J Biomech Eng 2002 Dec;124(6):734-41

Strain measurement in coronary arteries using intravascular ultrasound and deformable images.

Veress AI, Weiss JA, Gullberg GT, Vince DG, Rabbitt RD.

Atherosclerotic plaque rupture is responsible for the majority of myocardial infarctions and acute coronary syndromes. Rupture is initiated by mechanical failure of the plaque cap, and thus study of the deformation of the plaque in the artery can elucidate the events that lead to myocardial infarction. Intravascular ultrasound (IVUS) provides high resolution in vitro and in vivo cross-sectional images of blood vessels. To extract the deformation field from sequences of IVUS images, a registration process must be performed to correlate material points between image pairs. The objective of this study was to determine the efficacy of an image registration technique termed Warping to determine strains in plaques and coronary arteries from paired IVUS images representing two different states of deformation. The Warping technique uses pointwise differences in pixel intensities between image pairs to generate a distributed body force that acts to deform a finite element model. The strain distribution estimated by image-based Warping showed excellent agreement with a known forward finite element solution, representing the gold standard, from which the displaced image was created. The Warping technique had a low sensitivity to changes in material parameters or material model and had a low dependency on the noise present in the images. The Warping analysis was also able to produce accurate strain distributions when the constitutive model used for the Warping analysis and the forward analysis was different. The results of this study demonstrate that Warping in conjunction with in vivo IVUS imaging will determine the change in the strain distribution resulting from physiological loading and may be useful as a diagnostic tool for predicting the likelihood of plaque rupture through the determination of the relative stiffness of the plaque constituents.

Jpn Heart J 2002 Nov;43(6):581-91

Intravascular ultrasound assessment of longitudinal plaque distribution patterns in patients with angiographically silent coronary artery disease after heart transplantation.

Bocksch W, Wellnhofer E, Klimek W, Schartl M, Dreysse S, Musci M, Hummel M, Hetzer R.

AIMS; The purpose of this three-dimensional intracoronary ultrasound (ICUS) study was to assess longitudinal plaque distribution patterns in patients with angiographically silent coronary artery disease (CAD) after heart transplantation (HTX). METHODS AND RESULTS; Out of 334 patients without diameter stenosis >/=25% determined by coronary angiography, 321 underwent successful three-dimensional ICUS (30 MHz) of the left main coronary artery (LMCA) and all segments of the left anterior descending coronary artery (LAD). Early plaque formation was found in 296 patients (92.2%). Single (focal CAD, = 65) or multiple (polyfocal CAD, = 77), discrete coronary lesions were found in 142 patients and continuous plaque formation of at least one entire coronary segment (diffuse CAD) in 154 patients. Using multivariate regression analysis, male sex (= 0.01), increasing post-transplantation time (= 0.003) and increasing donor age (= 0.001) were independent clinical predictors for diffuse CAD. Both focal and diffuse CAD most frequently affected the proximal LAD (88% compared with 89.6%, NS). The mean intimal index of each LAD segment was significantly higher in patients with diffuse CAD (< 0.001) and showed a proximal-to-distal decline in patients with focal/polyfocal (LMCA, 10.1 +/- 14.3, LAD-6, 30.1 +/- 17.4%, LAD-7, 16.3 +/- 14.1%, LAD-8, 4.6 +/- 11.1%; < 0.001) and diffuse (LMCA, 27.0 +/- 16.0, LAD-6, 47.8 +/- 16.1%, LAD-7, 41.9 +/- 14.5%, LAD-8, 24.9 +/- 23.3%; < 0.01) CAD. CONCLUSION; Evaluation of longitudinal plaque distribution after HTX by three-dimensional ICUS revealed a time-dependent increase in the incidence of diffuse CAD and a proximal-to-distal decline in frequency and magnitude of early plaque formation.

J Interv Cardiol 2002 Dec;15(6):447-59

Intracoronary ultrasound in acute coronary syndromes: from characterization of vulnerable plaques to guidance of percutaneous treatment of complex stenoses.

Jimenez J, Escaned J.

Our current knowledge on the substrate and genesis of acute coronary syndromes (ACS) results from the integration of pathological, angiographic, and intracoronary imaging techniques. To summarize briefly the current paradigm, eight differentiated stages of development of atherosclerotic lesions are currently accepted, defined not only by the cellular elements involved, but also by the appearance of sudden alterations of plaque structure and coronary thrombosis. The latter constitutes not only the dominant substrate for the most devastating manifestations of coronary artery disease, but also accelerates plaque size at a faster pace than in earlier stages. The composition of atherosclerotic plaque varies significantly along the different evolutive stages, and thus includes cellular (macrophage, smooth muscle cells) and noncellular elements (glicosaminglycan or collagen-rich cellular matrix, extracellular lipid deposits, calcification, fresh, or organized thrombus) in a varying proportion. Furthermore, a dynamic process of vessel remodeling occurs along the atherosclerotic process, resulting, in most cases, in a protective mechanism against myocardial ischemia by preserving luminal dimensions during plaque enlargement. Intravascular ultrasound (IVUS) is one of the intracoronary imaging techniques that has contributed to the understanding of these changes in man. In addition, IVUS has the potential of being a useful clinical tool for predicting the chances of future acute coronary events by identifying vulnerable plaques, of characterizing which is the culprit lesion in ACS, and in guiding revascularization procedures in the treacherous field of thrombotic coronary syndromes. In this article, we review the current evidence on the potential of IVUS imaging for fulfilling these purposes.

Am J Cardiol 2002 Nov 21;90(10C):28L-31L

Usefulness of intravascular ultrasound-guided histological measurements after stenting in porcine coronary artery.

Strehblow C, Gyongyosi M, Sperker W, Shirazi M, Windberger U, Pugatsch T, Ben-Sasson S, Lotan C, Glogar D.

BACKGROUND: We evaluated the usefulness of intravascular ultrasound (IVUS) in the non-uniform distribution of in-stent neointimal hyperplasia, comparing macroscopic measurements with IVUS-guided histomorphometry. METHODS: Coronary stenting was performed in 45 left coronaries of 39 pigs, using 18 Tenax (Biotronik Gmbh and Co., Berlin, Germany), 11 bare Genius (Eurocor, Bonn, Germany), 10 polymer-coated Genius (Eurocor) and six Biodivysio Matrix LO (Biodivysio Ltd, Farnham, Surrey, UK) stents. After 4 weeks, coronary angiography and IVUS with automatic pullback were performed. IVUS images were analysed using three-dimensional analysis (EchoPlaque 2; INDEC Systems Inc., Mountain View, California, USA). The stented segments were formalin fixed, embedded in Technovit 9100 and cut to 4-8 microm thick slides. The most diseased in-stent segment was 4.49 +/- 4.54 mm away from the distal stent edge assessed by IVUS. Sections of these segments were stained for histomorphometry. RESULTS: A significant correlation was found between IVUS-guided histomorphometry and three-dimensional IVUS measurements of maximal intimal thickness ($r = 0.6985$, $P < 0.005$) and area ($r = 0.7736$, $P < 0.001$). Macroscopic measurements resulted in comparable maximal intimal thickness (0.83 +/- 0.43 mm compared with 0.81 +/- 0.46 mm) and area (4.44 +/- 1.73 mm2 compared with 3.45 +/- 1.55 mm2) by IVUS and histomorphometry, respectively. Although stent length, diameter, nominal inflation pressure and time and injury score did not differ between the stents, bare Genius stents resulted in significant smaller neointimal volume compared to Tenax, polymer-coated Genius and Biodivysio stents: 24.46 +/- 4.98 mm3 compared with 59.18 +/- 26.41, 60.46 +/- 10.03 and 61.41 +/- 16.27 mm3, respectively ($P < 0.05$). CONCLUSION: The significant correlation between IVUS-guided histomorphometry and IVUS measurements confirms the usefulness of IVUS in evaluation of experimental in-stent restenosis. Implantation of bare Genius stents resulted in significant lower neointimal hyperplasia compared to Tenax, polymer-coated Genius or phosphorylcholine-coated Biodivysio stents.

Circulation 2002 Oct 22;106(17):2200-6

Serial intravascular ultrasound assessment of the efficacy of intracoronary gamma radiation for preventing recurrent in-stent restenosis.

Ahmed JM.

Intracoronary stents reduce restenosis compared with balloon angioplasty. However, a major limitation of stenting is in-stent restenosis, which occurs in 10% to 40% of the patients depending upon risk factors. Serial intravascular ultrasound studies have shown that in-stent restenosis is primarily due to neointimal hyperplasia. Treatment of in-stent restenosis is challenging and recurrence rates are high regardless of interventional technique used. Several randomized clinical trials with intracoronary ionizing radiation using both beta (b) and gamma (g) emitters following primary catheter-based intervention have demonstrated a significant reduction in recurrence. The majority of these studies have used both serial angiographic and serial intravascular ultrasound endpoints to assess the efficacy of intracoronary radiation to prevent recurrence after the treatment of in-stent restenosis. As different mechanism of postradiation restenosis may operate in the original lesion segment, the ballooned segment and the actual irradiated segment, these imaging techniques have also helped to document any long-term affects of radiation including aneurysm formation, edge effects, geographical miss, and the presence or absence of remodeling. The angiographic results have correlated well with intravascular ultrasound results after radiation therapy and at follow-up. Thus, a combination of both serial intravascular ultrasound and careful angiography, which documents balloon, stent, and radiation source positioning, can fully assess the effectiveness of this modality of treatment.

Swiss Med Wkly 2002 Jun 1;132(21-22):279-84

Impact of intracoronary ultrasound guidance on long-term outcome of percutaneous coronary interventions in diabetics--insights from the randomized SIPS trial.

Mueller C, Mc Hodgson JB, Brutsche M, Perruchoud AP, Marsch S, Hunziker P, Buettner HJ.

BACKGROUND: The Strategy for Intravascular ultrasound (IVUS) guided PTCA and Stenting (SIPS) trial included a prospectively designed subgroup analysis to investigate whether routine IVUS-guidance during percutaneous intervention improves long-term outcome in diabetics. METHODS AND RESULTS: Consecutive diabetic patients (n = 43) with 57 lesions were randomly assigned to receive provisional stenting with angiographic guidance only (ANGIO) or with IVUS guidance provided by a combined IVUS/variable diameter balloon catheter (IVUS). The combined primary endpoint included death, nonfatal myocardial infarction and target vessel revascularisation (TVR) and was recorded for 28 months. The re-stenosis rate at 6-month follow-up angiography was defined as a secondary endpoint. A primary endpoint occurred in 6 diabetic patients (31.6%) in the IVUS-group and 11 diabetic patients (45.8%) in the ANGIO-group (relative risk for IVUS, 0.83, 95% confidence interval 0.28-2.35, p = 0.83). Kaplan-Meier analysis suggested that IVUS did slightly attenuate the negative effect of diabetes on long-term event-free survival. The quantitative assessment of follow-up angiography revealed that the incidence of re-stenosis was high in both groups (IVUS: 53% versus ANGIO: 52%, p = 0.94). There was no difference in the mean duration of hospitalisation (11.8 days with IVUS versus 11.2 days with ANGIO, p = 0.83) or total cost (US dollars 16,725 with IVUS versus US dollars 16,230 with ANGIO, p = 0.83) during follow-up. CONCLUSION: Routine IVUS-guidance during provisional stenting seems to slightly attenuate the negative effect of diabetes on long-term outcome. However, the re-stenosis rate remains very high.

Am Heart J 2002 Oct;144(4):589-96

Intravascular ultrasound catheter entrapment after coronary artery stenting.

Sasseen BM, Burke JA, Shah R, Costa MA, Zenni M, Gilmore P, Bass TA.

Intracoronary ultrasound (IVUS) facilitates optimal stent deployment in the treatment of coronary artery disease, which may favorably improve long-term outcome after stenting. Complications associated with IVUS include coronary vasospasm and rarely more serious adverse events such as vessel perforation or stent deformation. We report an IVUS catheter tip entrapment within a self-deploying nitinol stent.

Catheter Cardiovasc Interv 2002 Oct;57(2):155-60

Intravascular ultrasound and quantitative coronary angiography assessment of late in-stent restenosis: in vivo human correlation and methodological implications.

Prati F, Pawlowski T, Sommariva L, Labellarte A, Manzoli A, Boccanelli A, Motolese M.

Quantitative coronary angiography (QCA) is routinely used for assessment of strategies aimed at reducing in-stent restenosis. Yet QCA enables only the measurement of luminal variation of stented segments and, unlike intravascular ultrasound (IVUS), provides only an indirect estimation of late in-stent neointimal formation, which has a key role in the process of in-stent restenosis. The aims of the present study were to correlate the IVUS measurement of in-stent intimal hyperplasia (IH) with QCA indexes of restenosis, to find out whether QCA is an adequate surrogate of IVUS, and, using either QCA and IVUS data, to define the sample sizes needed to demonstrate the effectiveness of strategies to reduce in-stent restenosis. The database of the European Imaging Laboratory was used to screen 154 stents implanted between 1997 and 2001 and studied by IVUS at 6 +/- 1 months of follow-up. All cases underwent serial QCA assessment (preintervention, postintervention, and follow-up). Only 131 cases with single stent implantation in native coronary arteries were included in the study. Stent restenosis, defined as percent diameter stenosis (DS) > 50%, was present at QCA in 69 out of 131 cases (53%). Linear regression analyses were performed to correlate the amount of IH, calculated by IVUS as the average of all cross-section areas (CSA; mean % IH CSA) and QCA indexes of restenosis (late loss and % DS). A positive significant correlation was found between IVUS mean % IH CSA and QCA % DS ($r = 0.74$; $P < 0.0001$) and between IVUS mean % IH CSA and QCA late loss ($r = 0.72$; $P < 0.0001$). Based on IVUS measurements of mean % IH CSA, a total sample size of 74 stents would be required in a two-arm comparison to have 0.80 power to detect at 0.05 significant level a 30% difference between two compared groups. Alternatively, adopting the QCA late loss, 230 stents would be required. QCA measurements of late in-stent restenosis are well correlated with IVUS calculation of in-stent neointimal formation. IVUS assessment of IH allows smaller sample sizes than QCA to document significant reductions of in-stent restenosis. Therefore, the use of IVUS should be encouraged in comparison studies aimed at revealing significant neointimal differences in small sample size populations.

Int J Cardiol 2002 Nov;86(1):99-105

Morphologic and angiographic features of coronary plaque rupture detected by intravascular ultrasound.

Maehara A, Mintz GS, Bui AB, Walter OR, Castagna MT, Canos D, Pichard AD, Satler LF, Waksman R, Suddath WO, Laird JR Jr, Kent KM, Weissman NJ.

OBJECTIVES: This study was designed to report the clinical and angiographic correlates of plaque rupture detected by intravascular ultrasound (IVUS). BACKGROUND: Acute coronary syndromes result from spontaneous plaque rupture and thrombosis. METHODS: We report 300 plaque ruptures in 257 arteries in 254 patients. Plaque ruptures were detected during pre-intervention IVUS. Standard clinical, angiographic, and IVUS parameters were collected and/or measured. One lesion per patient was analyzed. RESULTS: Multiple ruptures were observed in 39 of 254 patients (15%), 36 in the same artery. Plaque rupture occurred not only in patients with unstable angina (46%) or myocardial infarction (MI, 33%), but also stable angina (11%) or no symptoms (11%). The tear in the fibrous cap could be identified in 157 of 254 patients; 63% occurred at the shoulder of the plaque and 37% in the center of the plaque. Thrombi were more common in patients with unstable angina or MI ($p = 0.02$) and in multiple ruptures ($p = 0.04$). The plaque rupture site contained the minimum lumen area (MLA) site in only 28% of patients; rupture sites had larger arterial and lumen areas and more positive remodeling than MLA sites. Intravascular ultrasound plaque rupture strongly correlated with complex angiographic lesion morphology: ulceration in 81%, intimal flap in 40%, thrombus in 7%, and aneurysm in 7%. CONCLUSIONS: Plaque ruptures occur with varying clinical presentations, strongly correlate with angiographic complex lesion morphology, may be multiple, and usually do not cause lumen compromise.

Catheter Cardiovasc Interv 2002 Sep;57(1):2-9

A new intracoronary measurement catheter, MetriCath, compared to intravascular ultrasound and quantitative coronary angiography in a stented porcine coronary model.

van der Giessen WJ, Carlier SG, Regar E, van Beusekom HM, Foley DP, de Feyter PJ, Verdouw PD, Boersma E, Wolthuis R, Serruys PW.

The purpose of this study was to compare measurements by MetriCath to intravascular ultrasound (IVUS) and quantitative coronary angiography (QCA). The MetriCath system consists of a low-pressure (200 mm Hg) balloon catheter connected to a pressure transducer and infusion pump linked to a computer that records pressure-volume curves. Cross-sectional area of blood vessels is obtained directly from the unrestrained and in-stent pressure-volume measurements. We compared stent cross-sectional area measurements by MetriCath, IVUS, and QCA in a porcine stented coronary artery model. Comparison of area measurements in 14 stents showed no significant differences between the three methods (P = 0.66). On average, values differed 0.37 +/- 0.60 mm(2) between MetriCath and QCA, 0.13 +/- 0.55 mm(2) between MetriCath and IVUS, and 0.22 +/- 0.80 mm(2) between IVUS and QCA. This corresponds to 6.2% +/- 10%, 3.0% +/- 9.0%, and 3.1% +/- 12.9% relative difference from the average of two corresponding measurements. Linear regression analysis showed excellent correlation between measurements (r = 0.99 for all comparisons). The differences in in-stent area measurements between MetriCath and both QCA and IVUS were small. Considering the ease and rapidity of obtaining MetriCath results, this technique may form an alternative to the others in evaluating stent expansion. Based on these findings, clinical evaluation seems warranted.

Circ J 2002 Aug;66(8):735-40

Coronary disease morphology and distribution determined by quantitative angiography and intravascular ultrasound-- re-evaluation in a cooperative multicenter intravascular ultrasound study (COMIUS).

Yamagishi M, Hosokawa H, Saito S, Kanemitsu S, Chino M, Koyanagi S, Urasawa K, Ito K, Yo S, Honye J, Nakamura M, Matsumoto T, Kitabatake A, Takekoshi N, Yamaguchi T.

Although previous studies have demonstrated that even quantitative coronary angiography (QCA) can not provide accurate disease morphology, there has not been a systematic comparison of disease morphology determined by QCA and intravascular ultrasound (IVUS), particularly in Japanese patients. Therefore, the present study prospectively examined patients in a multicenter cooperative study. A total of 491 coronary sites from 562 patients (446 men, 116 women; mean age, 64+/-11 years) who underwent coronary interventions were enrolled. The target lesions (>50% diameter stenosis) were evaluated pre-operatively by both QCA and IVUS operating at 30-40 MHz and the percent area stenosis, eccentricity index (EI) and lesion length were determined. The minimal (min) and maximal (max) distances from the center of the stenotic lesion to the outline of the vessel wall were measured, and the EI was calculated by the formula: [(max - min)/max]. By QCA, lesion length was determined by measuring the distance between the proximal and distal shoulders of the lesion. When the lesions were observed by IVUS with a motorized pull-back system, the length was calculated by multiplying the time for observation of the disease and 0.5 or 1 mm/s. Although the severity of the stenosis determined by QCA (86+/-10%, mean +/- SD) did not differ from that by IVUS (83+/-13%), there was no correlation between them (r=0.32, y=0.25x+65) and the correlation did not improve when lesions with remodeling, enlargement (n=176) or shrinkage (n=79) were omitted from the calculation. The EIs by QCA and IVUS were 0.51+/-0.26 and 0.52+/-0.22, respectively (NS), and there was no correlation between them (r=0.30, y=0.36x+33). However, when the lesions with remodeling were excluded, the correlation greatly improved (r=0.80, y=0.84x+10.6, $p<0.05$). Lesion length determined by QCA (12.4+/-6.1 mm) was significantly shorter than that by IVUS (16.3+/-8.9 mm, $p<0.01$). These results demonstrate that coronary angiography significantly misinterprets disease morphology in terms of severity, eccentricity and length, in part because of vessel remodeling that can be accurately determined only by IVUS.

Vnitr Lek 2002 Jul;48(7):675-7

Intravascular ultrasound guided direct stent implantation in the treatment of significant stenosis of the left coronary artery

Veselka J, Tesar D, Eisner T, Honek T.

The authors present the case of a 52-year-old patient with the symptomatology of unstable angina pectoris where they diagnosed a major stenosis of the trunk of the left coronary artery as the only significant lesion in the coronary circulation. The patient was successfully treated by means of an intravascular ultrasound--guided coronary stent implanted into the trunk of the left coronary artery. The authors discuss the possibilities and trends of contemporary catheterization treatment of major coronary affections.

Circulation 2002 Aug 13;106(7):804-8

Multiple atherosclerotic plaque rupture in acute coronary syndrome: a three-vessel intravascular ultrasound study.

Rioufol G, Finet G, Ginon I, Andre-Fouet X, Rossi R, Vialle E, Desjoyaux E, Convert G, Huret JF, Tabib A.

BACKGROUND: To test the hypothesis of general atherosclerotic plaque destabilization during acute coronary syndrome (ACS), the present study sought to analyze the 3 coronary arteries by systematic intravascular ultrasound scan (IVUS). METHODS AND RESULTS: Seventy-two arteries were explored in 24 patients referred for percutaneous coronary intervention after a first ACS with troponin I elevation. Fifty plaque ruptures (mean, 2.08 per patient; range, 0 to 6) were diagnosed by the association of a ruptured capsule with intraplaque cavity. Plaque rupture on the culprit lesion was found in 9 patients (37.5%). At least 1 plaque rupture was found somewhere other than on the culprit lesion in 19 patients (79%). These lesions were in a different artery than the culprit artery in 70.8% and were in both other arteries in 12.5% of these 24 patients. Complete IVUS examination of all 3 coronary axes in patients who had experienced a first ACS revealed that multiple atherosclerotic plaque ruptures were detected by IVUS; these multiple ruptures were present simultaneously with the culprit lesion; they were frequent and located (in three quarters of cases) on the 3 principal coronary trunks; and the multiple plaque ruptures in locations other than on the culprit lesion were less severe, nonstenosing, and less calcified. CONCLUSION: Although one single lesion is clinically active at the time of ACS, the syndrome seems nevertheless associated with overall coronary instability.

Circulation 2002 Aug 13;106(7):798-803

Intravascular ultrasound findings in the multicenter, randomized, double-blind RAVEL (RAndomized study with the sirolimus- eluting VElocity balloon-expandable stent in the treatment of patients with de novo native coronary artery Lesions) trial.

Serruys PW, Degertekin M, Tanabe K, Abizaid A, Sousa JE, Colombo A, Guagliumi G, Wijns W, Lindeboom WK, Ligthart J, de Feyter PJ, Morice MC; RAVEL Study Group.

BACKGROUND: The goal of this intravascular ultrasound investigation was to provide a more detailed morphological analysis of the local biological effects of the implantation of a sirolimus-eluting stent compared with an uncoated stent. METHODS AND RESULTS: In the RAVEL trial, 238 patients with single de novo lesions were randomized to receive either an 18-mm sirolimus-eluting stent (Bx VELOCITY stent, Cordis) or an uncoated stent (Bx VELOCITY stent). In a subset of 95 patients (sirolimus-eluting stent=48, uncoated stent=47), motorized intravascular ultrasound pullback (0.5 mm/s) was performed at a 6-month follow-up. Stent volumes, total vessel volumes, and plaque-behind-stent volumes were comparable. However, the difference in neointimal hyperplasia (2+/-5 versus 37+/-28 mm3) and percent of volume obstruction (1+/-3% versus 29+/-20%) at 6 months between the 2 groups was highly significant (P<0.001), emphasizing the nearly complete abolition of the proliferative process inside the drug-eluting stent. Analysis of the proximal and distal edge volumes showed no significant difference between the 2 groups in external elastic membrane or lumen and plaque volume at the proximal and distal edges. There was also no evidence of intrastent thrombosis or persisting dissection at the stent edges. Although there was a higher incidence of incomplete stent apposition in the sirolimus group compared with the uncoated stent group (P<0.05), it was not associated with any adverse clinical events at 1 year. CONCLUSIONS: Sirolimus-eluting stents are effective in preventing neointimal hyperplasia without creating edge effect and without affecting the plaque burden behind the struts.

J Am Soc Echocardiogr 2002 Aug;15(8):823-30

Impact of vessel curvature on the accuracy of three-dimensional intravascular ultrasound: validation by phantoms and coronary segments.

Stahr P, Voigtlander T, Rupprecht HJ, Aschenbrucker P, Mamtimin H, Brennecke R, Otto M, Fitzgerald PJ, Meyer J.

BACKGROUND: Three-dimensional intravascular ultrasound (IVUS) is used for volumetric assessment of arteriosclerotic plaque burden and restenotic tissue at follow-up after coronary interventions. However, the accuracy of these measurements, especially in tortuous vessels, is unclear. METHODS: A commercially available electrocardiogram (ECG)-gated 3-dimensional-IVUS system was tested in volume-validated straight and curved hydrocolloid phantoms and in volume-validated coronary specimens. Catheter withdrawal (30 MHz, 3.2F) was triggered using standardized ECG source with 0.2-mm step intervals per cardiac cycle simulation. RESULTS: On the basis of automated phantom volume measurements, IVUS overestimated true phantom volume (relative error = [measured V - true V]/true V x 100) by a median of 0.9%, 0.25%, and 1.96% for straight, mildly curved, and severely curved segments, respectively. The true volume of the coronary specimens was overestimated by a median of 5.79%. CONCLUSION: A median percentage deviation of 3-dimensional-IVUS-measured volumes from the true volumes of less than 10% in phantoms and coronary artery segments can be achieved.

J Invasive Cardiol 2002 Aug;14(8):452-6

Large coronary aneurysm complicated by acute myocardial infarction: combined intravascular ultrasound imaging and doppler flow assessment before and after PTFE-covered stent implantation.

Bartorelli AL, Grancini L, Montorsi P, Trabattoni D, Fabbiocchi F.

Large aneurysm of the proximal left anterior descending (LAD) coronary artery without angiographic evidence of atherosclerotic disease. IVUS evaluation revealed an 18 mm long and 12.2 x 10.8 mm wide aneurysm without atherosclerosis, thrombus or calcification. Pulsed wave Doppler showed significant reduction of LAD flow reserve, which normalized after successful obliteration of the aneurysm with polytetrafluoroethylene (PTFE)-covered stent implantation. Severe in-stent graft restenosis was found at 7-month angiographic and intravascular ultrasound follow-up, which was managed successfully with minimally invasive direct coronary bypass surgery. The patient did well, without symptoms over the following year.

J Am Coll Cardiol 2002 Jul 17;40(2):220-7

Intravascular ultrasound evaluation of coronary plaque regression by low density lipoprotein-apheresis in familial hypercholesterolemia: the Low Density Lipoprotein-Apheresis Coronary Morphology and Reserve Trial (LACMART).

Matsuzaki M, Hiramori K, Imaizumi T, Kitabatake A, Hishida H, Nomura M, Fujii T, Sakuma I, Fukami K, Honda T, Ogawa H, Yamagishi M.

OBJECTIVES: We sought to assess the effects of low density lipoprotein (LDL)-apheresis (LDL-A) for regression of coronary plaque in familial hypercholesterolemia (FH), we set up a one-year follow-up multicenter trial using coronary angiography and intravascular ultrasound (IVUS). BACKGROUND: It is still unclear whether aggressive lipid-lowering therapy by LDL-A leads to the regression of coronary plaque in patients with FH. METHODS: Eighteen patients with FH were assigned to one of two groups: medication + LDL-A (LDL-A group, n = 11) and medication only (medication group, n = 7). Total cholesterol, triglycerides, high density lipoprotein cholesterol and LDL cholesterol were measured in all subjects at the outset of treatment (baseline) and every three months thereafter. Coronary angiography and IVUS were performed at the outset and after the one-year follow-up period to measure minimal lumen diameter (MLD) by coronary angiogram and plaque area (PA) by IVUS. RESULTS: The LDL-A group showed 28.4% reduction in total cholesterol (from 275 +/- 27 mg/dl to 197 +/- 19 mg/dl) and 34.3% reduction in LDL cholesterol (from 213 +/- 25 mg/dl to 140 +/- 27 mg/dl) after one-year follow-up, while the medication group showed no changes in cholesterol levels. There were significant interactions between both treatments in total cholesterol ($p = 0.0001$), LDL cholesterol ($p = 0.0001$), MLD ($p = 0.008$) and PA ($p = 0.017$) using two-way repeated-measures analysis of variance by the SAS system (SAS Institute Inc., Cary, North Carolina). Significant differences were seen in net change in MLD ($p = 0.004$) and PA ($p = 0.008$) during the one-year follow-up period between both groups. CONCLUSIONS: These results suggest that aggressive lipid-lowering therapy using the combination of LDL-A and lipid-lowering drugs may induce regression of coronary atherosclerotic plaque in FH patients.

Am J Cardiol 2002 Jul 1;90(1):19-23

Discrimination of early/intermediate and advanced/complicated coronary plaque types by radiofrequency intravascular ultrasound analysis.

Stahr PM, Hofflinghaus T, Voigtlander T, Courtney BK, Victor A, Otto M, Yock PG, Brennecke R, Fitzgerald PJ.

Radiofrequency intravascular ultrasound (IVUS-RF) analysis, as an extension of conventional IVUS imaging, may provide more accurate plaque discrimination. Thirty-two autopsy atherosclerotic coronary arteries were investigated. Corresponding sectors in different plaques were matched by histologic and RF analysis. Histologic analysis utilized the American Heart Association plaque classification. The backscattered ultrasound RF signal was analyzed by fast-Fourier transform, providing the underlying frequency components of its power spectrum. The normalized backscattered signal power (in decibels [dB]) for frequencies between 15.3 and 40.3 MHz was then measured for plaque discrimination. Advanced/complicated plaque types showed a higher signal power at all frequencies than early/intermediate lesion types ($p < 0.001$ to $p = 0.005$). Discrimination of advanced/complicated lesion types was best at 15.3 MHz, with a cut-off point of 2.5 dB (sensitivity 93%, specificity 79%), and second best at 17.6 MHz (sensitivity 87%, specificity 71%, cut-off point 1.9 dB). With conventional IVUS, plaque discrimination was weaker; the best sensitivity for diagnosing early/intermediate lesion types was reached for "soft plaque" (sensitivity 63%, specificity 73%). Compared with conventional IVUS, IVUS-RF can discriminate between advanced/complicated and early/intermediate coronary atherosclerotic lesions with relatively high sensitivity and specificity in vitro.

Am J Cardiol 2002 Jun 15;89(12):1360-4

Relation of stent design and stent surface material to subsequent in-stent intimal hyperplasia in coronary arteries determined by intravascular ultrasound.

Hoffmann R, Mintz GS, Haager PK, Bozoglu T, Grube E, Gross M, Beythien C, Mudra H, vom Dahl J, Hanrath P.

A variety of different stent designs and coatings have become available. This study sought to determine the impact of stent design and gold-coating of stents on intimal hyperplasia (IH) in human atherosclerotic coronary arteries in relation to known predictors of restenosis. Angiographic and intravascular ultrasound (IVUS) studies were performed at 6-month follow-up on 311 native coronary lesions of 311 patients treated with 99 Multi-Link stents, 74 InFlow steel stents, 73 InFlow gold-coated stents, 41 Palmaz-Schatz stents, 12 NIR steel stents, and 12 gold-coated NIR Royal stents. Lumen and stent cross-sectional area (CSA) were measured at 1-mm axial increments. Mean IH CSA (stent CSA - lumen CSA) and mean IH thickness were calculated and averaged over the total stent length. IVUS demonstrated different levels of IH for the 6 stents. Mean IH thickness ranged from 0.20 +/- 0.13 mm for Multi-Link stents to 0.43 +/- 0.14 mm for InFlow goal-coated stents ($p < 0.001$). Multivariate analysis proved non-Multi-Link stent design (odds ratio 3.45, 95% confidence intervals 1.13 to 11.11, $p < 0.034$) and gold coating (odds ratio 3.78, 95% confidence intervals 1.88 to 7.54, $p < 0.001$) to be the only independent predictors of IH thickness >0.3 mm. In conclusion, stent design and surface material have an important impact on the IH response to stents implanted in human coronary arteries. However, the differences in IH thickness between the analyzed stents were relatively small compared with the absolute lumen dimensions.

J Invasive Cardiol 2002 Jun;14(6):315-20

In vivo quantitative tissue characterization of human coronary arterial plaques by use of integrated backscatter intravascular ultrasound and comparison with angioscopic findings.

Kawasaki M, Takatsu H, Noda T, Sano K, Ito Y, Hayakawa K, Tsuchiya K, Arai M, Nishigaki K, Takemura G, Minatoguchi S, Fujiwara T, Fujiwara H.

BACKGROUND: The purpose of the present study was to define whether integrated backscatter (IB) combined with conventional intravascular ultrasound (IVUS) makes tissue characterization of coronary arterial plaques possible. METHODS AND RESULTS: IB-IVUS was performed in coronary arteries (total 18 segments) of 9 patients at autopsy, and the findings were compared with the histology. RF signals, which were digitized at 2 GHz in 8-bit resolution, were obtained with an IVUS system with a 40-MHz catheter. IB values of the RF signal from the region of interest (ROI) (100-microm depth, 1.4 degrees per line) were calculated by use of a personal computer. IB values on the ROIs were divided into 5 categories, compared with each of the plaque histologies: category 1 (thrombus), -88 < IB < or = -80; category 2 (intimal hyperplasia or lipid core), -73 < IB < or = -63; category 3 (fibrous tissue), -63 < IB < or = -55; category 4 (mixed lesions), -55 < IB < or = -30; and category 5 (calcification), -30 < IB < or = -23. On the basis of these categories, we analyzed 5120 ROIs per segment in each ring-like arterial specimen. Color-coded maps of plaques were constructed by use of these IB data and conventional IVUS data, which reflected the plaque histology of autopsied coronary arteries well. Then, the same method was undertaken in 24 segments with plaque from 12 patients in vivo with angina pectoris. Comparisons between coronary angioscopy and IB-IVUS revealed that the surface color of plaques in angioscopy reflected the thickness of the fibrous cap rather than the size of the lipid core. CONCLUSIONS: IB-IVUS represents a new and useful tool for evaluating the tissue structure of human coronary arterial plaques

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Outcome of nonobstructive residual dissections detected by intravascular ultrasound following percutaneous coronary intervention.

Nishida T, Colombo A, Briguori C, Stankovic G, Albiero R, Corvaja N, Finci L, Di Mario C, Tobis JM.

The purpose of this study was to assess the outcome of nonobstructive (or non-flow-limiting) residual dissection (RD) after percutaneous coronary intervention. Results of 124 consecutive native coronary lesions with angiographic nonobstructive RD in 97 patients (RD group) were compared with outcomes of 124 lesions without RD in 100 patients (non-RD group), whose characteristics were matched with those of the RD group. RD occurred after stent implantation (81 of 124 lesions, 65%) or balloon angioplasty (43 of 124 lesions, 35%). Angiographic types of RD were type A in 8 lesions (6%), B in 101 (82%), and C in 15 (12%). Stents were implanted in 65% of the lesions in each group. Clinical success (94% in RD group vs 95% in non-RD group, p = 0.77) and the in-hospital major adverse cardiac event rates were found to be similar in the 2 groups (6% vs 3%, respectively; p = 0.33). The late angiographic and clinical outcomes were also comparable. By intravascular ultrasound (IVUS) evaluation of the dissections in the RD group, area stenosis correlated with the incidence of in-hospital major adverse cardiac events (p = 0.023), whereas the final minimal lumen area correlated inversely with the occurrence of restenosis (p = 0.011). An area stenosis > or =58% was the best predictor for the incidence of in-hospital major adverse cardiac events (sensitivity 0.68, specificity 0.68). Most nonobstructive RDs are "favorable" and do not need stent implantation. IVUS evaluation identifies "unfavorable" nonobstructive (or non-flow-limiting) dissections that might be prone to acute occlusion. Nonobstructive dissections can be left untreated when final IVUS reveals an area stenosis of < 60% at the site of a dissection.

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Impact of the cross-sectional geometry of the post-deployment coronary stent on in-stent neointimal hyperplasia: an intravascular ultrasound study.

Murata T, Hiro T, Fujii T, Yasumoto K, Murashige A, Kohno M, Yamada J, Miura T, Matsuzaki M.

To establish the relationship between the cross-sectional geometry of the post-deployment stent and the degree of in-stent neointimal hyperplasia (INH), intravascular ultrasound (IVUS) was used to examine cross-sections of the coronary arteries from 23 patients with coronary stents 6 months after implantation. Stent cross-sectional area (Sa) and stent perimeter (Sp) from 200 stent cross-sections, and the stent radius (Sr) and thickness of INH (Id) of 2,880 radial axes, were measured, and the mean degree of roundness (Rd) of stent cross-section was calculated for each stent as Rd=4piSa/Sp2. The degree of deformity (Df) of the stent cross-section was also calculated by comparing it with a hypothetical circle (the area of this hypothetical circle was equal to the Sa): Df=Sr/R, where R is the radius of the hypothetical circle. The area of INH was significantly larger in the Rd<0.87 group (n=84) than in the Rd> or =0.87 group (n=116) (3.83+/-1.26 vs 3.16+/-1.32 mm2, p<0.0005). There were significant differences in the thickness of INH among the 3 groups classified by the value of Df (Df<0.95: n=425, 0.21+/-0.12mm; 0.95< or =Df<1.05: n=2008, 0.29+/-0.15mm; Df> or =1.05: n=447, 0.34+/-0.15mm, overall p<0.0001). These data suggest that in-stent neointimal proliferation is more likely to occur in stented coronary arteries with a more oval than rounded cross-section, and particularly within the more pronounced and curved portion of the oval.

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Rapid evolution from coronary dissection to pseudoaneurysm after stent implantation: a glimpse at the pathogenesis using intravascular ultrasound.

Cafri C, Gilutz H, Kobal S, Esanu G, Weinstein JM, Abu-Ful A, Ilia R.

Coronary dissection during angioplasty can evolve into pseudoaneurysm. Stenting should prevent this complication. We present a case of coronary pseudoaneurysm after dissection that developed despite stent implantation. Intravascular ultrasound demonstrated no sealing of the false lumen due to undersizing and non-apposition to the wall by the stent

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Incidence, morphology, angiographic findings, and outcomes of intramural hematomas after percutaneous coronary interventions: an intravascular ultrasound study.

Maehara A, Mintz GS, Bui AB, Castagna MT, Walter OR, Pappas C, Pinnow EE, Pichard AD, Satler LF, Waksman R, Suddath WO, Laird JR Jr, Kent KM, Weissman NJ.

BACKGROUND: Intramural hematomas during percutaneous coronary intervention (PCI) have not been well studied. METHODS AND RESULTS: We used intravascular ultrasound to determine the incidence, morphology, and clinical features of post-PCI intramural hematomas. In 905 patients with 1025 consecutive native coronary artery, non-in-stent restenosis lesions undergoing PCI, 72 hematomas were detected in 69 arteries in 68 patients. The incidence of intramural hematomas per artery was 6.7% (69 of 1025); 36% (26 of 72) involved the proximal reference artery, 18% (13 of 72) were confined to the lesion, and 46% (33 of 72) involved the distal reference artery. The entry site from the lumen into the hematoma was identified in 86% of hematomas (62 of 72) and had the appearance of a dissection into the media. Conversely, a re-entry site was identifiable in only 8% (6 of 72). The axial extension of the hematoma was distal in 63% and proximal in 37%. In 60% of the hematomas (42 of 72) the angiogram had the appearance of a dissection; in 11% (8 of 72), it appeared to be a new stenosis; and in 29% (22 of 72), no significant abnormality was detected. Non-Q-wave myocardial infarctions occurred in 26% of patients (17 of 65). In 3 patients, the creatine kinase-MB was not measured during the hospital stay. Repeat revascularization occurred in 2 patients in-hospital, 2 additional patients at 1 month, and 8 additional patients at 1 year. There were 3 sudden deaths at 1 year. CONCLUSIONS: Intravascular ultrasound identified intramural hematomas after 6.7% of PCIs. The mechanism appeared to be a dissection into the media where blood accumulated because of a lack of re-entry. A third of ultrasound-identified hematomas showed no angiographic abnormalities. There was a high rate of non-Q-wave myocardial infarction, need for repeat revascularization, and sudden death in patients with hematomas.

Catheter Cardiovasc Interv 2002 May;56(1):40-5

Comparison of the self-expanding Radius stent and the balloon-expandable Multilink stent for elective treatment of coronary stenoses: a serial analysis by intravascular ultrasound.

Yu ZX, Tamai H, Kyo E, Kosuga K, Hata T, Okada M, Nakamura T, Komori H, Tsuji T, Takeda S, Motohara S, Uehata H.

We compared the outcome of the self-expanding Radius stent and the balloon-expandable Multilink stent serially by angiography and intravascular ultrasound. Successful stent deployment was achieved in 66 lesions of 56 stable angina patients (34 lesions with Radius stents and 32 lesions with Multilink stents). At follow-up, there were no significant differences in minimal lumen diameter or percent diameter stenosis between the groups, nor in restenosis rates, although the Radius stent group rate was slightly lower (23.5% vs. 31.3%). In the Radius stent group, stent cross-sectional area (CSA) increased gradually after implantation until the 6-month follow-up (8.37 +/- 1.83 to 10.16 +/- 2.59 mm(2); n = 15), giving a larger CSA (P = 0.03) than the Multilink stent group, which decreased (9.00 +/- 2.05 to 8.27 +/- 2.15 mm(2); n = 17). The lumen CSA was also slightly larger (6.82 +/- 3.06 vs. 5.84 +/- 1.85 mm(2); P = 0.29) in the Radius stent group. These findings indicated that the Radius stent enlarged progressively after implantation, which might be useful for prevention of restenosis.

Ital Heart J 2002 Jan;3(1 Suppl):71-7

Coronary angioplasty in women: risk factors and sex-related differences in coronary anatomy evaluated with intravascular ultrasonography

Petronio AS, Musumeci G, Limbruno U, Baglini R, Amoroso G, Merelli A, Mariani M.

BACKGROUND: The aim of this study was to evaluate the risk factors for cardiovascular diseases, clinical presentation and coronary anatomical size differences in women. METHODS: From January 1999 to December 2000, 244 female and 980 male patients were submitted to coronary angioplasty (PTCA). For both groups the following were considered: risk factors for cardiovascular diseases, clinical presentation and angiographic data. The clinically confirmed 6 months restenoses were evaluated. We performed intravascular ultrasound (IVUS) with three-dimensional reconstruction and quantitative coronary angiography (QCA) on the proximal left anterior descending (LAD) coronary artery segments free of significant atherosclerosis in 60 men and 50 women matched for age and clinical characteristics. The arterial and luminal areas were measured by planimetry and corrected for body surface area. We also evaluated the external elastic membrane diameter (EEMd), the minimal lumen diameter (MLD) and the intima-media thickness (IMT). RESULTS: At the time of admission, women were older than men, were shorter, weighed less, and had a smaller body surface area; they had more severe angina, diabetes mellitus and hypercholesterolemia. There was no difference between women and men in the incidence of clinical restenosis at 6 months of follow-up. At IVUS, the mean uncorrected LAD arterial area was smaller in women than in men (12.7 +/- 3 vs 15.9 +/- 3.3 mm2, $p < 0.05$), as was the mean LAD luminal area (9.9 +/- 3 vs 12.9 +/- 2.7 mm2, $p < 0.005$). Both the MLD and the EEMd as well as the IMT were smaller in women than in men (MLD 3.3 +/- 0.6 vs 3.9 +/- 0.5 mm, $p < 0.05$; EEMd 3.7 +/- 0.6 vs 4.2 +/- 0.4 mm, $p < 0.005$; IMT 0.29 +/- 0.1 vs 0.4 +/- 0.1 mm, $p < 0.05$). QCA confirmed the IVUS results (MLD 2.9 +/- 0.6 vs 3.5 +/- 0.8 mm, $p < 0.05$). After correction for body surface area, univariate associations between sex and both the arterial and luminal areas were no longer present. CONCLUSIONS: Women submitted to PTCA were older. The incidence of hypertension, diabetes mellitus and hypercholesterolemia was higher than in men. There was no sex difference in the rate of clinical restenosis at 6 months of follow-up. The LAD artery is smaller in women, independently of body size. This suggests an intrinsic sex effect on coronary dimensions.

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Application of intravascular ultrasound to characterize coronary artery disease and assess the progression or regression of atherosclerosis.

Nissen SE.

Angiography has major limitations in its ability to assess coronary disease. Intravascular ultrasound (IVUS) offers unique capabilities to assess coronary atherosclerotic burden. The tomographic orientation of ultrasound enables visualization of the full vessel wall, as opposed to the 2-dimensional projection of the lumen provided by angiography. The equipment required to perform coronary IVUS consists of a catheter with a miniaturized transducer and a console to reconstruct the image. High ultrasound frequencies are used, typically, 30 to 40 MHz, which provides excellent theoretical resolution. IVUS has been performed safely in a wide variety of clinical situations. Vessels with classic atherosclerosis exhibit a diversity of abnormal features that reflect the severity, composition, and distribution of the atheromata. Plaque rupture is sometimes evident in ultrasound examination of the culprit lesions after an acute coronary syndrome. Most laboratories routinely perform cross-sectional area measurements of the lumen and external elastic membrane boundaries and calculate atheroma area. IVUS commonly detects atherosclerosis at angiographically normal sites. It has contributed substantially to our understanding of remodeling and has shown that positive remodeling is more prevalent in unstable lesions. Studies in patients early after transplantation have shown the presence of advanced atherosclerosis in their apparently normal donors. In addition, the application of IVUS in detecting the rate of progression or regression of existing atherosclerosis is among the most dynamic areas of development. IVUS is likely to emerge as the "gold standard" in the study of atherosclerosis progression-regression over the next few years.

J Diabetes Complications 2002 Jan-Feb;16(1):50-5

Impact of insulin resistance on neointimal tissue proliferation after coronary stent implantation. Intravascular ultrasound studies.

Takagi T, Akasaka T, Yamamuro A, Honda Y, Hozumi T, Morioka S, Yoshida K.

Serial intravascular ultrasound (IVUS) studies in 55 nondiabetic patients showed that neointimal tissue proliferation after stent implantation in patients with impaired glucose tolerance (IGT) was greater than that in patients with normal glucose tolerance at follow-up. Multiple regression analysis showed that the sum of insulin levels was the best predictor of the greater neointimal index at follow-up. Another group of serial IVUS studies were performed in 62 stented lesions in 52 patients with Type 2 diabetes mellitus (DM). The study patients were randomized into a troglitazone group and a control group. The neointimal tissue proliferation at follow-up in the troglitazone group was significantly smaller than that in the control group.

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Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound.

Jang IK, Bouma BE, Kang DH, Park SJ, Park SW, Seung KB, Choi KB, Shishkov M, Schlendorf K, Pomerantsev E, Houser SL, Aretz HT, Tearney GJ.

OBJECTIVES: The aim of this study was to evaluate the feasibility and the ability of intravascular optical coherence tomography (OCT) to visualize the components of coronary plaques in living patients. BACKGROUND: Disruption of a vulnerable coronary plaque with subsequent thrombosis is currently recognized as the primary mechanism for acute myocardial infarction. Although such plaques are considered to have a thin fibrous cap overlying a lipid pool, imaging modalities in current clinical practice do not have sufficient resolution to identify thin (< 65 microm) fibrous caps. Optical coherence tomography is a new imaging modality capable of obtaining cross-sectional images of coronary vessels at a resolution of approximately 10 microm. METHODS: The OCT images and corresponding histology of 42 coronary plaques were compared to establish OCT criteria for different types of plaques. Atherosclerotic lesions with mild to moderate stenosis were identified on angiograms in 10 patients undergoing cardiac catheterization. Optical coherence tomography and intravascular ultrasound (IVUS) images of these sites were obtained in all patients without complication. RESULTS: Comparison between OCT and histology demonstrated that lipid-rich plaques and fibrous plaques have distinct OCT characteristics. A total of 17 IVUS and OCT image pairs obtained from patients were compared. Axial resolution measured 13 +/- 3 microm with OCT and 98 +/- 19 microm with IVUS. All fibrous plaques, macrocalcifications and echolucent regions identified by IVUS were visualized in corresponding OCT images. Intimal hyperplasia and echolucent regions, which may correspond to lipid pools, were identified more frequently by OCT than by IVUS. CONCLUSIONS: Intracoronary OCT appears to be feasible and safe. Optical coherence tomography identified most architectural features detected by IVUS and may provide additional detailed structural information.

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Use of preintervention intravascular ultrasound in patients with acute myocardial infarction.

Tanaka A, Kawarabayashi T, Taguchi H, Nishibori Y, Sakamoto T, Nishida Y, Yoshikawa J.

This study was designed to determine whether preintervention intravascular ultrasound (IVUS) imaging can assist in predicting the likelihood of acute coronary occlusion after primary angioplasty. Primary angioplasty is in widespread use for the treatment of acute myocardial infarction (AMI), although its usefulness is sometimes compromised by postprocedural acute coronary occlusion. If preintervention IVUS could be used to predict acute coronary occlusion, the task of determining treatment strategies for AMI would be significantly eased. Preintervention IVUS was performed without complications in 46 patients with AMI using manually prepared contrast medium. Coronary angiography was performed 1 hour after successful percutaneous transluminal coronary angioplasty. Acute coronary occlusion was seen in 13 of 46 patients (28%). There were no differences in the clinical characteristics and angiographic results between the patients with and without occlusion. In patients with acute occlusion, the incidence of eccentric plaque (85% vs 36%, $p < 0.01$) and echolucent area (92% vs 15%, $p < 0.01$) was significantly higher than in the occlusion-free patients. Most of the echolucent areas were associated with eccentric plaques (88%). Eccentric plaques characterized by echolucent areas are prone to acute occlusion after primary balloon angioplasty for AMI. Preintervention IVUS is both a safe and a useful adjunct to primary angioplasty.

Eur Heart J 2002 Feb;23(3):247-54

Discrepancy between angiography and intravascular ultrasound when analysing small coronary arteries.

Briguori C, Tobis J, Nishida T, Vaghetti M, Albiero R, Di Mario C, Colombo A.

AIMS: A small reference diameter may be the consequence of high plaque burden and diffuse disease. The reference vessel diameter in small coronary arteries may vary according to the method of measurement used. We endeavoured to confirm the difference between data from examinations conducted using angiography with that revealed by intravascular ultrasound. METHODS AND RESULTS: Between March 1993 and October 1999, 344 consecutive patients with 419 lesions in small vessels (< or =2.75 mm, Small group) and 953 patients with 1161 lesions in large vessels (Large group) underwent intravascular ultrasound-guided percutaneous transluminal angioplasty in our Institution. The mean difference between the intravascular ultrasound and the angiographic reference diameter (Delta(IVUS-Angio)) was 1.3+/-0.5 mm in the Small group and 1.0+/-0.6 mm in the Large group (P<0.001). There was a stronger correlation between plaque burden and Delta(IVUS-Angio)in the Small group (r=0.80, P<0.001) than in the Large group (r=0.59, P<0.001). An Delta(IVUS-Angio)> or =0.30 mm occurred in 99.5% of cases in the Small group and in 90% in the Large group (P<0.001). An Delta(IVUS-Angio)> or =0.50 mm occurred in 96% of case in the Small group and 80% in the Large group (P<0.001). Predictors of Delta(IVUS-Angio)> or =0.50 in the Small group were: proximal or middle lesion site, vessel type (left anterior descending artery, diagonal and obtuse marginal branches) and female sex. An Delta(IVUS-Angio)> or =1.0 mm occurred in 71% of cases in the Small group and in 49% in the Large group (P<0.001). Predictors of Delta(IVUS-Angio)> or =1.0 mm in the Small group were: proximal or middle lesion site, female sex, and lesion length. CONCLUSIONS: A high percentage of vessels measuring < or =2.75 mm are large vessels with a high plaque burden. This condition is particularly prevalent in females, with lesions in the proximal or middle left anterior descending artery, and in obtuse marginal and diagonal branches.

Z Kardiol 2002;91 Suppl 3:89-97

Ten years after introduction of intravascular ultrasound in the catheterization laboratory: tool or toy?

Regar E, Serruys PW.

Intravascular ultrasound (IVUS) represents the gold standard in the assessment of atherosclerotic disease. It has deeply affected our understanding of coronary artery disease and therapeutic strategies. We learned that a phenomenon described in pathologic series plays a very important role during life--that of vessel remodeling. The type of remodeling (positive or negative) cannot been assessed by angiography but is clinically relevant for optimal, procedural lumen gain. The modern stent implantation technique with a high balloon to artery ratio and high balloon pressure is the result of the IVUS finding that the majority of stents are not optimally deployed despite appropriate angiographic results. IVUS is essential in the clinical practice for the assessment of ambiguous angiography, left main stem disease, complex lesion and in-stent restenosis. Furthermore, IVUS has become an indispensable research tool in the analysis of new therapeutic strategies such as coronary brachytherapy.

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Intravascular ultrasound-guided balloon angioplasty compared with stent: immediate and 6-month results of the multicenter, randomized Balloon Equivalent to Stent Study (BEST).

Schiele F, Meneveau N, Gilard M, Boschat J, Commeau P, Ming LP, Sewoke P, Seronde MF, Mercier M, Gupta S, Bassand JP; Balloon Equivalent to Stent Study.

BACKGROUND: Balloon angioplasty guided by intravascular ultrasound (IVUS) makes it possible to choose the balloon size according to the true vessel diameter and to detect suboptimal results requiring subsequent stent implantation. The Balloon Equivalent to STent (BEST) study aimed to assess whether this strategy would give the same results as systematic stenting. METHODS AND RESULTS: A total of 132 of 254 patients were randomized to IVUS-guided percutaneous transluminal coronary angioplasty (aggressive PTCA), and 122 were randomized to stenting (stent group). We hypothesized that a difference of <8% in the 6-month angiographic restenosis rate (primary end point) could be considered noninferior. The aggressive PTCA procedure was longer and had a greater use of contrast medium than stenting. In the aggressive PTCA group, crossover to stent was needed in 58 patients (44%). At 6 months, 20 of 119 patients (16.8+/-6.7%) in the aggressive PTCA group and 21 of 116 patients (18.1+/-7.0%) in the stent group had restenosis. The difference was -1.3%, with an upper limit of 95% confidence interval of 7.1% (ie, less than the noninferiority boundary). The in-stent restenosis rate was higher in the stent group (15.5% versus 5%; P=0.02). The differences in minimum lumen diameter, lumen cross-section area, and 1-year event rate were not significant. CONCLUSIONS: A strategy of IVUS-guided angioplasty with provisional stenting is feasible and safe. At the cost of a more complex procedure, it reduces the stent rate by half, with similar 6-month angiographic IVUS and clinical outcome compared with stent implantation.

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J Am Coll Cardiol , 2001;37(5):1329-34

Long-term vessel response to a self-expanding coronary stent: a serial volumetric intravascular ultrasound analysis from the ASSURE Trial.A Stent vs. Stent Ultrasound Remodeling Evaluation.

Kobayashi Y, Honda Y, Christie GL, Teirstein PS, Bailey SR, Brown CL 3rd, Matthews RV, De Franco AC, Schwartz RS, Goldberg S, Popma JJ, Yock PG, Fitzgerald PJ.

OBJECTIVES: We sought to investigate the in vivo mechanical properties of a new self-expanding coronary stent (RADIUS) and, particularly, the subsequent vessel response over time. BACKGROUND: Preclinical studies have suggested that self-expanding stents may produce less vessel wall injury at initial deployment, leading to larger follow-up lumens than with balloon-expandable stents. However, the influence of the chronic stimulus from self-expanding stents on the vessel wall remains unknown. METHODS: Sixty-two patients were randomly assigned to either the RADIUS self-expanding stent group (n = 32) or the Palmaz-Schatz balloon-expandable stent group (n = 30). Intravascular ultrasound was performed after stent deployment and at six-month follow-up. RESULTS: At follow-up, the RADIUS stents had increased 23.6% in overall volume, while the Palmaz-Schatz stents had remained unchanged. Due to the greater mean neointimal area (3.0 +/- 1.7 mm2 vs. 1.9 +/- 1.2 mm2, p = 0.02) in the RADIUS group, no significant difference in net late lumen loss was observed between the two groups. On the other hand, analysis at the peristent margins demonstrated that mean late loss was significantly smaller in the RADIUS group than it was in the Palmaz-Schatz group (0.1 +/- 2.1 mm2 vs. 1.9 +/- 2.4 mm2, p = 0.02). CONCLUSIONS: Serial volumetric IVUS revealed that the RADIUS stents continued to enlarge during the follow-up period. In this stent implantation protocol, this expansion was accompanied by a greater amount of neointima than the Palmaz-Schatz stents, resulting in similar late lumen loss in both configurations. In the peristent margins, however, late lumen loss was minimized with the RADIUS stents.

Catheter Cardiovasc Interv , 2001;52(4):420-4

Intravascular ultrasound findings in patients with abnormal coronary flow reserve after stenting.

Muramatsu T, Tsukahara R, Ho M, Ito Y, Ishimori H, Saiki N.

A coronary flow reserve (CFR) of 2.0 has been advocated as the endpoint for coronary intervention therapy. Experience shows, however, that CFR does indeed exceed 2.0 in many cases poststenting, while remaining below 2.0 in others. In this study, we assessed the clinical characteristics and IVUS findings of patients whose CFR remained below 2.0 after stent implantation, specifically 16 patients with CFR below 2.0 (22 lesions, 64 +/- 9 years, 4 female), and 102 patients with CFR above 2.0 (112 lesions, mean age 66 +/- 11 years, 22 female). Patient population comprised patients selected for retrospective study, but participants were selected on the basis of matching patient and lesion characteristics. The IVUS findings showed that incidence of calcified lesions and post-PTCA dissection of hard plaque were higher among patients with CFR < 2.0. Further, IVUS-obtained vascular measurements showed post-PTCA area stenosis to be 58.7 +/- 15.2% in the CFR < 2.0 group, and 45.3 +/- 12.5% among CFR > or = 2.0 patients (P < 0.05). These findings indicate that patients with diffuse calcified lesions or high post-PTCA % area stenosis, as determined by IVUS, are more likely to have lower CFR after stenting.

Am J Cardiol , 2001 ;87:1246-9

Usefulness of intravascular ultrasound in preventing stenting of hazy areas adjacent to coronary stents and its support of support spot-stenting.

Grewal J, Ganz P, Selwyn A, Kinlay S.

The uncertain significance of hazy areas at the margins of coronary stents may lead to further, at times unnecessary, stenting. However, the risk of restenosis increases substantially when additional stents are deployed. We used intravascular ultrasound (IVUS) to identify the causes of hazy segments adjacent to stents. We identified 13 cases with hazy regions adjacent to coronary stents and 20 controls without hazy regions matched by age, gender, and vessel stented. Hazy regions were defined from the angiogram as reduced contrast density without a clearly defined intimal tear, dissection, thrombus, or stenosis (> 50%). IVUS images

were obtained from the reference, stent, and hazy and control regions adjacent to the stent. Computerized planimetery was used to measure the vessel, lumen, and plaque cross-sectional areas (CSAs), the maximum arc of calcium, and the eccentricity ratio (minimum:maximum lumen diameter). There were no significant differences between hazy and control segments in the vessel, lumen, and plaque CSAs. All lumen CSAs were >4.0 mm2. Compared with control regions, the hazy regions had calcified plaque more often (69% vs 25%; odds ratio [OR] 6.75, 95% confidence intervals [CI] 1.82 to 25.0]) and more frequent intimal tears (23% vs 0%, OR 6.67, 95% CI 1.98 to 35.0). Haziness was particularly associated with calcified plaque and eccentric lumen ($p = 0.037$). Thus, haziness at the margins of coronary stents is often caused by calcified plaque. IVUS can differentiate calcified plaques from intimal tears and thereby obviate unnecessary stenting.

J Am Coll Cardiol , 2001;37(7):1864-70

Plaque distribution and vascular remodeling of ruptured and nonruptured coronary plaques in the same vessel: an intravascular ultrasound study in vivo.

von Birgelen C, Klinkhart W, Mintz GS, Papatheodorou A, Herrmann J, Baumgart D, Haude M, Wieneke H, Ge J, Erbel R.

OBJECTIVES: This study was designed to identify potential differences between the intravascular ultrasound (IVUS) characteristics of spontaneously ruptured and nonruptured coronary plaques. BACKGROUND: The identification of vulnerable plaques in vivo may allow targeted prevention of acute coronary events and more effective evaluation of novel therapeutic approaches. METHODS: Intravascular ultrasound was used to identify 29 ruptured plaques in arteries containing another nonruptured plaque in an adjacent segment. Intravascular ultrasound characteristics of these plaques were compared with plaques of computer-matched controls without evidence of plaque rupture. Plaque distribution was assessed by measuring the eccentricity of lumen location (inside the total vessel). Lumen cross-sectional area narrowing was calculated as [1 - (target/reference lumen area)] x 100%. A remodeling index was calculated as lesion/reference arterial area (>1.05 = compensatory enlargement, <0.95 = shrinkage). RESULTS: Among the three groups of plaques, there was no significant difference in quantitative angiographic parameters, IVUS reference dimensions and IVUS lumen cross-sectional area narrowing. There was a difference in plaque distribution; lumen location by IVUS was significantly more eccentric in ruptured than in nonruptured ($p = 0.002$) and control plaques ($p < 0.0001$). The arc of disease-free vessel wall was larger in ruptured than in control plaques ($p < 0.0001$). The remodeling

pattern of ruptured and nonruptured plaques differed significantly from that of the control plaques (p = 0.0001 and 0.003); compensatory enlargement was found in 66%, 48%, and 17%, whereas shrinkage was found in 7%, 10% and 48%, respectively. CONCLUSIONS: Intravascular ultrasound assessment of plaque distribution and vascular remodeling may help to classify plaques with the highest probability of spontaneous rupture

Circulation 2001 ;104(8):856-9

Serial intravascular ultrasound assessment of the efficacy of intracoronary gamma-radiation therapy for preventing recurrence in very long, diffuse, in-stent restenosis lesions.

Ahmed JM, Mintz GS, Waksman R, Mehran R, Leiboff B, Pichard AD, Satler LF, Kent KM, Weissman NJ.

BACKGROUND: The efficacy of coronary gamma-irradiation in preventing recurrent in-stent restenosis (ISR) is well established. However, brachytherapy may be less effective in very long, diffuse ISR lesions. METHODS AND RESULTS: We used serial intravascular ultrasound (IVUS) to study patients with long, diffuse ISR lesions (length, 36 to 80 mm) who were enrolled in (1) Long WRIST (Washington Radiation In-Stent Restenosis Trial), a double-blind, placebo-controlled trial of intracoronary gamma-irradiation (15 Gy at 2 mm from the source) and (2) high-dose (HD) Long WRIST, a registry that used a dose prescription of 18 Gy at 2 mm from the source. IVUS was performed using automated pullback (0.5 mm/s). Stent, lumen, and intimal hyperplasia were measured at 2-mm intervals. Complete postintervention and follow-up IVUS imaging was available in 30 irradiated and 34 placebo patients from Long WRIST and in 25 patients from HD Long WRIST. Stent length was longer in HD Long WRIST than in placebo or treated patients in Long WRIST (P=0.0064 and P=0.0125, respectively). Otherwise, baseline measurements were similar. At follow-up, the minimum lumen area was largest in the HD Long WRIST patients (4.0+/-1.4 mm(2)); areas were 2.9+/-1.0 mm(2) in irradiated patients in Long WRIST and 1.9+/-1.1 mm(2) in placebo patients in Long WRIST (P<0.005 for all comparisons). CONCLUSIONS:- Serial IVUS analysis shows that gamma-irradiation reduces recurrent in-stent neointimal hyperplasia in long, diffuse ISR lesions; however, it is even more effective when given at a higher dose.

Circulation , 2001 ;104(16):1917-22

Fractional flow reserve compared with intravascular ultrasound guidance for optimizing stent deployment.

Fearon WF, Luna J, Samady H, Powers ER, Feldman T, Dib N, Tuzcu EM, Cleman MW, Chou TM, Cohen DJ, Ragosta M, Takagi A, Jeremias A, Fitzgerald PJ, Yeung AC, Kern MJ, Yock PG

BACKGROUND: Determination of fractional flow reserve (FFR) has been proposed as a means to assess stent deployment. In this prospective, multicenter trial, we evaluate the use of FFR to optimize stenting by comparing it with standard intravascular ultrasound (IVUS) criteria. METHODS AND RESULTS: Eighty-four stable patients with isolated coronary lesions underwent coronary stent deployment starting at 10 atm and increased serially by 2 atm until the FFR was >/=0.94 or 16 atm was achieved. IVUS was then performed. FFR was measured with a coronary pressure wire with intracoronary adenosine to induce hyperemia. The diagnostic characteristics of an FFR <0.94 to predict suboptimal stent expansion by IVUS, defined in both absolute and relative terms, were calculated. Over a range of IVUS criteria, the highest sensitivity, specificity, and predictive accuracy of FFR were 80%, 30%, and 42%, respectively. Receiver operator characteristic analysis defined an optimal FFR cut point at >/=0.96; at this threshold, the sensitivity, specificity, and predictive accuracy of FFR were 75%, 58%, and 62%, respectively (P=0.03 for comparison of predictive accuracy, P=0.01 for concordance between FFR and IVUS). The negative predictive value was 88%. Significantly better diagnostic performance was achieved in a subgroup that received higher doses (>30 microgram) of intracoronary adenosine during pressure measurements, suggesting that FFR might be overestimated in the other group. CONCLUSIONS: A fractional flow reserve <0.96, measured after stent deployment, predicts a suboptimal result based on validated intravascular ultrasound criteria; however, an FFR >/=0.96 does not reliably predict an optimal stent result. Higher doses of intracoronary adenosine than previously used to measure FFR improve these results.

J Am Coll Cardiol , 2001 ;38(5):1427-33

Intravascular ultrasound-guided percutaneous transluminal coronary angioplasty with provisional spot stenting for treatment of long coronary lesions.

Colombo A, De Gregorio J, Moussa I, Kobayashi Y, Karvouni E, Di Mario C, Albiero R, Finci L, Moses J.

OBJECTIVES: The purpose of this study was to evaluate the approach of intravascular ultrasound (IVUS)-guided percutaneous transluminal coronary angioplasty (PTCA) with spot stenting (SS) for the treatment of long coronary lesions. BACKGROUND: Treating long coronary lesions with balloon angioplasty results in suboptimal short- and long-term outcomes. Full lesion coverage with traditional stenting (TS) has been associated with a high restenosis rate. METHODS: We prospectively evaluated a consecutive series of 130 long lesions (>15 mm) in 101 patients treated with IVUS-guided PTCA and SS. The results were compared with those of TS in a matched group of patients. Coronary angioplasty was performed with a balloon to vessel ratio of 1:1, according to the IVUS media-to-media diameter of the vessel at the lesion site, to achieve prespecified IVUS criteria: lumen cross-sectional area (CSA) > or =5.5 mm(2) or > or =50% of the vessel CSA at the lesion site. The stents were implanted only in the vessel segment where the criteria were not met. RESULTS: In the SS group, stents were implanted in 67 of 130 lesions, and the mean stent length was shorter than that of lesions in the matched TS group (10.4 +/- 13 mm vs. 32.4 +/- 13 mm, $p < 0.005$). The 30-day major adverse cardiac event (MACE) rate was similar (5%) for both groups. Angiographic restenosis was 25% with IVUS-guided SS, as compared with 39% in the TS group ($p < 0.05$). Follow-up MACE and target lesion revascularization rates were lower in the SS group than in the TS group (22% vs. 38% [$p < 0.05$] and 19% vs. 34% [$p < 0.05$], respectively). CONCLUSIONS: Intravascular ultrasound-guided SS for the treatment of long coronary lesions is associated with good acute outcome. Angiographic restenosis and follow-up MACE rates were significantly lower than those with TS.

Am J Cardiol , 2001 ;88(10A):7M-20M

Coronary intravascular ultrasound: implications for understanding the development and potential regression of atherosclerosis.

De Franco AC, Nissen SE.

The incremental value of intravascular ultrasound (IVUS), compared with angiographic analysis of coronary atherosclerosis, originates principally from 2 key features-its tomographic perspective and the ability to image coronary atheroma directly. Whereas angiography depicts the cross-sectional coronary anatomy as a planar silhouette of the lumen, ultrasound directly images the atheroma within the vessel wall, allowing measurement of atheroma size, distribution, and to some extent, composition. Although angiography remains the principal method to assess the extent of coronary atherosclerosis and to guide percutaneous coronary interventions,

IVUS is rapidly altering conventional paradigms in the diagnosis and therapy of coronary artery disease. Thus, IVUS has become a vital adjunctive imaging modality for the aggressive coronary interventional cardiologist. As such, ultrasound has earned a role as a viable complementary technique relative to angiography, rather than an alternative to conventional angiographic methods. This article reviews the rationale, technical advantages and limitations, and interpretation of intravascular ultrasonography from the perspective of the general and invasive cardiologist. We emphasize the impact that IVUS studies have had on our understanding of the atherosclerotic coronary artery disease process, because these findings have important implications for all cardiologists. We then review several trials that are currently using intravascular ultrasonography for the study of coronary artery disease regression.
J Am Coll Cardiol , 2001 ;38(5):1427-33

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J Am Coll Cardiol , 2001 ;38(6):1622-7

Optimizing stent expansion with new stent delivery systems.

Takano Y, Yeatman LA, Higgins JR, Currier JW, Ascencio E, Kopelson KA, Tobis JM.

OBJECTIVES: The purpose of this study was to assess whether the newer stent delivery systems provide a stented lumen cross-sectional area (CSA) that is equal to the delivery balloon nominal dimensions. BACKGROUND: First generation stents were often not adequately expanded with their delivery system and frequently required higher pressure or a larger balloon after deployment. Newer stents were designed to optimize expansion with noncompliant, high-pressure balloons provided as the delivery systems. METHODS: Intravascular ultrasound (IVUS) was used to evaluate 38 stents in 32 patients after deployment at 14 to 16 atm with their delivery balloon system. Minimum stent lumen CSA and stent minimum lumen diameter (MLD) were measured by IVUS imaging. The manufacturer? expected stent diameter was defined as the balloon diameter measured by the company at the maximum pressure used. The manufacturer? expected stent area was calculated based on the manufacturer? expected stent diameter. RESULTS: The MLD (2.5 +/- 0.5 mm) and minimum stent CSA (6.0 +/- 1.7 mm(2)) by IVUS were significantly smaller than the manufacturer? expected stent diameter (3.5 +/- 0.4 mm) and area (9.5 +/- 1.9 mm(2)) ($p < 0.0001$, respectively). The mean MLD by IVUS was 72 +/- 8% of the expected stent diameter, and the mean minimum stent CSA by IVUS was 62 +/- 10% of the expected stent area. CONCLUSIONS: Despite moderately high-pressure inflations, the mean minimum stent CSA actually achieved was, on average, only 62% of the manufacturer? expected stent area. To optimize stent deployment, these IVUS observations should be considered during coronary artery stenting.

J Am Coll Cardiol , 2001;38(7):2001-5

Impact of pre-interventional arterial remodeling on subsequent vessel behavior after balloon angioplasty: a serial intravascular ultrasound study.

Okura H, Hayase M, Shimodozono S, Bonneau HN, Yock PG, Fitzgerald PJ.

OBJECTIVES: The purpose of this study was to assess the impact of pre-intervention arterial remodeling on subsequent vessel behavior following balloon angioplasty. BACKGROUND: Positive arterial remodeling before intervention has been shown to have a negative impact on the clinical outcome after nonstented coronary interventional procedures. However, the mechanism of interventions in coronary vessel geometry over time is less well characterized. METHODS: Serial (pre-, post- and follow-up) intravascular ultrasound analysis was performed in 46 native coronary lesions. Positive remodeling (PR) was defined as vessel area (VA) at the target lesion greater than that of average reference segments. Intermediate or negative remodeling (IR/NR) was defined as VA at the target lesion less than or equal to that of average reference segment. Remodeling index was defined as VA at the target lesion site divided by that of average references. RESULTS: Pre-interventional PR and IR/NR were present in 21 (46%) and 25 (54%) of 46 patients, respectively. At follow-up, the change in plaque area was similar between the two groups (1.3 +/- 2.1 vs. 1.2 +/- 2.1 mm(2), p = 0.840). Lesions with PR showed a significantly smaller change in VA than those with IR/NR (-0.2 +/- 2.5 vs. 1.4 +/- 2.3 mm(2), p = 0.03). As a result, late lumen loss was significantly larger in lesions whose pre-intervention configuration exhibited PR (-1.5 +/- 1.8 vs. 0.2 +/- 1.6 mm(2), p = 0.002). CONCLUSIONS: Lesions with PR appear to have less capacity to compensate for further plaque growth after balloon angioplasty and thus show a proportional increase in late lumen loss. This may in part explain the less favorable clinical outcomes of positively remodeled lesions.

J Am Coll Cardiol, 2001 ;38(7):1866-71

Do beta-adrenergic blocking agents increase coronary flow reserve?

Billinger M, Seiler C, Fleisch M, Eberli FR, Meier B, Hess OM.

BACKGROUND: Beta-adrenergic blocking agents are the cornerstone in the treatment of coronary artery disease (CAD). The exact pathophysiologic mechanism is not clear but depends largely on the oxygen-sparing effect of the drug. Thus, the effect of metoprolol on coronary flow reserve and coronary flow velocity reserve (CFVR) was determined in patients with CAD. METHODS: Coronary blood flow velocity was measured with the Doppler flow wire in 23 patients (age: 56 +/- 10) undergoing percutaneous transluminal coronary angioplasty for therapeutic reasons. Measurements were carried out at rest, after 1-min vessel occlusion (postischemic CFVR) as well as after intracoronary adenosine (pharmacologic CFVR) before and after 5 mg

intravenous metoprolol. In a subgroup (n = 15), absolute flow was measured from coronary flow velocity multiplied by coronary cross-sectional area. RESULTS: Rate-pressure product decreased after metoprolol from 9.1 to 8.0 x 10(3) mm Hg/min ($p < 0.001$). Pharmacologic CFVR was 2.1 at rest and increased after metoprolol to 2.7 ($p = 0.002$). Likewise, postischemic CFVR increased from 2.6 to 3.3 ($p < 0.001$). Postischemic CFVR was significantly higher than pharmacologic CFVR before as well as after metoprolol. Coronary vascular resistance decreased after metoprolol from 3.4 +/- 2.0 to 2.3 +/- 0.7 mm Hg x s/cm ($p < 0.02$). CONCLUSIONS: The following conclusions were drawn from this study. Metoprolol is associated with a significant increase in postischemic and pharmacologic CFVR. However, postischemic CFVR is significantly higher than pharmacologic CFVR. The increase in CFVR by metoprolol can be explained by a reduction in vascular resistance. The increase in CFVR (= increased supply) and the reduction in oxygen consumption (= decreased demand) after metoprolol explain the beneficial effect of this beta-blocker in patients with CAD.
Am Heart J, 2001 ;142(6):970-4

The contribution of ?echanical?problems to in-stent restenosis: An intravascular ultrasonographic analysis of 1090 consecutive in-stent restenosis lesions.

Castagna MT, Mintz GS, Leiboff BO, Ahmed JM, Mehran R, Satler LF, Kent KM, Pichard AD, Weissman NJ.

OBJECTIVES: Serial intravascular ultrasonographic (IVUS) studies have shown that in-stent restenosis is the result of intimal hyperplasia (IH). However, routine preintervention IVUS imaging has suggested that many restenotic stents were inadequately deployed. The purpose of this IVUS study was to determine the incidence of mechanical problems contributing to in-stent restenosis (ISR). METHODS: Between April 1994 and June 2000, 1090 patients with ISR were treated at the Washington Hospital Center. All underwent preintervention IVUS imaging. IVUS measurements included proximal and distal reference lumen areas and diameters; stent, minimum lumen, and IH (stent minus lumen) areas; and IH burden (IH/stent area). RESULTS: In 49 ISR lesions (4.5%), there were morphologic findings that contributed to the restenosis. These were termed mechanical complications. Examples include (1) missing the lesion (eg, an aorto-ostial stenosis), (2) stent ?rush,?and (3) having the stent stripped off the balloon during the implantation procedure. Excluding mechanical complications, stent underexpansion was common. In 20% of the ISR cases the stents had a cross-sectional area (CSA) at the site of the lesion <80% of the average reference lumen area. Twenty percent of lesions had a minimum stent area <5.0 mm(2) and an additional 18% had a minimum stent area of 5.0 to 6.0 mm(2). Twenty-four percent of lesions had an IH burden <60%. CONCLUSION: Mechanical problems related to stent deployment procedures contribute to a significant minority of ISR lesions (approximately 25%).

Circulation , 2002 ;105(8):939-43

Relationship between coronary artery remodeling and plaque vulnerability.

Varnava AM, Mills PG, Davies MJ.

BACKGROUND: In vivo studies with intravascular ultrasound have shown that complex plaque anatomy and plaque rupture are more frequent in the presence of marked outward remodeling. A large lipid core and a high macrophage count are recognized histological markers for plaque vulnerability. The link between plaque vulnerability in terms of these markers and remodeling in coronary arteries has not been explored. METHODS AND RESULTS: In 88 male subjects who died suddenly with coronary artery disease, 108 plaques were studied. The percent remodeling was calculated. Lesions with remodeling > or = 0% were considered to have positive remodeling, and those in which remodeling was < 0% were considered to have negative remodeling. Percent lipid core and macrophage count at the plaque were assessed. Of 108 plaque sites, 64 (59.2%) had undergone no remodeling or positive remodeling, and 44 (40.7%) had negative remodeling (vessel shrinkage). Lesions with positive remodeling, compared with lesions with vessel shrinkage, had a larger lipid core (percent mean lipid core was 39.0 +/- 21.0% versus 22.3 +/- 23.1%, respectively; P < 0.0001) and a higher macrophage count (mean macrophage count was 15.6 +/- 12.3 versus 8.9 +/- 11.6, respectively; P = 0.005). CONCLUSIONS: We have shown that coronary artery plaques with positive remodeling have a higher lipid content and macrophage count, both markers of plaque vulnerability. These results may explain why plaque rupture is often apparent at sites with only modest luminal stenoses (but marked positive remodeling).

Circulation, 1995;91:1959-1965

Patterns of Calcification in Coronary Artery Disease
A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions

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Background. Target lesion calcium is a marker for significant coronary artery disease and a determinant of the success of transcatheter therapy.

Methods and Results. Eleven hundred fifty-five native vessel target lesions in 1117 patients were studied by intravascular ultrasound (IVUS) and coronary angiography. The presence, magnitude, location, and distribution of IVUS calcium were analyzed and compared with the detection and classification (none/mild, moderate, and severe) by angiography. Angiography detected calcium in 440 of 1155 lesions (38%): 306 (26%) moderate calcium and 134 (12%) severe. IVUS detected lesion calcium in 841 of 1155 (73%, P<.0001 versus angiography). The mean arc of lesion calcium measured 115±110°; the mean length measured 3.5±3.7 mm. Target lesion calcium was only superficial in 48%, only deep in 28%, and both superficial and deep in 24%. The mean arc of superficial calcium measured 85±108°; the mean length measured 2.4±3.4 mm. Three hundred seventy-three of 1155 reference segments (32%) contained calcium (P<.0001 compared with lesion site). The mean arc of reference calcium measured 42±80°; the mean length measured 1.7±3.6 mm. Only 44 (4%) had reference calcium in the absence of lesion calcium. Angiographic detection and classification of calcium depended on arcs, lengths, location, and distribution of lesion and reference segment calcium. By discriminant analysis, the classification function for predicting angiographic calcium included the arc of target lesion calcium, the arc of superficial calcium, the length of reference segment calcium, and the location of calcium within the lesion. This model correctly predicted the angiographic detection of calcification in 74.4% of lesions and the angiographic classification (none/moderate/severe) of calcium in 62.8% of lesions.

Conclusions. IVUS detected calcium in >70% of lesions, significantly more often than standard angiography. Although angiography is moderately sensitive for the detection of extensive lesion calcium (sensitivity, 60% and 85% for three- and four-quadrant calcium, respectively), it is less sensitive for the presence of milder degrees.

Circulation, 1996;94:35-43

Arterial Remodeling After Coronary Angioplasty
A Serial Intravascular Ultrasound Study

Gary S. Mintz, MD; Jeffrey J. Popma, MD; Augusto D. Pichard, MD; Kenneth M. Kent, MD, PhD; Lowell F. Satler, MD; S. Chiu Wong, MD; Mun K. Hong, MD; Julie A. Kovach, MD; Martin B. Leon, MD

Background. Restenosis occurs after 30% to 50% of transcatheter coronary procedures; however, the natural history and pathophysiology of restenosis are still incompletely understood.

Methods and Results. Serial (postintervention and follow-up) intravascular ultrasound imaging was used to study 212 native coronary lesions in 209 patients after percutaneous transluminal coronary angioplasty, directional coronary atherectomy, rotational atherectomy, or excimer laser angioplasty. The external elastic membrane (EEM) and lumen cross-sectional areas (CSA) were measured; plaque plus media (P+M) CSA was calculated as EEM minus lumen CSA. The anatomic slice selected for serial analysis had an axial location within the target lesion at the smallest follow-up lumen CSA. At follow-up, 73% of the decrease in lumen (from 6.6±2.5 to 4.0±3.7 mm2, P<.0001) was due to a decrease in EEM (from 20.1±6.4 to 18.2±6.4 mm2, P<.0001); 27% was due to an increase in P+M (from 13.5±5.5 to 14.2±5.4 mm2, P<.0001). (Lumen CSA correlated more strongly with (EEM CSA (r=.751, P<.0001) than with △P+M CSA (r=.284, P<.0001). (EEM was bidirectional; 47 lesions (22%) showed an increase in EEM. Despite a greater increase in P+M (1.5±2.5 versus 0.5±2.0 mm2, P=.0009), lesions exhibiting an increase in EEM had (1) no change in lumen (-0.1±3.3 versus 3.6±2.3 mm2, P<.0001), (2) a reduced restenosis rate (26% versus 62%, P<.0001), and (3) a 49% frequency of late lumen gain (versus 1%, P<.0001) compared with lesions with no increase in EEM.

Conclusions. Restenosis appears to be determined primarily by the direction and magnitude of vessel wall remodeling (△EEM). An increase in EEM is adaptive, whereas a decrease in EEM contributes to restenosis.

Summary

Circulation, 1996;94:1247-1254

Patterns and Mechanisms of In-Stent Restenosis
A Serial Intravascular Ultrasound Study

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Background Studies have suggested that restenosis within Palmaz-Schatz stents results from neointimal

hyperplasia or chronic stent recoil and occurs more frequently at the articulation.
Methods and Results Serial intravascular ultrasound (IVUS) was performed after intervention and at follow-up in 142 stents in 115 lesions. IVUS measurements (external elastic membrane [EEM], stent, and lumen cross-sectional areas [CSAs] and diameters) were performed, and plaque CSA (EEM lumen in reference segments and stent lumen in stented segments), late lumen loss ((lumen), remodeling ((EEM in reference segments and (stent in stented segments), and tissue growth ((plaque) were calculated. After intervention, the lumen tended to be smallest at the articulation because of tissue prolapse. At follow-up, tissue growth was uniformly distributed throughout the stent; the tendency for greater neointimal tissue accumulation at the central articulation reached statistical significance only when normalized for the smaller postintervention lumen CSA. In stented segments, late lumen area loss correlated strongly with tissue growth but only weakly with remodeling. Stents affected adjacent vessel segments; remodeling progressively increased and tissue growth progressively decreased at distances from the edge of the stent. These findings were similar in native arteries and saphenous vein grafts and in lesions treated with one or two stents. There was no difference in the postintervention or follow-up lumen (at the junction of the two stents) when overlapped were compared with nonoverlapped stents.
Conclusions Late lumen loss and in-stent restenosis were the result of neointimal tissue proliferation, which tended to be uniformly distributed over the length of the stent.

Summary

1. After intervention, the lumen tended to be smallest at the articulation because of tissue prolapse.
2. At follow-up, tissue growth was uniformly distributed throughout the stent.
3. In stented segments, late lumen area loss correlated strongly with tissue growth but only weakly with remodeling.
4. Remodeling progressively increased and tissue growth progressively decreased at distances from the edge of the stent.

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Intravascular Ultrasound Predictors of Restenosis After Percutaneous Transcatheter Coronary Revascularization

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Objectives. This study sought to evaluate preintervention and postintervention intravascular ultrasound studies for potential predictors of angiographic restenosis and to use ultrasound predictors of restenosis to enhance our understanding of the pathopysiology of the restenosis disease process.

Background. Restenosis remains the major limitation of percutaneous transcatheter coronary revascularization. Although its mechanisms remain incompletely understood, numerous studies have identified some of the clinical, anatomic and procedural risk factors for restenosis. Intravascular ultrasound imaging of target lesions before and after catheter-based treatment consistently demonstrates more target lesion calcium, more extensive reference segment atherosclerosis, smaller final lumen dimensions, significant residual plaque burden and a greater degree of tissue trauma than is evident by angiography.

Methods. Intravascular ultrasound studies were performed in 360 nonstented native coronary artery lesions (final diameter stenosis 18±11%) in 351 patients for whom follow-up angiographic data were available 6.4±3.6 months later. Hospital charts were reviewed, and qualitative and quantitative coronary angiographic and intravascular ultrasound analyses were performed by independent core laboratories. Four dependent angiographic end points were tested: restenosis as a binary definition (≥50% diameter stenosis at follow-up) was the primary end point; follow-up diameter stenosis, late lumen loss and follow-up minimal lumen diameter were the secondary end points.

Results. Reference vessel size, the preintervention quantitative coronary angiographic assessment of lesion severity and the postintervention intravascular ultrasound cross-sectional measurements predicted the late angiographic results. In particular, the intravascular ultrasound postintervention cross-sectional narrowing (plaque plus media cross-sectional area divided by external elastic membrane cross-sectional area) predicted the primary end point (restenosis) and two of the three secondary end points (follow-up diameter stenosis and late lumen loss) and was therefore the most consistent predictor of restenosis.

Conclusions. Intravascular ultrasound variables are more powerful and consistent predictors of angiographic restenosis than currently accepted clinical or angiographic risk factors.

Summary

1. Multivariate predictors of restenosis: IVUS reference lumen CSA($p<0.001$), QCA diameter stenosis($p<0.01$), postintervension IVUS CSN($p<0.001$)

2. Multivariate predictors of F/U diameter stenosis: QCA MLD($p<0.001$), postintervention IVUS CSN($p<0.001$)

3. Multivariate predictors of late lumen loss: QCA DS($p<0.05$), postintervention QCA DS($p<0.001$), postintervention IVUS CSN($p<0.05$)

4. Multivariate predictors of F/U MLD: QCA ref diameter($p<0.05$), IVUS ref lumen CSA($p<0.01$), QCA MLD($p<0.001$), IVUS EEM CSA($p<0.001$), IVUS lumen CSA($p<0.001$)

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Intravascular Ultrasound Findings After Successful Primary Angioplasty for Acute Myocardial Infarction: Predictors of Abrupt Occlusion

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Objectives. This study sought to evaluate the intravascular structure as depicted by intravascular ultrasound after successful primary angioplasty (i.e., without thrombolytic therapy) for acute myocardial infarction and to investigate the related predictors of acute coronary occlusion.

Background. The usefulness of primary angioplasty for acute myocardial infarction is still limited by early reocclusion. There are few data regarding the intravascular ultrasound findings after primary angioplasty.

Methods. Intravascular ultrasound was performed in 27 patients after successful primary angioplasty. Repeat coronary angiography was performed 15 min later, on the following day and 1 month after angioplasty.

Results. Abrupt occlusion occurred in 8 of 27 patients. Angiographic variables in patients with versus those without abrupt occlusion were not significantly different. Intravascular ultrasound disclosed a significantly smaller lumen area ([mean ± SD] 2.49 ± 0.72 vs. 5.06 ± 1.52 mm2, $p < 0.001$) and a significantly greater percent plaque area (80.5 ± 9.1% vs. 63.7 ± 7.8%, $p < 0.001$) in patients with abrupt occlusion. There was no significant difference in external elastic membrane cross-sectional area. We classified the ultrasound appearance of the intravascular structure as smooth, irregular or filled. Abrupt occlusion occurred in none of 6 patients with a smooth intravascular structure, 24% of 17 patients with an irregular structure and in all 4 with a filled structure ($p < 0.05$). In the latter group, the lumen was filled with bright speckled or low echogenic material, although angiography revealed excellent coronary dilation in all these arteries.

Conclusions. Intravascular ultrasound revealed a narrow lumen in coronary arteries showing abrupt occlusion after successful primary angioplasty, even though angiography disclosed successful dilation. Arteries with a lumen filled with bright speckled or low echogenic material frequently develop abrupt occlusion.

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Remodeling of Human Coronary Arteries Undergoing Coronary Angioplasty or Atherectomy

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Background. Recently, long-term constriction of the vessel has been suggested as an alternative mechanism of restenosis after coronary angioplasty.

Methods and Results. To understand remodeling of human coronary arteries undergoing coronary angioplasty or atherectomy, serial intravascular ultrasonographic examinations were performed at preintervention and postintervention examinations and at 24 hours, 1 month, and 6 months. Complete serial data were obtained in 61 lesions (balloon angioplasty, 35 lesions; directional atherectomy, 26 lesions). Lumen area improved from 6.81 ±2.24 mm2 after intervention to 8.22±2.79 mm2 at 1 month (P=.0001) and decreased to 4.88±2.86 mm2 at 6 months (P=.0001). Vessel area enlarged from 17.32±5.35 mm2after intervention to 19.39±5.33 mm2 at 1 month (P=.0001) and decreased to 16.33±5.54 mm2 at 6 months (P=.0001). Plaque+media area increased significantly from postintervention examination to 24 hours (10.51±4.38 versus 10.96±4.49 mm2, P=.0008) and from 24 hours to 6 months (10.96±4.49 versus 11.45±4.45 mm2, P=.03). Changes in lumen area in each study interval correlated more closely with changes in vessel area than with changes in plaque+media area. Restenotic lesions compared with nonrestenotic lesions had a greater decrease in the vessel area between 1 month and 6 months (-4.33±2.73 versus -2.49±2.15 mm2, P=.006) and greater increase in the plaque+media area both within 24 hours (0.84±1.22 versus 0.27±0.38 mm2, P=.04) and between 24 hours and 6 months (1.19±2.19 versus 0.18±1.46 mm2, P=.04). Conclusions. Remodeling after coronary angioplasty or atherectomy was characterized by early adaptive enlargement and late constriction of the vessel.

Summary

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Intimal hyperplasia thickness at follow-up is independent of stent size: a serial intravascular ultrasound study

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The purpose of this study was to determine whether the thickness of the intimal hyperplasia (IH) layer that accumulates within Palmaz-Schatz stents is dependent on stent size. Intravascular ultrasound (IVUS) and quantitative angiographic (QCA) studies were performed after stent implantation and at follow-up (5.4 ± 3.8 months) in 161 patients with 177 lesions treated with 221 Palmaz-Schatz stents. Stent and lumen cross-sectional area (CSA) were measured. IH CSA and thickness at follow-up were calculated and compared with stent CSA and circumference. Maximum IH CSA and thickness were measured at the smallest follow-up lumen CSA; mean IH CSA and thickness was averaged over the length of the stent. Maximum IH CSA measured 4.8 ± 2.4 mm2, and mean IH CSA measured 2.8 ± 2.2 mm2. Maximum IH thickness (at the smallest follow-up lumen CSA) measured 0.60 ± 0.36 mm, and mean IH thickness (over the length of the stent) measured 0.30 ± 0.19 mm. There was a weak, but significant correlation between mean and maximum IH CSA versus stent CSA ($r = 0.215$, $p < 0.0001$ and $r = 0.355$, $p < 0.0001$, respectively). However, there was no correlation between mean or maximum IH thickness versus stent CSA ($r = 0.018$, $p = 0.643$ and $r = 0.056$, $p = 0.463$, respectively) or stent circumference ($r = 0.002$, $p = 0.956$ and $r = 0.069$, $p = 0.361$, respectively). IH thickness was found to be independent of the stent size. This explains the known higher frequency of restenosis in smaller stents compared with larger stents.

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Serial volumetric (threedimensional) intravascular ultrasound analysis of restenosis after directional coronary atherectomy

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Objectives. We report the use of three-dimensional (volumetric) intravascular ultrasound (IVUS) analysis to assess serial changes after directional coronary atherectomy (DCA).
Background. Recent serial planar IVUS studies have described a decrease in external elastic membrane (EEM) area following catheter-based intervention as an important mechanism of late lumen renarrowing.
Methods. Thirty-one patients with de novo native coronary lesions treated with DCA in the Serial Ultrasound Restenosis (SURE) Trial and in Optimal Atherectomy Restenosis Study (OARS) were enrolled in this study. Serial IVUS was performed before and after intervention and at 6 months' follow-up. In a subgroup of 18 patients from the SURE trial, IVUS was also performed at 24 h and at 1 month postintervention. Segments, 20-

mm-long (200 image slices), were analyzed using a previously validated three-dimensional, computerized, automated edge-detection algorithm. The EEM, lumen, and plaque+media (P+M = EEM-lumen) volumes were calculated.

Results. At follow-up, lumen volume was smaller than at postintervention (159 ± 69 mm3 vs. 179 ± 49 mm3, $p = 0.0003$). From postintervention to follow-up, there was a decrease in EEM volume (377 ± 107 to 352 ± 125 mm3, $p < 0.0001$), but no change in P+M volume ($p = 0.52$). The △lumen volume correlated strongly with △ EEM volume ($r = 0.842$, $p < 0.0001$), but not with △P+M volume. In the 18 patients from the SURE Trial, the decrease in lumen and EEM volumes occurred late, between 1 month and 6 months of follow-up.

Conclusions. Volumetric IVUS analysis demonstrated that late lumen volume loss following DCA was a result of a decrease in EEM volume. This was a late event, occurring between 1 and 6 months' postintervention.

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Relation of arterial geometry to luminal narrowing and histologic markers for plaque vulnerability: the remodeling paradox

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Objective. To relate local arterial geometry with markers that are thought to be related to plaque rupture.

Background. Plaque rupture often occurs at sites with minor luminal stenosis and has retrospectively been characterized by colocalization of inflammatory cells. Recent studies have demonstrated that luminal narrowing is related with the mode of atherosclerotic arterial remodeling.

Methods. We obtained 1,521 cross section slices at regular intervals from 50 atherosclerotic femoral arteries. Per artery, the slices with the largest and smallest lumen area, vessel area and plaque area were selected for staining on the presence of macrophages (CD68), T-lymphocytes (CD45RO), smooth muscle cells (alpha-actin) and collagen.

Results. Inflammation of the cap or shoulder of the plaque was observed in 33% of all cross sections. Significantly more CD68 and CD45RO positive cells, more atheroma, less collagen and less alpha-actin positive staining was observed in cross sections with the largest plaque area and largest vessel area vs. cross sections with the smallest plaque area and smallest vessel area, respectively. No difference in the number of inflammatory cells was observed between cross sections with the largest and smallest lumen area.

Conclusion. Intraindividually, pathohistologic markers previously reported to be related to plaque vulnerability were associated with a larger plaque area and vessel area. In addition, inflammation of the cap and shoulder of the plaque was a common finding in the atherosclerotic femoral artery.

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Quantitative Coronary Angiographic and Intravascular Ultrasound Assessment of a New Nonarticulated Stent: Report From the Advanced Cardiovascular Systems MultiLink Stent Pilot Study

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Objectives. The purpose of this study was to evaluate the safety, feasibility, optimal deployment technique and 1-year clinical outcome for the Advanced Cardiovascular Systems (ACS) MultiLink stent.

Background. Optimal stent deployment assessed by quantitative coronary angiography and intravascular ultrasound (IVUS) is associated with improved clinical outcome.

Methods. Forty-nine consecutive patients with a discrete stenosis in a native coronary artery 3 to 4 mm in diameter were treated with the new, balloon-expandable ACS MultiLink stent. Stent expansion was assessed in all patients using quantitative coronary angiography and serial IVUS imaging after 8-, 12- and 16-atm inflations. Clinical follow-up was obtained at 30 days and 1 year.

Results. All 49 patients had successful placement of a MultiLink stent without death, emergency coronary artery bypass graft surgery or Q wave myocardial infarction. After placement of the MultiLink stent, the minimal lumen diameter increased from 1.24 to 2.98 mm ($p < 0.001$), and diameter stenosis decreased from 61% to 7% ($p = 0.001$). Minimal lumen cross-sectional area by IVUS increased progressively after 8, 12 and 16 atm (5.6 to 6.8 to 7.4 mm2, respectively, $p < 0.001$). However, only 64% of stents achieved a lumen/reference area ratio$\geq$70%. No adverse clinical events occurred by 30 days, and by 1 year only one patient (2.0%) required revascularization of the stented artery

Conclusions. Treatment of stenoses in native coronary arteries with the MultiLink stent is associated with a high success rate and a low incidence of adverse events by 1 year, despite the fact that the majority of stents did not meet IVUS-defined criteria for ?ptimal stenting?derived from first-generation devices.

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Intravascular Ultrasound Predictors of Angiographic Restenosis in Lesions Treated With Palmaz-Schatz Stents

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Objectives. This study sought to evaluate the clinical, procedural, preinterventional and postinterventional quantitative coronary angiographic (QCA) and intravascular ultrasound (IVUS) predictors of restenosis after Palmaz-Schatz stent placement.

Background. Although Palmaz-Schatz stent placement reduces restenosis compared with balloon angioplasty, in-stent restenosis remains a major clinical problem.

Methods. QCA and IVUS studies were performed before and after intervention (after stent placement and high pressure adjunct balloon angioplasty) in 382 lesions in 291 patients treated with 476 Palmaz-Schatz stents for whom follow-up QCA data were available 5.5 ± 4.8 months (mean ± SD) later. Univariate and multivariate predictors of QCA restenosis (≥50% diameter stenosis at follow-up, follow-up percent diameter stenosis [DS] and follow-up minimal lumen diameter [MLD]) were determined.

Results. Three variables were the most consistent predictors of the follow-up angiographic findings: ostial lesion location, IVUS preinterventional lesion site plaque burden (plaque/total arterial area) and IVUS assessment of final lumen dimensions (whether final lumen area or final MLD). All three variables predicted both the primary (binary restenosis) and secondary (follow-up MLD and follow-up DS) end points. In addition, a number of variables predicted one or more but not all the end points: 1) restenosis (IVUS preinterventional lumen and arterial area); 2) follow-up DS (QCA lesion length); and 3) follow-up MLD (QCA lesion length and preinterventional MLD and DS and IVUS preinterventional lumen and arterial area).

Conclusions. Ostial lesion location and IVUS preinterventional plaque burden and postinterventional

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Impact of intravascular ultrasound guidance in stent deployment on 6-month restenosis rate: a multicenter, randomized study comparing two strategies-with and without intravascular ultrasound guidance

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Objectives. We aimed to investigate the impact of intravascular ultrasound (IVUS)-guided stent implantation on the 6-month restenosis rate, which has not yet been fully established in randomized trials.
Background. The 6-month angiographic restenosis rate was compared in patients with symptomatic ischemic heart disease who were randomly allocated to angioplasty and stent deployment, with versus without IVUS guidance.
Methods. After successful stent implantation, patients were randomized into two groups: Group A had no further dilation, and Group B had additional balloon dilation until achievement of IVUS criterion for stent expansion. The study group consisted of 164 patients, assuming a 50% reduction of the restenosis rate in Group B (15% vs. 30%) (alpha = 10%, beta = 20%).
Results. We enrolled 155 patients. Overdilation was carried out in 31 (39%) of 79 Group B patients, with the IVUS criterion being achieved in 63 (80%) of 79. No significant difference was observed in the minimal luminal diameter (MLD), but the stent lumen cross-sectional area (CSA) was significantly larger in Group B (mean ± SD) (7.16 ± 2.48 vs. 7.95 ± 2.21 mm2, p = 0.04). At 6 months, there was no significant difference in the restenosis rate, (28.8% [21 of 73] in Group A vs. 22.5% [16 of 71] in Group B, p = 0.25), but according to the observed difference in the restenosis rate, the power of the study was only 40%. The difference in MLD was also nonsignificant (1.60 ± 0.65 mm in Group A vs. 1.70 ± 0.64 mm in Group B, p = 0.20), whereas the lumen CSA was 20% larger in the IVUS-guided group (4.47 ± 2.59 vs. 5.36 ± 2.81 mm2, p = 0.03). Lumen CSA was the only predictor of restenosis by multivariate logistic regression analysis.
Conclusions. A nonsignificant 6.3% absolute reduction in the restenosis rate and a nonsignificant difference in MLD were observed in this study. Nonetheless, we still cannot rule out a beneficial effect of IVUS guidance, although this may have gone undetected owing to a lack of statistical power. A significant increase was observed in immediate and 6-month lumen size, as detected by IVUS, indicating that ultrasound guidance in stent deployment may be beneficial.

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Remodeling of In-Stent Neointima, Which Became Thinner and Transparent Over 3 Years : Serial Angiographic

and Angioscopic Follow-up

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Background-Recently, it has been reported that the luminal diameter shows phasic changes after stenting: the progression of luminal narrowing followed by its regression. To elucidate the mechanisms involved in the phasic changes in luminal diameter after stenting, we examined the changes in neointimal thickness and the appearance of neointima by a series of angiographic and angioscopic observations for 3 years after stent implantation.

Methods and Results-In 12 patients who received a Wiktor coronary stent, serial angiographic and angioscopic examinations were performed immediately, 2 to 4 weeks, 3 months, 6 months, and 3 years after the stenting without repetition of angioplasty. Neointimal thickness was determined by angiography as the difference between stent and luminal diameters. The angioscopic appearance of neointima over the stent was classified as transparent or nontransparent according to the visibility of the majority of the stent. Neointimal thickness increased significantly at 3 months (0.75±0.32 mm) without further changes at 6 months (0.74±0.32 mm). Thereafter, however, it decreased significantly over 3 years (0.51±0.26 mm). The angioscopic appearance was classified as transparent in 8 patients (100%) immediately after stenting, 6 patients (100%) at 2 to 4 weeks, 2 patients (17%) at 3 months, 2 patients (20%) at 6 months, and 7 patients (58%) at 3 years.

Conclusions-The neointima became thick and nontransparent until 6 months and then became thin and transparent by 3 years. We conclude that neointimal remodeling exists after stenting and plays a major role in the alteration of coronary luminal diameter after stenting.

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Clinical, Intravascular Ultrasound, and Quantitative Angiographic Determinants of the Coronary Flow Reserve Before and After Percutaneous Transluminal Coronary Angioplasty

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This study evaluated the clinical, intravascular ultrasound (IVUS), and angiographic determinants of the coronary flow reserve (CFR) as measured by guidewire Doppler velocimetry. Using standard methodology, 86 consecutive patients were studied before intervention (n = 73 patients, including the assessment of intermediate stenoses) and/or after intervention (n = 39 patients, including after percutaneous transluminal coronary angioplasty (PTCA) in 27 and post-Palmaz-Schatz stent placement + high-pressure adjunct PTCA in 12). Only 5 patients were studied before intervention, post-PTCA, and poststent. Univariate and multivariate clinical, quantitative coronary angiography (QCA), and IVUS correlates of the CFR were evaluated. There was a linear relation between CFR and IVUS minimum lumen cross-sectional area (CSA): r = 0.771, p <0.0001 for the overall cohort; r = 0.831, p <0.0001 before intervention; r = 0.514, p = 0.0061 post-PTCA; and r = 0.623, p = 0.0306 poststent placement. Overall, an IVUS minimum lumen CSA of ≥4.0 mm2 had a diagnostic accuracy of 89% in identifying a CFR of ≥2.0. This diagnostic accuracy increased slightly to 92% when only the preintervention observations were considered. Using multivariate linear regression analysis, the independent determinants of the CFR in the overall cohort of 112 observations were IVUS minimum lumen CSA (p <0.0001), angiographic lesion length (p = 0.0101), and diabetes mellitus (p = 0.0371): r2 = 0.6224. When the subset of preintervention observations were analyzed separately, the independent determinants of the CFR were minimum lumen CSA (p <0.0001) and angiographic lesion length (p = 0.0095): r2 = 0.7176. Thus, the major determinants of the CFR in patients with coronary artery disease are lumen compromise (which is best assessed by the IVUS measurement of the minimum lumen CSA) and lesion length. A minimum lumen CSA ≥4.0 mm2 has a high diagnostic accuracy in predicting a CFR ≥2.0, especially before intervention.

1.Independent determinants of CFR in the overall cohort of 112 observations: IVUS minimum lumen CSA (p <0.0001), angiographic lesion length (p = 0.0101), and diabetes mellitus (p = 0.0371): r2 = 0.6224.
2. Independent determinants of the CFR in the subset of observations performed before intervention: minimum lumen CSA (p <0.0001), angiographic lesion length (p = 0.0095); r2 = 0.7176

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One-year follow-up after intravascular ultrasound assessment of moderate left main coronary artery disease in patients with ambiguous angiograms

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OBJECTIVES

The purpose of this study was to correlate angiographic and intravascular ultrasound (IVUS) findings in left main coronary artery (LMCA) disease and identify the predictors of coronary events at one year in patients with LMCA stenoses.

BACKGROUND

Significant (≥50% diameter stenosis [DS]) LMCA disease has a poor long-term prognosis.

METHODS

One hundred twenty-two patients who underwent angiographic and IVUS assessment of the severity of LMCA disease and who did not have subsequent catheter or surgical intervention were followed for one year. Standard clinical, angiographic and IVUS parameters were collected.

RESULTS

The quantitative coronary angiography (QCA) reference diameter (3.91 ± 0.76 mm, mean ± 1 SD) correlated moderately with IVUS (4.25 ± 0.78 mm, r = 0.492, p = 0.0001). The lesion site minimum lumen diameter (MLD) (2.26 ± 0.82 mm) by QCA correlated less well with IVUS (2.8 ± 0.82 mm, r = 0.364, p = 0.0005). The QCA DS measured 42 ± 16%. During the follow-up period, 4 patients died, none had a myocardial infarction, 3 underwent catheter-based LMCA intervention and 11 underwent bypass surgery. Univariate predictors of events ($p < 0.05$) were diabetes, presence of another lesion whether treated with catheter-based intervention or untreated with DS > 50% and IVUS reference plaque burden and lesion lumen area, maximum lumen diameter, MLD, plaque area and area stenosis. Using logistic regression analysis diabetes mellitus, an untreated vessel (with a DS > 50%) and IVUS MLD were independent predictors of cardiac events.

CONCLUSIONS

In selected patients assessed by IVUS, moderate LMCA disease had a one-year event rate of only 14%. Intravascular ultrasound MLD was the most important quantitative predictor of cardiac events. For any given MLD, the event rate was exaggerated in the presence of diabetes or another untreated lesion (>50% DS).

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Intravascular ultrasound predictors of target lesion revascularization after stenting of protected left main coronary artery stenoses

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We evaluated the predictors of late clinical outcomes after stenting of protected left main coronary artery (LMCA) stenoses. Intravascular ultrasound (IVUS) guided stenting of protected LMCA stenoses was performed in 87 consecutive patients between January 1994 and December 1996. Results were evaluated using conventional (clinical, angiographic, and IVUS) methodology. Late (12 month) clinical follow-up information was obtained in all patients. Initial procedural success was achieved in 86 patients (99%). There was 1 in-hospital death (in the 1 patient with a procedural failure). There were no other in-hospital complications, including Q-wave myocardial infarction, emergency bypass surgery, or repeat coronary angioplasty. The overall target lesion revascularization (TLR) rate was 13%. Using multivariate logistic regression analysis, the only independent predictor of TLR was the postintervention lumen area by IVUS. A final lumen area $\geq$7.0 mm2 was obtained in 74 patients (86%); the TLR rate for these patients was 7%. This was compared with patients with a final lumen area <7.0 mm2 in whom the TLR rate was 50% ($p = 0.0011$). Stenting of protected LMCA stenoses is safe and effective with acceptable long-term clinical outcomes. The most important factor determining long-term success was the postintervention lumen area by IVUS.

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Reduction of restenosis by vessel size adapted percutaneous transluminal coronary angioplasty using intravascular ultrasound

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Restenosis following percutaneous transluminal coronary angioplasty (PTCA) remains a serious problem in interventional cardiology. Recent trials using stent implantation have proposed a reduction in restenosis, presumably due to a higher initial luminal gain. This study was conducted to evaluate if the short- and long-term results following conventional PTCA may be favorable, if balloon dilation was performed according to measurements gained by intravascular ultrasound (IVUS) (vessel size adapted PTCA). The use of intracoronary stents might be omitted if comparable long-term results could be achieved by this modified technique of balloon angioplasty. This unicenter and nonrandomized pilot trial was initiated in January 1995 with 252

patients who had 271 lesions. IVUS was performed before and after intervention to determine the external elastic membrane (EEM) diameter at the lesion site. The balloon catheter was sized according to the EEM diameter measured by IVUS (EEM 10%). The mean balloon diameter was 4.1 ± 0.5 mm, the dilation time 130 ± 60 seconds with a balloon pressure of 7.0 ± 2.0 atm. Clinical acute and 1-year long-term follow-up were obtained for all patients and follow-up angiography in 71% of patients. Acute events occurred postinterventionally in 5 patients (2%). The cumulative event rate during long-term follow-up was 14%. The angiographic restenosis rate (diameter stenosis >50%) after 1 year was 19%. Vessel size adapted PTCA using IVUS led to favorable acute and long-term results with a low restenosis rate and a low 1-year clinical event rate. Despite dissections that occur frequently using large balloon sizes, an increased rate of major complications did not occur, indicating a safe procedure and substantiating the philosophy of ?therapeutic dissections.?The results need to be verified in a randomized trial.

The American Journal of Cardiology, 83:1518-1523

Intravascular ultrasound assessment of the relation between early and late changes in arterial area and neointimal hyperplasia after percutaneous transluminal coronary angioplasty and directional coronary atherectomy

Gary S. Mintz, Takeshi Kimura, Masakiyo Nobuyoshi, Martin B. Leon

Previous serial intravascular ultrasound (IVUS) analysis after percutaneous transluminal coronary angioplasty or directional coronary atherectomy showed (1) early (within 1 month) increase in arterial area, (2) late (1- to 6-month) decrease in arterial area, and (3) an increase in plaque area from immediately to 6 months after intervention. To further understand these findings, we used serial IVUS to study the relations between changes in arterial and plaque area during the follow-up period after coronary intervention. Serial IVUS was performed before intervention and immediately, 24 hours, 1 month, and 6 months after percutaneous transluminal coronary angioplasty (n = 35) or directional coronary atherectomy (n = 26) in 57 patients. Arterial, lumen, and plaque areas were measured at the lesion site with the smallest preintervention and follow-up lumen areas at all time points. The increase in plaque area in the first month after intervention was accompanied by an equal or greater increase in arterial area ($r = 0.670$, $p < 0.0001$). There was a decrease in arterial area from 1 to 6 months after intervention, which correlated inversely with both the increase in plaque area ($r = 0.434$, $p < 0.0001$) or arterial area ($r = 0.515$, $p < 0.0001$) during the first month after intervention and directly with the 1- to 6-month increase in plaque area ($r = 0.460$, $p < 0.0001$). Comparison of the late (1 to 6 months) and early (within 1 month) △arterial versus △plaque area regression lines suggested that the late decrease in arterial area was

superimposed on the relation between △arterial area and △plaque area. These relations were especially strong in restenotic (vs nonrestenotic) lesions. The early increase and late decrease in stenosis arterial area and neointimal hyperplasia appear to be interrelated, especially in restenotic stenoses.

The American Journal of Cardiology, 83:1012-1017

Does the specific intravascular ultrasound criterion used to optimize stent expansion have an impact on the probability of stent restenosis?

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Intravascular ultrasound (IVUS) imaging has been used to optimize stent implantation in coronary arteries, but the criteria used were chosen on an empiric basis. The aim of this study was to determine whether any of these criteria have an independent role in predicting the probability of freedom from restenosis. The study population consisted of 425 patients (496 lesions) who underwent angiographically successful IVUS-guided stenting. Five IVUS criteria were studied: (1) intrastent minimal lumen cross-sectional area (ISMLCSA) ≥9 mm2; (2) ISMLCSA≥(9 mm2 and 80% of average reference lumen cross-sectinla area [CSA]); (3) ISMLCSA ≥ 90% of average reference lumen CSA; (4) ISMLCSA ≥90% of distal reference lumen CSA; and (5) ISMLCSA≥ 55% of average reference vessel CSA. These criteria were met in 33%, 29%, 68%, 82%, and 69% of lesions, respectively. Angiographic follow-up was performed in 335 of 421 eligible patients (80%) at 5.3 ± 2.7 months. An absolute ISMLCSA 9 mm2 was associated with the lowest restenosis, but this criterion was primarily achieved in large vessels. The only criterion that was associated with higher probability of freedom from restenosis independently from vessel size was an ISMLCSA 55% of average reference vessel CSA. Therefore, when IVUS is used to guide stent implantation an effort should be made to achieve the largest lumen safely possible. An ISMLCSA 55% of the average reference vessel CSA seems to be the most appropriate criterion in terms of frequency of achievement and in terms of increasing the probability of freedom from restenosis.

The American Journal of Cardiology, 83:5:687-690

Clinical utility of negative contrast intravascular ultrasound to evaluate plaque morphology before and after coronary interventions

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Although intravascular ultrasound (IVUS) is used for evaluation of plaque volume and lumen size as well as detection of vessel wall structures after catheter-based interventions, differentiation between the lumen and plaque structures can be difficult. This study attempted to evaluate the efficacy of negative contrast IVUS imaging for assessment of vessel wall morphology after coronary interventions. IVUS studies were performed in 67 lesions in 66 patients before and after coronary interventions. After the baseline ultrasound imaging run, warm 5% glucose solution was injected manually through the guiding catheter into the coronary artery to washout blood from the lumen to avoid speckled reflections from red blood cells (negative contrast). Quantitative measurements were obtained and plaque morphology was assessed for the presence and extent of medial dissections and intimal flaps. There was no difference in each quantitative parameter between baseline images and negative contrast images. The vessel wall boundary was clearly delineated from the lumen, which was defined as effective negative contrast in 51 of 67 lesions (76%). The baseline images revealed plaque dissection in 9 lesions (18%) and an intimal flap in 13 lesions (25%). In addition, 4 dissections (8%) and 16 intimal flaps (31%) were visualized during the infusion of negative contrast. Additional treatment was performed in 4 lesions (8%) based on the images with negative contrast. Negative contrast IVUS was more sensitive in demonstrating a plaque fracture than were baseline images. This method is useful for enhancing the diagnostic capability of IVUS imaging and may influence the decision-making process during interventional procedures.

Circulation 2000 102: 617-623

Characterization of Plaque Components With Intravascular Ultrasound Elastography in Human Femoral and Coronary Arteries In Vitro

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Background-The composition of plaque is a major determinant of coronary-related clinical syndromes. Intravascular ultrasound (IVUS) elastography has proven to be a technique capable of reflecting the mechanical properties of phantom material and the femoral arterial wall. The aim of this study was to investigate the capability of intravascular elastography to characterize different plaque components.
Methods and Results-Diseased human femoral (n=9) and coronary (n=4) arteries were studied in vitro. At each location (n=45), 2 IVUS images were acquired at different intraluminal pressures (80 and 100 mm Hg). With the use of cross-correlation analysis on the high-frequency (radiofrequency) ultrasound signal, the local strain in the tissue was determined. The strain was color-coded and plotted as an additional image to the IVUS echogram. The visualized segments were stained on the presence of collagen, smooth muscle cells, and macrophages. Matching of elastographic data and histology were performed with the use of the IVUS echogram. The cross sections were segmented in regions (n=125) that were based on the strain value on the elastogram. The dominant plaque types in these regions (fibrous, fibro-fatty, or fatty) were obtained from histology and correlated with the average strain and echo intensity. The strain for the 3 plaque types as determined by histology differed significantly (P=0.0002). This difference was mainly evident between fibrous and fatty tissue (P=0.0004). The plaque types did not reveal echo-intensity differences in the IVUS echogram (P=0.882).
Conclusions-Different strain values are found between fibrous, fibro-fatty, and fatty plaque components, indicating the potential of intravascular elastography to distinguish different plaque morphologies.

Journal of the American College of Cardiology, 33:1870-1878

Clinical validation of intravascular ultrasound imaging for assessment of coronary stenosis severity : Comparison with stress myocardial perfusion imaging

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OBJECTIVES

To validate intravascular ultrasound (IVUS) measurements for differentiating functionally significant from

nonsignificant coronary stenosis.

BACKGROUND

To date, there are no validated criteria for the definition of a flow-limiting coronary artery stenosis by IVUS.

METHODS

Preinterventional IVUS imaging (30-MHz imaging catheter) of 70 de novo coronary lesions was performed. The lesion lumen area and three IVUS-derived stenosis indixes comparing lesion lumen area with the lesion external elastic lamina (EEL) area, the mean reference lumen area and the mean reference EEL area were compared with the results of stress myocardial perfusion imaging.

RESULTS

The lesion lumen area and three IVUS-derived stenosis indexes showed sensitivities and specificities ranging between 80% and 90% using stress myocardial perfusion imaging as the gold standard. The lesion lumen area≤ 4 mm2 is a simple and highly accurate criterion for significant coronary narrowing.

CONCLUSIONS

Quantitative IVUS indices can be reliably used for identifying significant epicardial coronary artery stenoses.

Circulation, 1999 , 99: 1660-1665

Effects of Intracoronary ß-Radiation Therapy After Coronary Angioplasty : An Intravascular Ultrasound Study

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Background-Endovascular radiation is emerging as a potential solution for the prevention and treatment of restenosis. Its effects on the morphology of unstented vessels cannot be determined by angiography and therefore require the use of intravascular ultrasound.

Methods and Results-Through a 5F noncentered catheter for delivery of a 90Sr/Y source train, 12, 14, or 16 Gy at 2 mm was delivered to native coronary arteries after successful balloon angioplasty in 30 patients. Four patients required stent deployment in the first week. Quantitative coronary angiography and IVUS were performed during the initial procedure and at 6-month follow-up. Binary angiographic restenosis was present in 3 of 30 patients, with target lesion and vessel revascularization performed in 3 and 5 patients, respectively. Angiographic late loss was -0.02±0.60 mm, with a -0.09±0.46 loss index. IVUS demonstrated no significant reduction in lumen area (from 5.69±1.72 mm2 after treatment to 6.04±2.63 mm2 at follow-up), with no significant change in external elastic membrane area (13.71±4.54 to 14.22±4.71 mm2) over the 6-month follow-

up. Wall area was 8.01±3.85 mm2 after radiation therapy and 8.19±3.44 mm2 at follow-up (P=NS). No significant differences were noted between the different dose groups.
Conclusions-ß-Radiation therapy resulted in a low restenosis rate with negligible late loss by angiography. By IVUS, ß-radiation was shown to inhibit neointima formation, with no reduction of total vessel area at 6-month follow-up.

Am J Cardiol , 1999 ;84(11):1298-303

Acute and long-term results of an intravascular ultrasound-guided percutaneous transluminal coronary angioplasty/provisional stent implantation strategy.

Abizaid A, Pichard AD, Mintz GS, Abizaid AS, Klutstein MW, Satler LF, Mehran R, Leiboff B, Kent KM, Leon MB

Two hundred eighty-four consecutive patients with 438 native coronary artery stenoses were enrolled prospectively in a study of intravascular ultrasound (IVUS)-guided provisional percutaneous transluminal coronary angioplasty (PTCA): (1) IVUS-guided, aggressive lesion-site media-to-media balloon sizing, (2) IVUS assessment of residual lumen dimensions to identify optimal PTCA results (minimum lumen area > or =65% of the average of the proximal and distal reference lumen areas or > or =6.0 mm2 and no major dissection), and (3) liberal stent crossover. Overall, 206 stenoses in 134 patients were treated with PTCA alone. Reasons for crossover were flow-limiting or lumen compromising dissections in 28% of patients or a suboptimal IVUS minimum lumen area in 72% of patients. Sixty-three stenoses (27%) were treated with Gianturco-Roubin stents and 169 (73%) with Palmaz-Schatz stents. The clinical success rate and major in-hospital complication rates were similar in the optimal PTCA and stent crossover groups. At 1 year, 42 patients (15%) with 53 stenoses (12%) underwent revascularization: 8% of stenoses in the PTCA group and 16% in the stent crossover group. In approximately half of the patients treated using an IVUS guided aggressive PTCA strategy, stent implantation could be avoided without sacrificing an increase in acute complications or late clinical outcome. This provides an alternative strategy for interventionalists less inclined to use routine elective stenting.

Summary

Am J Cardiol, 1999 ;84(9):981-6

Evaluation of scaffolding effects of five different types of stents by intravascular ultrasound analysis.

Okabe T, Asakura Y, Ishikawa S, Asakura K, Mitamura H, Ogawa S

The acute elastic recoil of 5 types of stents immediately after deployment by intravascular ultrasound and quantitative coronary angiography measurements was analyzed. Successfully implanted stents were: Palmaz-Schatz in 104 lesions, Gianturco-Roubin in 65, Wiktor in 45, gfx in 22, and Multi-Link stents in 22. Before and after stenting, the cross section of the smallest luminal area and vessel area was measured with intravascular ultrasound. The postdilatation balloon area was calculated by quantitative coronary angiography. Percent recoil was calculated as: [1-(preluminal area)/balloon area)] x 100. The ratio of balloon area-to-vessel area was also compared. Although preluminal areas in Gianturco-Roubin and Palmaz-Schatz stents were similar (2.4 +/- 0.1 vs 2.5 +/- 0.1 mm2, p = NS), postluminal area in the Gianturco-Roubin was significantly smaller than the area in the Palmaz-Schatz (6.3 +/- 0.2 vs 8.3 +/- 0.3 mm2, p <0.05). Although both the balloon area/vessel area (0.68 +/- 0.05, 0.80 +/- 0.08 vs 0.83 +/- 0.02, p <0.05) and the preluminal area (2.1 +/- 0.4, 1.6 +/- 0.2 vs 2.5 +/- 0.1 mm2, p <0.05) were smaller in gfx and Multi-Link than in the Palmaz-Schatz, postluminal area was comparable to the area in the Palmaz-Schatz (7.8 +/- 0.4, 7.4 +/- 0.4 vs 8.3 +/- 0.3 mm2, p = NS). Percent recoil in the Gianturco-Roubin was poorest among these 5 groups. More favorable initial gain can be obtained with Palmaz-Schatz, Wiktor, gfx, and Multi-Link stents than with the Gianturco-Roubin stent.
Figure. Comparison of luminal gain index and percent recoil (%RECOIL) among 5 stents. Luminal gain index = [(postluminal area)-(preluminal area)]/prevessel area; %RECOIL = [1-(postluminal area)/(balloon area)]×100%. Luminal gain index was significantly larger in PS, W, and ML groups than in the GR group. PS, gfx, and ML groups provided significantly less percent recoil than the GR group.

Am J Cardiol, 1999 ;84(6):650-4

Measuring maximal percent area stenosis poststent placement with intracoronary Doppler and the continuity equation and correlation with intracoronary ultrasound and angiography.

Al Suwaidi J, Higano ST, Holmes DR Jr, Rihal CS, Lerman A

Quantitative coronary angiography (QCA) and intracoronary ultrasound (ICUS) are methods for anatomic assessment of stent deployment. Intracoronary Doppler is primarily a method for the physiologic assessment of coronary stenoses. It correlates well with traditional noninvasive measurements of lesion significance. Intracoronary Doppler was used for the anatomic assessment of de novo coronary artery stenosis with variable success; however, its use for anatomic assessment of adequate stent deployment is unavailable. A rapid, automated software program was developed based on a modified continuity equation to calculate the maximal in-stent percent area stenosis by comparing the maximal in-stent velocity to an average reference velocity (proximal and distal). This study was designed to compare the Doppler method of an anatomic assessment with QCA and ICUS in 15 patients. Physiologic success of stent deployment was determined by the distal coronary flow reserve to 24 to 36 microg of intracoronary adenosine. Following successful stent deployment, distal coronary flow reserve increased significantly from a baseline of 1.6 +/- 0.5 to 2.9 +/- 1.1. There was a significant correlation between the maximal in-stent percent area stenosis as measured by Doppler and both QCA ($r = 0.78$, $p < 0.01$) and ICUS ($r = 0.84$, $p < 0.01$). This study demonstrates that maximal in-stent percent area stenosis can be measured by intracoronary Doppler and a novel software program. The intracoronary Doppler guidewire method can assess the adequacy of stent deployment using both anatomic and physiologic principles and may supplement other quantitative methodologies.

Figure. Relation between percent area stenosis determined by Doppler continuity equation and by intravascular ultrasound (IVUS)

Figure. Relation between percent area stenosis determined by Doppler continuity equation and by QCA

Catheter Cardiovasc Interv , 1999 ;47(4):434-40

Quantitative changes in reference segments during IVUS-guided stent implantation: impact on the criteria for optimal stent expansion.

Regar E, Klauss V, Werner F, Henneke KH, Rieber J, Konig A, Theisen K, Mudra H

Intravascular ultrasound is an established method to optimize stent implantation. Stent expansion is estimated

from the relation between minimal in-stent cross-sectional area and reference lumen area. We analyzed the periprocedural lumen increment in the reference segments and its impact on intravascular ultrasound (IVUS) criteria for optimized stenting. Seventy-five consecutive patients were studied with a 2.9 Fr, 30-MHz system and motorized pullback (0.5 mm/sec). Lumen area was measured by planimetry; absolute and relative differences in area (delta area) were calculated. Lumen area increment for reference segments proximal and distal to the stent was 6.4% +/- 10.3% and 6.1% +/- 10.8%; 49/75 patients fulfilled all IVUS criteria for optimal stent expansion at the final IVUS assessment, and 10/75 patients met all the IVUS criteria in relation to the first measurement of reference lumen area, but not in relation to the final measurement of reference lumen area. During high-pressure dilatation within the stent, reference lumen increment is visible. If reference lumen planimetry is not repeated after additional high-pressure balloon inflation, the final relative stent expansion may be overestimated.

Summary

Circulation ,1999 ;99(24):3149-54

Preintervention arterial remodeling as an independent predictor of target-lesion revascularization after nonstent coronary intervention: an analysis of 777 lesions with intravascular ultrasound imaging.

Dangas G, Mintz GS, Mehran R, Lansky AJ, Kornowski R, Pichard AD, Satler LF, Kent KM, Stone GW, Leon MB

BACKGROUND: Pathological and intravascular ultrasound (IVUS) studies have documented arterial remodeling during atherogenesis. However, the impact of this remodeling process on the long-term outcome after percutaneous intervention is unknown. METHODS AND RESULTS: We used preintervention IVUS to define positive and negative/intermediate remodeling in a total of 777 lesions in 715 patients treated with nonstent techniques. Positive remodeling (lesion external elastic membrane area greater than average reference) was present in 313 lesions; intermediate/negative remodeling (lesion external elastic membrane area less than or equal to reference) was present in the other 464. Baseline clinical and angiographic characteristics were similar, except for a slightly higher percentage of insulin-dependent diabetic patients (10.2% versus 6.1%; P=0.054) in the negative/intermediate-remodeling group. Angiographic success and in-hospital and short-term complications were comparable in the 2 groups. There was no significant correlation between remodeling (as a continuous variable) and final lumen area (r=0.06) or final lesion plaque burden (r=0.17). At 18+/-13 months of

clinical follow-up, both groups had similar rates of death and Q-wave myocardial infarction: 3.4% and 2.5% for the negative/intermediate-remodeling group versus 2.7% and 2.7% for the positive-remodeling group. However, the target-lesion revascularization (TLR) rate was 20.2% for the negative/intermediate-remodeling group versus 31.2% for the positive-remodeling group (P=0.007), and remodeling, as a continuous variable, was strongly correlated with probability of TLR (P=0.0001). By multivariable logistic regression analysis, diabetes (OR=2.3), left anterior descending artery location (OR=1.8), and remodeling (OR=5.9) were independent predictors of TLR. CONCLUSIONS: Positive lesion-site remodeling is associated with a higher long-term TLR after a nonstent interventional procedure. Thus, long-term clinical outcome appears to be determined in part by preintervention lesion characteristics.

Summary

Am Heart J , 2000;139:643-8

Role of intracoronary ultrasound after high-pressure stent implantation

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Background Poststent high-pressure balloon inflation has been shown to improve clinical outcomes. However, it is unknown whether intracoronary ultrasound (ICUS) provides additional clinical guidance after initial high-pressure balloon inflation is used during stent placement. Thus the purpose of this study was to determine if stent deployment techniques are improved with ICUS imaging despite an optimal angiographic result achieved with high-pressure balloon inflation.

Methods and Results Prospective data were collected on 96 consecutive patients in whom 151 stents were deployed. Stents and high-pressure balloons were angiographically sized 1:1 by visual estimation. High-pressure (≥12 atm in all cases) balloon inflations were continued until angiographic completion (<10% residual stenosis), after which index ICUS imaging was performed. Stent apposition, symmetry, and lumen dimensions were evaluated. An optimal ICUS result was defined as full apposition of the stent, symmetry ratio≥0.80, and acute gain≥0.80 of the reference lumen area. If inadequate ICUS results were found, further dilations with higher pressures or larger balloons and subsequent stent reevaluation with ICUS were performed. Sixty-nine (46%) stents required additional balloon inflations. Of these stents, 35 (23%) had initial acute gains that were

<80% of the reference lumen area. Forty-six (30%) stents were found to have unapposed struts and 24 (16%) had a symmetry ratio <0.80. In patients requiring additional inflations, minimum stent area increased from 7.6 ± 2.2 mm2 to 9.2 ± 2.4 mm2 (P < .0001). Similarly, complete stent apposition improved from 33% to 68% of total stents (P < .0001). After initial ICUS, higher-pressure dilations were performed in 40 patients, whereas larger balloons greater than or equal to ICUS reference vessel diameter were used in 33 patients. Follow-up was obtained in 95 (99%) patients. The overall major adverse cardiac event rate at 6 months was 9.3%, which consisted of 8 target vessel revascularizations and 1 abrupt closure requiring repeat intervention.
Conclusions Even when poststent high-pressure balloon inflation achieves an optimal angiographic result, ICUS assists in optimizing acute gain, symmetry, and apposition of intracoronary stents in approximately 50% of patients. Moreover, ICUS guidance is associated with low rates for target vessel revascularization and major adverse cardiac events at 6-month follow-up.

Circulation, 2000; 102: 1484-1489

Three-Dimensional Intravascular Ultrasound Assessment of Noninjured Edges of ß-Irradiated Coronary Segments

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Background-The ?dge effect,?late lumen loss at the margins of the treated segment, has become an important issue in the field of coronary brachytherapy. The aim of the present study was to assess the edge effect in noninjured margins adjacent to the irradiated segments after catheter-based intracoronary ß-irradiation.
Methods and Results-Fifty-three vessels were assessed by means of 3-dimensional intravascular ultrasound after the procedure and at 6- to 8-month follow-up. Fourteen vessels (placebo group) did not receive radiation (sham source), whereas 39 vessels were irradiated. In the irradiated group, 48 edges (5 mm in length) were identified as noninjured, whereas 18 noninjured edges were selected in the placebo group. We compared the volumetric intravascular ultrasound measurements of the noninjured edges of the irradiated vessels with the fully irradiated nonstented segments (IRS, n=27) (26-mm segments received the prescribed 100% isodose) and the noninjured edges of the vessels of the placebo patients. The lumen decreased (6 mm3) in the noninjured edges of the irradiated vessels at follow-up (P=0.001). We observed a similar increase in plaque volume in all segments: noninjured edges of the irradiated group (19.6%), noninjured edges of the placebo group (21.5%),

and IRS (21.0%). The total vessel volume increased in the IRS in the 3 groups. No edge segment was subject to repeat revascularization.
Conclusions-The edge effect occurs in the noninjured margins of radiation source train in both irradiated and placebo patients. Thus, low-dose radiation may not play an important role in this phenomenon, whereas nonmeasurable device injury may be considered a plausible alternative explanation.

Journal of the American College of Cardiology, 35:106-111

Morphology of vulnerable coronary plaque: insights from follow-up of patients examined by intravascular ultrasound before an acute coronary syndrome

Masakazu Yamagishi, Mitsuyasu Terashima, Kojiro Awano, Mikihiro Kijima, Satoshi Nakatani, Satoshi Daikoku, Kenichi Ito, Yoshio Yasumura, Kunio Miyatake

OBJECTIVES
To determine the morphologic features of coronary plaques associated with acute coronary syndrome, we prospectively followed patients with atherosclerotic disease identified by intravascular ultrasound (IVUS).
BACKGROUND
Although clinical evaluation of the vulnerable atherosclerotic plaque is important, few data exist regarding the morphology of the vulnerable plaque in clinical settings.
METHODS
We examined 114 coronary sites without significant stenosis by angiography (<50% diameter stenosis) in 106 patients. All the sites exhibited atherosclerotic lesions by IVUS. These lesions consisted of 22 concentric and 92 eccentric plaques with a percent plaque area averaging 59 ± 12%.
RESULTS
During the follow-up period of 21.8 ± 6.4 months (range 1 to 24), 12 patients had an acute coronary event at a previously examined coronary site at an average of 4.0 ± 3.4 months after the initial IVUS study. All the preexisting plaques related to the acute events exhibited an eccentric pattern and the mean percent plaque area was 67 ± 9%, which was greater than plaque area in the other 90 patients without acute events (57 ± 12%, $p < 0.05$). There was no statistically significant difference in lumen area between two patient groups (6.7 ± 3.0 vs. 7.5 ± 3.7 mm2). Among 12 coronary sites with an acute occlusion, 10 sites contained the echolucent zones, eight of these shallow and two deep, likely representing a lipid-rich core. In 90 sites without acute events, an

echolucent zone in the shallow portion was seen at only four sites ($p < 0.05$).

CONCLUSIONS

Large eccentric plaque containing an echolucent zone by IVUS can be at increased risk for instability even though the lumen area is preserved at the time of initial study. Compensatory enlargement of vessel wall due to remodeling may contribute to the relatively small degree of stenosis by angiography.

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Evaluation of direct stent implantation without predilatation by intravascular ultrasound

Jose Maria de la Torre Hernandez, Isabel Gomez, Felipe Rodriguez-Entem, Javier Zueco, Alvaro Figueroa, Thierry Colman

Direct stenting, stenting without predilatation, aims to reduce procedural time (ischemic, fluoroscopic) and cost, saving the balloon needed for predilatation. Other benefits could be the avoidance of the eventual abrupt vessel closure or dissection after balloon dilatation and the reduction of the restenosis rate due to less arterial injury. This technique has proved to be feasible and safe in selected lesions. In conventional stenting, even using high pressures, nearly 40% of stents with an acceptable angiographic result still require additional dilatation to achieve an optimal result by intravascular ultrasound (IVUS). Lumen dimensions after stenting may be only 50% to 60% of the maximum achieved due to inadequate balloon expansion and elastic recoil. This problem could be even more pronounced in direct stenting because there is no predilatation. There are no published studies addressing IVUS examination of stents implanted without predilatation. The present study provides insights into the exact impact of this method on the arterial lumen and stent expansion

Circulation, 2000 ;101(6):604-10

Atherosclerotic plaque burden and CK-MB enzyme elevation after coronary interventions : intravascular ultrasound study of 2256 patients.

Mehran R, Dangas G, Mintz GS, Lansky AJ, Pichard AD, Satler LF, Kent KM, Stone GW, Leon MB

BACKGROUND: Elevation of serum creatine kinase MB fraction (CK-MB) after percutaneous coronary interventions has been associated with early and late mortality; however, the pathogenesis of CK-MB elevation is still unknown. We hypothesized that CK-MB elevation was related to atherosclerotic plaque burden as assessed by preintervention intravascular ultrasound (IVUS). METHODS AND RESULTS: We studied 2256 consecutive patients who underwent intervention of 2780 native coronary lesions and had complete high-quality preintervention IVUS imaging in the era before routine use of platelet glycoprotein IIb/IIIa inhibitors. Patients were divided into 3 groups: CK-MB within normal range (1675 patients; 2061 lesions); CK-MB elevation 1 to 5 times upper limit of normal (292 patients; 355 lesions); and CK-MB elevation > or = 5 times upper limit of normal (289 patients; 364 lesions). Qualitative angiographic lesion morphology and quantitative analysis were similar among the 3 groups. On preintervention IVUS, progressively more reference segment and lesion site plaque burden and lesion site calcium occurred in the groups with CK-MB elevation. Positive remodeling was more common in lesions with CK-MB elevation. As levels of CK-MB increased, cross-sectional narrowing (percentage plaque burden) increased, both at the reference site (mean cross-sectional narrowing values were 45.1%, <49.3%, and <52.2% for normal CK-MB, 1 to 5 times upper limit of normal, and > or =5 times upper limit of normal groups, respectively; P=0.03) and at the lesion site (81.9%, <85.4%, and <87.1%, respectively; P=0.04). Multivariate analysis indicated that de novo lesions, atheroablative technique, plaque burden at the lesion and reference segments, and final minimal lumen diameter were independent predictors of CK-MB elevation. CONCLUSIONS: CK-MB elevation correlates with a greater atherosclerotic plaque burden. CK-MB elevation after intervention may be a marker of diffuse atherosclerotic disease or a consequence of catheter-based intervention in more diseased arteries or both.
Independent predictors of CK-MB elevation: de novo lesions, atheroablative technique, plaque burden at the lesion and reference segments, and final MLD

Summary

American Journal of Cardiology. 86:1318-1321, 2000

Effect of Preintervention Plaque Burden on Subsequent Intimal Hyperplasia in Stented Coronary Artery Lesions.

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We sought to determine if axial and circumferential distribution of plaque before stenting determines the axial and circumferential distribution of subsequent intimal hyperplasia (IH). We studied 22 patients with a single Palmaz-Schatz stent implanted in a native coronary artery, who underwent intravascular ultrasound (IVUS) imaging before intervention, after stenting, and at 6-month follow-up. For each lesion, 7 locations were analyzed: proximal and distal reference, proximal and distal edge of the stent, proximal and distal location within the body of the stent, and the articulation. Pre- and postintervention and follow-up image slices were precisely aligned and analyzed for pre- and postintervention plaque area and follow-up IH area and thickness. The location of maximal IH area was at or adjacent to the location of maximal preintervention plaque in 17 of 22 of the patients (77%). Similiarly, the circumferential distribution of IH at follow-up paralleled the eccentricity pattern of the native plaque burden in 69% (24 of 35 slices). Using multivariant analysis, the strongest predictor of IH was preintervention plaque area ($p = 0.001$). IH accumulates axially and circumferentially preferentially at the site of maximal preintervention plaque.

TABLE 1. Location of Maximal Intimal Hyperplasia Cross-Sectional Area (CSA) at Follow-Up in Relation to Maximal Preintervention or Final Poststenting Plaque CSA

TABLE 2. Univariate Predictors of Intimal Hyperplasia Cross-Sectional Area (CSA) at Follow-Up

American Journal of Cardiology. 86(7):753-758,2000.

Relation Between Vascular Morphologic Changes During Stent Implantation and the Magnitude of In-Stent Neointimal Hyperplasia

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Intimal hyperplasia usually occurs after balloon over-stretch injury or wire coil stimuli to coronary arteries. We examined whether the degree of vessel wall stretch during coronary stent placement could predict the amount of in-stent neointimal hyperplasia after a 6-month follow-up. Serial (preintervention, postballooning, poststent implantation, and a follow-up after 6 months) intravascular ultrasound (IVUS) was used to study 457 consecutive cross-sectional areas in 28 patients. IVUS imaging, using a motorized pullback system at 0.5 mm/s, allowed 1-mm axial increment measurements of the total vascular, stent, and lumen cross-sectional areas. The mean total vascular area changed from 10.89 +/- 2.50 mm2 before to 11.27 +/- 2.49 mm2 after ballooning, to 12.80

+/- 2.59 mm2 after stenting, and to 12.58 +/- 2.41 mm2 at follow-up (p <0.0001). The mean lumen area changed from 3.36 +/- 1.95 mm2 before to 4.21 +/- 1.65 mm2 after ballooning, to 5.16 +/- 1.09 mm2 after stenting, and to 3.57 +/- 1.23 mm2 at follow-up (p <0.0001). The mean stent area decreased from 5.25 +/- 1.17 mm2 after stenting to 5.09 +/- 0.90 mm2 at follow-up (p <0.0001). Stepwise logistic regression analysis showed that [DELTA] total vascular area (after stent implantation-before intervention) was a strong predictor of the amount of intimal hyperplasia (r = 0.57, p <0.0001). Vascular overstretch caused by the stenting procedure promotes intimal hyperplasia in proportion to the degree of sectional vascular stretch.

TABLE 3. Univariate Analysis of Predictors (during stent implantation procedure) of the Amount of Neointimal Hyperplasia at Six-Month Follow-Upl

* p <0.001 by stepwise logistic regression analysis.

legend before = before intervention; LA = luminal area; NA = amount of neointimal hyperplasia; PA = plaque area (TA-LA); TA = total vascular area

Figure2. Predictor of the neointimal cross-sectional area (NA)/total vascular area (TA) at 6-month follow-up. There was a significant positive correlation between TA(Post Stent-Pre)and the percent amount of NA (r=0.57,p<0.0001).

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Intravascular ultrasound findings of negative arterial remodeling at sites of focal coronary spasm in patients with vasospastic angina.

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Background: There are few data about the intravascular ultrasound (IVUS) findings in patients with vasospastic angina, especially regarding patterns of vascular remodeling.

Methods and Results: Coronary spasm was documented by angiography and electrocardiographic evidence of ischemia in 36 patients after administration of ergonovine (cumulative doses up to 350 [mu]g). After relief of spasm with 1000 [mu]g of intracoronary nitroglycerin, quantitative angiography and IVUS imaging were performed and analyzed by standard methods. The 36 focal spasm sites were compared with the proximal and

distal reference segments. The angiographic baseline minimum lumen diameter measured 1.78 +/- 0.66 mm, which decreased to 0.66 +/- 0.38 mm with ergonovine provocation (P < .0001), increased to 2.66 +/- 0.64 mm after intracoronary nitroglycerin (P < .0001 compared with baseline and after ergonovine), and did not change after IVUS imaging (2.66 +/- 0.63, P = .9). By IVUS, atherosclerotic lesions were observed at all coronary spasm sites; the mean plaque burden measured 56% at the spasm site and 35% at the reference. Spasm site plaque composition was hypoechoic in 31 and hyperechoic, noncalcific in 5; there was no calcium. The mean eccentricity index (maximum divided by minimum plaque thickness) was 6.7. Positive remodeling (spasm site arterial area greater than proximal reference) was present in 5; intermediate remodeling (proximal reference greater than spasm site greater than distal reference arterial area) was present in 7; and negative remodeling (spasm site arterial area less than distal reference) was present in 24.

Conclusions: Sites of vasospasm in patients with variant angina showed characteristics of early atherosclerosis, except for an unusually high incidence of negative arterial remodeling.

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Final Results of the Can Routine Ultrasound Influence Stent Expansion (CRUISE) Study

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Background: Intravascular ultrasound (IVUS) can assess stent geometry more accurately than angiography. Several studies have demonstrated that the degree of stent expansion as measured by IVUS directly correlated to clinical outcome. However, it is unclear if routine ultrasound guidance of stent implantation improves clinical outcome as compared with angiographic guidance alone.

Methods and Results: The CRUISE (Can Routine Ultrasound Influence Stent Expansion) study, a multicenter study IVUS substudy of the Stent Anti-thrombotic Regimen Study, was designed to assess the impact of IVUS on stent deployment in the high-pressure era. Nine centers were prospectively assigned to stent deployment

with the use of ultrasound guidance and 7 centers to angiographic guidance alone with documentary (blinded) IVUS at the conclusion of the procedure. A total of 525 patients were enrolled with completed quantitative coronary angiography, quantitative coronary ultrasound, and clinical events adjudicated at 9 months for 499 patients. The IVUS-guided group had a larger minimal lumen diameter (2.9+/-0.4 versus 2.7+/-0.5 mm, P <0.001) by quantitative coronary angiography and a larger minimal stent area (7.78+/-1.72 versus 7.06+/-2.13 mm2, P <0.001) by quantitative coronary ultrasound. Target vessel revascularization, defined as clinically driven repeat interventional or surgical therapy of the index vessel at 9 month-follow-up, occurred significantly less frequently in the IVUS-guided group (8.5% versus 15.3%, P <0.05; relative reduction of 44%).
Conclusions: These data suggest that ultrasound guidance of stent implantation may result in more effective stent expansion compared with angiographic guidance alone.

Figure 4. Clinical outcomes at 9 months in both study groups.

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True 3-Dimensional Reconstruction of Coronary Arteries in Patients by Fusion of Angiography and IVUS (ANGUS) and Its Quantitative Validation.

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Background: True 3D reconstruction of coronary arteries in patients based on intravascular ultrasound (IVUS) may be achieved by fusing angiographic and IVUS information (ANGUS). The clinical applicability of ANGUS was tested, and its accuracy was evaluated quantitatively.

Methods and Results: In 16 patients who were investigated 6 months after stent implantation, a sheath-based catheter was used to acquire IVUS images during an R-wave-triggered, motorized stepped pullback. First, a single set of end-diastolic biplane angiographic images documented the 3D location of the catheter at the beginning of pullback. From this set, the 3D pullback trajectory was predicted. Second, contours of the lumen or stent obtained from IVUS were fused with the 3D trajectory. Third, the angular rotation of the reconstruction was optimized by quantitative matching of the silhouettes of the 3D reconstruction with the actual biplane images. Reconstructions were obtained in 12 patients. The number of pullback steps, which determines the pullback length, closely agreed with the reconstructed path length (r =0.99). Geometric measurements in silhouette images of the 3D reconstructions showed high correlation (0.84 to 0.97) with corresponding measurements in the actual biplane angiographic images.
Conclusions: With ANGUS, 3D reconstructions of coronary arteries can be successfully and accurately obtained in the majority of patients.
Figure 2. A and C, Longitudinal cut planes through a vessel. A, Series of pullback transducer locations of free-floating catheter. C, Pullback trajectory for sheath-based type. Imaging planes are indicated at 2 locations (I1, I2). Note that in A, imaging plane is not necessarily perpendicular to path. B, Possible distortion of path induced by respiration. D and E, Potential views of a 3D reconstructed catheter coreline combined with an IVUS cross-sectional plane for 2 different angular rotations (see also text).
Figure 6. A, Lateral angiographic view of RCA. B, Corresponding 3D lumen reconstruction. There is close similarity between lumen diameters and position of catheter coreline relative to lumen. C, Vessel wall is added to reconstruction.

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Mechanism of Lumen Enlargement During Intracoronary Stent Implantation: An Intravascular Ultrasound Study.

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Background: Intravascular ultrasound analysis has assessed mechanisms of lumen enlargement after nonstent interventions, but not after stenting.

Methods and Results: Preintervention and postintervention intravascular ultrasound was used to study 25 de novo native coronary lesions treated with single MultiLink stents without preatheroablation. External elastic membrane, lumen, and plaque and media (P&M) areas were measured every 1 mm to include the lesion and reference segments that were 5 mm proximal and distal to it. Lesion mean lumen area increased from 4.0+/-1.0 mm2 before the intervention to 8.8+/-2.0 mm2 after the intervention (P <0.0001) as a result of an increase in mean external elastic membrane area (14.2+/-2.7 to 16.1+/-3.0 mm2, P <0.0001) and a decrease in mean P&M area (10.2+/-2.2 to 7.2+/-1.8 mm2, P <0.0001). The decrease in lesion P&M was accompanied by an increase in both proximal reference mean P&M (7.0+/-1.9 to 8.4+/-2.0 mm2, P <0.0001) and distal reference mean P&M (5.8+/-2.1 to 7.2+/-2.1 mm2, P <0.0001). Volumetric analysis showed an axial redistribution of plaque away from the center of the lesion toward the reference segments to increase the plaque burden in both the proximal and distal reference segments. Total (lesion plus reference) mean P&M decreased from 8.6+/-2.1 to 7.5+/-1.8 mm2 (P <0.0001).

Conclusions: The mechanisms of lumen enlargement after stenting involved (1) significant axial redistribution of plaque from the lesion into the reference segments, (2) vessel expansion, and (3) either plaque embolization or compression.

Figure 2. The postintervention P&M CSA correlated with preintervention P&M CSA (A). The decrease in P&M CSA correlated with preintervention P&M CSA (B).

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Sex differences in coronary artery size assessed by intravascular ultrasound

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Background: Women have worse outcomes after myocardial infarction and coronary revascularization. The explanations are likely multifactorial but may include smaller coronary artery size. Smaller luminal diameter has been confirmed angiographically; however, because of possible confounding effects of coronary

remodeling, angiographically silent atherosclerosis, and body size, it is unclear if there is a true sex influence on arterial size.

Methods: We performed intravascular ultrasound on left main (LM) and proximal left anterior descending (LAD) coronary artery segments that were free of significant atherosclerosis in 50 men and 25 women. Arterial and luminal areas were measured by planimetry and corrected for body surface area. We evaluated associations between sex and coronary dimensions with univariate and then multiple linear regression analyses.

Results: Mean uncorrected LM and LAD arterial areas were smaller in women than in men (21.53 vs 26.95 mm2, P < .001, and 14.68 vs 19.94 mm2, P = .002, respectively), as were mean LM and LAD luminal areas (15.94 vs 18.79 mm2, P = .020, and 10.13 vs 12.71 mm2, P = .036, respectively). In multivariate models accounting for body surface area and controlling for other factors, sex independently predicted corrected LM and LAD arterial area. In analyses that additionally controlled for plaque area, sex independently predicted corrected LAD luminal area.

Conclusions: LM and LAD arteries are smaller in women, independent of body size. This suggests an intrinsic sex effect on coronary dimensions. Future studies should investigate underlying mechanisms because they may lead to novel therapeutic strategies and improved outcomes for women with coronary artery disease.

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Reproducibility of neointima quantification with motorized intravascular ultrasound pullback in stented coronary arteries

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Background: Intravascular ultrasound (IVUS) imaging has shown excellent reproducibility immediately after coronary stent implantation. However, the variability of measurements in lesions late after stent implantation, when neointima formation is present, has not been studied. Neointimal tissue is generally low echogenic and thus difficult to quantify. We therefore sought to analyze the reproducibility of morphometric measurements late after stent implantation.

Methods and Results: Fifty consecutive patients were investigated 6 months after Palmaz-Schatz stent implantation (motorized catheter pullback 0.5 mm/s). Two experienced investigators independently identified the stent area, lumen area, and neointimal area at different sites within the stent. Planimetric measurements

were performed with commercially available software. Correlation coefficient and mean difference for corresponding measurements were calculated for the intraobserver and interobserver comparisons. Variability for the intraobserver and interobserver comparisons was similar. Observer agreement regarding the presence of neointimal hyperplasia was as high as 71% (interobserver comparison 62%). The mean difference for neointima area was 0.06 +/- 1.5 mm2 (-0.6 +/- 1.5 mm2); mean differences for lumen area were 0.02 +/- 0.19 mm2 (0.03 +/- 0.17 mm2) and for stent area 0.01 +/- 0.09 mm2 (-0.02 +/- 0.12 mm2) (values for interobserver comparison are given in parentheses). Correlation between measurements was high for all structures: correlation coefficients were 0.66 (0.69) for neointima, 0.94 (0.95) for lumen, and 0.95 (0.91) for stent area.
Conclusions: Morphometric measurements of IVUS investigations with motorized IVUS pullback late after stent placement show good reproducibility. Intraobserver variability and interobserver variability are low. Differences for corresponding measurements were more pronounced for neointima area. Motorized catheter pullback guarantees high reliability of IVUS measurements and should be used routinely for clinical IVUS studies. 1215

American Journal of Cardiology, 85(5):559-562, 2000

Comparison of Coronary Stent Expansion by Intravascular Ultrasonic Imaging in Younger Versus Older Patients With Diabetes Mellitus

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The poor long-term outcome in young diabetic patients receiving stents is not well understood. The purpose of this study was to characterize the postprocedural results of stent placement in diabetic patients using intravascular ultrasound to identify factors that might be associated with poor clinical outcome. The acute dimensions from intravascular ultrasound studies after stent deployment at 5 sites were measured from 39 coronary segments from patients with diabetes mellitus (DM) and 161 segments from nondiabetic patients (non-DM). Within these 2 groups, segments were subgrouped into young (y) and old (o) in reference to the mean study age of 64 years, forming 4 groups: yDM (n = 20), y non-DM (n = 65), oDM (n = 19), and o non-DM (n = 96). Results are reported as mean +/- 1 SD. Diabetic patients had smaller mean lumen area within the treated segment than o non-DM (8.37 +/- 2.59 vs 9.11 +/- 3.35 mm2, p <0.01). These differences were more pronounced at the distal reference vessel lumen of yDM than y non-DM (7.6 +/- 2.3 vs 10.3 +/- 4.5 mm2, p <0.003), and were associated with greater percent plaque area in the distal reference vessel (43.4 +/- 13% vs 34.1

+/- 11.2%, p <0.003). In young diabetic patients undergoing elective stent placement, underexpansion of the stented segment is common, which may contribute to the relatively poor long-term outcome in these patients. We suggest that when stenting is the procedure of choice in this subgroup of high-risk patients, special attention should be given to optimizing lumen

Figure 2. Lumen area. Distribution of lumen areas in the 4 groups, showing differences in lumen area in the young group, (y DM vs y ND, p <0.02), and in the older patients group (oDM vs oND p <0.08). Clinical groups: young DM patients (yDM, n = 20), young non-DM patients (yND, n = 65), old DM patients (oDM, n = 19), old non-DM patients (oND, n = 96). DR = distal reference; DSE = distal stent edge; MSA = minimal stent area; PR = proximal reference; PSE = proximal stent edge.

TABLE III. Quantitative IVUS Analysis of Proximal and Distal Reference Segments Comparing the Four Clinical Groups

* Comparing yDM versus y non-DM as well as oDM versus o non-DM patients, p <0.05.

Comparing oDM versus o non-DM patients, p <0.02.

Comparing yDM versus y non-DM patients, p <0.003.

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Accentuated Remodeling on the Upstream Side of Atherosclerotic Lesions

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Although it has been postulated that atherosclerotic stenotic lesions cannot remodel in response to altered flow, evidence to support or refute this hypothesis has been elusive. In vitro models have shown that accelerated endothelial shear stress occurs on the upstream side of stenoses, while turbulent lower shear stress is seen on the downstream side. We therefore compared vascular remodeling at paired sites 2 mm upstream and 2 mm downstream of the site of minimal lumen area in 25 atherosclerotic lesions in 23 patients using intravascular ultrasound. Remodeling was compared by 2 methods: normalized vessel area (vessel arealesion/vessel areareference) and remodeling index (change in vessel area/change in plaque area from reference). Normalized vessel area was significantly greater upstream than downstream (1.21 +/- 0.06 vs 1.12 +/- 0.09; p <0.05), despite similar plaque burden (8.84 +/- 0.81 vs 8.42 +/- 0.85 mm2) resulting in larger lumen area (8.15 +/- 1.02 vs 6.10 +/- 0.88 mm2; p <0.05). Remodeling index was also significantly higher upstream than downstream (0.67 +/- 0.20 vs

0.12 +/- 0.24, respectively, p <0.05). Accentuation of remodeling on the upstream side was significantly correlated (r = 0.54, p = 0.01) with the mean degree of shear acceleration expected by stenosis severity. Impaired remodeling on the downstream side may partly explain stenosis propagation down a vessel.

Figure 1. Flow convergence on the proximal side of a stenosis results in accelerated shear forces, whereas turbulent flow distal to the stenosis results in lower shear stress. Remodeling index (upper left), normalized plaque area (upper right), vessel area (lower left), and lumen area (lower right) at the lesion (LES) and 1 and 2 mm upstream (UL1, UL2) and downstream (DL1, DL2). Bars represent mean ± SEM.

*p <0.05 versus 2 mm downstream.

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Intravascular Ultrasonic Predictors of Angiographic Restenosis After Long Coronary Stenting

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The intravascular ultrasound (IVUS) criteria for stent optimization have not been determined in stenting long lesions. We evaluated the predictors of angiographic restenosis and compared it with stent lumen cross-sectional area (CSA) and stent length between short (stent length <20 mm) and long (>=20 mm) coronary stenting. IVUS-guided coronary stenting was successfully performed in 285 consecutive patients with 304 native coronary lesions. Six-month follow-up angiogram was performed in 236 patients (82.8%) with 246 lesions (80.9%). Results were evaluated using conventional (clinical, angiographic, and IVUS) methods. The overall angiographic restenosis rate was 22.8% (56 of 246 lesions) (short stent 17.6% vs long stent 32.2%, p = 0.009). Using multivariate logistic regression analysis, the independent predictors of angiographic restenosis were the IVUS stent lumen CSA (odds ratio 1.51, 95% confidence intervals 1.18 to 1.92, p = 0.001) and stent length (odds ratio 0.95, 95% confidence intervals 0.91 to 1.00, p = 0.039). The angiographic restenosis rate was 54.8% for stent lumen CSA of <5.0 mm2 (short stent 37.5% vs long stent 73.3%, p = 0.049), 27.4% for CSA between 5.0 and 7.0 mm2 (short stent 24.1% vs long stent 31.7%, p = 0.409), 10.5% for CSA between 7.0 and 9.0 mm2 (short stent 10.0% vs long stent 12.5%, p = 0.772), and 11.4% for stent lumen CSA of >=9.0 mm2 (short stent 10.4% vs long stent 13.3%, p = 0.767) (p = 0.001). Compared with short coronary stenting, long coronary stenting is effective treatment modality to cover long lesions with comparable long-term clinical outcomes in cases of stent lumen CSA of >=7.0 mm2. Regardless of the stent length, the most important factor determining angiographic restenosis was the IVUS stent lumen CSA in relatively large coronary artery lesions.

TABLE V. Angiographic and Intravascular Ultrasound (IVUS) Findings Between Restenosis and Non-Restenosis

TABLE VI. Angiographic Restenosis Rate (%) According to Postintervention Lumen Cross-Sectional Area (CSA) and Stent Length

American Journal of Cardiology. 85(1):37-40, 2000.

Pathologic Validation of a New Method to Quantify Coronary Calcific Deposits In Vivo Using Intravascular Ultrasound

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Current methods of calcium quantification by intravascular ultrasound (IVUS) measure the arc of calcium using the cross-sectional image at the lesion and at the reference site while neglecting calcium elsewhere. Calcium at these sites may not adequately represent the extent of total epicardial coronary calcium. We devised a new method to quantify calcium as a percentage of the coronary luminal surface. This study examines whether this new method accurately reflects coronary calcium determined by histology. Seventeen postmortem coronary arteries were pressure-fixed and imaged by IVUS using a motorized pullback device. Total plaque-luminal circumferential length and calcified plaque-luminal circumferential length were measured from serial cross-sectional IVUS images every 1 mm. With use of Simpson's method, the total plaque and calcified plaque surface area was then calculated. Histologic sections were stained with hematoxylin-eosin and Movat pentachrome at 3-mm intervals. Calcium was independently quantified by planimetry under light microscopy. Histologic analysis (n = 253 sections) revealed a wide range of calcium (0 to 47 mm2; mean 12 16 mm3). The IVUS-derived calcified plaque surface area was 17 23 mm2), which represented 3.1 4.1% (range 0% to 13.9%) of the total plaque surface area. The histologic and IVUS quantification of calcium by this method was strongly related (r = 0.84, p <0.0001), which was an improvement over current 2-dimensional measures of calcium arc (r = 0.41, p = 0.18). Calculation of calcified plaque surface area from sequential IVUS images appears to accurately reflect the degree of total coronary calcification.

Figure 5. A, scatter plot of histologic calcium volume on the y axis and IVUS-derived calcified plaque-luminal area on the x axis. The relation between both methods of calcium quantification (r = 0.82) was highly significant (p <0.0001). B, scatter plot of histologic calcium volume on the y axis and IVUS-derived percent calcified plaque-luminal area on the x axis. The percent calcified plaque-luminal area is the proportion of the luminal

surface that is calcified. The relation between both methods of calcium quantification (r = 0.84) was highly significant (p <0.0001).

American Heart Journal, 139(1, Part 1):59-63, 2000

Natural history of intravascular ultrasound-detected edge dissections from coronary stent deployment.

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Background: High-resolution intravascular ultrasound (IVUS) performed immediately after stent deployment often reveals dissection at the stent margin that may not be appreciated by angiography. However, the natural history of these edge dissections is unknown. These intimal disruptions at the stent margins have been previously reported to occur in 5% to 23% of stent implantations. The short-term prognosis of these lesions appears to be good; however, the longer-term effect on restenosis and/or vessel remodeling is not known. We therefore studied a cohort of patients with the use of IVUS immediately after stent implantation and at 6 months to assess the incidence and prognosis of coronary edge dissections.

Methods and Results: One hundred fifty patients undergoing Palmaz-Shatz stent implantation were imaged with IVUS with the use of a motorized pullback, and the incidence of edge dissections was determined and graded according to depth and circumferential extent. Arterial and lesional morphometric parameters were assessed by digital planimetry. Six-month IVUS images were aligned with the poststent IVUS to determine the natural history of these lesions. Sixteen (10.7%) of 150 had edge tears. All were angiographically silent. Most lesions (n = 9) were superficial intimal tears. Vessel, lumen, and plaque area were similar in the nondissection and dissection groups in both the proximal and distal reference segments. Plaque eccentricity was likewise similar in both groups. At 6 months, lesions (n = 12) healed without a change in plaque burden, undergoing a "tacking down" process. Vessel area (19.1 +/- 6.4 vs 18.4 +/- 7.1 mm2, P = not significant), lumen area (8.2 +/- 4.1 vs 9.2 +/- 4.0 mm2, P = not significant), and plaque area (10.0 +/- 3.3 vs 9.8 +/- 3.3 mm2, P = not significant) were unchanged when compared with the lesion site taken at stent deployment.

Conclusions: Edge dissections as detected by IVUS do not necessarily proscribe an adverse prognosis at 6 months. This finding may provide reassurance to interventionalists because these lesions are frequently seen by IVUS after stent deployment. Further studies are warranted to precisely define specific morphometric features of edge dissections that affect the long-term clinical outcome. (Am Heart J 2000;139:59-63.)

Circulation,102(20):2497-2502, 2000

Ultrasound-Guided Strategy for Provisional Stenting With Focal Balloon Combination Catheter: Results From the Randomized Strategy for Intracoronary Ultrasound-Guided PTCA and Stenting (SIPS) Trial

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Background: Intracoronary ultrasound (ICUS) has provided insights into vascular pathology and interventional therapy. The Strategy for ICUS-Guided PTCA and Stenting (SIPS) trial tested the hypothesis that routine ICUS guidance of coronary interventions improves outcome.

Methods and Results: A single-center consecutive-patient randomized design (with 6-month angiographic and 2-year clinical follow-up) was used. Consecutive patients (no chronic total occlusions or emergency procedures) were randomized to ICUS-guided provisional stenting or standard angiographic guidance. Quantitative angiographic minimal lumen diameter (MLD), angiographic restenosis, clinically driven target lesion revascularization, and major adverse cardiac events (MACEs) were evaluated. A total of 291 procedures (356 lesions) were included. Procedure success was higher in the ICUS-guided group than the group randomized to standard guidance (94.7% versus 87.4%, respectively;P =0.033), whereas time (65.2+/-31.0 versus 60.5+/-34.0 minutes, P =0.18) and contrast use (209.3+/-94.1 versus 197.5+/-89.5 mL, P =0.23) were not significantly different. Stenting rates were similar (49.7% versus 49.5%, P =0.89). Acute gain was greater in the ICUS-guided group than in the standard guidance group (1.85+/-0.72 versus 1.67+/-0.76 mm, respectively;P =0.02). Angiographic 6-month analysis revealed no difference in MLD (1.71+/-0.94 versus 1.57+/-0.90, P =0.19) or binary restenosis rate (>50% diameter stenosis) (29% versus 35%, P =0.42). Clinical follow-up (602+/-307 days) showed a significant decrease in clinically driven target lesion revascularization in the ICUS group compared with the standard guidance group (17% versus 29%, respectively;P =0.02).

Conclusions: Although angiographic MLD did not differ significantly after 6 months, ICUS-guided provisional stenting improved 2-year clinical results after intervention.

Figure. Kaplan-Meier survival curve showing freedom from TLR for ICUS-guided (solid line, circles) and Angio-guided (dashed line, squares) groups

Table 5. Major Adverse Cardiac EventsMACE includes death, myocardial infarction, re-PTCA, and CABG; 2-y, per patient

IVUS

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