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Current Advances in CAD Imaging
OCT, NIRS, RF IVUS

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Disclosure

FINANCIAL DISCLOSURE:

Grants/Research Support: LightLab Imaging/St. Jude Medical, Medtronic, Astra Zeneca, InfraReDx

Consulting: LightLab Imaging/St. Jude, Japan Stent Technology

Intravascular Diagnostics for VP

Modality	Resolution	Penetration	Cap	Lipid	Inflam	Ca
OCT	**10 um**	**poor**	**+++**	**+++**	**+**	**++**
Spectroscopy	**-**	**poor**	**-**	**+++**	**-**	**-**
IVUS (RF, IB)	**100 um**	**good**	**+**	**+**	**-**	**+++**
Angioscopy	100 um	poor	+	++	-	-
Thermography	500 um	poor	-	-	+++	-
IV MR	160 um	good	+	++	++	++

Suh, Jang. Circ CV Imaging 2011;4:169

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Intravascular Modalities

- OCT
- Spectroscopy
- RF IVUS

Intravascular Modalities

- OCT
- Spectroscopy
- RF IVUS

OCT History

1992	OCT (Fujimoto)	MIT
1995	1.3 micron, high resolution source	
1996	Radial scanning catheter	
1998	Non-reciprocal interferometer	
1998	MGH Cardiac OCT Group	MGH
1999	Clinically viable system for cardiology	
2000	FIM study in cardiology	
2004	In vivo plaque characterization	
2006	FD-OCT	
2010	FDA approval	
2010	MGH OCT Registry	

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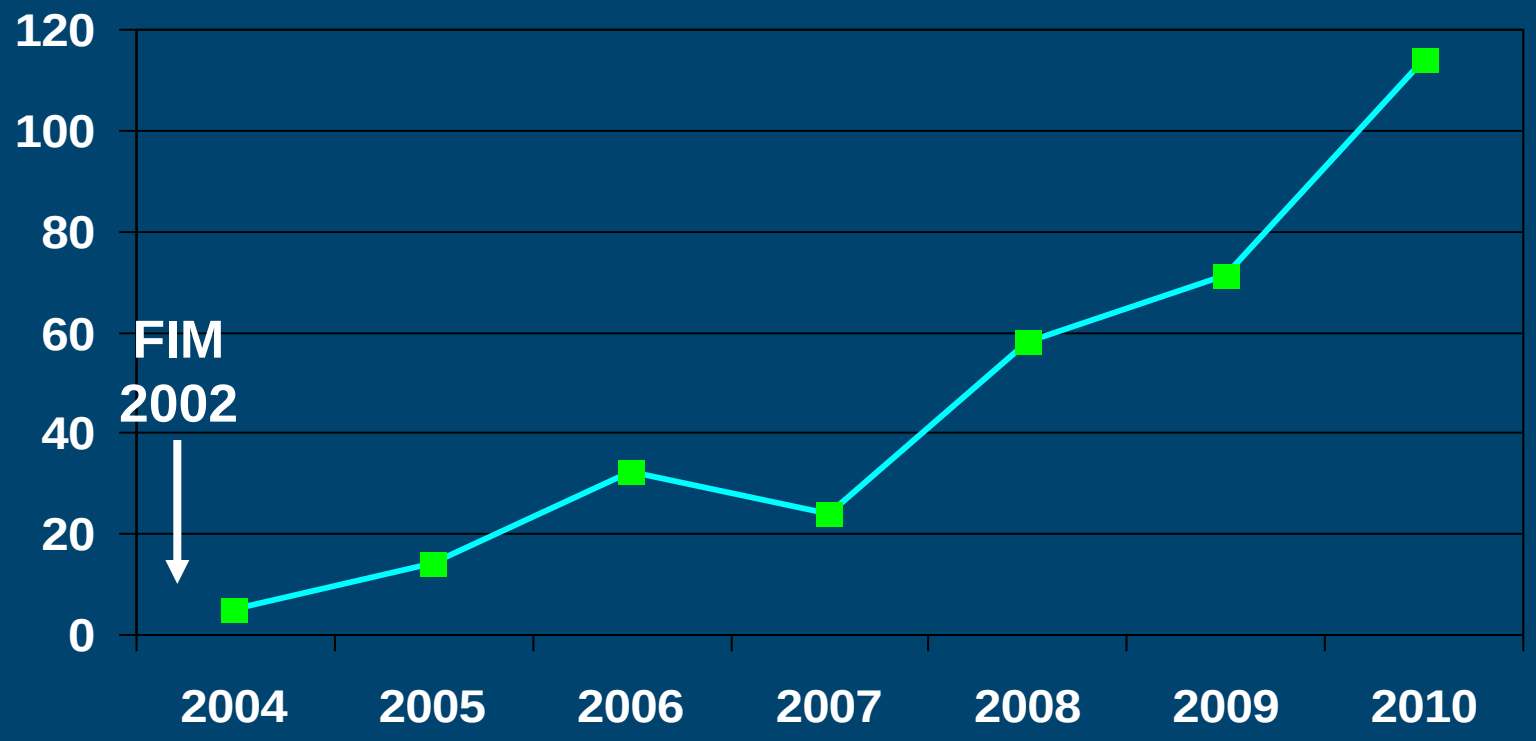
Intra-coronary OCT Publication



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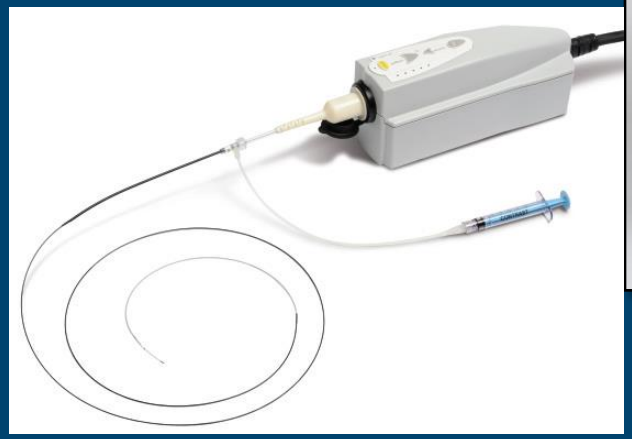
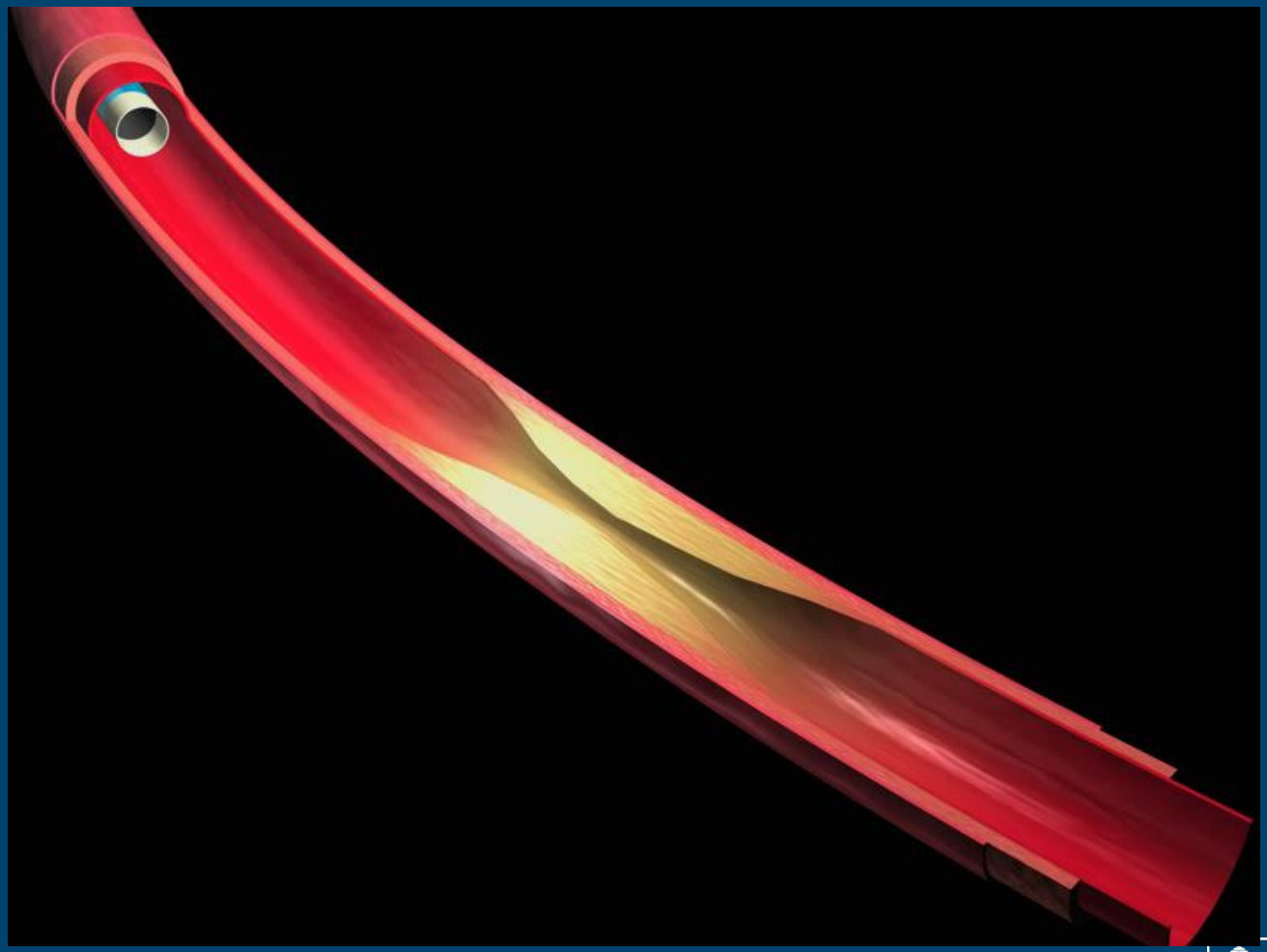
C7XR System

- Balloon occlusion not required
- Fast flush, spiral pullback acquisition
- 5 cm arterial segment in 2.5 sec
- Rapid exchange (Rx) imaging catheter



FD OCT



AMI vs ACS vs SAP

	AMI (n=20/30/35)	ACS (n=20/24/--)	SAP (n=17/31/20)
LRP (%)	90/93/--	75/71/--	58/42/--
FCT (μm)	47/49/--	54/79/--	103/196/--
TCFA (%)	72/83/77	50/46/--	20/3/25
MΦ (%)	5.7±1.4	5.9±2.1	4.2±1.7

Jang 2005/Kubo 2007/Fujii 2008

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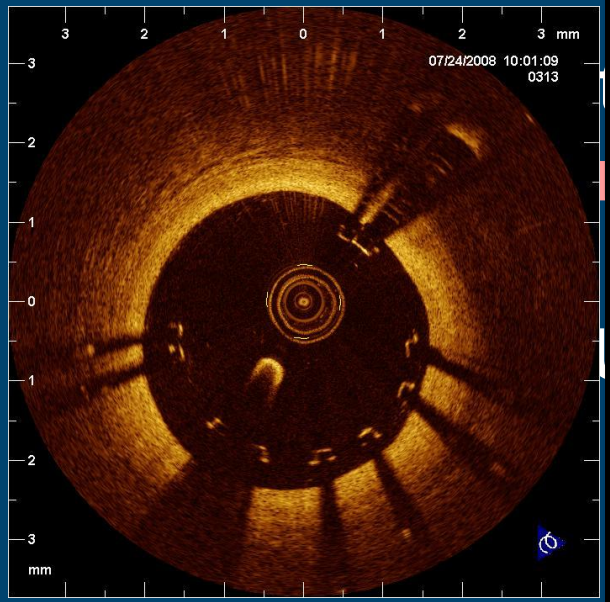
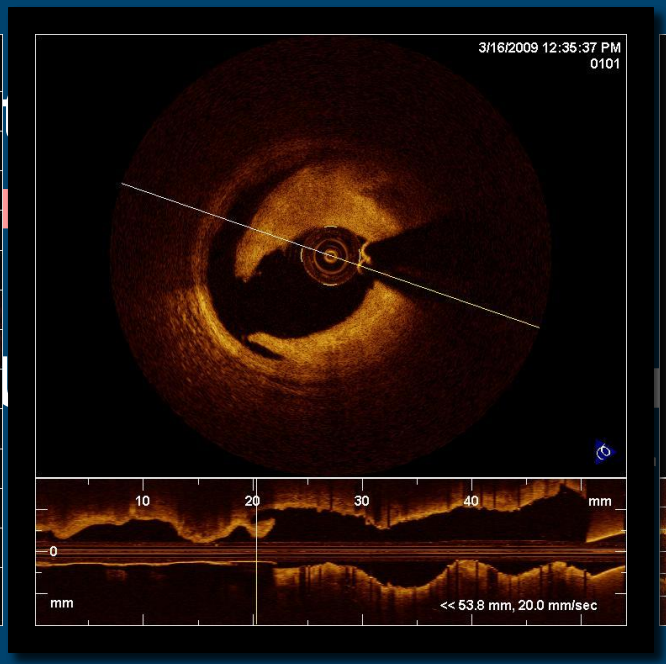
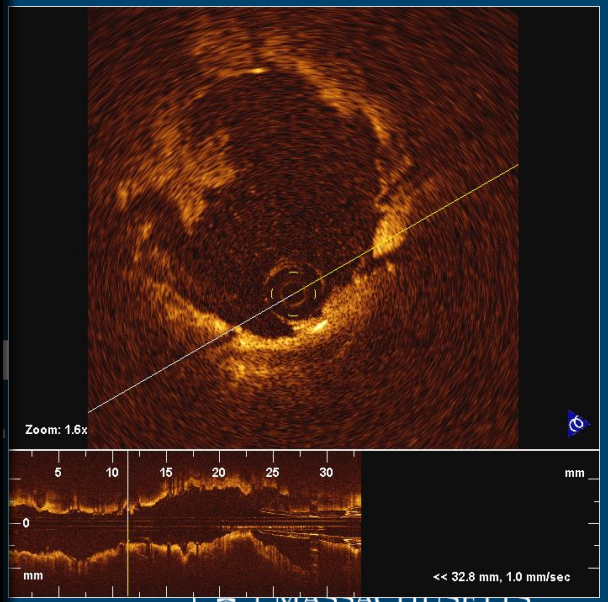
PCI

1. **Immediately post:**

   Malapposition, dissection, thrombus







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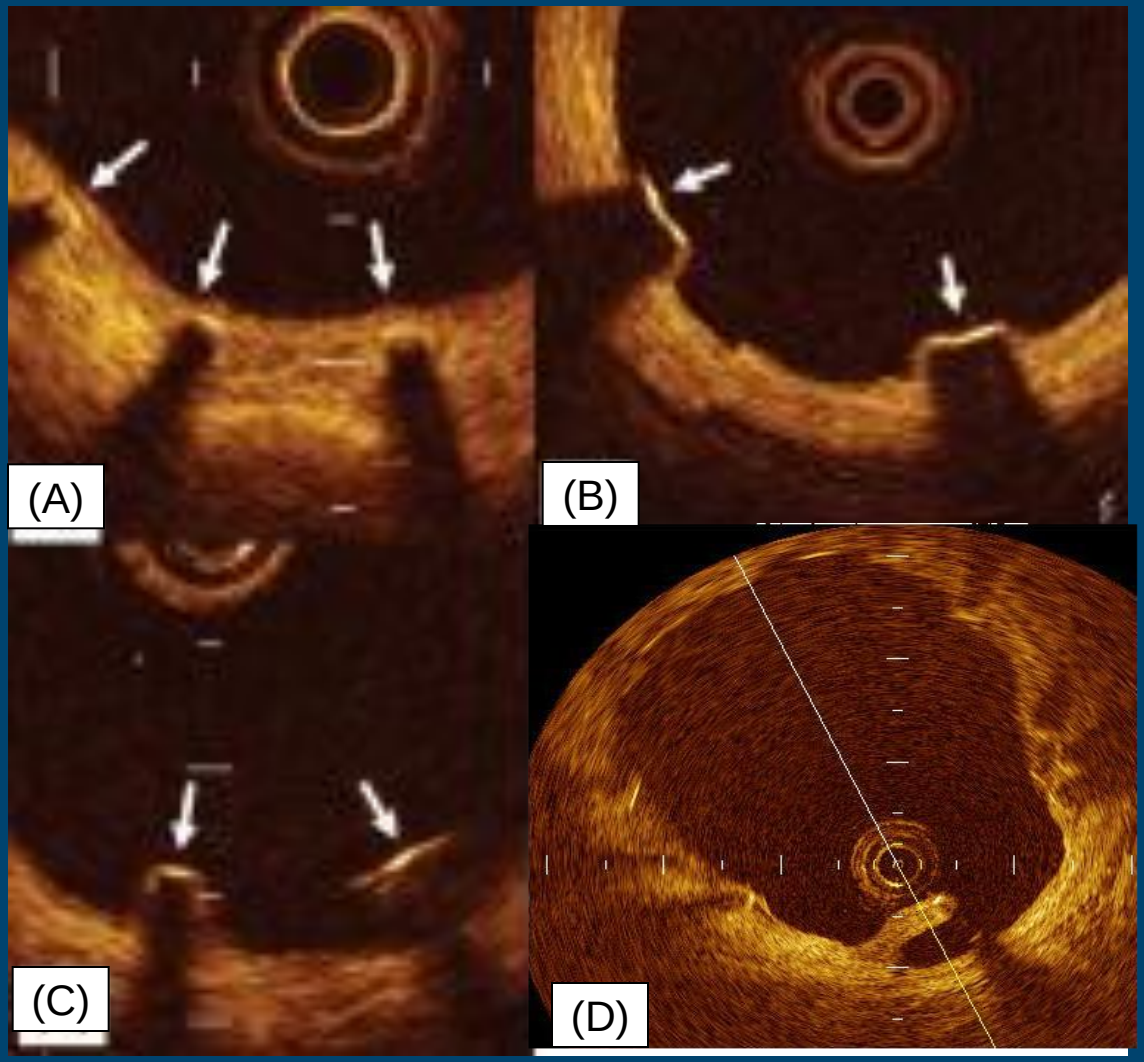
PCI

1. **Immediately post:**
   Malapposition, dissection, thrombus

2. **Intermediate F/U: DES**
   Strut surface coverage

3. **Chronic F/U: BMS after 5 years**
   DES after 2 years
   Neoatherosclerosis

Stent Struts Coverage/Apposition



A: well apposed and covered
B: well apposed, not covered
C: malapposed, not covered
D: malapposed, but covered

Lowe, Narula, Fujimoto, Jang. JACC CV Interv. In press.

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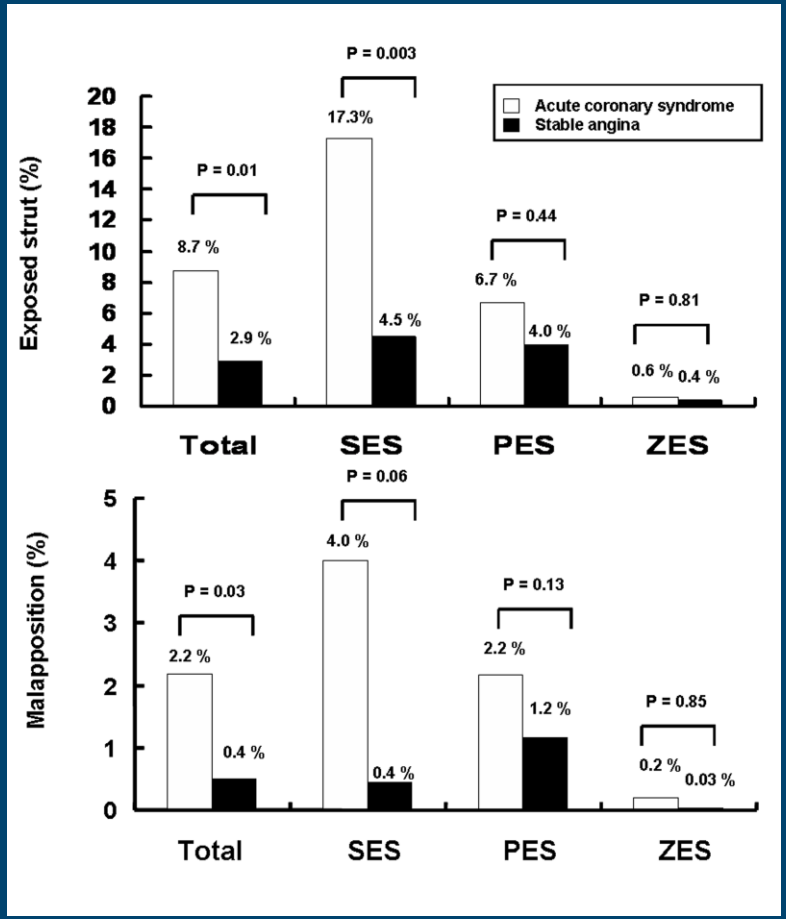
SES v PES v ZES: 9 mo F/U



Kim JS. JACC CV Interv 2009

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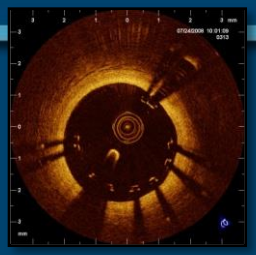
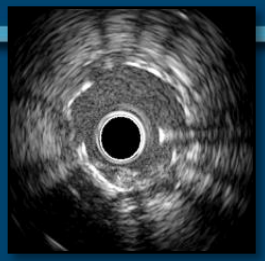
FD-OCT vs IVUS



C7XR

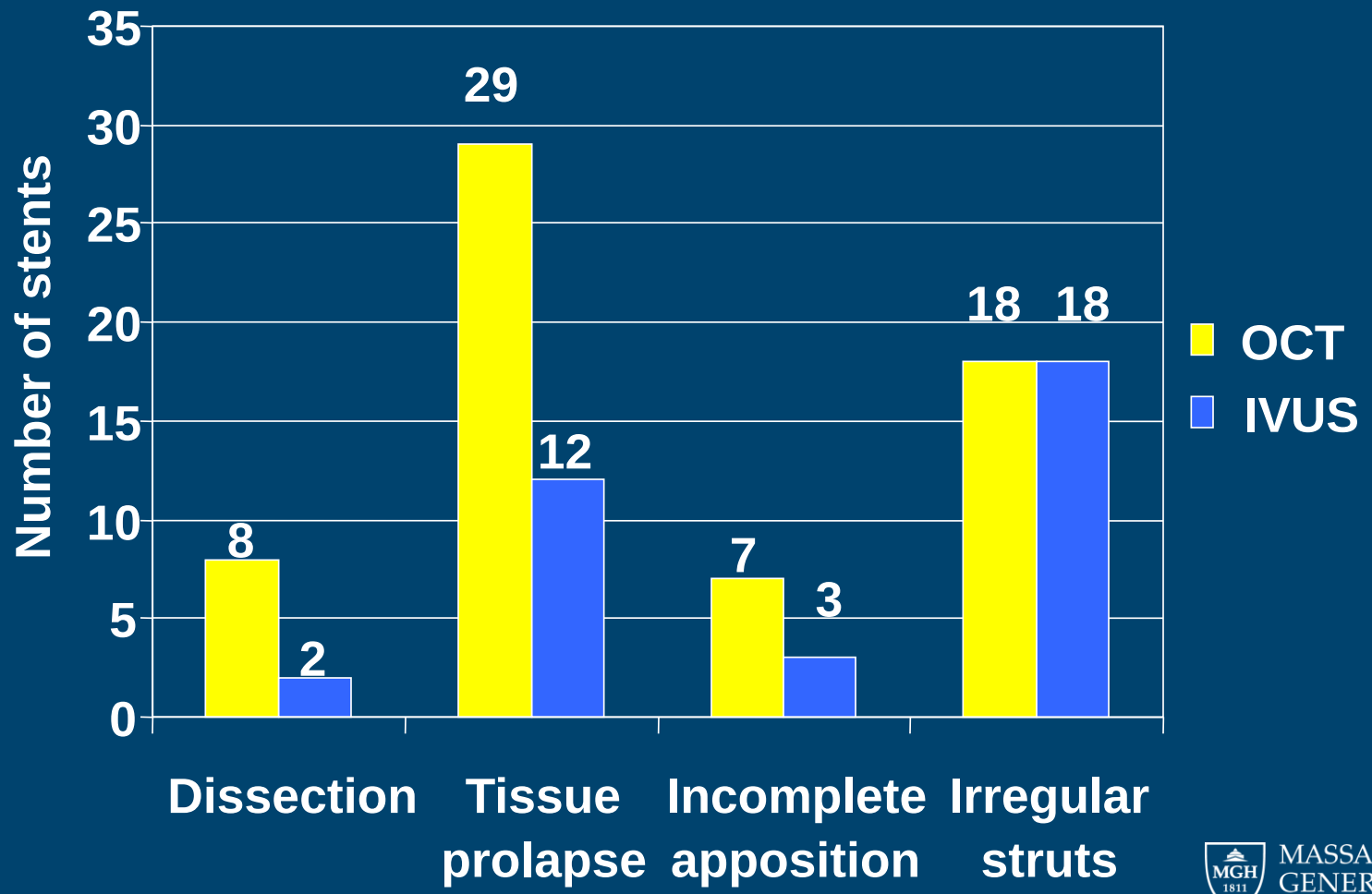


IVUS

Axial Resolution	12 - 15 μm	100 - 200 μm
Beam Width	20 – 40 μm	200 – 300 μm
Frame Rate	100 frames/s	30 frames/s
Pullback Speed	20 mm/s	0.5 - 1 mm/s
Scan Diameter	10 mm	15-20 mm
Tissue Penetration	1.0 - 2.0 mm	10 mm
Lines per Frame	500	256
Lateral Sampling (3mm Artery)	19 μm	225μm
Blood Clearing	Required	Not Required

Jang IK. JACC CV Interv 2011;4:492

Comparison of OCT and IVUS Findings Post Stenting



Bouma, Jang. Heart 2003

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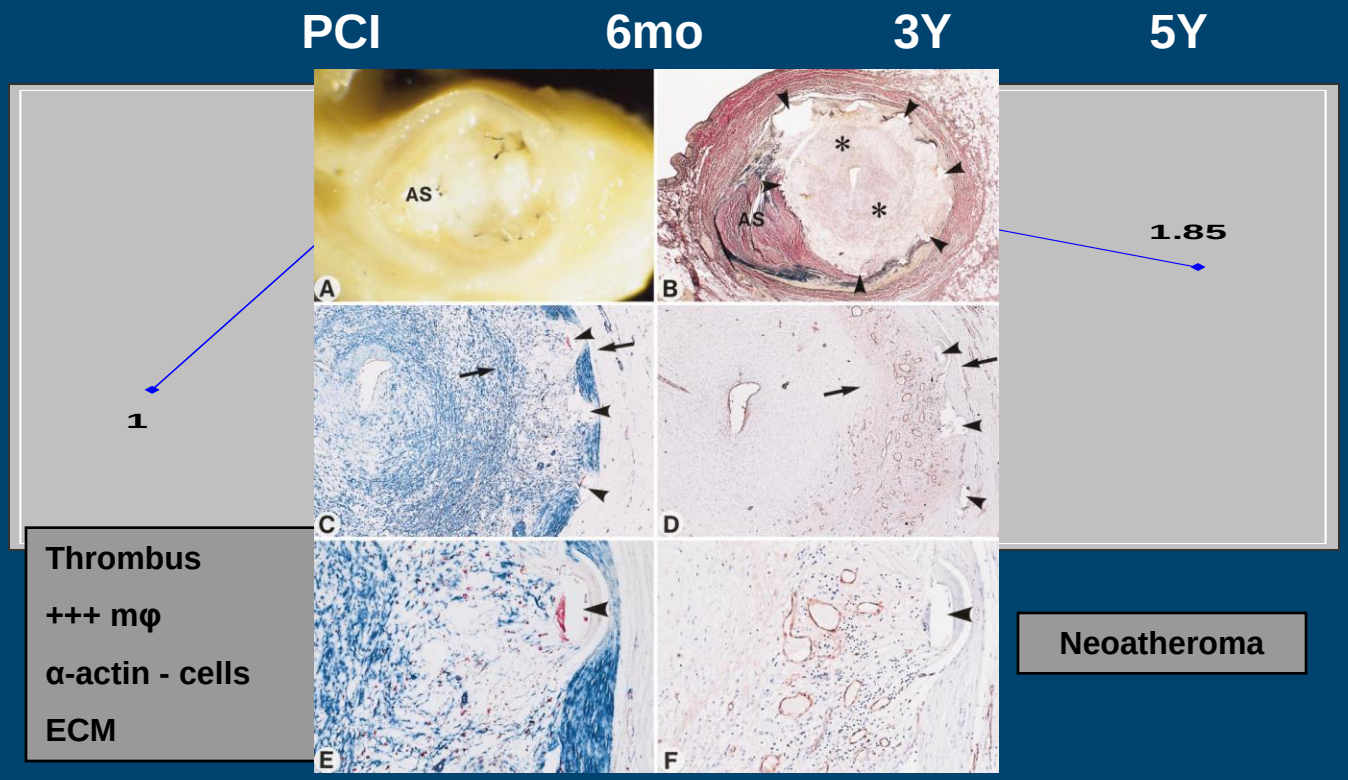
Neoatherosclerosis



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Neoatherosclerosis inside BMS

	< 6 mo (n=20)	> 5 yrs (n=21)	
Lipid laden intima	0	67%	< 0.05
Intimal disruption	0	38%	< 0.05
Thrombus	5%	25%	< 0.05
Intraintimal neovascularization	0	62%	0.01

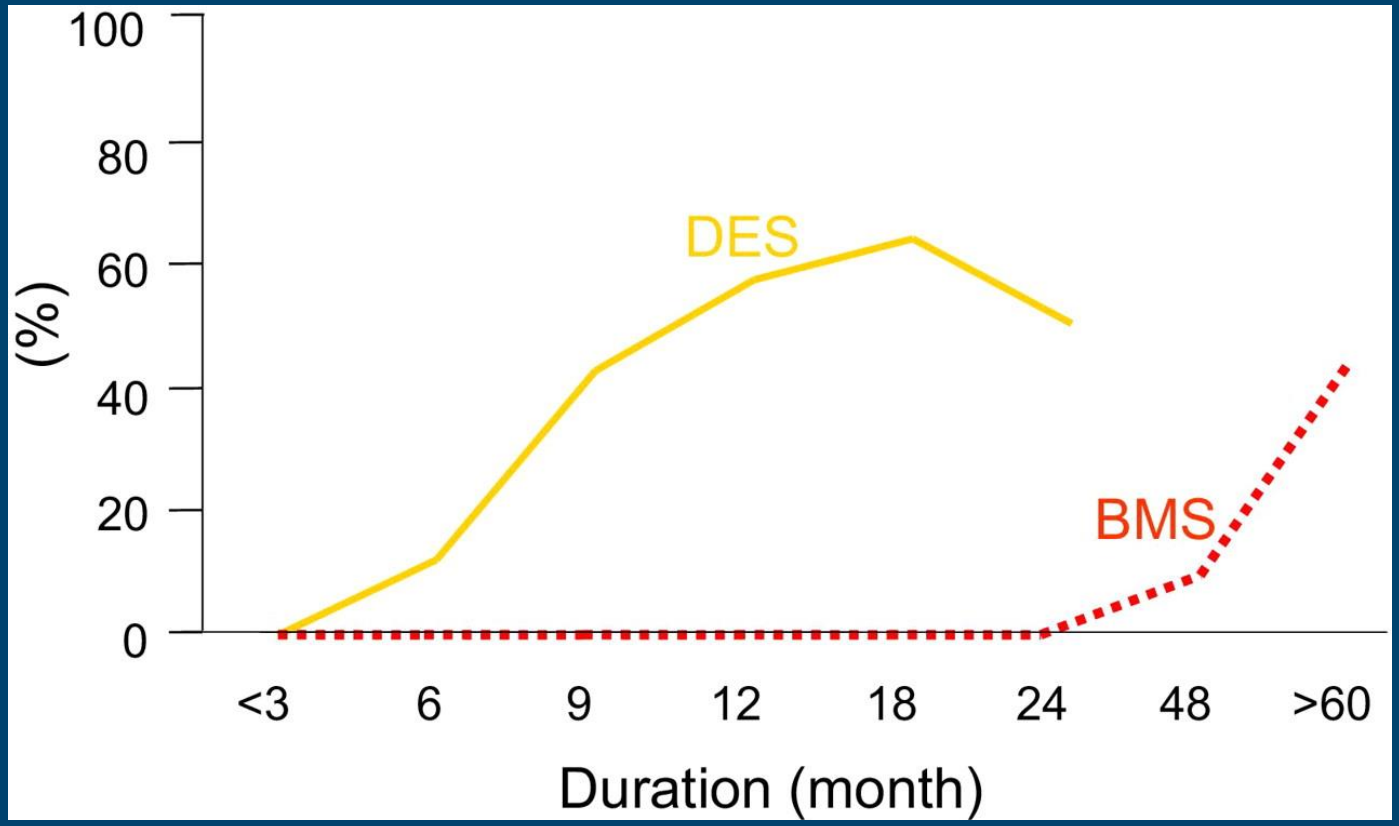
Takano, Mizuno. JACC 2010

Lipid-rich plaque inside BMS

- 39 pts with 6.5 yr f/u
- 20/60 (33%) stents, 16/39 (41%) patients
- Fibrous cap thickness: 56.7 ± 5.8 μm
- Lipid arc: 173 ± 57.7˚
- Plaque disruption: 6/20 (30%)
- Thrombus: 1/20 (5%)
- Macrophage: 7/20 (35%)

Hou, Jang. Heart 2010;96:1187

Percentage of Patients With Atherosclerotic Change in DES Versus BMS in Relation to Duration of Implant at Autopsy



Nakazawa, G. et al. J Am Coll Cardiol Img 2009;2:625-628

JACC cardiovascular Imaging

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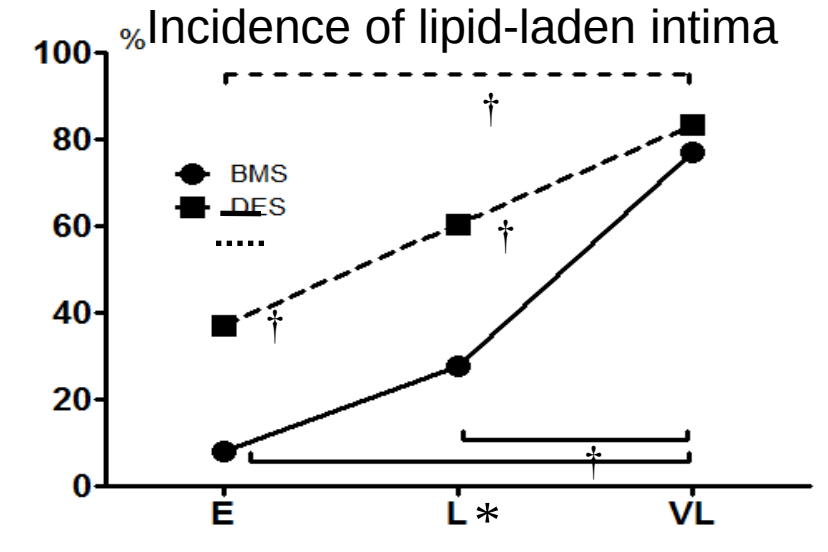
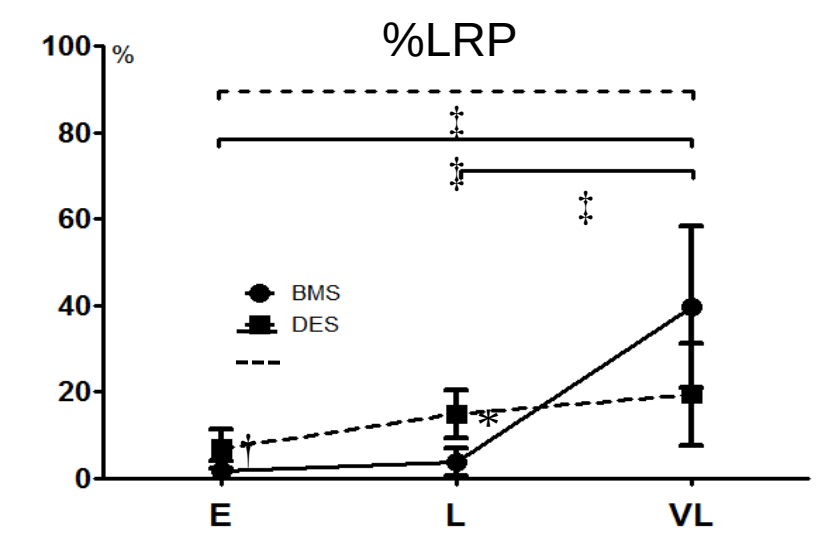
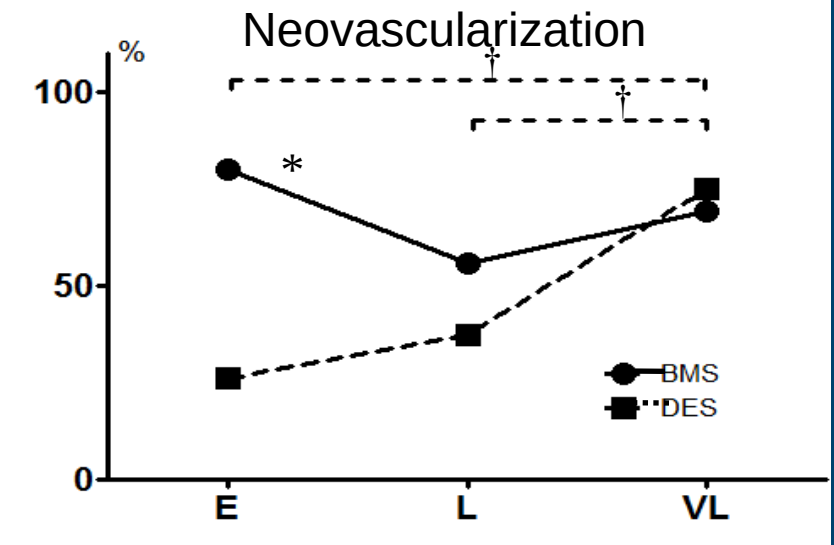
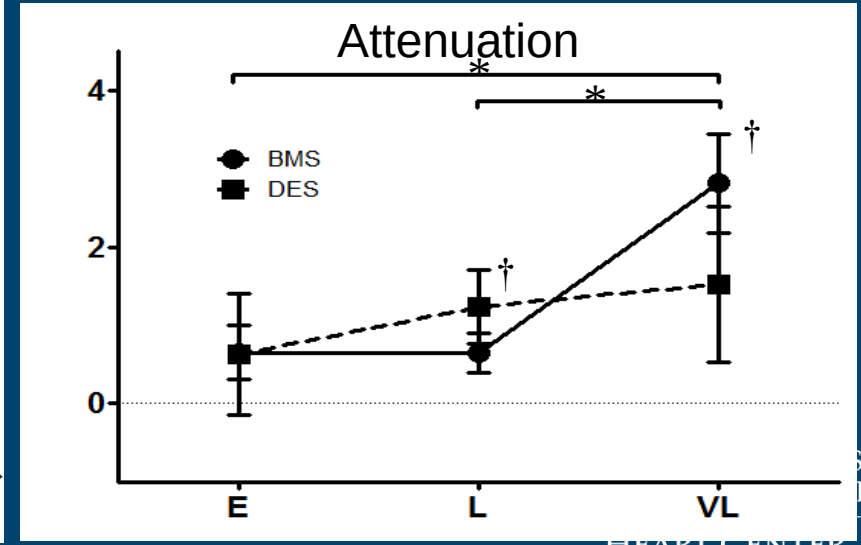
NIH Characteristics

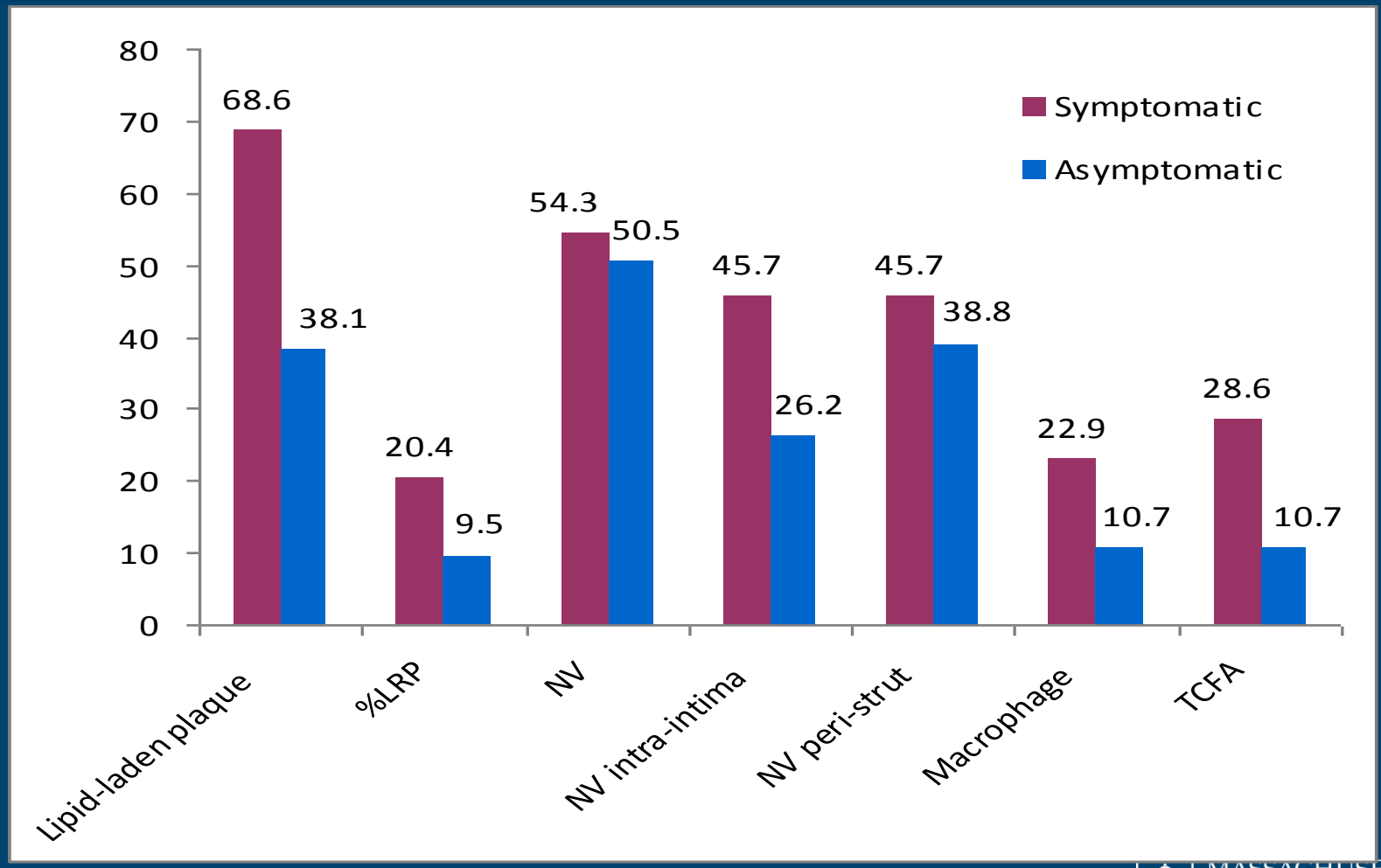








NIH Characteristics



Yonetsu T, Kato K, Kim SJ, L Xing, Jang IK. Submitted

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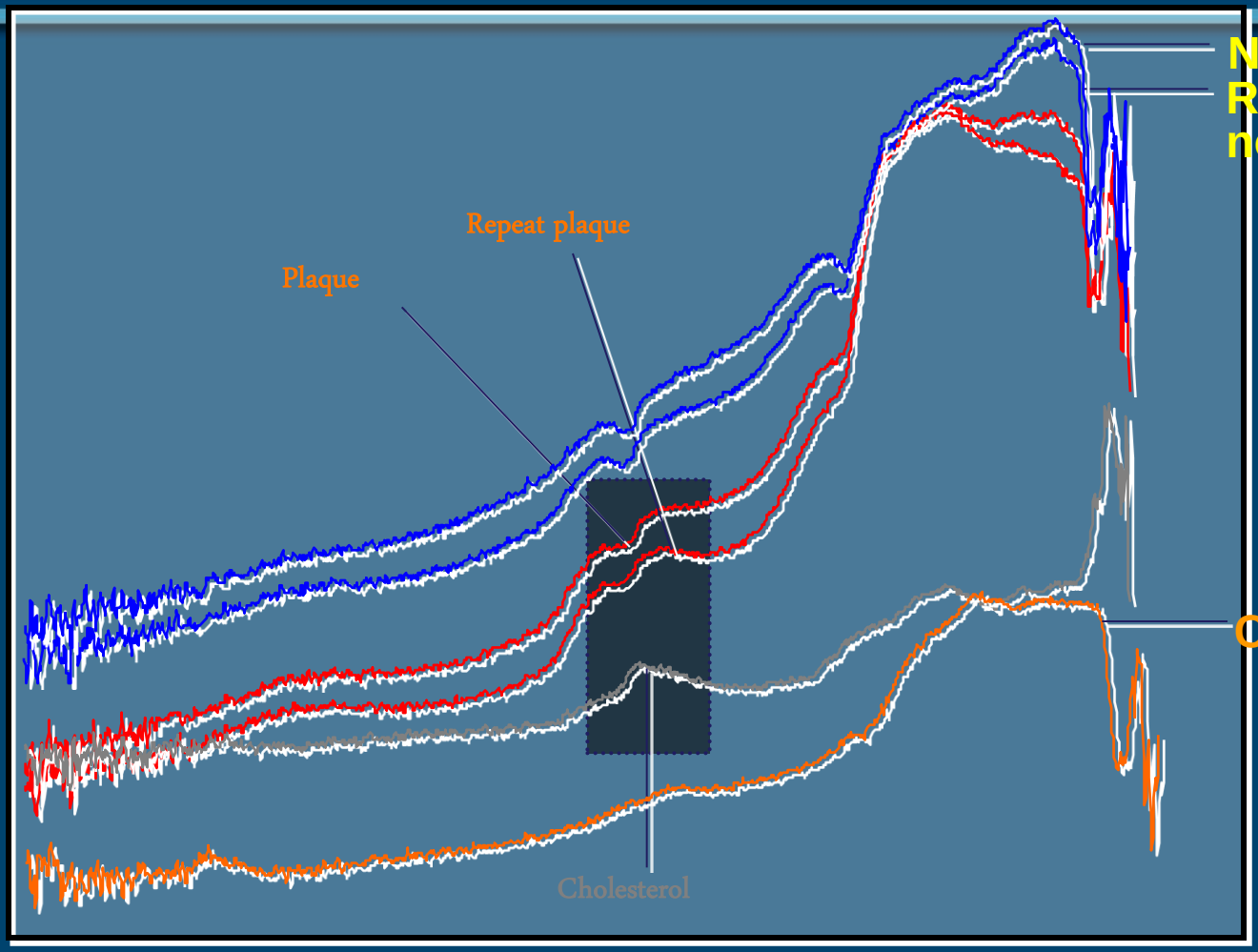
Intravascular Modalities

- OCT
- **Spectroscopy**
- RF IVUS

Near-IR Spectra of Human Aortic Samples



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Characterization of plaque histology by NIR spectroscopy (*ex vivo, no blood, no motion)*

All values in %.			
Sensitivity			
Specificity			
Positive predictive value			
Negative predictive value			

Moreno P et al. Circulation 2002

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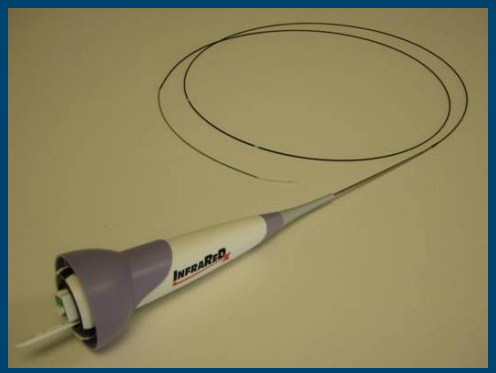
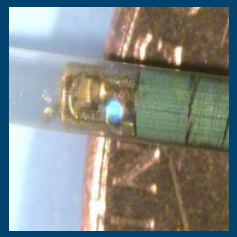
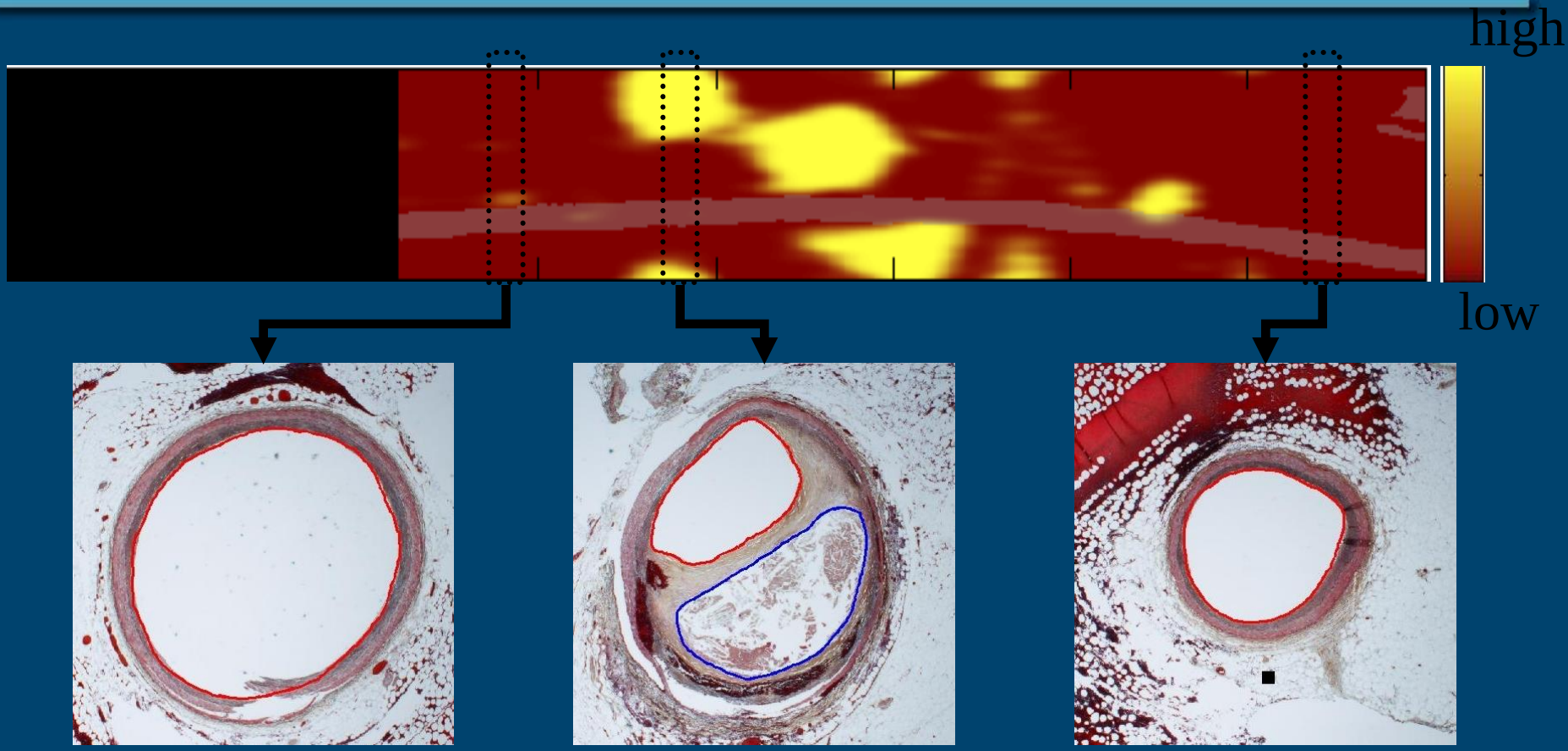
InfraReDx Spectroscopy System

- Three components: console, PBR, catheter (3.2 Fr, monorail, 0.014” compatible)
- Automatically scans artery
- Spectra processed by algorithm and displayed to user as a chemical image of lipid rich plaque probability (“Chemogram”)





LipiScan versus Histology



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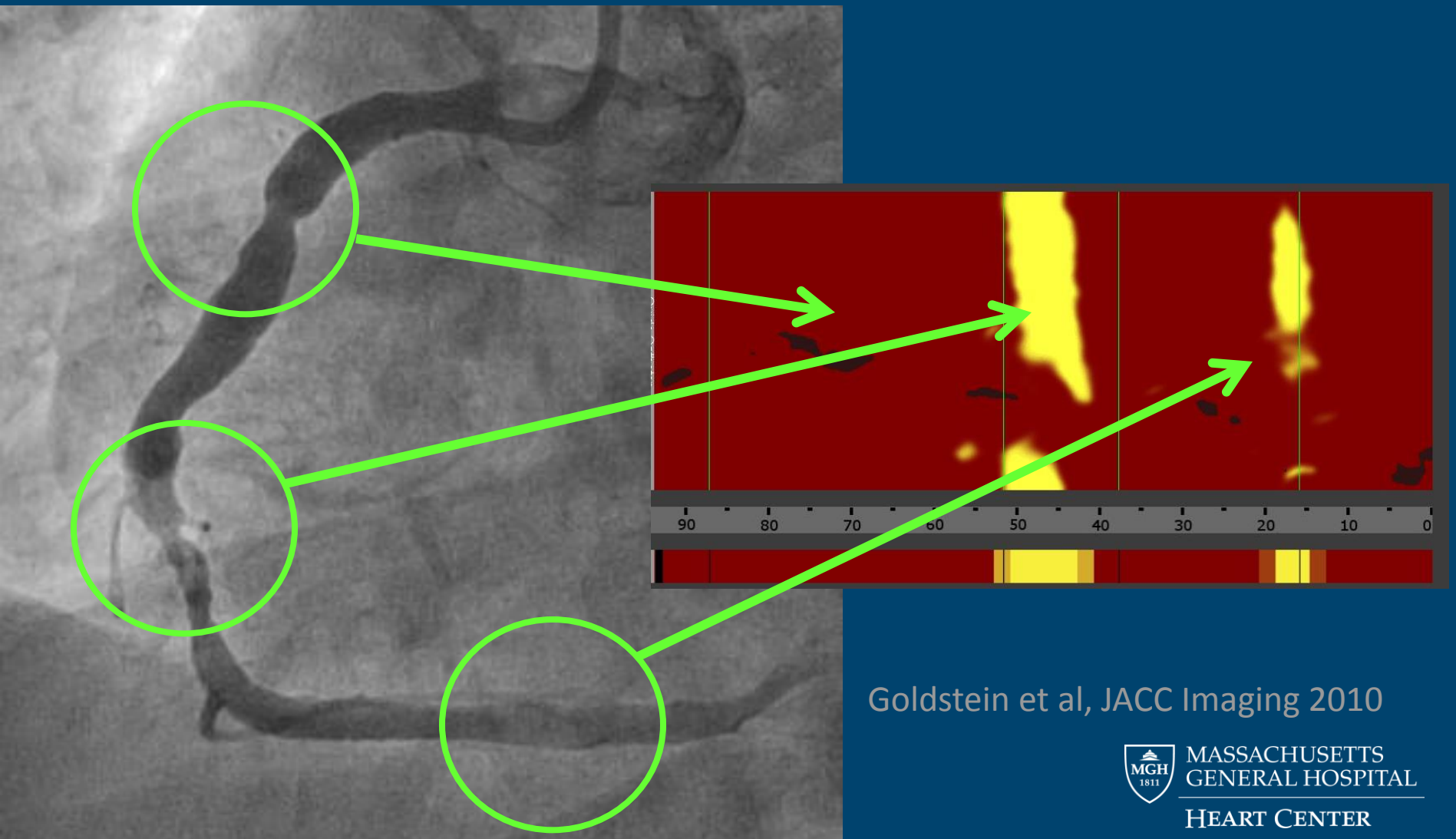
NIRS



Goldstein et al, JACC Imaging 2010

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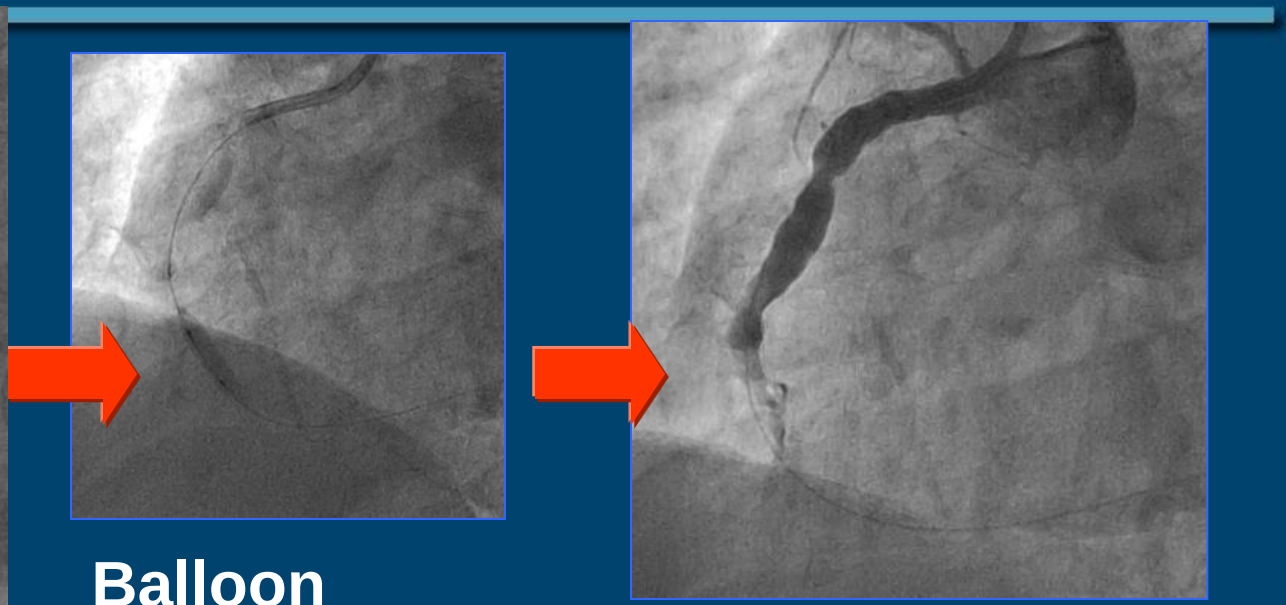
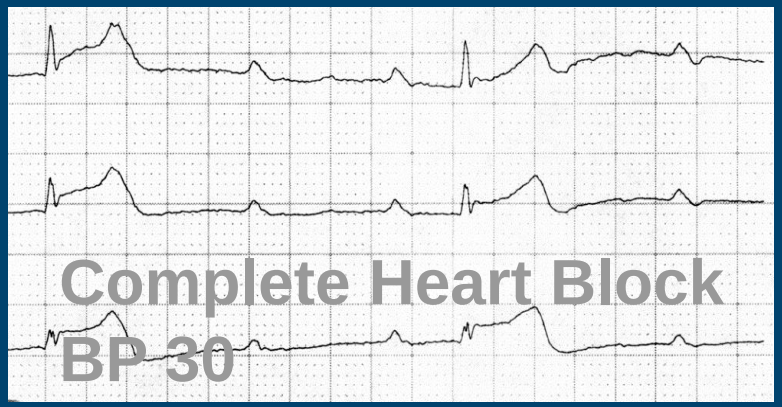
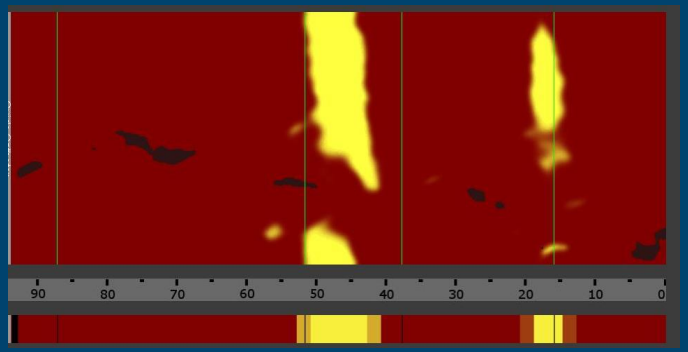
NIRS



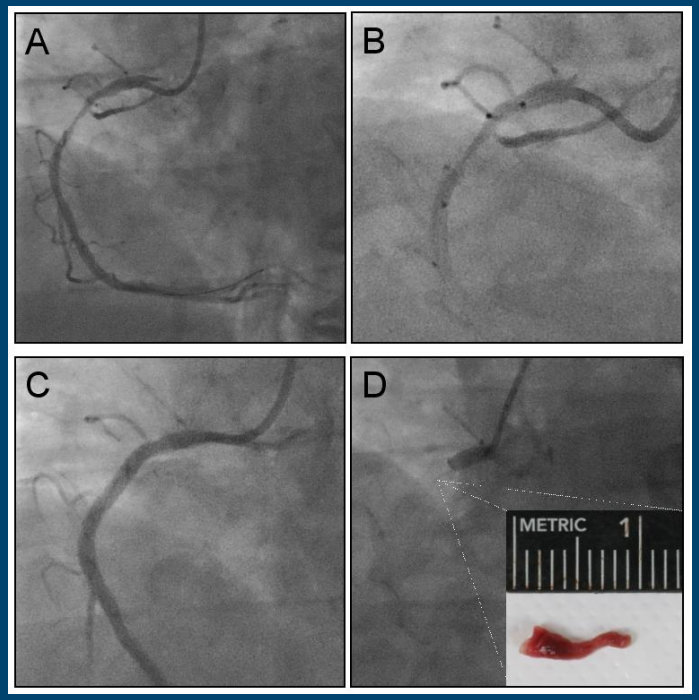
Balloon inflation

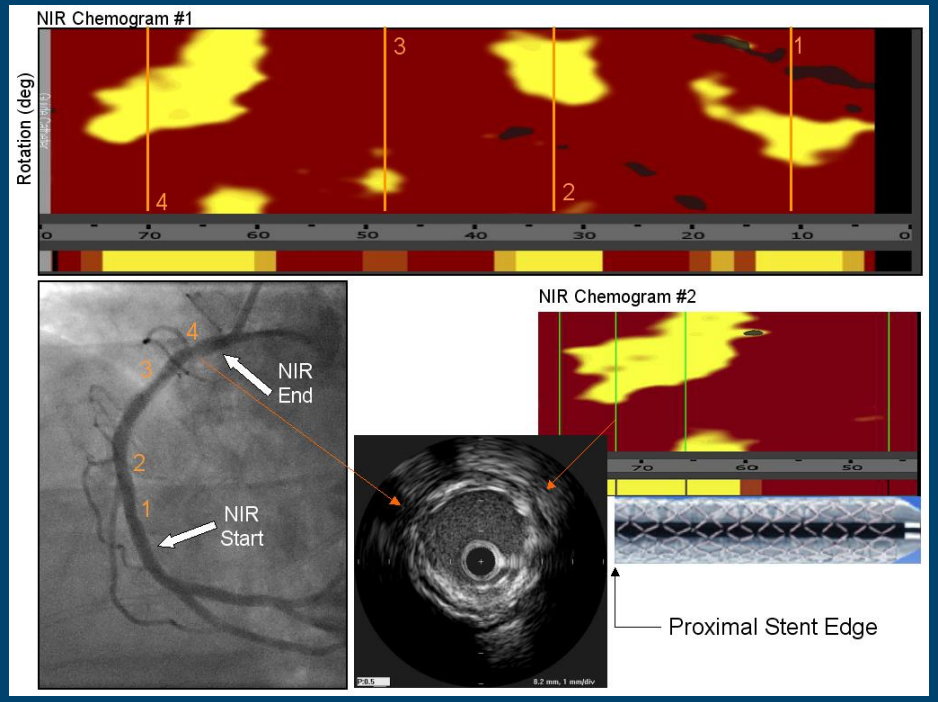
No flow





Acute Stent Thrombosis





Sakhuja, Jang. Circulation 2010

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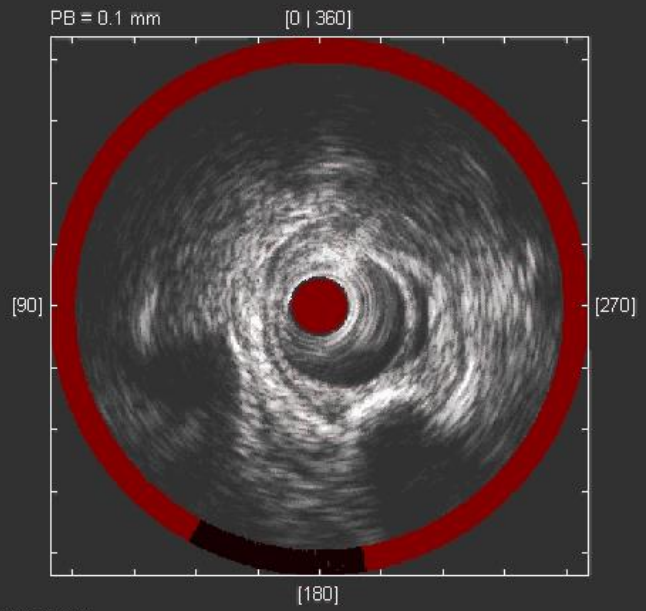
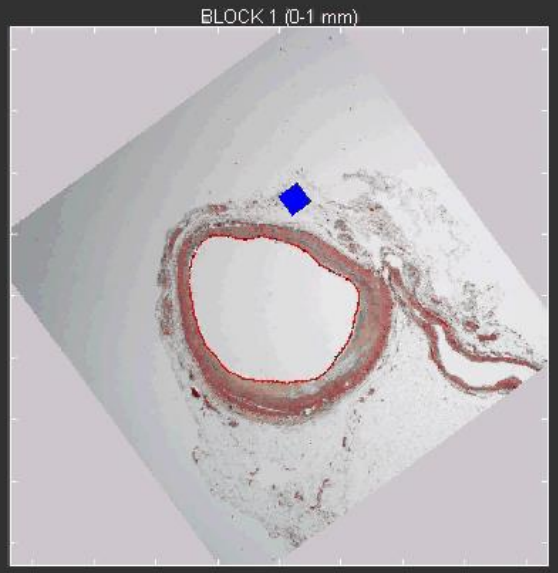
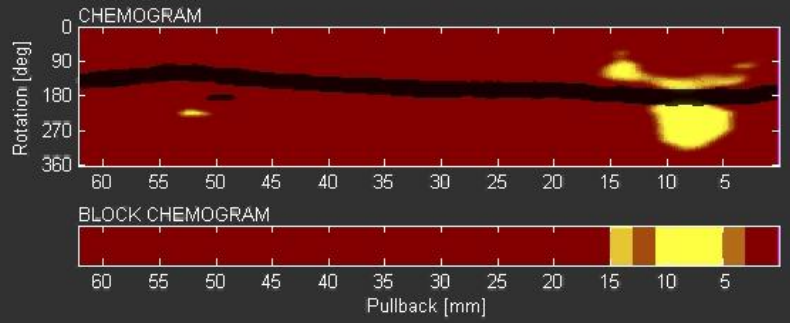
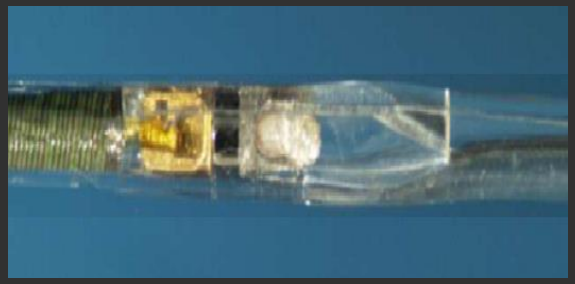
LipiScan IVUS





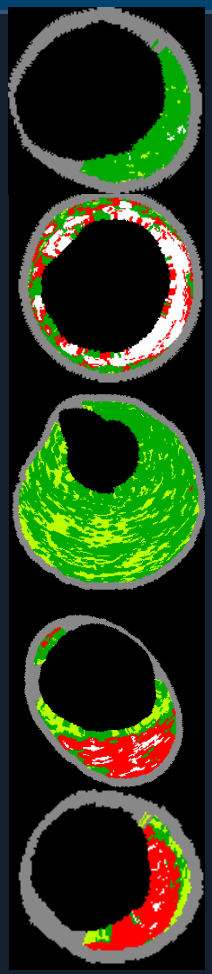




Intravascular Modalities

- OCT
- Spectroscopy
- **RF IVUS**

Virtual histology lesion classification



1. Fibrotic
2. Fibrocalcific
3. Pathological intimal thickening (PIT)
4. Thick cap fibroatheroma (ThCFA)
5. VH-thin cap fibroatheroma (VH-TCFA)

The PROSPECT Trial (700 ACS pts)

3-vessel imaging post PCI: Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n=~350)

Proximal 6-8 cm of each coronary artery

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: 1 mo, 6 mo, 1 yr, 2 yr, ±3-5 yrs

MSCT Substudy
N=50-100

Repeat imaging in pts with events

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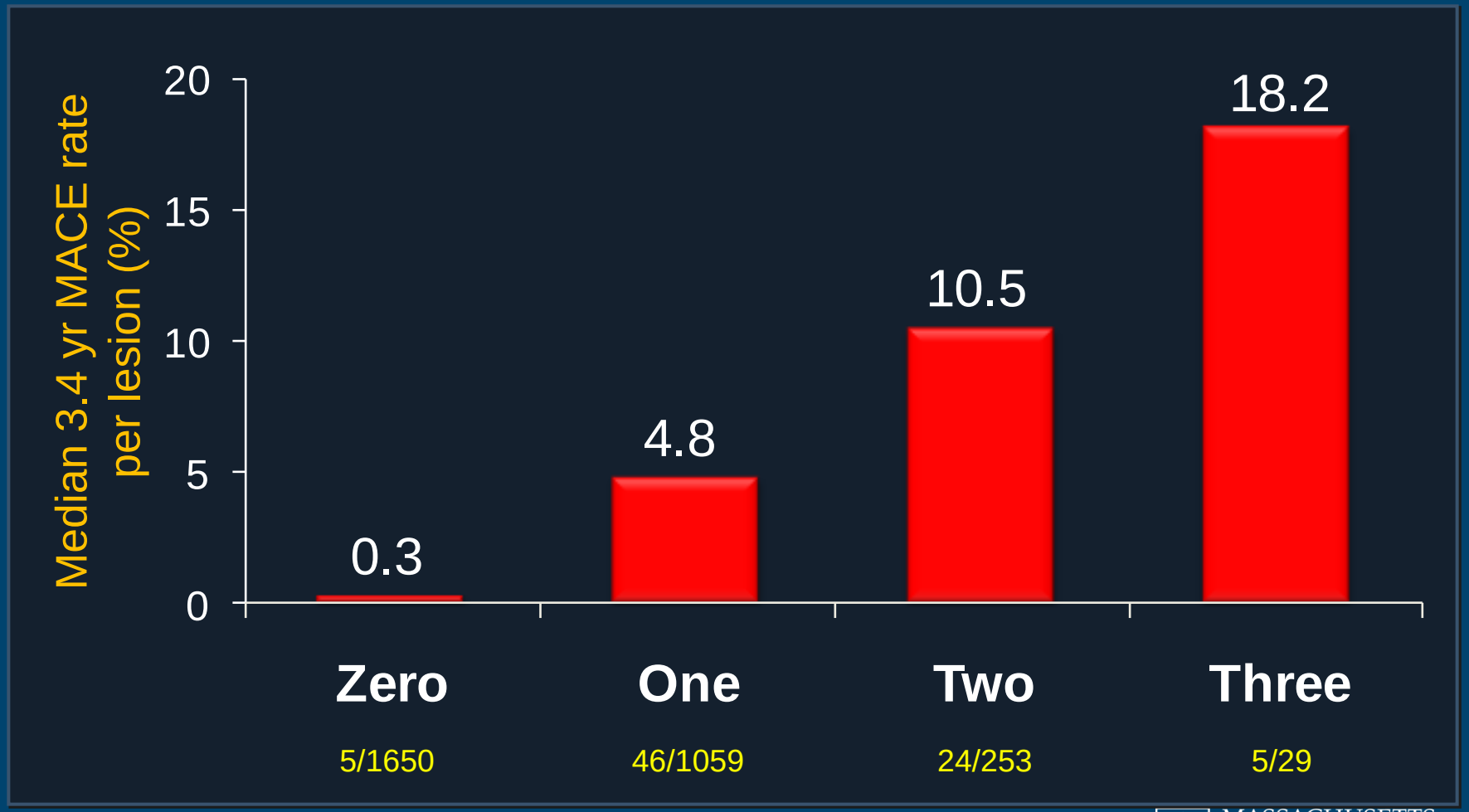
Independent predictors of lesion level events

Variable	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Variables entered into the model: minimal luminal area (MLA) ≤4.0 mm^2; plaque burden at the MLA (PB_{MLA}) ≥70%; external elastic membrane at the MLA (EEM_{MLA}) <median (14.1 mm^2); lesion length ≥median (11.2 mm); distance from ostium to MLA ≥median (30.4 mm); remodeling index ≥median (0.94); VH-TCFA.

Number of factors present: PB_{MLA} ≥70%, MLA ≤4.0mm² or TCFA



PB = plaque burden at the MLA

PROSPECT: MACE
3-year follow-up, hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter-minate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.7% (11)
Cardiac arrest	0.3% (2)	0.3% (2)	0% (0)	0% (0)
MI (STEMI or NSTEMI)	2.7% (17)	1.7% (11)	1.0% (6)	0.2% (1)
Rehospitalization for unstable or progressive angina	15.4% (101)	10.4% (69)	10.7% (68)	0.8% (5)
Composite MACE	20.4% (132)	12.9% (83)	11.6% (74)	2.7% (17)
Cardiac death, arrest or MI	4.9% (31)	2.2% (14)	1.0% (6)	1.9% (12)

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Rates are 3-yr Kaplan-Meier estimates (n of events)

Summary

	PCI Pre-	PCI Immediate Post	PCI F/U	Plaque Study
OCT	+++	+++	+++	+++
NIR IVUS	+	+/-	+/-	+
RF IVUS	++	++	+	++

Limitation

1. OCT: Lack of clinical outcome data

2. Spectroscopy: Very limited data

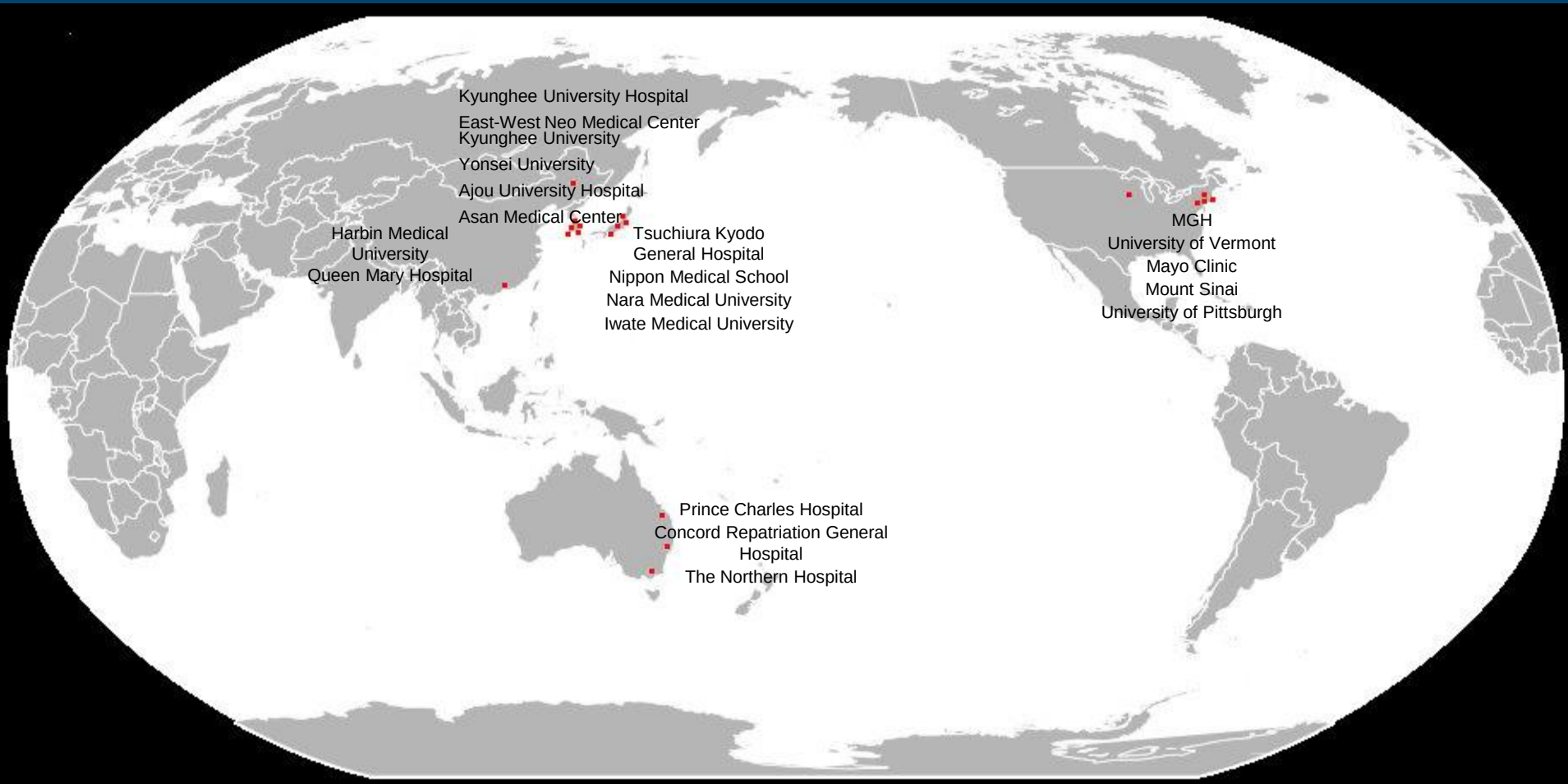
3. VH IVUS: Low resolution
   Little additional value

MGH OCT Registry

- Target 3000 patients x 3 years
- 20 sites from Australia, China, Singapore, Japan, Korea, USA
- Data collection started in 6/2010

http://www.massgeneral.org/octregistry

Site Locations



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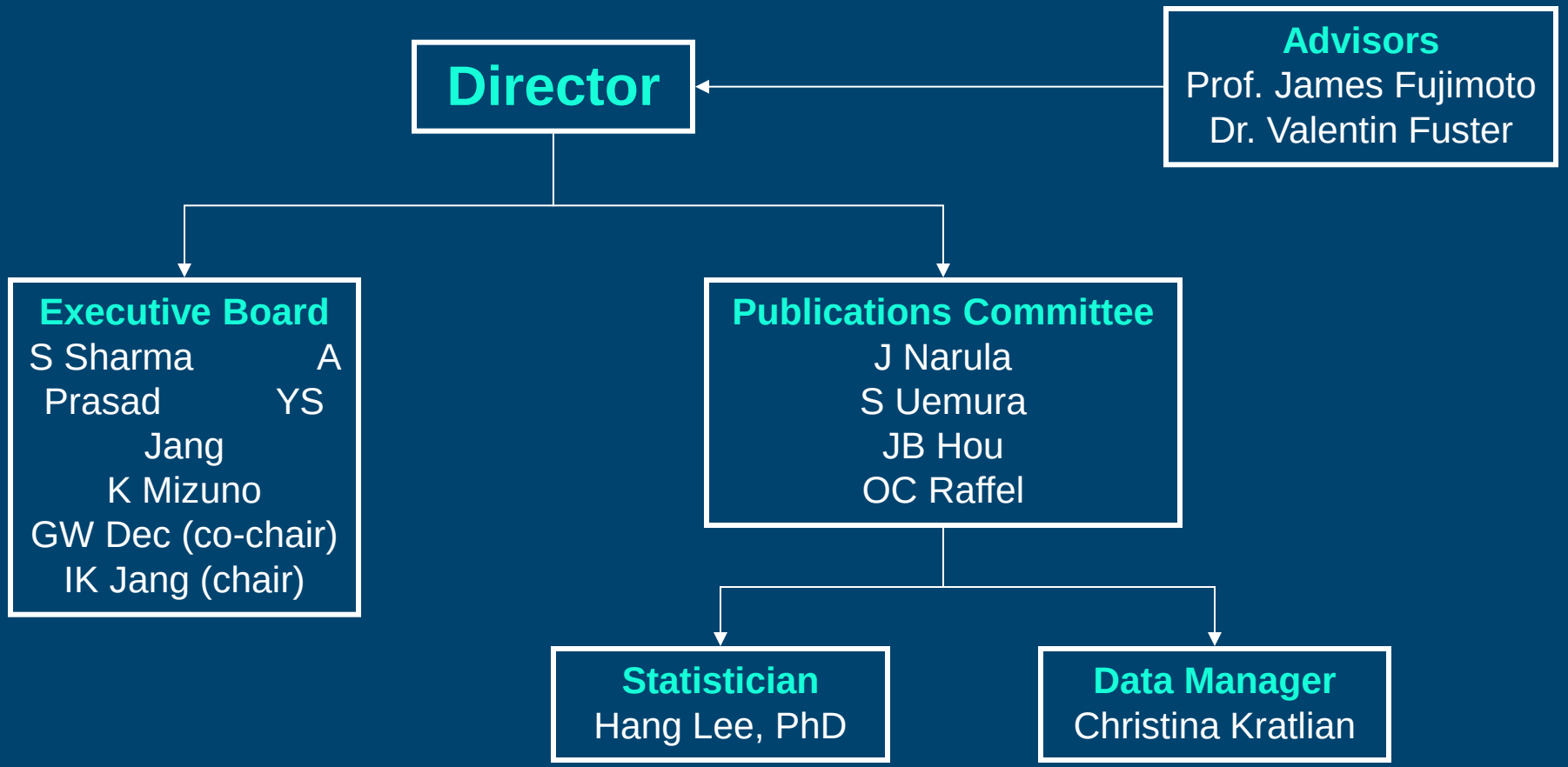
Organization



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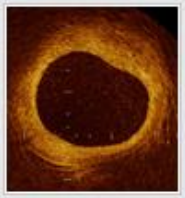
OCT Fellowship in MGH

- “Dr. John Nam OCT fellowship”
  - K. Kato from Japan for 3 years
  - SJ Kim from Korea for 2 years
  - T. Yonetsu from Japan for 2 years
  - L. Xing from China for 6 months
  - JH Yoon from US for 2 year
  - R. Lee from Singapore for 1 mo
  - HB Jia from China for 1 year from 2/2012
  - MGH clinical fellows

Website, cont.



Massachusetts General Hospital Optical Coherence Tomography (OCT) Registry

- Support our research
- Learn more about the OCT Registry by e-mailing Christina Kratlian at ckratlian@partners.org

Massachusetts General Hospital researchers are spearheading an international effort to study optical coherence tomography (OCT), an imaging technology that could help doctors identify the vulnerable coronary plaques that cause heart attacks or sudden cardiac death.

OVERVIEW | GROUP MEMBERS | RESEARCH PROJECTS | NEWS & EVENTS | PUBLICATIONS | CONTACT

The Massachusetts General Hospital Optical Coherence Tomography (OCT) Registry is led by a team of world class researchers who have devoted their careers to pioneering OCT imaging. Meet the team behind the OCT registry, including:

Ik-Kyung Jang, MD, PhD

Ik-Kyung Jang, MD, PhD is Professor of Medicine at Harvard Medical School, Director of the Cardiology Laboratory for Integrative Physiology and Imaging (CLIPI) at Massachusetts General Hospital.

Dr. Jang came to Massachusetts General Hospital in 1987 from Leuven University in Belgium, where he has completed his residency in medicine and fellowship in cardiology. He also successfully defended his doctorate thesis at the same university. After his advanced fellowship in cardiology at Mass General, he joined the staff and is currently working as a physician and an interventional cardiologist in the Cardiology Division.

His research interest has been acute coronary syndromes including acute myocardial infarction. His earlier research focused on pharmacology and physiology of thrombosis and thrombolysis including thrombin hypothesis and platelet inhibition. For the last twelve years he has pioneered the application of intravascular Optical Coherence Tomography (OCT) to patients to better characterize coronary plaques and to understand the mechanisms of plaque rupture. Dr. Jang was the first to perform intravascular OCT procedure in a patient. In addition, he was the principal investigator for the recent US multicenter OCT trial. Dr. Jang has been invited to lectures at numerous national and international meetings. His publications number more than 200.

Iris McNulty, RN, Research Nurse and Coordinator

Iris A. McNulty received a BA in Anthropology from Brown University and her BSN from Simmons College. She has worked at Massachusetts General Hospital since 1995, with a focus in Cardiology since 2000. In 2003 she started working with Dr. Ik-Kyung Jang as a research nurse, and has coordinated multiple investigational drug trials, investigational device trials and observational studies. Iris has significant experience working on OCT trials; she was the site coordinator of the OCT trial that resulted in FDA approval of Lightlab Imaging's OCT system. She also helped plan the first Mass General OCT Registry Symposium, which took place in March 2010 and was attended by international OCT experts.

Dr. Hang Lee, PhD, Statistician

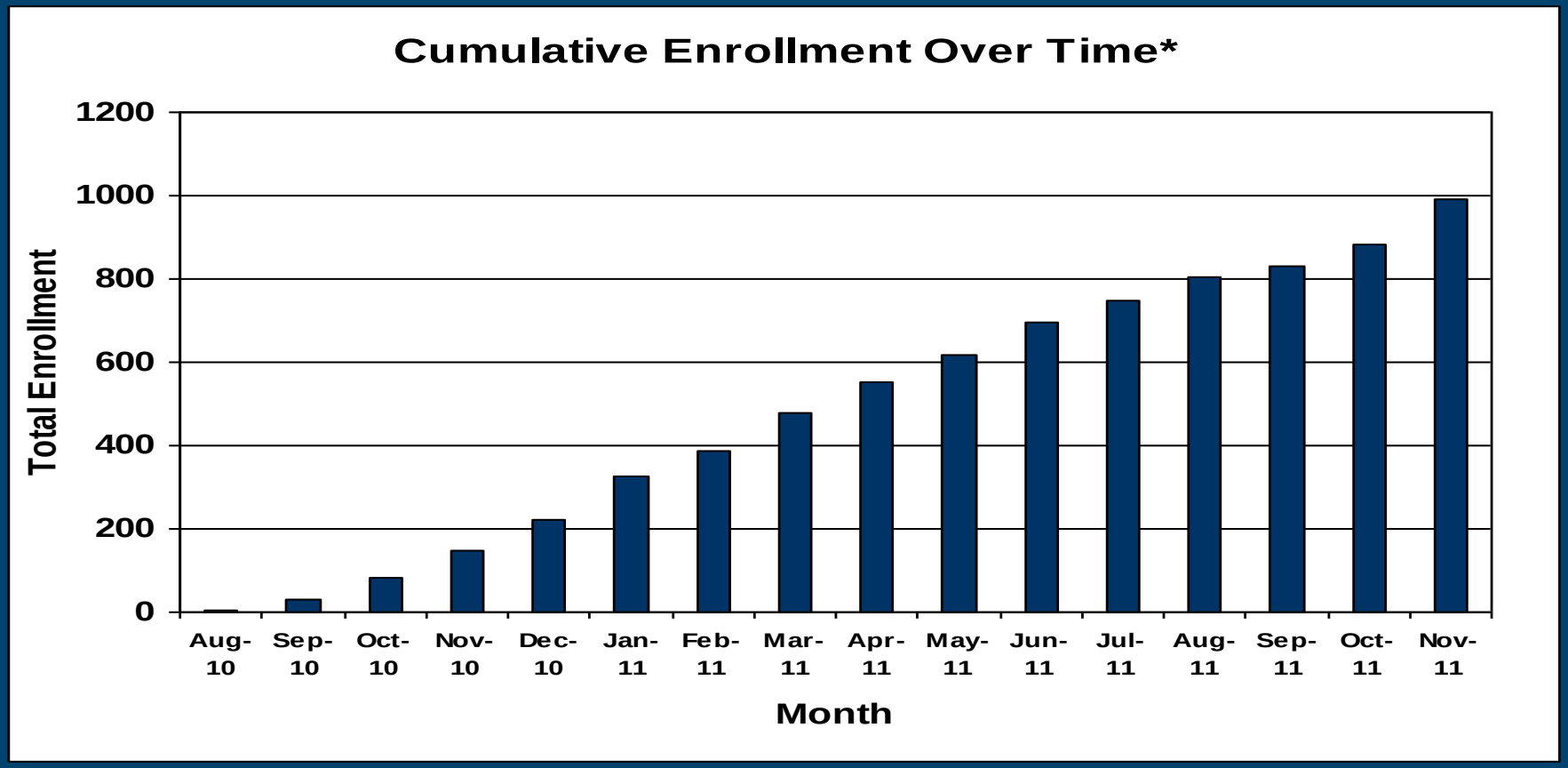
Dr. Lee is the study statistician of the OCT Registry. He is the lead statistician of the Harvard Catalyst Biostatistics Program at Mass General and the Mass General Clinical Research Program Biostatistics Consulting Laboratory, and he serves as the primary statistician of the Gynecologic Oncology Program at Dana-Farber Harvard Cancer Center. He is also the lead statistician of the NHLBI-funded ROMICAT trial (Rule Out Myocardial Ischemia/Infarction Using Computer Assisted tomography - A Randomized, Controlled, Multicenter Diagnostic Trial). Dr. Lee is Assistant Professor of Medicine at Harvard Medical School and has over 10 years of experience in a wide range of Mass General and Harvard-based collaborative clinical trials and epidemiologic investigations. His statistical expertise is in the longitudinal data, statistical genetics, clinical trials design and complex data analysis, and he has authored and co-authored over 120 clinical study articles.

Christina Kratlian, MA, Coordinator/Data Manager

Christina Kratlian received her BA in Psychology from Boston University and her MA in Medical Science from Boston University School of Medicine. As an undergraduate, Christina worked as a research assistant in medical education at BUSM. Her responsibilities included compiling an extensive literature review, assisting with study development, and contributing to a grant proposal, which subsequently led to funding. As a Masters student, Christina developed a unique study investigating distress and anxiety in children during routine immunizations. In August 2011, Christina came to Mass General to work under Dr. Ik-Kyung Jang as a clinical research coordinator and is the data manager for the Registry.

Enrollment Overview

- As of November 28, 2011, data for **1009 subjects** has been entered into the eCRF



MASSACHUSETTS GENERAL HOSPITAL
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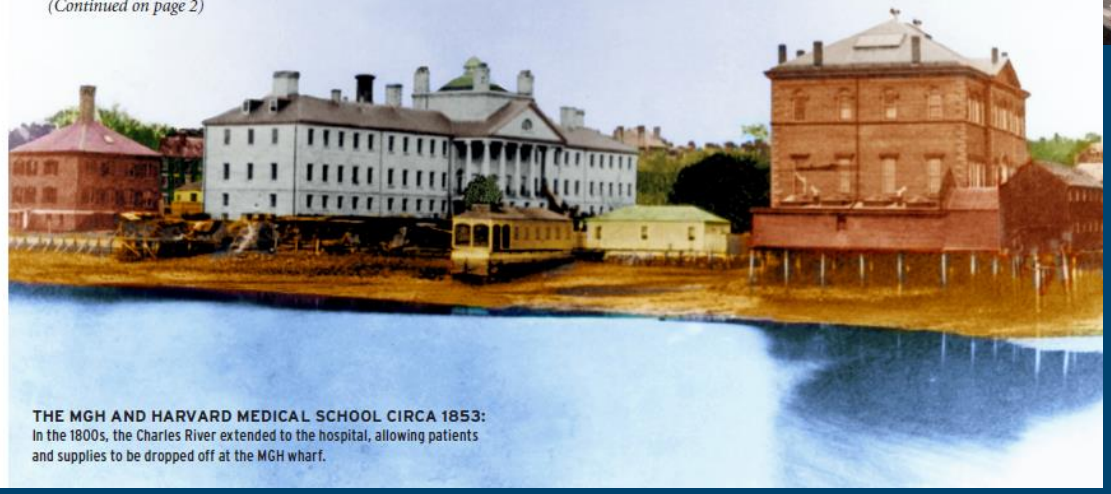
Thank You

MGH history book to commemorate bicentennial

AS PART OF the MGH's bicentennial celebrations, a commemorative book covering the hospital's unique beginnings and illustrious history will be published in 2011. "Something in the Ether, A Bicentennial History of Massachusetts General Hospital, 1811 to 2011," was written by author and publisher Webster Bull. Much of the content was drawn from interviews with longtime MGH staff and countless hours of research of historical records and archival material. The book is scheduled to be released in March and will be available at the MGH General Store and select booksellers.

(Continued on page 2)



THE MGH AND HARVARD MEDICAL SCHOOL CIRCA 1853:
In the 1800s, the Charles River extended to the hospital, allowing patients and supplies to be dropped off at the MGH wharf.

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