

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

A Prospective Natural History Study of Coronary Atherosclerosis

Gregg W. Stone MD, Akiko Maehara MD, Alexandra J. Lansky MD, Bernard de Bruyne MD, Ecaterina Cristea MD, Gary S. Mintz MD, Roxana Mehran MD, John McPherson MD, Naim Farhat MD, Steve Marso MD, Helen Parise ScD, Barry Templin MBA, Roseann White MA, Zhen Zhang PhD, Patrick W. Serruys MD, PhD, for the PROSPECT Investigators

Contents

Table 1. Inclusion and exclusion criteria.....	Page 2
Table 2. Medication use.....	Page 3
Table 3. Length of imaged coronary arteries available for core laboratory analysis.....	Page 4
Table 4. Residual lesion characterization by angiographic and ultrasound core laboratory analysis after successful percutaneous coronary intervention.....	Page 5
Table 5. Clinical predictors of non-culprit lesion-related major adverse cardiac events occurring per patient during median 3.4 year follow-up.....	Page 6
Table 6. Intravascular ultrasound predictors of non-culprit lesion-related major adverse cardiac events occurring at the specific lesion site during median 3.4 year follow-up.....	Page 8
Table 7. Multivariable models for non-culprit lesion-related major adverse cardiac events occurring at the specific lesion site during median 3.4 year follow-up.....	Page 10
Table 8. PROSPECT study organization and list of participating sites and investigators.....	Page 11
Figure 1. Lesion classification according to radiofrequency IVUS.....	Page 14
Figure 2. Example from the PROSPECT study.....	Page 15
Figure 3. Event rates at median 3.4 year follow-up according to grayscale and radiofrequency-IVUS plaque type, minimal lumen area and plaque burden.....	Page 16

Table 1. Inclusion and exclusion criteria

<u>Clinical inclusion criteria</u>	<ol style="list-style-type: none"> 1. Age ≥ 18 years 2. Acute coronary syndrome (ACS; unstable angina, non ST-segment elevation myocardial infarction (NSTEMI) or ST-segment elevation myocardial infarction (STEMI) with ≥ 10 minutes of angina or anginal equivalent consistent with unstable angina or myocardial infarction (MI) within 72 hours, with either elevated cardiac biomarkers (CK-MB or troponin) or ST-segment deviation of >1 mm in ≥ 2 contiguous electrocardiographic leads. 3. Patient agrees and is able to follow all protocol procedures. 4. Patient provides written, informed consent.
<u>Clinical exclusion criteria</u>	<ol style="list-style-type: none"> 1. STEMI within 24 hours. 2. Serum creatinine ≥ 2.5 mg/dl. 3. Decompensated hypotension, heart failure, shock, refractory ventricular arrhythmias, acute conduction system disease, implanted defibrillator, or left ventricular ejection fraction $\leq 30\%$. 4. Known severe allergy, hypersensitivity or contraindication to aspirin, heparin, thienopyridines or contrast which cannot be adequately pre-medicated. 5. Stroke or transient ischemic attack within 6 months. 6. Significant gastrointestinal or urinary bleed within the past 6 months, coagulopathy, bleeding diathesis, or refusal of blood transfusions. 7. Percutaneous coronary intervention (PCI) within 6 months or any prior bypass graft surgery. 8. Prior or planned heart transplant or any other organ transplant. 9. Anticipated life expectancy <1 year. 10. Prior participation in this study or current enrollment in another investigational study that has not reached its primary endpoint. 11. Pregnant or nursing patients and those who plan pregnancy in the period up to 1 year following index procedure. Female patients of child-bearing potential must have a negative pregnancy test done within 7 days prior to the index procedure.
<u>Angiographic inclusion criteria</u>	<ol style="list-style-type: none"> 1. Successful and uncomplicated PCI performed in 1 or 2 major epicardial coronary arteries (including their branches). <ul style="list-style-type: none"> - Successful PCI was defined as residual diameter stenosis of $<50\%$ in all lesions with TIMI-3 flow in all vessels. - Uncomplicated PCI was defined as the absence of intra-procedural chest pain or ST-segment changes lasting >10 minutes, sustained vessel closure, slow or no reflow, sidebranch loss, distal embolization, perforation, residual dissection ($>$type B), or requirement for cardiopulmonary resuscitation, cardioversion or defibrillation, pacemaker insertion, intubation, intraaortic balloon insertion or intravenous pressors.
<u>Angiographic exclusion criteria</u>	<ol style="list-style-type: none"> 1. PCI required in all 3 major epicardial coronary arteries 2. Anatomic conditions precluding 3-vessel intravascular ultrasound (IVUS) imaging (e.g. marked calcification or tortuosity, chronic total occlusion or thrombus) 3. Left main coronary artery culprit lesion 4. Any remaining lesion with diameter stenosis $>50\%$ after PCI 5. Coronary artery bypass graft surgery planned within 1-year after PCI

Table 2. Medication use

<u>Aspirin use</u>	
- at discharge	675/697 (96.8%)
- at 6 months	625/653 (95.7%)
- at 1-year	606/640 (94.7%)
- at 2-years	572/616 (92.9%)
- at 3 years	527/575 (91.7%)
<u>Thienopyridine use</u>	
- at discharge	676/696 (97.1%)
- at 6 months	555/652 (85.1%)
- at 1-year	455/640 (71.1%)
- at 2-years	254/616 (41.2%)
- at 3 years	202/575 (35.1%)
<u>Statin or lipid lowering therapy use</u>	
- at discharge	594/695 (85.5%)
- at 6 months	552/652 (84.7%)
- at 1-year	537/639 (84.0%)
- at 2-years	514/615 (83.6%)
- at 3 years	485/574 (84.5%)
<u>Beta blocker use</u>	
- at discharge	632/697 (90.7%)
- at 6 months	570/653 (87.3%)
- at 1-year	550/640 (85.9%)
- at 2-years	507/616 (82.3%)
- at 3 years	466/575 (81.0%)
<u>ACEI or ARB use</u>	
- at discharge	479/693 (69.1%)
- at 6 months	447/652 (68.6%)
- at 1-year	443/639 (69.3%)
- at 2-years	433/615 (70.4%)
- at 3 years	405/574 (70.6%)

ACEI or ARB denotes angiotensin converting enzyme inhibitor or angiotensin receptor blocker

Table 3. Length of imaged coronary arteries available for core laboratory analysis

Coronary artery	Angiography (N=697)	Grayscale-IVUS (N=673)	Radiofrequency-IVUS (N=623)
Left main	9.3 ± 4.3 mm	12.8 ± 9.8 mm	12.8 ± 9.7 mm
Left anterior descending	153.5 ± 41.1 mm	73.3 ± 34.1 mm	73.8 ± 33.7 mm
Left circumflex	132.7 ± 49.9 mm	63.3 ± 36.1 mm	63.6 ± 36.0 mm
Right	148.3 ± 45.1 mm	85.2 ± 39.6 mm	85.5 ± 39.4 mm
Total per patient	437.9 ± 86.4 mm	192.0 ± 97.7 mm	206.7 ± 85.4 mm
Total all patients	305,228.3 mm	129,216.8 mm	128,757.9 mm

IVUS denotes intravascular ultrasound imaging.

Table 4. Residual lesion characterization by angiographic and ultrasound core laboratory analysis after successful percutaneous coronary intervention

Angiographic diameter stenosis $\geq 50\%$	110 lesions in 697 patients
Reference vessel diameter (mm, median [IQR])	2.3 [1.9, 3.1]
Minimal luminal diameter (mm, median [IQR])	0.9 [0.7, 1.3]
Diameter stenosis (% , median [IQR])	57.5 [52.9, 64.7]
Lesion length (mm, median [IQR])	11.3 [8.1, 16.3]
Grayscale-IVUS lesion analysis	3,160 lesions in 673 patients
Minimal lumen area (mm ² , median [IQR])	5.9 [4.3, 8.1]
- Minimal lumen area $\leq 4.0\text{mm}^2$	620/3160 (19.6%)
External elastic membrane area* (mm ² , median [IQR])	14.1 [10.5, 18.2]
Plaque and media cross sectional area* (mm ² , median [IQR])	7.8 [5.8, 10.6]
Plaque burden* (% , median [IQR])	55.5 [49.1, 62.8]
- Plaque burden* $\geq 70\%$	283/3160 (9.0%)
Remodeling index* (median [IQR])	0.9 [0.8, 1.0]
Lesion length (mm, median [IQR])	11.2 [5.8, 21.7]
Distance to the minimal lumen area** (mm, median [IQR])	30.0 [13.5, 54.0]
Radiofrequency-IVUS lesion analysis	2,811 lesions in 623 patients
Tissue composition (% , median [IQR])	
- Fibrous tissue	60.1 [53.9, 65.7]
- Fibrofatty	19.0 [12.1, 28.0]
- Dense calcium	4.4 [1.8, 8.9]
- Necrotic core	11.5 [5.9, 18.4]
Lesion classification [†]	N=2759
- Pathological intimal thickening	1008 (36.5%)
- Thick-cap fibroatheroma	1018 (36.9%)
- Thin-cap fibroatheroma	596 (21.6%)
- Fibrotic plaque	104 (3.8%)
- Fibrocalcific plaque	33 (1.2%)

3-vessel, 2-vessel and 1-vessel IVUS imaging were performed in 588, 106 and 3 patients, respectively (mean 2.8 ± 0.4 vessels per patient).

* Denotes measurement at the minimal lumen area. **From the coronary ostium. [†] In lesions with multiple patterns, the most severe pattern present was selected according to the following hierarchy: thin-cap fibroatheroma; thick-cap fibroatheroma; fibrotic/fibrocalcific/pathologic intimal thickening. IVUS denotes intravascular ultrasound. IQR denotes interquartile range.

Table 5. Clinical predictors of non-culprit lesion-related major adverse cardiac events occurring per patient during median 3.4 year follow-up

Variable	Patients with variable and non-culprit lesion events (n)	Total patients with variable (N)	Event rate*	HR [95%CI]	P value
Age ≥58.1 years [†]	38	344	12.1%		
Age <58.1 years [†]	38	345	12.2%	1.02 [0.65, 1.60]	0.92
Sex - Male	56	527	11.8%		
Sex - Female	20	162	13.2%	1.17 [0.70, 1.95]	0.55
Diabetes mellitus - No	56	569	10.7%		
Diabetes mellitus - Yes	20	117	20.1%	1.91 [1.15, 3.18]	0.01
- Not requiring insulin	14	96	16.3%	1.55 [0.86, 2.79]	0.14
- Requiring insulin	6	21	41.4%	4.07 [1.75, 9.46]	0.001
Metabolic syndrome - No	35	344	11.1%		
Metabolic syndrome - Yes	40	321	13.8%	1.28 [0.81, 2.02]	0.29
Current smoker - No	39	355	11.9%		
Current smoker - Yes	36	324	12.4%	1.05 [0.67, 1.66]	0.82
Hypertension - No	31	369	9.1%		
Hypertension - Yes	42	314	14.7%	1.64 [1.03, 2.60]	0.04
Hyperlipidemia - No	34	348	10.6%		
Hyperlipidemia - Yes	31	276	12.3%	1.16 [0.71, 1.89]	0.55
Prior myocardial infarction - No	66	613	11.8%		
Prior myocardial infarction - Yes	10	72	15.5%	1.34 [0.69, 2.60]	0.39
Family history or CAD - No	28	336	9.1%		
Family history of CAD - Yes	35	275	14.1%	1.59 [0.97, 2.62]	0.07
Framingham risk score <7 [†]	30	320	10.3%		
Framingham risk score ≥7 [†]	46	369	13.6%	1.30 [0.82, 2.05]	0.27
Prior PCI - No	61	613	10.8%		
Prior PCI - Yes	15	75	23.1%	2.20 [1.25, 3.86]	0.006
Presentation – NSTEMI or UA	49	481	11.3%		
Presentation - STEMI	27	208	14.1%	1.26 [0.79, 2.02]	0.33
BMI < 27.9 kg/m ^{2†}	33	342	10.6%		
BMI ≥27.9 kg/m ^{2†}	43	343	13.8%	1.30 [0.83, 2.05]	0.25
Total cholesterol ≥170.0 mg/dl [†]	35	311	12.2%		
Total cholesterol <170.0 mg/dl [†]	33	304	12.2%	1.01 [0.63, 1.62]	0.97

LDL cholesterol <93.6 mg/dl [†]	29	285	11.3%		
LDL cholesterol ≥93.6 mg/dl [†]	38	294	14.1%	1.28 [0.79, 2.07]	0.32
HDL cholesterol ≥38.6 mg/dl [†]	37	341	11.8%		
HDL cholesterol <38.6 mg/dl [†]	30	264	12.9%	1.13 [0.70, 1.82]	0.63
Triglycerides <124.0 mg/dl [†]	34	303	12.3%		
Triglycerides ≥ 124.0 mg/dl [†]	34	305	12.4%	1.02 [0.64, 1.65]	0.92
Hemoglobin A1C <5.8% [†]	30	280	11.6%		
Hemoglobin A1C ≥5.8% [†]	34	287	13.4%	1.15 [0.70, 1.88]	0.58
Creatinine clearance ≥60 ml/min	51	436	13.0%		
Creatinine clearance <60 ml/min	6	48	15.8%	1.19 [0.51, 2.77]	0.69
C-reactive protein ≥7.2 mg/dl [†]	37	334	12.0%		
C-reactive protein <7.2 mg/dl [†]	36	331	12.1%	1.01 [0.64, 1.60]	0.95
# of diseased coronary arteries					
- One	6	149	4.5%		
- Two	29	283	11.7%	2.65 [1.10, 6.37]	0.03
- Three	41	265	16.5%	3.99 [1.69, 9.38]	0.002
PCI vessels - One	51	496	11.3%		
PCI vessels - Two	25	188	14.9%	1.37 [0.85, 2.21]	0.20
Aspirin at discharge - Yes	73	667	12.0%		
Aspirin at discharge - No	3	22	15.8%	1.29 [0.41, 4.10]	0.66
Thienopyridine at discharge - Yes	74	668	12.1%		
Thienopyridine at discharge - No	2	20	15.2%	1.11 [0.27, 4.50]	0.89
Statin or LLT at discharge - Yes	64	587	11.9%		
Statin or LLT at discharge - No	12	100	14.0%	1.2 [0.62, 2.14]	0.65
Beta blocker at discharge - Yes	67	624	11.8%		
Beta blocker at discharge - No	9	65	15.4%	1.32 [0.66, 2.64]	0.44
ACEI or ARB at discharge - No	22	211	11.3%		
ACEI or ARB at discharge - Yes	54	474	12.6%	1.07 [0.65, 1.76]	0.78

* Kaplan-Meier estimate at median 3.4 years; [†] Median value; BMI denotes body mass index; CAD denotes coronary artery disease; NSTEMI denotes non ST-segment elevation myocardial infarction; PCI denotes percutaneous coronary intervention; STEMI denotes ST-segment elevation myocardial infarction; UA denotes unstable angina with electrocardiographic changes. LLT denotes lipid lowering therapy; ACEI denotes angiotensin converting enzyme inhibitor; ARB denotes angiotensin receptor blocker.

Table 6. Intravascular ultrasound predictors of non-culprit lesion-related major adverse cardiac events occurring at the specific lesion site during median 3.4 year follow-up

Variable	Lesions with variable and non-culprit lesion events (n)	Total lesions with variable (N)	Event rate*	HR [95%CI]	P value
<u>Grayscale-IVUS measures</u>					
MLA ≥ 5.9 mm ^{2†}	7	1569	0.5%		
MLA < 5.9 mm ^{2†}	48	1569	3.3%	6.89 [3.12, 15.23]	<0.001
- MLA > 4.0 mm ²	25	2522	1.1%		
- MLA ≤ 4.0 mm ²	30	616	5.3%	5.00 [2.94, 8.51]	<0.001
EEM [‡] ≥ 14.1 mm ^{2†}	21	1569	1.5%		
EEM [‡] < 14.1 mm ^{2†}	34	1569	2.3%	1.61 [0.93, 2.77]	0.09
P&M CSA [‡] ≥ 7.8 mm ^{2†}	23	1567	1.6%		
P&M CSA [‡] < 7.8 mm ^{2†}	32	1571	2.3%	1.40 [0.82, 2.40]	0.22
Plaque burden [‡] $< 56\%^\dagger$	7	1568	0.5%		
Plaque burden [‡] $\geq 56\%^\dagger$	48	1570	3.3%	6.92 [3.13, 15.30]	<0.001
- Plaque burden [‡] $< 70\%$	30	2855	1.2%		
- Plaque burden [‡] $\geq 70\%$	25	283	9.6%	8.72 [5.13, 14.82]	<0.001
Remodeling index $< 0.94^\dagger$	24	1568	1.7%		
Remodeling index $\geq 0.94^\dagger$	30	1568	2.1%	1.25 [0.73, 2.15]	0.41
Lesion length < 11.2 mm [†]	10	1569	0.7%		
Lesion length ≥ 11.2 mm [†]	45	1569	3.1%	4.44 [2.24, 8.81]	<0.001
Distance to MLA < 30.0 mm [†]	15	1395	1.2%		
Distance to MLA ≥ 30.0 mm [†]	34	1395	2.7%	2.30 [1.25, 4.22]	0.007
<u>Radiofrequency-IVUS measures</u>					
Tissue composition					
- Fibrous tissue area < 2.3 mm ^{2†}	22	1397	1.7%		
- Fibrous tissue area ≥ 2.3 mm ^{2†}	29	1397	2.3%	1.33 [0.77, 2.32]	0.31
- Fibrofatty area ≥ 0.7 mm ^{2†}	24	1397	1.9%		
- Fibrofatty area < 0.7 mm ^{2†}	27	1397	2.1%	1.16 [0.67, 2.01]	0.59

- DC area <0.2 mm ^{2†}	17	1397	1.3%		
- DC area ≥0.2 mm ^{2†}	34	1397	2.7%	2.01 [1.12, 3.59]	0.02
- NC area <0.4 mm ^{2†}	17	1397	1.3%		
- NC area ≥0.4 mm ^{2†}	34	1397	2.7%	2.06 [1.15, 3.68]	0.02
- Fibrous tissue area ≥75.0% [‡]	18	1397	1.4%		
- Fibrous tissue area <75.0% [‡]	33	1397	2.6%	1.88 [1.06, 3.33]	0.03
- Fibrofatty area ≥22.0% [‡]	18	1397	1.4%		
- Fibrofatty area <22.0% [‡]	33	1397	2.6%	1.94 [1/09, 3.45]	0.02
- DC area <5.4% [‡]	20	1397	1.6%		
- DC area ≥5.4% [‡]	31	1397	2.4%	1.55 [0.89, 2.73]	0.12
- NC area <13.6% [‡]	21	1397	1.6%		
- NC area ≥13.6% [‡]	30	1397	2.4%	1.48 [0.85, 2.59]	0.17
Lesion classification					
- Fibrotic plaque - yes	0	71	0.0%		
- Fibrotic plaque - no	51	2638	2.1%	-	0.99
- Fibrocalcific plaque - no	50	2676	2.0%		
- Fibrocalcific plaque - yes	1	33	3.1%	1.56 [0.22, 11.30]	0.66
- PIT - yes	6	1005	0.7%		
- PIT - no	45	1704	2.9%	4.57 [1.95, 10.71]	<0.001
- Thick-cap FA - yes	18	1005	2.0%		
- Thick-cap FA - no	33	1704	2.1%	1.09 [0.61, 1.93]	0.77
- Thin-cap FA - no	25	2114	1.3%		
- Thin-cap FA - yes	26	595	4.9%	3.90 [2.25, 6.76]	<0.001

* Kaplan-Meier estimate at median 3.4 years; [†] Median value; [‡] Denotes measurement at the minimal lumen area. CSA denotes cross sectional area; DC denotes dense calcium; EEM denotes external elastic membrane; FA denotes fibroatheroma; IVUS denotes intravascular ultrasound; MLA denotes minimal lumen area; P&M denotes plaque and media; NC denotes necrotic core; PIT denotes pathological intimal thickening.

Note: Patients with indeterminate events were excluded. Gray-scale and radiofrequency volumetric analyses were consistent with area measures but did not provide incremental utility (data not shown).

Table 7. Multivariable models of non-culprit lesion-related major adverse cardiac events occurring at the specific lesion site during median 3.4 year follow-up

	HR [95% CI]	P value
<u>Model 1, pre-specified</u> (C-statistic 0.82)*		
Plaque burden $\geq 70\%$	5.03 [2.51, 10.11]	<0.001
Thin-cap fibroatheroma	3.35 [1.77, 6.36]	<0.001
Minimal lumen area $\leq 4.0\text{mm}^2$	3.21 [1.61, 6.42]	0.001
<u>Model 2</u> (C-statistic 0.84)*		
Plaque burden $\geq 63\%$	6.50 [3.19, 13.26]	<0.001
Thin-cap fibroatheroma	2.72 [1.48, 5.00]	0.001
Minimal lumen area $\leq 4.58\text{mm}^2$	3.42 [1.72, 6.78]	<0.001
<u>Model 3</u> (C-statistic 0.84)*		
Plaque burden (per 10% increase)	2.39 [1.60, 3.57]	<0.001
Thin-cap fibroatheroma	2.78 [1.52, 5.08]	<0.001
Minimal lumen area (per 1.0mm^2 decrease)	1.44 [1.16, 1.79]	0.001

MACE denotes major adverse cardiac events (cardiac death, cardiac arrest, myocardial infarction or rehospitalization due to unstable or progressive angina).

*Angiographic, grayscale-IVUS and radiofrequency-IVUS variables, as well as the significant patient-level predictors were considered for entry into the lesion-level multivariable regression model. The final variables entered were: minimal lumen area (MLA), plaque burden at the MLA, external elastic membrane at the MLA, lesion length, distance from the coronary ostium to the MLA, remodeling index, thin-cap fibroatheroma, insulin-requiring diabetes and prior percutaneous coronary intervention. In Model 1, MLA $\leq 4.0\text{mm}^2$ and plaque burden $\geq 70\%$ were selected as frequently used dichotomous values from prior studies. In Model 2 (post hoc), cut points for all continuous variables were selected by receiver operator characteristic analysis which best predicted non-culprit MACE. In Model 3 (post hoc), continuous data were used for all variables.

Table 8. PROSPECT study organization and list of participating sites and investigators

Executive Committee – G.W. Stone (Principal Investigator), Columbia University Medical Center/New York-Presbyterian Hospital and the Cardiovascular Research Foundation, New York, NY; P.W. Serruys (Co-Principal Investigator), Erasmus University, Heartcenter Rotterdam, The Netherlands; B. de Bruyne (European Co-Principal Investigator), Cardiovascular Center, OLV Hospital, Aalst, Belgium; G. Johnson, Abbott Vascular, Santa Clara, CA.

Operations Committee – G.W. Stone, A. J. Lansky, G. Mintz, E. Cristea, and A. Maehara, Columbia University Medical Center/New York-Presbyterian Hospital and the Cardiovascular Research Foundation, New York, NY; W. Cheong, Abbott Vascular, Santa Clara, CA; T. Engels, Abbott Vascular, Santa Clara, CA; W. Pierson, Abbott Vascular, Santa Clara, CA; S. Veldhof, Abbott Vascular, Brussels, Belgium; B. Templin, Abbott Vascular, Santa Clara, CA; P. Margolis and M Lussier, Volcano Therapeutics, San Diego, CA.

Site Monitoring – Abbott Vascular, Santa Clara, CA.

Data Management and Biostatistical Analysis – Abbott Vascular, Santa Clara, CA.

Clinical Events Adjudication Committees – Cardiovascular Research Foundation, New York, NY: R. Mehran (Director); Duke Clinical Research Institute, Durham, NC: K. Mahaffey (Director).

Angiographic Core Laboratory – Cardiovascular Research Foundation, New York, NY: A. J. Lansky (Director), E. Cristea.

IVUS Core Laboratory – Cardiovascular Research Foundation, New York, NY: A. Maehara (Director), G. S. Mintz.

Palpography Core Laboratory – Cardialysis B.V., The Netherlands: G. van Es (Director).

Biomarker Core Laboratory – Clinical Reference Laboratory, Lenexa, KS: R. Prasad (Vice President).

Data and Safety Monitoring Board – S. Steinhubl (Chair), University of Kentucky, Lexington, KY; S. King, Piedmont Hospital, Atlanta, GA; A. Allen, Duke University, Durham, NC.

Electronic Data Capture – Phase Forward, Waltham, MA.

Study Sites, Principal Investigators, and Primary Study Coordinators – North Mississippi Medical Center, Tupelo, MS, USA: Barry Bertolet; Skejby Sygehus, Aarhus, Denmark: Hans-Erik Bøtker; The Christ Hospital, Cincinnati, OH, USA: Thomas Broderick; Piedmont Hospital, Atlanta, GA, USA: Charles Brown; Pinnacle Health at Harrisburg Hospital, Wormleysburg, PA, USA: Rajesh Dave; Northwestern University, Chicago, IL, USA: Charles Davidson; Onze-Lieve-Vrouweziekenhuis, Aalst, Belgium: Bernard de Bruyne; University Hospital, Krakow, Poland: Dariusz Dudek; Cleveland Clinic, Cleveland, OH, USA: Stephen Ellis; Clinique Pasteur, Toulouse, France: Jean Fajadet; Allegheny General Hospital, Pittsburgh, PA, USA: Tony Farah; NOHC/EMH Regional Medical Center, Elyria, OH, USA: Naim Farhat; Stanford University Hospital, Stanford, CA, USA: William Fearon; Sisters of Charity Providence Hospital, Columbia, SC, USA: Michael Foster; University Hospital Gregorio Maranon, Madrid, Spain: Eulogio Garcia; Kerckhoff Klinik, Bad Nauheim, Germany: Christian Hamm; Indiana Heart Center, Indianapolis, IN, USA: James Hermiller; Hospital do Meixoeiro, Vigo, Spain: Andres Iñiguez; Mayo Clinic, Rochester, MN, USA: Amir Lerman; Hospital Clinico San Carlos, Madrid, Spain: Carlos Macaya; Universitätsspital, Zürich, Switzerland: Willibald Maier; St. Luke's Hospital, Kansas City, MO, USA: Steve Marso; Azienda Ospedaliera S. Orsola-Malpighi, Bologna, Italy: Antonio Marzocchi; Kardiologische Gemeinschaftspraxis, Hamburg, Germany: Detlef Mathey; Vanderbilt University Medical Center, Nashville, TN, USA: John McPherson; Mt Sinai Medical Center, New York, NY, USA: Pedro Moreno; Presbyterian Hospital, Charlotte, NC, USA: Gary Niess; Columbia

University, New York, NY, USA: Leroy Rabbini; London Chest Hospital, London, United Kingdom: Martin Rothman; CHU Jean Minjoz, Besancon, France: Francois Schiele; Erasmus University Thoraxcentrum, Rotterdam, The Netherlands: Patrick Serruys; Hospital Santa Cruz, Carnaxide, Portugal: Rui Teles; Academisch Ziekenhuis Middelheim, Antwerp, Belgium: Stefan Verhey; Washington Hospital Center, Washington DC, USA: Ron Waksman; Sahlgrenska Sjukhuset, Göteborg, Sweden: Per Albertsson; Herzzentrum, Bad Oeynhausen, Germany: Marcus Wiemer; Riverside Methodist Hospital, Columbus, OH, USA: Steve Yakubov.

Figure 1. Lesion classification according to radiofrequency IVUS. Fibroatheromas (FA) were defined by the presence of >10% confluent necrotic core (NC; red color). If more than 30 degrees of the NC abutted the lumen in 3 or more consecutive frames, the fibroatheroma was classified as a thin-cap fibroatheroma (TCFA); otherwise it was categorized as a thick-cap fibroatheroma (ThCFA). Fibrotic plaque was defined as consisting mainly of fibrous tissue (FT; dark green color) with <10% confluent NC, <10% confluent dense calcium (DC; white color), and <15% of fibrofatty (FF; light green color). Fibrocalcific plaque was defined as mainly FT with >10% of confluent DC, with <10% of confluent NC. Pathological intimal thickening (PIT) was defined as $\geq 15\%$ FF, with <10% confluent NC and <10% confluent DC. In addition, fibroatheromas were sub-classified as having single or multiple confluent NCs and containing or not containing DC. The entire lesion was evaluated for lesion level radiofrequency-IVUS classification. Multiple lesion subtypes were considered as separate lesions if they were separated by ≥ 3 consecutive image slices of different morphology; for example, multiple TCFAs were considered separate if they were separated by ≥ 3 consecutive non-TCFA containing image slices. In segments with more than one lesion subtype, a hierarchy was utilized wherein TCFA took precedence over ThCFA, and any FA took precedence over any non-FA lesion type.

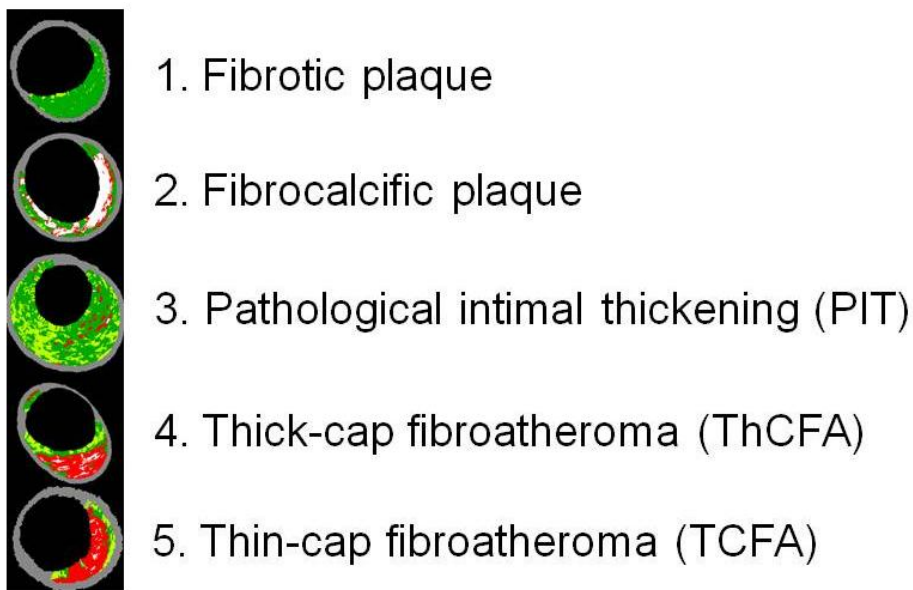


Figure 2. Example from the PROSPECT study. A 52 year old man was admitted on February 13th, 2006 with a non ST-segment elevation myocardial infarction due to an occluded mid left anterior descending artery which was successfully stented. Three vessel angiography and gray-scale and radiofrequency-IVUS was then performed (left coronary artery shown, left angiogram). The patient was asymptomatic until 51 weeks later when on February 6th, 2007 he developed a non ST-segment elevation myocardial infarction due to a progressive thrombotic lesion in the mid left circumflex artery (diameter stenosis 71.3%, thick arrow, right angiogram). At the index procedure the angiographic diameter stenosis of this lesion (thin arrows, left angiogram) had been 28.6% with lesion length 6.8 mm, and by intravascular ultrasound the minimal lumen area was 5.3 mm² and the plaque burden was 74%. The lesion was classified by the core laboratory as a thick-cap fibroatheroma (necrotic core 31%). Two additional fibroatheromas are present proximal to the lesion which did not progress.

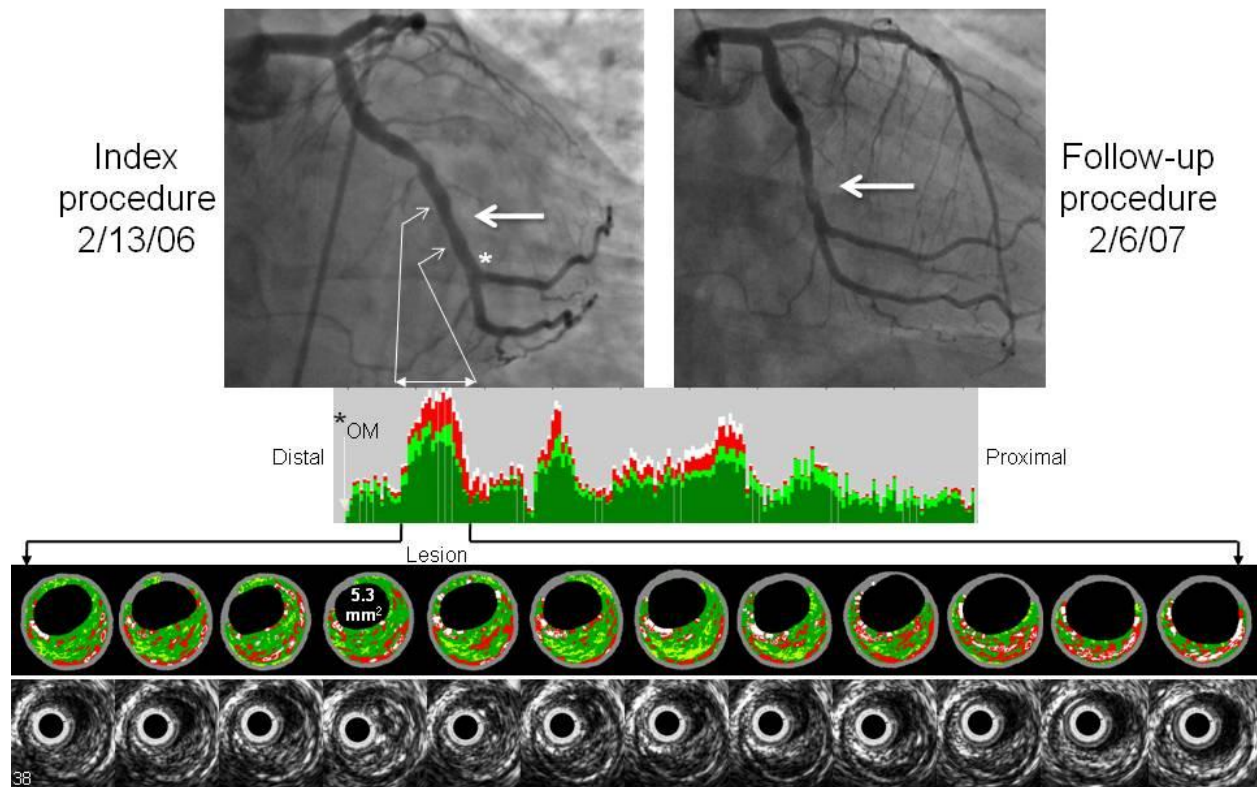
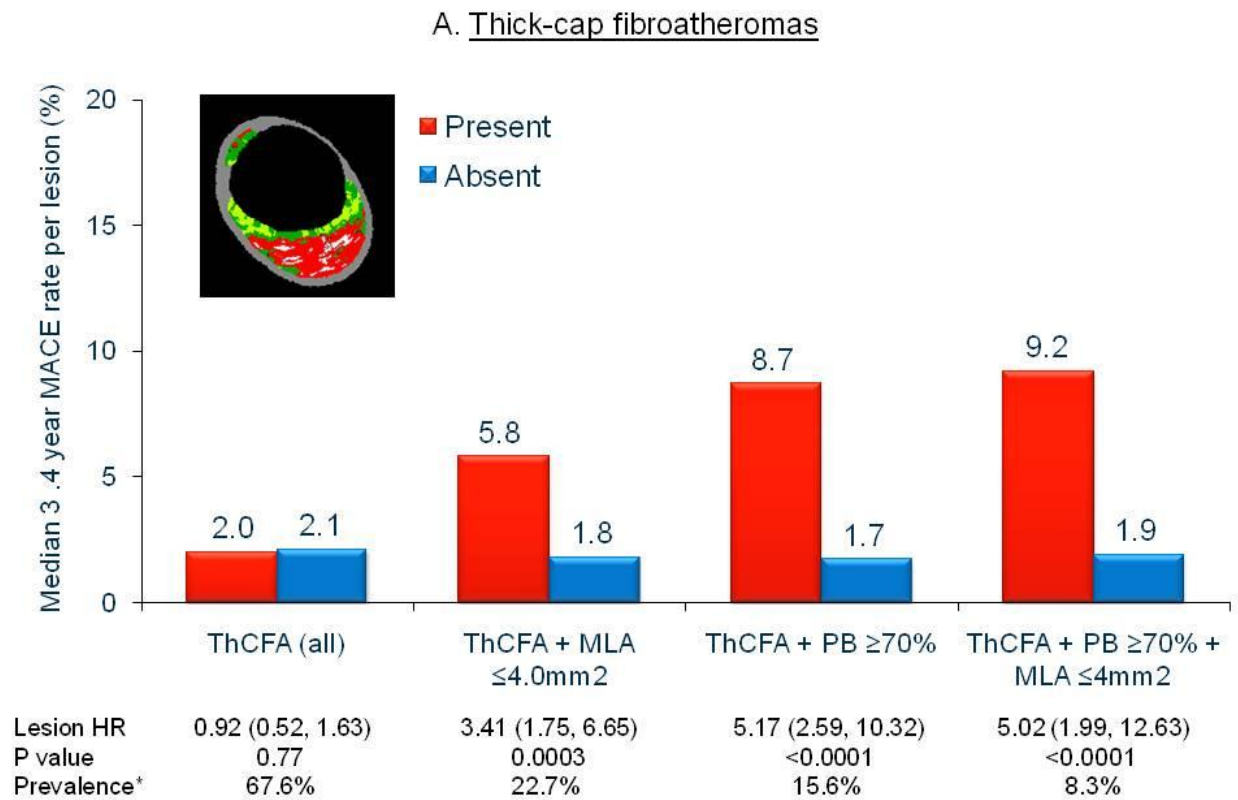


Figure 3. Event rates at median 3.4 year follow-up according to grayscale and radiofrequency-IVUS plaque type, minimal lumen area and plaque burden. A) Thick-cap fibroatheromas (n=1005 lesions); B) Non fibroatheromas (n=1109 lesions), consisting of pathological intimal thickening (n=1005 lesions), fibrotic lesions (n=71), and fibrocalcific lesions (n=33). FA denotes fibroatheroma. MLA denotes minimal lumen area; HR denotes the hazard ratio with 95% confidence interval for a non-culprit lesion related event developing at a lesion site with those characteristics; MACE denotes major adverse cardiac events; PB denotes plaque burden; ThCFA denotes thick-cap fibroatheroma. * Denotes the prevalence of one or more such lesions being present per patient.



B. Non fibroatheromas

