J Am Coll Cardiol (2004);44:53-6
Clinical, angiographic, and intravascular ultrasound characteristics of early saphenous vein graft failure
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OBJECTIVES: We sought to examine saphenous vein graft (SVG) lesions that fail within the first year after operation. BACKGROUND: Saphenous vein grafts remain patent for approximately 10 years; however, up to 15% to 20% of SVGs become occluded within the first year. METHODS: We studied 100 patients who underwent percutaneous coronary intervention (PCI) for early (<1 year post-implantation) SVG failure lesions and compared them with a diabetes- and hypercholesterolemia-matched cohort of late SVG failures (>1 year). Coronary angiography and intravascular ultrasound images were analyzed. RESULTS: The majority of patients in both groups were males who presented with unstable angina; 36% were diabetic. Graft ages were 6.0 +/- 2.9 months and 105.4 +/- 50.8 months, respectively. The early SVG failure lesion location was more often ostial or proximal (62% vs. 42%, respectively). Early SVG failures were angiographically smaller than late failures (reference: 2.47 +/- 0.86 mm vs. 3.26 +/- 0.83 mm, $p < 0.001$) but had similar lesion lengths. Intravascular ultrasound showed that early failure lesions had smaller proximal and distal reference lumen areas (7.3 +/- 6.8 mm2 vs. 10.6 +/- 3.8 mm2, $p = 0.026$) and greater reference plaque burden than late failures (52.3% vs. 36.1%, $p < 0.001$). After PCI, 20.6% of early and 30.6% of late failure lesions had creatine kinase-myocardial band (CK-MB) greater than twice normal. CONCLUSIONS: Early SVG failure is mostly proximal or ostial, lesions appear focal, and early SVGs appear smaller than late SVGs. Intravascular ultrasound shows significant reference segment plaque burden, suggesting more severe, diffuse SVG disease.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15234406

Am J Cardiol (2004);94:1067-70
Vascular remodeling and plaque composition between focal and diffuse coronary lesions assessed by intravascular ultrasound
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Coronary remodeling and plaque composition were compared between focal and diffuse coronary lesions. Negative remodeling and fibrous and calcified plaque compositions contribute to stenosis development in diffuse lesions more frequently than in focal lesions.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15476629

Am Heart J (2004);147:158-64
Association between plasmin activation system and intravascular ultrasound signs of plaque instability in patients with unstable angina and non-st-segment elevation myocardial infarction

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BACKGROUND: The association between intravascular ultrasound (IVUS) signs of plaque instability and plasma levels of biomarkers was determined in patients with unstable angina and non-ST-segment elevation myocardial infarction (UA/NSTEMI). METHODS: Fifty-two patients underwent coronary angiography and IVUS 8 +/- 5 hours after the onset of chest pain. IVUS analysis included plaque morphology, disruption, thrombi and eccentricity, lumen, external elastic membrane, and plaque plus media areas of culprit lesion and reference segments and arterial remodeling. Plasma levels of the thrombin activation system (thrombin-antithrombin complex [TAT], tissue factor pathway inhibitor [TFPI], and prothrombin fragments 1+2 [F1+2]) and plasmin activation system (tissue and urokinase-type plasminogen activator [t-PA and u-PA], plasminogen activator inhibitor-1 [PAI-1], and D-dimer) were measured with enzyme-linked immunosorbent assay kits before angiography. RESULTS: Elevated levels of TAT (7.2 +/- 6.0 microg/L), F1+2 (1.8 +/- 1.0 nmol/L), TFPI (179.1 +/- 131.0 ng/mL), PAI-1 (95.4 +/- 54.6 ng/mL), t-PA (10.6 +/- 8.8 ng/mL), and u-PA (2.6 +/- 0.9 ng/mL) were found in patients with UA/NSTEMI. The serum levels of D-dimer (40.0 +/- 39.5 ng/mL) remained in reference range. Expansive and constrictive remodeling were found in 18 (35%) and 12 (23%) patients, respectively. Expansive remodeling of the culprit lesion was associated with significantly higher plasma levels of PAI-1 (121.6 +/- 55.0 vs 87.7 +/- 61.5 and 77.4 +/- 42.8 ng/ml, P =.039), and u-PA (3.0 +/- 1.2 vs 2.2 +/- 0.5 and 2.5 +/- 0.7 ng/mL, P =.026) as compared with constrictive and neutral remodeling. Increased plasma levels of u-PA were associated with plaque rupture (3.0 +/- 0.7 vs 2.5 +/- 0.9 ng/mL, P =.062). Plasma levels of PAI-1 and u-PA correlated positively with plaque plus media (P =.0297 and P =.0093) and external elastic membrane areas (P =.010 and P =.0002). CONCLUSIONS: Elevated levels of biomarkers of plasmin activation system are associated with signs of plaque instability of culprit lesion in UA/NSTEMI and might therefore serve as non-invasive determinants of the population that is at high risk for subsequent adverse events.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14691435

Circulation (2004);110:928-33
Comparison of coronary plaque rupture between stable angina and acute myocardial infarction: a three-vessel intravascular ultrasound study in 235 patients
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BACKGROUND: We evaluated the incidence and predictors of single and multiple plaque ruptures in acute myocardial infarction (AMI) and stable angina pectoris (SAP). METHODS AND RESULTS: We performed 3-vessel intravascular ultrasound (IVUS) examination in 235 patients: 122 had AMI, and 113 had SAP. Plaque rupture of infarct-related or target lesions occurred in 80 AMI patients (66%) and in 31 SAP patients (27%) (P<0.001). Non-infarct-related or non-target artery plaque ruptures occurred in 21 AMI patients (17%) and 6 SAP patients (5%) (P=0.008). Multiple plaque ruptures were observed in 24 AMI (20%) and 7 SAP patients (6%) (P=0.004). T TDie17 TD0004 Tc0.

at least 1 plaque rupture in any coronary artery was noted in 84 AMI patients (69%) and 35 SAP patients (31%) (P<0.001). Overall, the only independent clinical predictor of plaque rupture in the infarct-related/target lesion was AMI (P<0.01; OR, 4.867; 95% CI, 2.734 to 8.661). The only independent clinical predictor of plaque rupture in AMI patients was an elevated C-reactive protein (CRP) level (P=0.035; OR, 2.139; 95% CI, 1.053 to 4.343). Conversely, in SAP patients, the only independent clinical predictor of plaque rupture was diabetes mellitus (P=0.034; OR, 2.553; 95% CI, 1.071 to 6.085). The only independent clinical predictor of multiple plaque ruptures was AMI (P=0.003; OR, 3.752; 95% CI, 1.546 to 9.105). CONCLUSIONS: Three-vessel IVUS imaging showed that culprit lesion plaque rupture, secondary remote plaque ruptures, and multiple plaque ruptures were all more common in AMI patients than SAP patients. In AMI patients, plaque rupture was associated with a high CRP level, whereas in SAP patients, plaque rupture was more common in those with diabetes.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15313951

Circulation (2004);110:2831-6
Correlations between fractional flow reserve and intravascular ultrasound in patients with an ambiguous left main coronary artery stenosis
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BACKGROUND: Intravascular ultrasound (IVUS) is being used to assess the significance of a left main coronary artery stenosis (LMCS). However, the cutoff values of IVUS parameters at which to predict a fractional flow reserve (FFR) of 0.75 are unknown. METHODS AND RESULTS: In 55 patients with an angiographically ambiguous LMCS, a pressure guidewire was used to calculate FFR, and IVUS parameters were calculated after automatic pullback. FFR averaged 0.86+/-0.13 (range, 0.55 to 1.0). IVUS minimum lumen diameter (MLD), minimum lumen area (MLA), cross-sectional narrowing (CSN), and area stenosis (AS) were 3.8+/-0.61 mm, 7.65+/-2.9 mm2, 59+/-13%, and 47+/-19%, respectively. Regression analysis demonstrated strong correlations between FFR and MLD (r=0.79, P<0.0001) as well as between FFR and MLA (r=0.74, P<0.0001). There were inverse, moderate correlations between FFR and CSN (r=0.69, P<0.0001), followed by those between FFR and AS (r=0.54, P<0.0001). Compared with FFR as the "gold standard," an MLD of 2.8 mm had the highest sensitivity and specificity (93% and 98%, respectively) for determining the significance of an LMCS, followed by an MLA of 5.9 mm2 (93% and 95%, respectively). Based on an FFR <0.75 and an FFR > or =0.75, the 38-month survival and event-free survival estimates (EFSEs) were both 100% and 100% versus 90%, respectively (P=NS). CONCLUSIONS: We conclude that (1) an IVUS MLD and MLA of 2.8 mm and 5.9 mm2, respectively, strongly predict the physiological significance of an LMCS and (2) among patients with an LMCS, an FFR of 0.75 is a strong predictor of survival and EFSE.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15492302

Circulation (2004);110:265-70
Regression of coronary atherosclerosis by simvastatin: a serial intravascular ultrasound

study
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BACKGROUND: Angiography of the coronary arteries reflects only changes in luminal dimensions. With intravascular ultrasound, cross-sectional images can be obtained and area measurements can be added to calculate volumes of the external elastic membrane (EEM), plaque plus media (P+M), and lumen. The aim of this study was to investigate the effect of lipid lowering by simvastatin on coronary atherosclerotic P+M as changes in volumes of EEM, P+M, and lumen. METHODS AND RESULTS: In 40 male patients with hypercholesterolemia, ischemic heart disease, and a nonsignificant coronary artery lesion in a not previously revascularized coronary artery, serial intravascular ultrasound studies with an ECG-triggered pullback were performed at baseline, after 3 months on a lipid-lowering diet, and after another 12 months on simvastatin 40 mg/d. Mean length of the analyzed atherosclerotic segments was 5.9+/-3.3 mm. After 12 months on simvastatin, a significant reduction in P+M volume of 6.3% (P=0.002) was observed, whereas only a nonsignificant reduction in EEM volume of 1.8% was seen without any concomitant change in lumen volume. A significant reduction in total cholesterol of 31.0% (6.1+/-0.8 versus 4.2+/-0.7 mmol/L, P<0.001) and LDL cholesterol of 42.6% (4.0+/-0.8 versus 2.2+/-0.6 mmol/L, P<0.001) was obtained. CONCLUSIONS: Lipid-lowering therapy with simvastatin for 12 months is associated with a significant P+M regression in coronary arteries measured as reduction in P+M and EEM volumes without any concomitant change in lumen volume.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15238460

J Am Coll Cardiol (2004);43:1241-7
Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intracoronary ultrasound
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OBJECTIVES: We evaluated the accuracy of contrast-enhanced multidetector spiral computed tomography (MDCT) for the noninvasive detection and classification of coronary plaques and compared it with intracoronary ultrasound (ICUS). BACKGROUND: Noninvasive determination of plaque composition and plaque burden may be important to improve risk stratification and to monitor progression of coronary atherosclerosis. METHODS: We included 46 consecutive patients with a distinctive risk profile, who were investigated by ICUS (Goldvision, 20 MHz, Jomed Inc., Rancho Cordova, California). Due to the inability to slow the heart rate below 65 beats/min (n = 7) and due to renal insufficiency (n = 2), nine of 46 consecutive patients could not be studied by MDCT (Sensation 16, Siemens, Forchheim, Germany). RESULTS: In the remaining 37 patients, 68 vessels were investigated by ICUS, and 58 of these vessels were visualized by MDCT with image quality sufficient for analysis. In these vessels that were divided in 3-mm sections, MDCT correctly classified 62 of 80 (78%) sections containing hypoechoic plaque areas, 87 of 112 (78%) sections containing hyperechoic

plaque areas, and 150 of 158 (95%) sections containing calcified plaque tissue. In 484 of 525 (92%) sections, atherosclerotic lesions were correctly excluded. The MDCT-derived density measurements within coronary lesions revealed significantly different values for hypoechoic (49 HU [Hounsfield Units] +/- 22), hyperechoic (91 HU +/- 22), and calcified plaques (391 HU +/- 156, p < 0.02). CONCLUSIONS: This study demonstrates that, in the case of diagnostic image quality, contrast-enhanced MDCT permits an accurate identification of coronary plaques and that computed tomography density values measured within plaques reflect echogenity and plaque composition.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15063437

Am J Cardiol (2005);95:107-9
Intravascular ultrasound assessment of neointima distribution and the length of stent that was free of intravascular ultrasound-detectable intimal hyperplasia in paclitaxel-eluting stents
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Using data from the ASian Paclitaxel-Eluting Stent Clinical Trial, a 3-center, randomized, placebo-controlled trial of nonpolymeric paclitaxel-coated stents with a single center, 81-patient intravascular ultrasound (IVUS) substudy, the length of a stent that was free of IVUS-detectable intimal hyperplasia measured 3.2 +/- 4.8 mm in placebo stents, 6.1 +/- 5.6 mm in low-dose stents, and 8.7 +/- 6.1 mm in high-dose stents (p = 0.0029). IVUS percent neointima volume obstruction correlated with the length of this IVUS neointima-free segment (r = 0.785, p <0.0001); angiographic late lumen loss and follow-up diameter stenosis also correlated with the IVUS neointima-free length of the stents (r = 0.670, p <0.0001 and r = 0.679, p <0.0001, respectively.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15619404

Am J Cardiol (2005);95:105-7
Comparison of quantitative angiographic parameters with the magnitude of neointimal hyperplasia measured by volumetric intravascular ultrasound in patients treated with bare metal and nonpolymeric paclitaxel-coated stents
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We used data from the ASian Paclitaxel-Eluting Stent Clinical Trial (a 3-center, randomized, placebo-controlled trial of nonpolymeric paclitaxel-coated stents with a single-center intravascular ultrasound substudy) to compare angiographic indexes of drug-eluting stent efficacy with the magnitude of intimal hyperplasia (IH) assessed by intravascular ultrasound. Overall, percent IH (IH volume divided by stent volume) was larger in restenotic lesions than in nonrestenotic lesions (46 +/- 19% vs 15 +/- 13%, p <0.0001); angiographic late loss and follow-up diameter stenoses correlated strongly with percent IH.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15619403

Am J Cardiol (2004);93:470-3

significant associated stenosis (minimal lumen cross-sectional area >4 mm2) were included and systematically treated with 40 mg statin and antiplatelet agent (clopidogrel and aspirin for > or =9 months). Mean clinical and IVUS follow-up was 22+/-13 months (median, 22 months). No clinical event related to the lesion under study occurred. On final IVUS examination, half (14 of 28) of the ruptured plaques had healed, and the degree of stenosis tended to diminish (stenosis, 22+/-17% versus 29+/-17% at baseline; P=0.056). No healing-prediction criterion could be identified. CONCLUSIONS: Nearly 2 years of follow-up found that spontaneous coronary atheromatous plaque rupture without significant stenosis detected on first acute coronary syndrome healed without significant plaque modification in 50% of cases with medical therapy.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15492303

Eur Heart J (2004);25:2026-33
Soft plaque detected on intravascular ultrasound is the strongest predictor of in-stent restenosis: an intravascular ultrasound study
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AIMS: Although various predictors of in-stent restenosis (ISR) have been reported, the subject of parameters relating to ISR on intravascular ultrasound (IVUS) still leaves room for discussion. The aim of this study was to clarify the strongest predictors of ISR using IVUS. METHODS AND RESULTS: Ninety-two native coronary lesions undergoing single bare-metallic stent implantation were investigated retrospectively. We classified them into the ISR (n=46) and non-ISR (n=46) groups using quantitative coronary angiography. On serial IVUS studies, plaque morphology, and areas and volumes of each component in vessel were evaluated. Among all parameters, diabetes mellitus and soft plaque appearing hypoechoic on IVUS were associated with ISR. By multivariate analysis, soft plaque was the only independent predictor of ISR (p=0.0057). Compared with non-soft plaque, soft plaque had a larger plaque reduction rate (-7.1% vs. -1.6%, p=0.0613) and smaller percent plaque volume (53.0% vs. 55.5%, p=0.0273) after stenting. Conversely, soft plaque had a larger neointimal area (4.39 vs. 3.33 mm2, p=0.0437) and percent plaque area (80.5% vs. 75.1%, p=0.0503) at follow-up. CONCLUSION: Soft plaque detected on IVUS was the strongest predictor of ISR. Soft plaque was compressed more easily by stenting, however, causing more proliferation of neointima subsequently and resulted in a worse prognosis.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15541839

Circulation (2004);109:627-33
Vascular responses at proximal and distal edges of paclitaxel-eluting stents: serial intravascular ultrasound analysis from the TAXUS II trial
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BACKGROUND: On the basis of brachytherapy experience, edge stenosis has been raised as a potential limitation for drug-eluting stents. We used serial intravascular

ultrasound (IVUS) to prospectively analyze vessel responses in adjacent reference segments after implantation of polymer-controlled paclitaxel-eluting stents. METHODS AND RESULTS: TAXUS II was a randomized, double-blind trial with 2 consecutive patient cohorts that compared slow-release (SR) and moderate-release (MR) paclitaxel-eluting stents with control bare metal stents (BMS). By protocol, all patients had postprocedure and 6-month follow-up IVUS. Quantitative IVUS analysis was performed by an independent core laboratory, blinded to treatment allocation, in 5-mm vessel segments immediately proximal and distal to the stent. Serial IVUS was available for 106 SR, 107 MR, and 214 BMS patients. For all 3 groups, a significant decrease in proximal-edge lumen area was observed at 6 months. The decrease was comparable (by ANOVA, P=0.194) for patients in the SR (-0.54+/-2.1 mm2) and MR (-0.88+/-1.9 mm2) groups compared with the BMS (-1.02+/-1.9 mm2) group. For the distal edge, a significant decrease in lumen area was only observed with BMS (-0.91+/-2.0 mm2, P<0.0001); this decrease was significantly attenuated with SR (0.08+/-2.0 mm2) and MR (-0.19+/-1.7 mm2) stents (P<0.0001 by ANOVA). Negative vessel remodeling was observed at the proximal (-0.48+/-2.2 mm2, P=0.011) but not the distal edges of BMS and at neither edge of SR or MR stents. CONCLUSIONS: The marked reduction in in-stent restenosis with SR or MR stents is not associated with increased edge stenosis at 6-month follow-up IVUS. In fact, compared with BMS, there is instead a significant reduction in late lumen loss at the distal edge with TAXUS stents.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14769685

Am J Cardiol (2005);95:498-502
Intravascular ultrasound assessment of lesions with target vessel failure after sirolimus-eluting stent implantation
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Intravascular ultrasound (IVUS) evaluation was performed in 33 lesions with sirolimus-eluting stent (SES) failure: 4 thromboses, 26 in-stent restenoses (including 6 edge stenoses), 4 new stenoses >5 mm proximal to the stent, and 1 patient with no evidence of the implanted SES (presumably because of embolization). A minimum stent

quantitative intravascular ultrasound (IVUS) analyses in the TAXUS II trial. METHODS AND RESULTS: TAXUS II was a randomized, double-blind study with 536 patients in 2 consecutive cohorts comparing slow-release (SR; 131 patients) and moderate-release (MR; 135 patients) paclitaxel-eluting stents with BMS (270 patients). This IVUS substudy included patients treated with one study stent who underwent serial IVUS examination after the procedure and at 6-month follow-up (BMS, 152 patients; SR, 81; MR, 81). The analyzed stented segment (15 mm) was divided into 5 subsegments in which mean vessel area (VA), stent area (SA), lumen area (LA), intrastent neointimal hyperplasia area (NIHA), and peristent area (VA-SA) were measured. NIHA was significantly reduced in SR (0.7+/-0.9 mm2, P<0.001) and MR (0.6+/-0.8 mm2, P<0.001) compared with BMS (1.9+/-1.5 mm2), with no differences between the two paclitaxel-eluting release formulations. Longitudinal distribution of neointimal hyperplasia throughout the paclitaxel-eluting stent was uniform. Neointimal growth was independent of peristent area at postprocedure examination in all groups. There were progressive increases in peristent area from BMS to SR to MR (0.5+/-1.7, 1.0+/-1.8, and 1.4+/-2.0 mm2, respectively; P<0.001). The increase in peristent area was directly correlated with increases in VA. CONCLUSIONS: Both SR and MR paclitaxel-eluting stents prevent neointimal formation to the same degree compared with BMS. However, the difference in peristent remodeling suggests a release-dependent effect between SR and MR.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14691036

Am J Cardiol (2004);93:1107-13
Spectrum of remodeling behavior observed with serial long-term (>/=12 months) follow-up intravascular ultrasound studies in left main coronary arteries
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Most intravascular ultrasound (IVUS) studies of arterial remodeling in native coronary arteries reported a remodeling index obtained at a single time point. We analyzed serial IVUS examinations, including the vessel cross-sectional area changes (remodeling behavior), of 60 hemodynamically nonstenotic left main lesions (baseline vs 18.4 +/- 9.4 months follow-up). Lumen reduction resulted from vessel reduction (sometimes despite plaque + media decrease), plaque + media increase (with or without vessel increase), or both. The percent annual changes in lumen area correlated strongly with changes in vessel (r = 0.84), but not with changes in plaque + media area. Plaques were classified as group A lesions, reflecting positive remodeling behavior (vessel changes >0), or group B lesions, reflecting negative (or intermediate) remodeling behavior (vessel changes <==0). Both groups did not differ significantly in demographics, laboratory data, and medications. Group A lesions (n = 40) more often showed plaque + media increase than group B lesions (32 of 40 [80%] vs 9 of 20 [45%]; p = 0.02). Group A lesions had, on average, mild annual lumen increase despite mild plaque + media increase, i.e, overcompensation of remodeling for plaque + media increase (vessel increase greater than plaque + media area increase, 19 of 40 [47%]). Conversely, group B lesions (n = 20) showed a significant lumen area reduction (-2.8 +/- 2.6 mm(2)/year) as a result of a decrease in vessel area only. Thus, serial long-term [illegible]

from vessel shrinkage (sometimes despite plaque decrease), plaque increase (with or without vessel increase), or both; overall, only the remodeling behavior has a significant relation to lumen changes. More than 30% of lesions show a negative remodeling behavior, which shows no relation to patient characteristics or initial plaque burden.
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