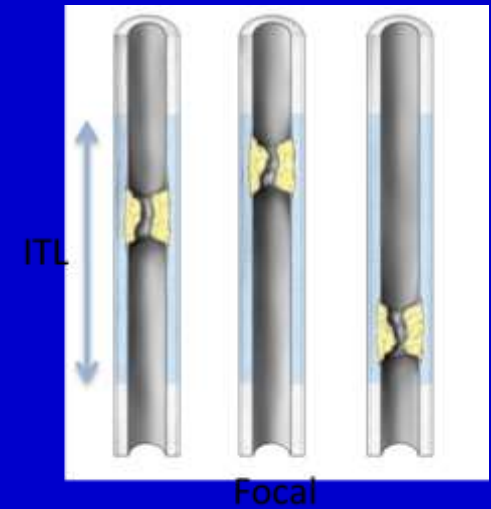# Results: Scoring System

Type 1: Focal lesions <20% ITL

Edge proximal <2cm of proximal ITL margin
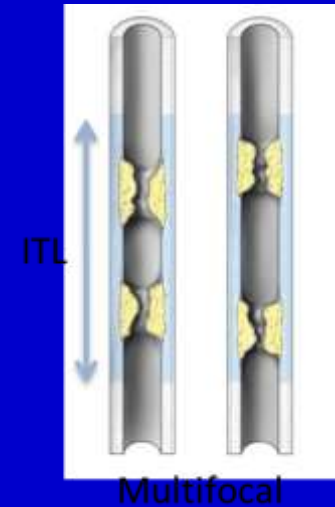
Edge distal <2cm of distal ITL margin

Index Pre-Tx   Index Post-Tx   TLR

Blue arrow denotes ITL

ITL

Focal

ITL = Index treated length.

Results: Scoring System

Type 1: Focal lesions <20% ITL

    Edge proximal <2cm of proximal ITL margin

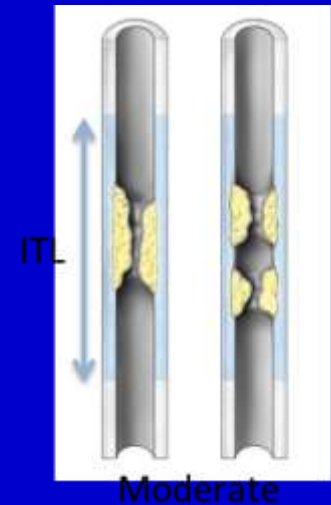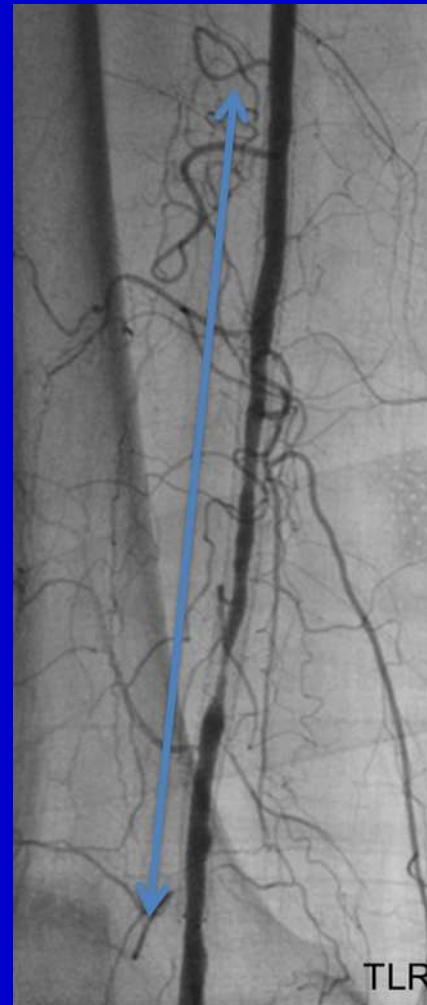   Edge distal <2cm of distal ITL margin

Type 2: Multifocal lesions

    Multiple lesions combining to <50% ITL but with ≥3cm separation

    Edge bilateral within 2cm of both ITL margins

ITL

Multifocal

TLR

Blue arrow denotes ITL

ITL = Index treated length.

Results: Scoring System

Type 1: Focal lesions <20% ITL

    Edge proximal <2cm of proximal ITL margin

    Edge distal <2cm of distal ITL margin

Type 2: Multifocal lesions

    Multiple lesions combining to <50% ITL but with ≥3cm separation

    Edge bilateral within 2cm of both ITL margins

Type 3: Moderate lesions
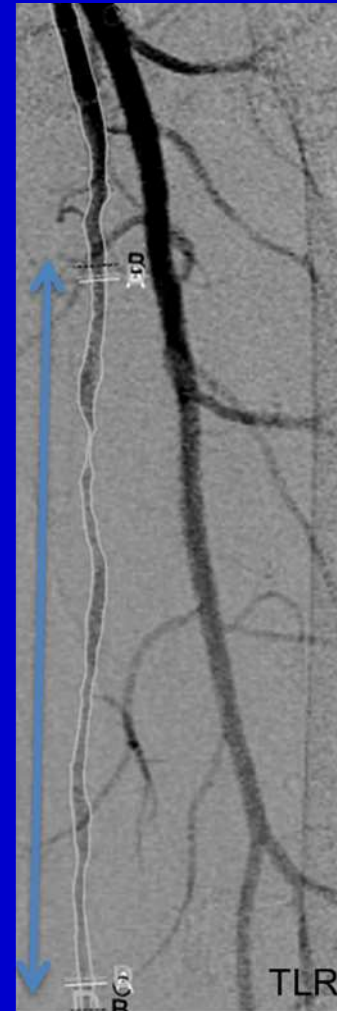
    Lesions ≥20% but <50% of the ITL

    Multiple lesions with <3cm separation

ITL = Index treated length.

TLR

Blue arrow denotes ITL

ITL

Moderate

Results: Scoring System

Type 1: Focal lesions <20% ITL

    Edge proximal <2cm of proximal ITL margin

    Edge distal <2cm of distal ITL margin

Type 2: Multifocal lesions

    Multiple lesions combining to <50% ITL but with ≥3cm separation

    Edge bilateral within 2cm of both ITL margins

Type 3: Moderate lesions

    Lesions ≥20% but <50% of the ITL
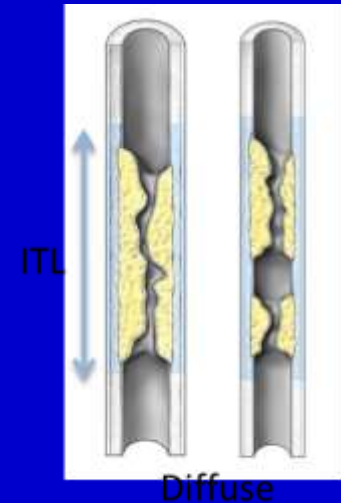
    Multiple lesions with <3cm separation

Type 4: Diffuse lesions

    Lesions ≥50% ITL regardless of separation

ITL = Index treated length.

Blue arrow denotes ITL

ITL

Diffuse

Results: Scoring System

Type 1: Focal lesions <20% ITL

    Edge proximal <2cm of proximal ITL margin

    Edge distal <2cm of distal ITL margin

Type 2: Multifocal lesions

    Multiple lesions combining to <50% ITL but with ≥3cm separation

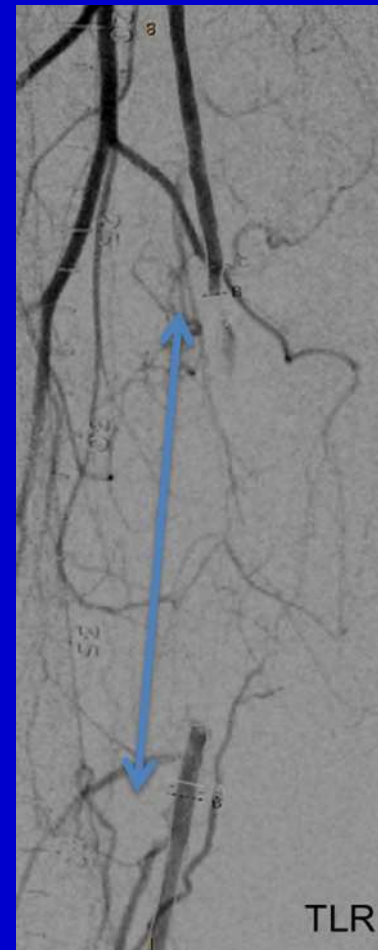   Edge bilateral within 2cm of both ITL margins

Type 3: Moderate lesions

    Lesions ≥20% but <50% of the ITL
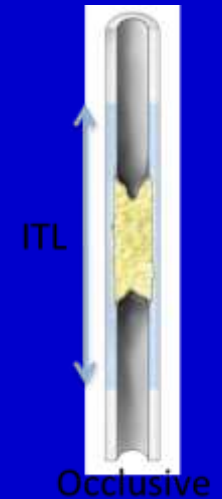
    Multiple lesions with <3cm separation

Type 4: Diffuse lesions

    Lesions ≥50% ITL regardless of separation

Type 5: Occlusive lesions

ITL = Index treated length.

ITL

Occlusive

TLR

Blue arrow denotes ITL

Results: Scoring System

Type 1: Focal lesions <20% ITL

    Edge proximal <2cm of proximal ITL margin

    Edge distal <2cm of distal ITL margin

Type 2: Multifocal lesions

    Multiple lesions combining to <50% ITL but with ≥3cm separation

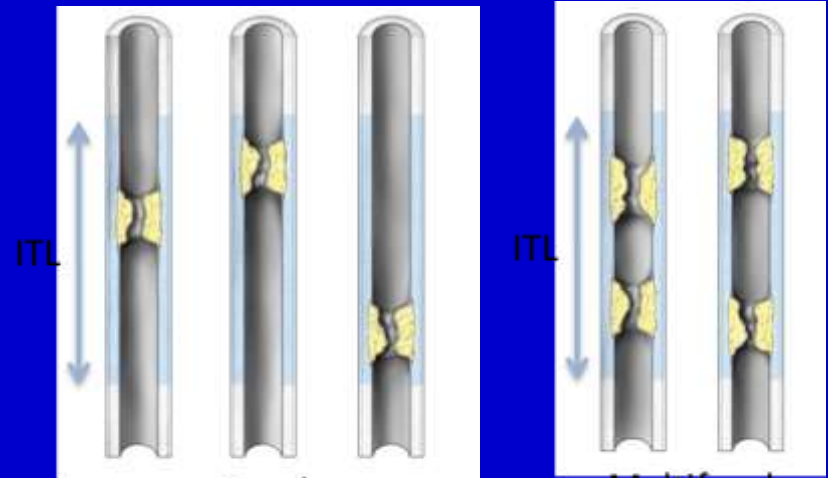   Edge bilateral within 2cm of both ITL margins

Type 3: Moderate lesions

    Lesions ≥20% but <50% of the ITL

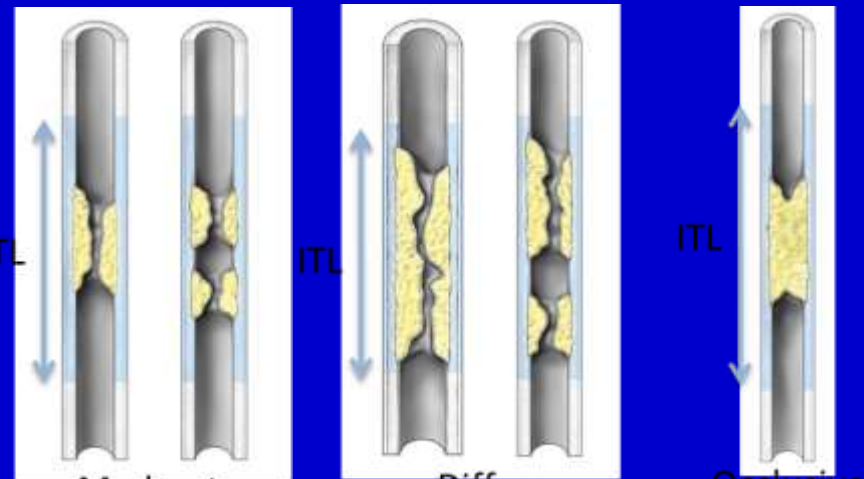   Multiple lesions with <3cm separation

Type 4: Diffuse lesions

    Lesions ≥50% ITL regardless of separation

Type 5: Occlusive lesions

ITL = Index treated length.

Limitations

- **Only MDT devices evaluated**
  - **Atherectomy cases were only directional atherectomy (SilverHawk & TurboHawk)**
  - **DCB cases were only IN.PACT Admiral**
  - **No peripheral stent-grafts**
  - **No peripheral drug-eluting stents**
- **Only complete / high-quality imaging studies were evaluable**
- **Procedural and technical variables, such as catheter placement and remote device complications, are not part of the analysis**

Analytical Plans

Treatment Modality

Baseline Stenosis

Association with Calcium

Time-to-TLR
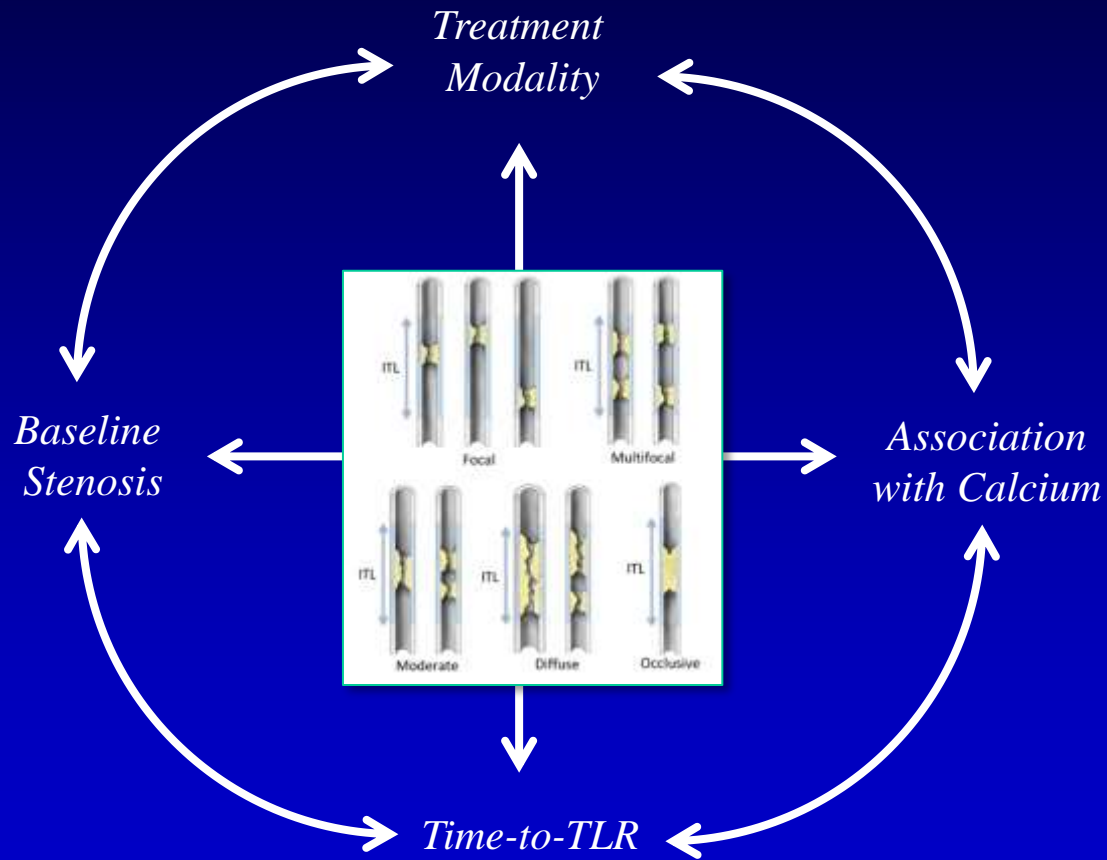
Baseline Stenosis Preliminary Analysis

- **202 TLRs analyzed of the 410 cases available with baseline imaging**
  - **410 total less 145 unevaluable and 63 disqualified as BTK lesions or restenoses <50%**
- **Focal lesions exhibited tendency to fail in a focal restenosis pattern**
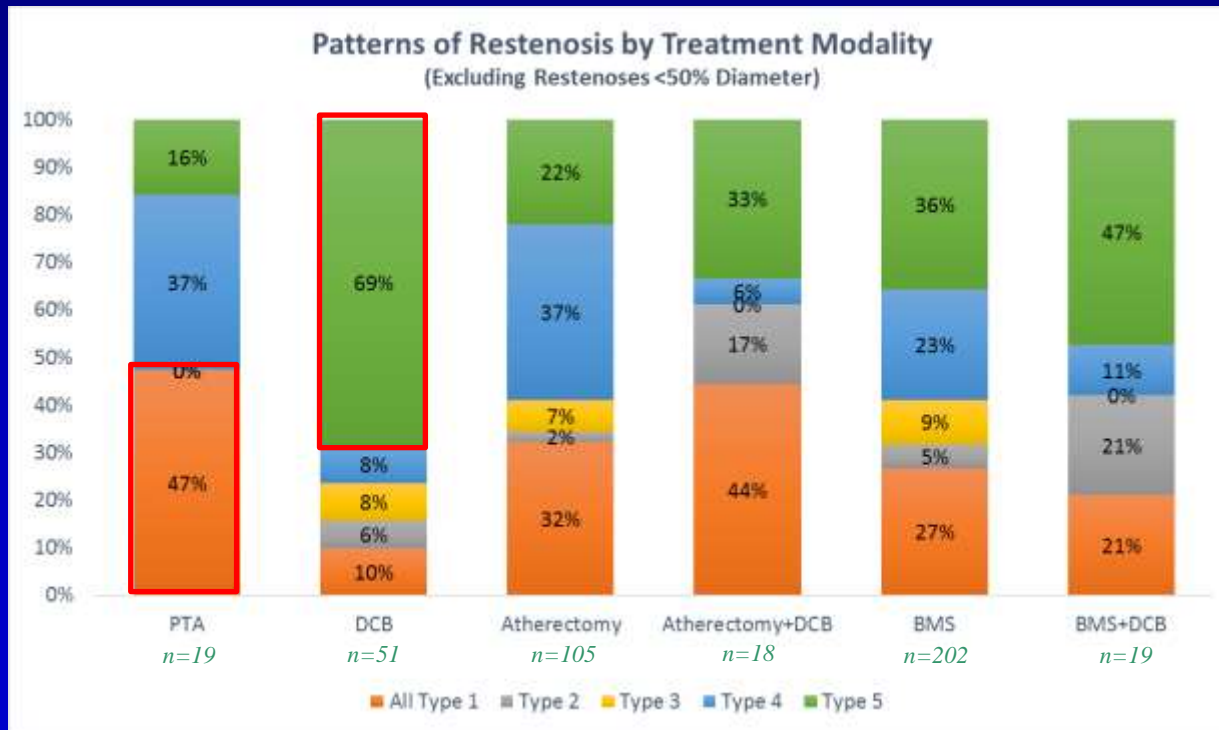- **Diffuse and occlusive lesions tended to fail in diffuse and occlusive patterns**

Patterns of Restenosis by Baseline Stenosis Score (Excluding Restenoses <50% Diameter)
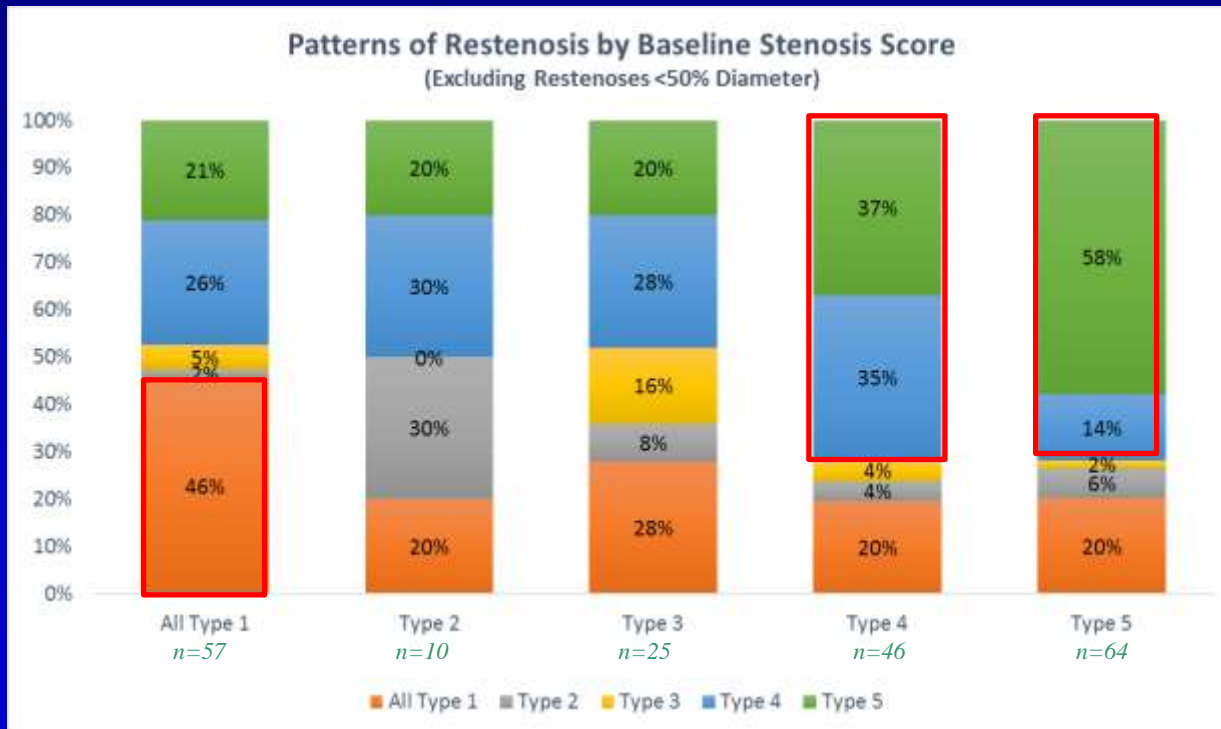
Restenosis Pattern at TLR

Baseline Pattern

Treatment Modality Preliminary Analysis

- **414 TLRs analyzed**
  - **486 total less 7 unevaluable and 65 disqualified as BTK lesions or restenoses <50%**
- **Lesions treated with PTA tended to fail in focal pattern**
- **Lesions treated with DCB tended to fail in occlusive pattern**

Patterns of Restenosis by Treatment Modality (Excluding Restenoses <50% Diameter)

Treatment Modality Preliminary Analysis

- Deeper dive of restenosis associated with baseline stenosis by treatment
- Lesions treated with PTA exhibited evenly-distributed baseline stenosis pattern, suggesting focal failure pattern of PTA
- Lesions treated with DCB tended to consist of more occlusions at baseline, potentially confounding high rate of occlusive restenosis pattern

Patterns of Restenosis with Respect to Baseline Stenosis by Treatment Modality
(Excluding Restenosis <50% Diameter)
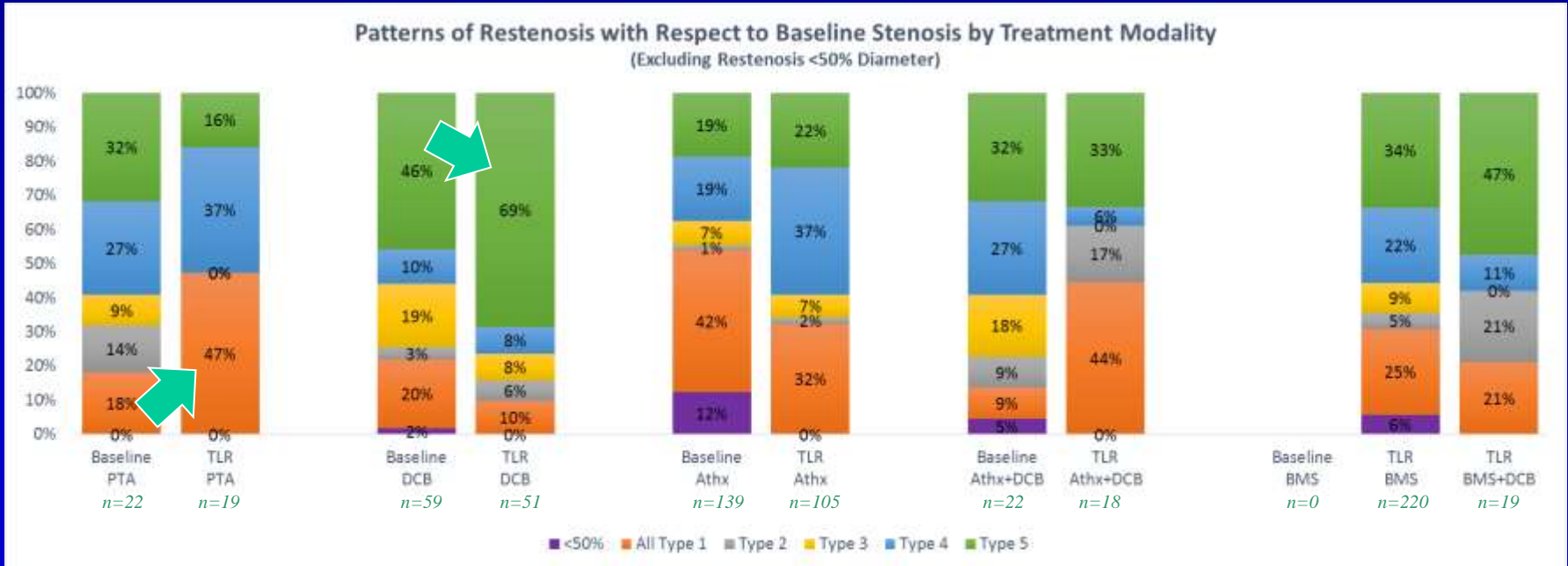
Calcium Association PreliminaryAnalysis

- **194 TLRs analyzed**
  - **241 total less 47 disqualified as BTK lesions or restenoses <50%**
- **No clear trend emerges between calcium severity and restenosis morphology**
- **Device-specific analysis regarding the effect of calcium may add clarity**

Patterns of Restenosis by Baseline Calcium Severity
(Excluding Restenoses <50% Diameter)
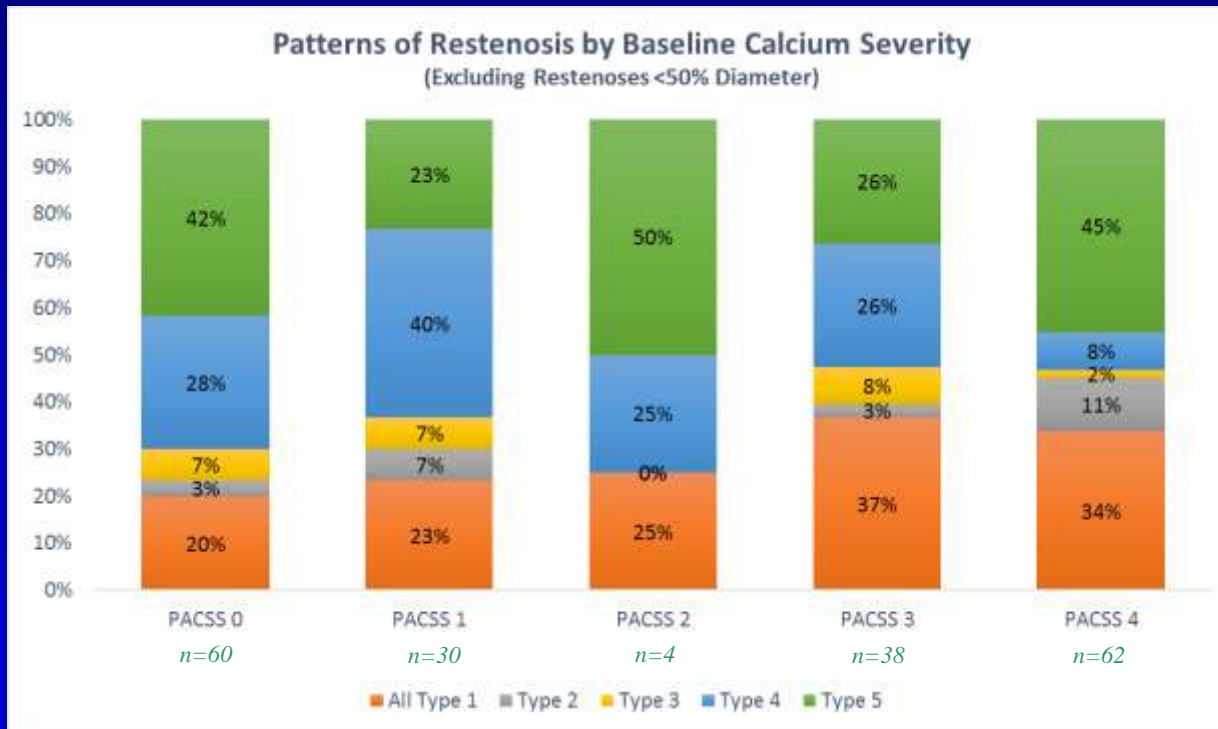
Restenosis Pattern at TLR

Baseline Pattern

Summary

- Existing restenosis scoring systems lack descriptive value for non-stent treatments and long, complex FPA lesions
- Proposed system provides all-inclusive nomenclature with more description of failure morphologies
  - These may provide for more information regarding subsequent therapy (ies)
  - Potential determinant for index procedural technology
- **The proposed "patterns of restenosis" may unify previous and future device trials regardless of technology**
- Initial scoring"patterns" is effective and consistent among all modalities
- Initial review suggests there are differences between modalities in patterns of restenosis.
- Further analysis will become important in describing critical health economics