# What is the Definition of Moderate to Heavy Calcification? Based on Fluoroscopy or Intravascular Imaging

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### 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 signifitant commany artery disease and a determinant of the success of transcatheter theraps.

Methods and Renalty Eleven hundred fifty-five native vesseltarget lessons in 1117 patients were studied by intravascular ultranound (IVUS) and contnary 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< 600) versus angiography). The mean arc of lesion calcium measured 135 ± 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 are of superficial calcium measured 85:: 1085; the mean length measured 24::34 mm. There hundred seventy-three of 1355 reference segments (32%) contained calcium (P<.0001 compared with lesion site). The mean are of reference calcium measured 42:30°; the mean

Selective coronary arteriography has been the "gold standard" for guiding revascularization in coronary artery disease. Despite its widespread acceptance, it has many inherent limitations, including its inability to assess plaque composition with negative contrast imaging. Recently, it has been suggested that coronary arteriography has a limited ability to detect and localize target lesson calcium. 12 Target lesson calcium is both a marker for significant coronary artery disease and the major determinant of the success of various transcatherer therapies. 115

Intravascular ultrasound (IVUS) provides transmural images of cotonary arteries in vivo. The normal coronary arterial wall, the major components of the atherosclerotic pluque, and the changes that occur during the atherosclerotic disease process, after transcutherer therapy, and during restenosis can be studied in humans in a

length measured 1.7-5 h mm. Only 44 (473) had reference calcium in the absence of lesson calcium. Angingraphic decision and obsenbations of calcium depended on aris, lengths location, and doorthalms of beam and reference segment calcium. Bu decremonant analysis, the dissolution facilities in predicting angingraphic culcium included the arc of target lesson calcium, the arcs of soperficial calcium, the length of reference segment colcum, and the location of calcium within the festor. This model correctly predicted the angingraphic chaodication in real-27 of fessons and the angiographic chaodication in non-moderate sessore) of calcium in 62-87 of fessons.

Conclusion: IVUS detected calcium at ~391 of besons, significantly more often than standard argography. Although angography is moderated sentime for the distoction of extension related to the control of extension calcium, temperaturely, the size sentime for the presence of middle digrees. Commandor, 1995;48:1993-1985.

Key Words • coronary disease • calcium • ultrasomo • angesgraphs

manner previously not possible. The purpose of this words is (1) to use IVUS to evaluate the patterns (e.g. magnitude, location, and distribution) of coronary arreys calcum in a large number of patients undergoing transcattleter therapy for coronary arreys disease and (2) to compare IVUS and coronary argingraphy in the evaluation of coronary arreys calcification.

### Methods

### Patient Population

From July 1, 1991, to March 1, 1994, 1155 target lessons in 1117 patients were studied by IVUS and coronary angiographs These lesons met the following criteria (1) native vessel location (thereby excluding von graft and internal mammary lesions) and (2) ability to assess target lesion morphology by both IVUS and coronary arguigraphy etherelose excluding lessons with presume stem placement). There were 862 men and 255 women 61 ± 14 years old. Target lessen location was left. main in 47, left amenor descending in 467, left circumflex in 190, and right commany artery in 441, diagonal branches were considered part of the left america descending and marginal branches were considered part of the left circumflex arters One hundred morti-us learns were ontal in location. No catheter based intercentain was performed in 144 lessons (2) of which were treated instead with operative ecvascularization). halioon angoplasty was performed in 127 lesions, directional commun atherectoms (Devices for Vascular Interventions in

## Definition of Calcified Lesions – Angiography/Fluoroscopy

- Readily apparent densities noted within the vascular wall at the site of the stenosis
  - Moderate: Densities seen prior to contrast injection, but only during cardiac motion
  - Severe: Densities seen prior to contrast injection, but w/o cardiac motion and usually involve both sides of the arterial wall

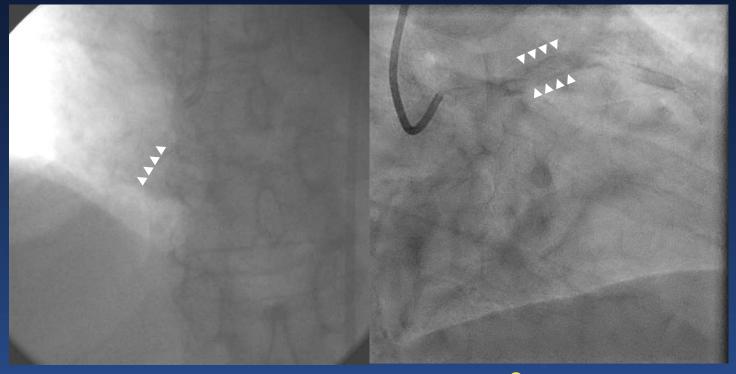
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E. 1995 American Hourt Association, Inc.

## Definition of Calcified Lesions – Angiography/Fluoroscopy



Moderate:
Seen only during cardiac motion on one side of vessel

Severe:
Seen without cardiac motion on both sides of vessel



## Meta-analysis of 13 studies and 66,361 pts assessing the association between angiographic arget lesion calcification and adverse outcomes in pts undergoing DES implantation

Endpoint	# of studies	HR
All cause mortality	4	1.41 (1.27-1.56)
Cardiac mortality	5	1.97 (1.68-2.31)
Myocardial infarction	6	1.33 (1.13-1.57)
MACE	5	1.37 (1.19-1.58)
TLR	8	1.47 (1.18-1.83)
Early TLR (<1 year)	7	1.63 (1.43-1.85)
Stent thrombosis	12	1.63 (1.36-1.96)
Early ST (<30 days)	5	1.69 (1.16-2.45)

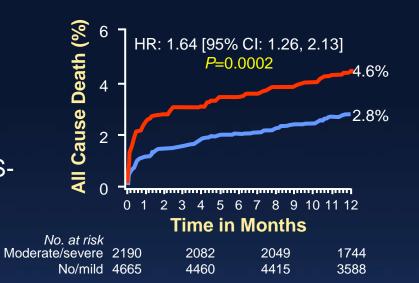
10/13 studies compared moderate/severe calcium vs no/mild calcium



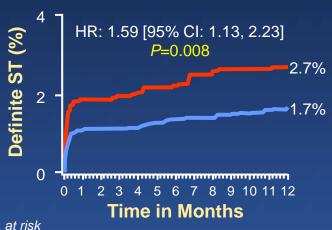
## Ischemic Outcomes After PCI of Calcified Vessels in ACS Pts

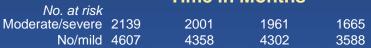
Pooled Analysis from the HORIZONS-AMI and ACUITY Trials

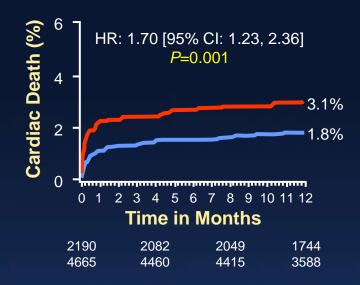
The presence of moderate/severe target lesion calcification was an independent predictor of 1-year definite ST (hazard ratio [HR]: 1.62; 95% confidence interval [CI]: 1.14 to 2.30; p=0.007) and ischemic TLR (HR: 1.44; 95% CI: 1.17 to 1.78; p=0.0007)

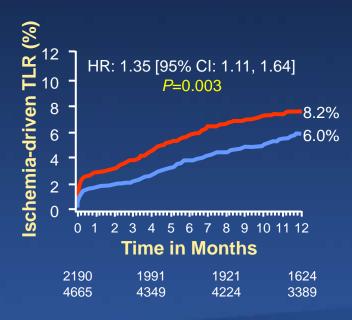












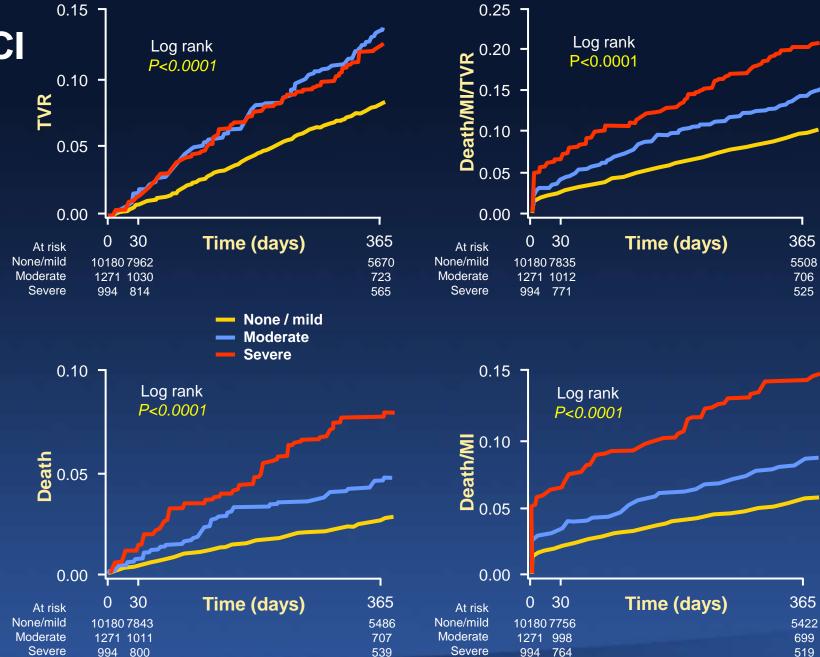


### Adverse Events Post-PCI And Calcification

Findings from a large multiethnic registry

The three strongest independent predictors of moderate to severe coronary calcification were lesion length, pt age, and LM location (c-statistic 0.73).

After adjusting for age, race, BMI, CKD, hypertension, smoking, prior MI or CABG, PAD, anemia, and lesion length, location, and angiographic characteristics, moderate or severe calcification remained associated with MACE (HR 1.63 [1.42, 1.86], P<0.001) and mortality (HR 1.64 [1.26, 2.15], P<0.001).



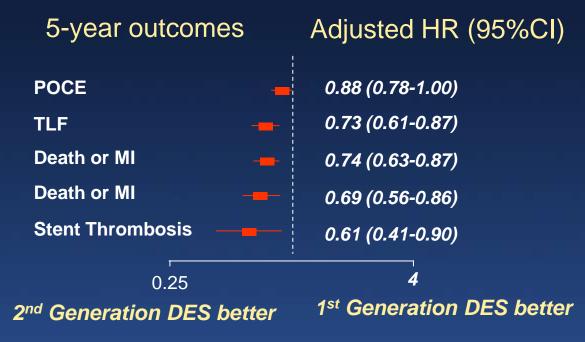


## 10-yr clinical outcomes: Pooled analysis of the ISAR-TEST 4 and 5 randomized trials

	No calcium	Mild calcium	Moderate calcium	Severe calcium	P-value
#	1212	2069	1276	396	
All cause mortality	25.3%	32.1%	41.7%	46.5%	0.004
TLR	17.4%	16.5%	19.8%	28.7%	0.001
MI	4.9%	5.9%	6.0%	10.5%	0.02
Definite/probable ST	1.3%	1.4%	1.8%	3.6%	0.6



## Moderate/Severe Angiographic Coronary Calcification and Long-Term Outcomes According to DES Generation



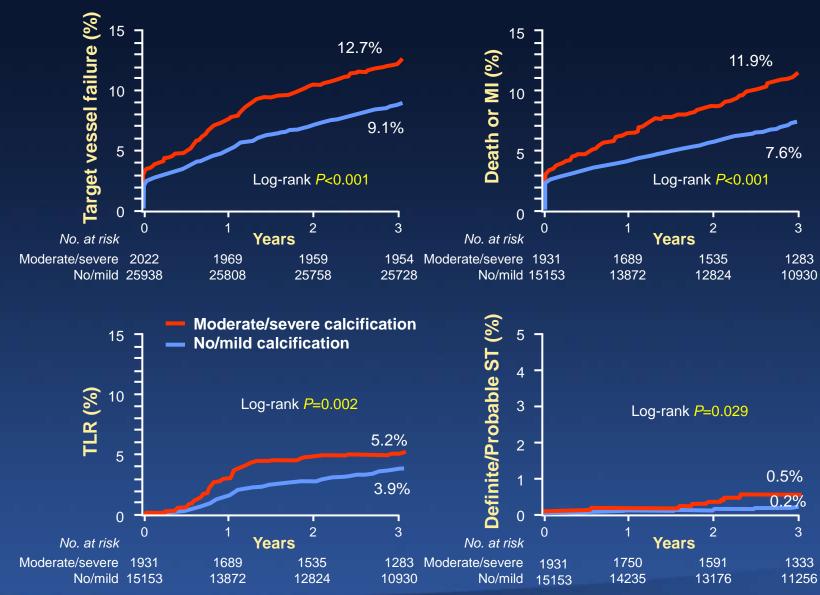
- Individual pt data were pooled from 18 RCT evaluating DES, categorized according to the presence of angiography core laboratoryconfirmed moderate or severe coronary artery calcium.
- A total of 19,833 patients were included. Moderate or severe calcium was present in 1 or more target lesions in 6,211 patients (31.3%).
- Major endpoints were the patient-oriented composite endpoint (POCE; death, MI, or any revascularization) and the device-oriented composite endpoint of target lesion failure (cardiac death, target vessel MI, or ischemia-driven TLR).



### IRIS-DES Registries (n=17,084 pts with 27,739 lesions)

The presence of moderate/severe coronary artery calcium was significantly associated with an adjusted risk of TVF at 3 yrs [hazard ratio, 1.37; 95% confidence interval (CI), 1.19-1.58; P < 0.001].

For severe calcium, optimal lesion preparation was associated with a lower 3-year rate of TVF (22.3vs. 12.8%) in the late F-U period of 1–3yrs (HR, 0.28; 95% CI, 0.12–0.69; P=0.003), but not in the early F-U period <1yr (HR, 1.16; 95% CI, 0.37–3.71; P=0.80). However, post-dilation with a high-pressure noncompliant balloon had no effect on the outcome. There was no impact of technique on lesser amounts of calcium.





### Randomized clinical trials using the fluoroscopic definition of moderate/severe calcium

Circulation: Cardiovascular Interventions

The Randomized PREPARE-CALC Trial

BACKGROUND: Balloon distration or debulking everys to be repertial to

allow-supportal start implantation in calcified coronary lesions. Compared

with standard balloon preditation, debuting using high-spired rotational

atherectomy (RA) is associated with higher initial procedural suscess albeit

with higher in-stent, late turner loss at intermediate-term follow-up. Whether

modified (scoons or cultimal balloons (MB) could achieve similar procedural

success compared with RA is not known. In addition, whether new-peneration

sing-eluting stents could countedralance the expensive repirtimal problemation

METHODS AND RESURTS: We randomly assigned potients with documented

maccardial achemia and severely calcified native commany leasons undergoing

print rollineages; nakel to ypetivite a st rollinivatro ywronos escenatures;

MB or RA followed by drug-eluting views implantation. Starting was performed

using a third-pereration septimus-eluting stant with a bisubsorbable polymer.

delivery and expansion with attainment of <20% in litera residual stances in

the presence of TIMI (Thrombolysis in Myocardia) infunction (3 flow without

crossover or stent failure; powered for superiority) and in-stent late lumen loss

at 9 months (noweed for annarheonists). Tan hundred nations were enrolled

at 2 centers in Germany in-100 in each treatment group). The mean age of the

study population was 74.047.0 years, 76% owns man, and 33.5% had diabetes

melitus. Strategy suscess was significantly more common in the RA group IRTN versus 98%, relative risk of Salura with an MS- versus BA-based strotegy, 9.5.

95% Ct 2:3-39.7; A=0.0001), but mean fluoroscopy time was longer (19.6x13.4)

versus 23 9±12 2 minutes: Av0 031, At 9 months, regan in-stant late lumen.

loss was 0.16±8.39 mm in the MR group and 0.27±0.40 mm in the RA group

(P=0.21, A=0.02 for noninferority). Target lesion revisioulascenori (7% versio

2%; Aug. 17); definite or probable stem thrombosis (D% verus 0%; Auf. D0).

different Setween the Millians SA groups.

and target was at falter 07% versus 6%, 760 70) were low and not agrificantly

CONCLUSIONS: Lesion prepuration with uptions RA before drug-druting stent

employments in a few late or neverty all parties to severely calculated commany leadons.

is more commanly suppressful as a primary strategy companed with MB, and is not

Resulting halfs; and offective as long as bolicust RA is readily available and may offer

associated with exceptive late furnish line. A strategy of productinal ME remains.

the advertages of compatibility with smaller sized catheters and less inadiation.

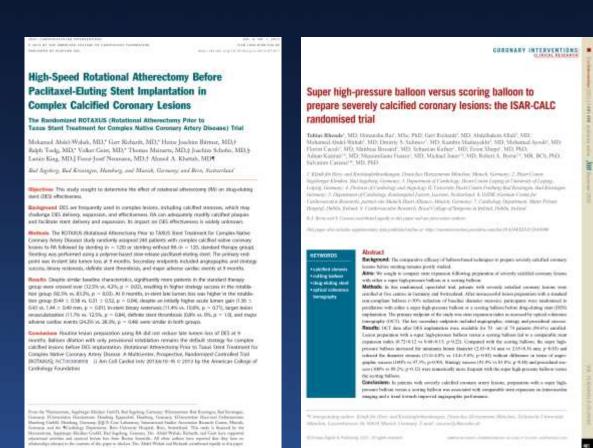
CLINICAL TRIAL REGISTRATION: URL https://www.shricattish.gov.Urtgue

Both strategies are associated with excellent clinical outcome at 9 months.

The brail had 2 premary and points: strategy success (defined as successful stert)

High-Speed Rotational Atherectomy Versus

ORIGINAL ARTICLE



Abdel-Wahab et al. JACC Cardiovasc Interv 2013;6:10-9

Rheude et al. EuroIntervention. 2021:17:481-488.

Abdel-Wahab et al. Circ Cardiovasc

Modified Balloons Prior to Drug-Eluting Stent Implantation in Severely Calcified Coronary Lesions Michaeled Abdel Walner Ralph Toelg, MD Robert A. Ryme, MB BOL Volker Geist, MD Mohamed El-Mewerds Abdolhakim Alfali, MD Tobias Rheude, MD Derek R. Robinson, D. Phil Mohammad Abdelphani. Drettriy S. Sulimov, MD Adner Kestrati, MD Gert Richardt, MD Rackground \* Intercent \* this every zero \* furban \* Idi

Committee contains at the surface. Cardiovascular Revascularization Medicine Randomized Compartson of Strategies to PrepAre SeveRely CALCified Coronary Lesions 2: Design and Rationale of the ISAR-CALC 2 Trial larta Scalamogna 14, Mohamed Abdel-Wahab , Kambis Mashayekhi , Massimiliano Fusam , lavid M. Leistner 12, Mohamed Ayoub 1, Erion Xhepa 1, Michael Joner 11, Adnan Kastrati 11, alwatore Cassese 4, Tobias Rheude 44 sematted to Assistage, Natures and Links Letters, Surveys but to circletor and hypotopy Advanta bilation, alternat. Green ott mar for 1864. 3. Kortingat, fligantige, blever klankleriter florikke filos, frankler i Jersen Jenser Control for Control (1864), fligantig (1874), fligant film filosophis, frankler (1874), fligantig OTHE BESIES ARRYMACT harigement. The previous course traduced of severally sale that consules forces has been associated with low performance of consulery stress and poor cliental image even cultivation. Admission below proporation telling colodito initial for, to linearity 3GE Usphil 27 his price 2GE soluble palser Militarium (KE) more productions in of the absorpt course to any recomming the risk of soort failure. Author-Appel to begin Hady-design and electron. The ISBLONG I Electron Productor INCTION TO Be to temporal infrared, and question, translatations, translatements, amendes historia, apen-street mod disrigand to company a tomas proportion strategy with differ report high-processor fulform or retinourcable little report SPU before drug-desiring street 1987 Insulantation is parameter with properly calculated partitional property between the total All contrasts are in quiesd for trial completion. The primary endpoint will be final applicable, estated former dissector (MEX) after since implicit alone. By secondary endpoints in faile since impaction companily applical coloring over tomag tanks (CC), promised and statem species, seed for complementary being recognition or 8 of about other prioring, both factors goth, and inspecialments careful correct opins 18-day follows up.

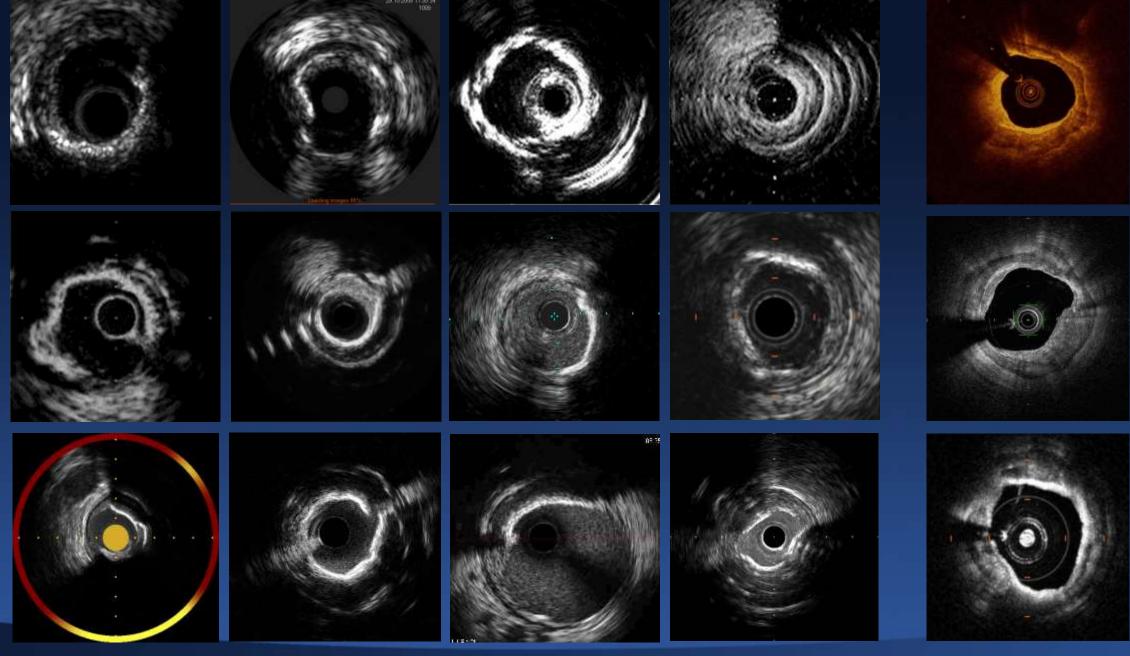
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Interv. 2018;11:e007415

Scalamogna et al. Cardiovasc Revasc Med 2023;49:22-27







### Angiography is only moderately sensitive for detection of extensive lesion calcium (sensitivity 60% and 85% for 3- and 4-quadrant calcium, n=1155)

Patterns of Calcification in Coronary Artery Disease

A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions

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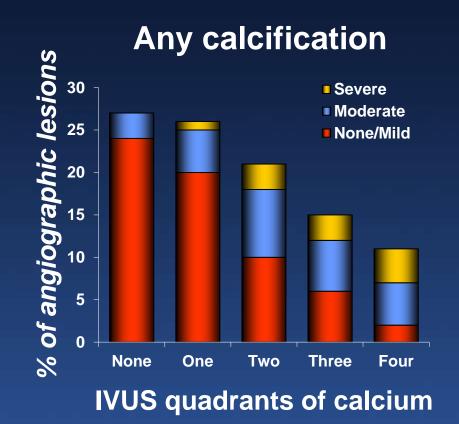
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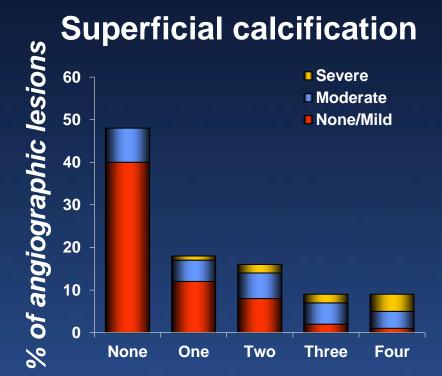
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Condition (NVS directal calculation of 197) of forest agedyante more other than standard argography. Writingly exposingly is modulately scenarios for the detection of cricelour quadrant calcom, respectively; it is less sensitive for the protected of militar degrees, illimination, 1990,90,1969-1965.

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**IVUS** quadrants of superficial calcium



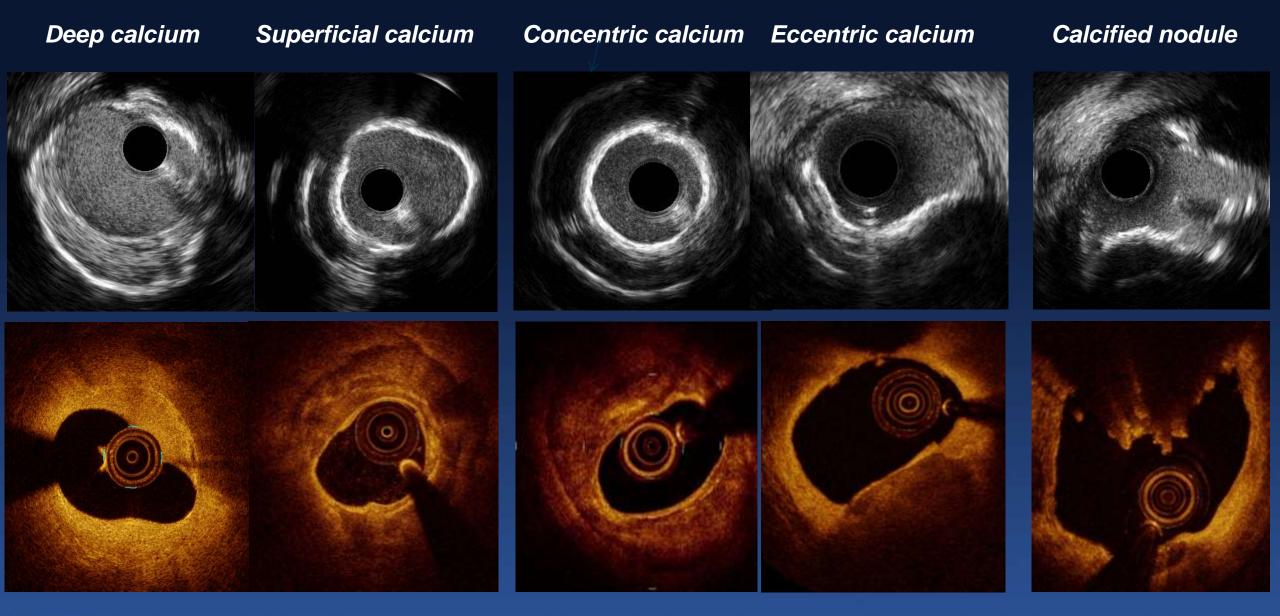
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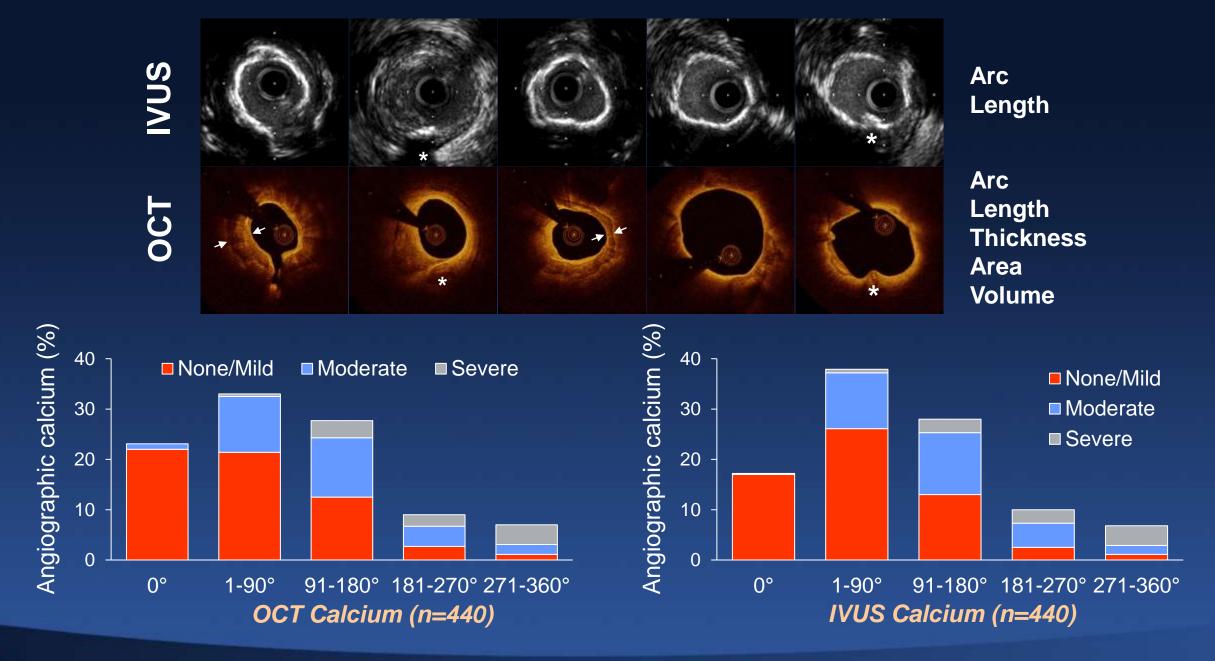
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Consequenties of Mario R Laure, MD Director of Breschill, Washington Cardinings Comm. 10 Dwing St NW 149-11, Work-

	Angiographic Calcification					
IVUS	None/Mild	Moderate	Severe			
#	715	306	134			
Target lesion Ca++	61%	90%	98%			
Arc of lesion Ca++ (°)	71±83	165±106	238±104			
Superficial lesion Ca++	37%	72%	92%			
Arc of Superficial lesion Ca++ (°)	44±74	124±110	215±119			
Arc of reference Ca++ (°)	25±63	61±93	87±98			
Total length of Ca++ (mm)	3.6±4.4	7.2±6.4	9.7±6.4			

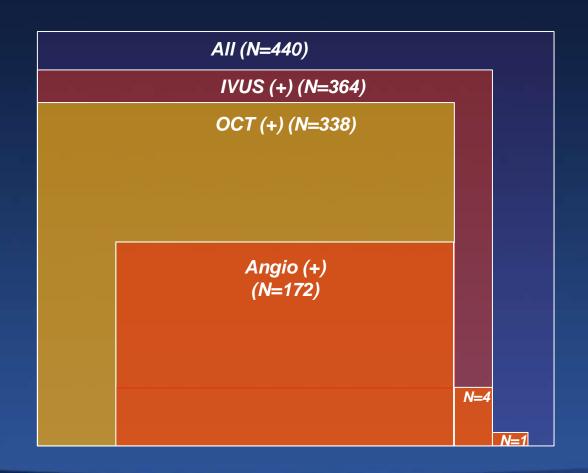








	IVUS (+)	IVUS (-)		OCT (+)	OCT (-)		OCT (+)	OCT (-)
Angio (+)	176	1	Angio (+)	172	5	IVUS (+	) 338	26
Angio (-)	188	75	Angio (-)	166	97	IVUS (-)	0	76





## Pre and post-OCT calcium scoring system predicting stent expansion

	Test cohor	t of 128 p	ots						
	Regression Coefficient	95% CI	P-value	P-value Calcium Score					
Mayimum adaium angla (nar 1900)	7 40	10.045.0.04	-0.01	Maximum calcium angle		≤180°	0		
Maximum calcium angle (per 180°)	-7.43	-12.6 to -2.21	<0.01			>180°	2		
Marian and in this language (and 0.5 and 0.5	2.40	0.0545.0.45	0.00	Maximum calcium thickness		≤0.5mm	0		
Maximum calcium thickness (per 0.5 mm)	-3.40	-6.35 to -0.45	0.02			>0.5mm	1		
0-1-:	0.00	4.00.1- 0.55	0.04	Calcium length		≤5mm	0		
Calcium length (per 5 mm)	-3.32	-4.09 to -0.55	0.01			>5mm	1		
	Validation co	hort of 13	3 pts						
Score	(n=27)	(n=45)	(n=34) (n=3) <b>(n=2</b>		<b>4)</b> P-\	P-value			
MSA, mm²	7.2	6.3	5.9	6.7	5.7	'n	.21		
MOA, IIIII	(5.4, 9.2)	(5.2, 8.4)	(4.8, 8.0)	(5.8, 7.1)	(4.4, 7	7.4) °			
Stent expansion at target lesion calcium, %	99	98	86	98	78	<(	0.01		
Ctont expansion at target resion calcium, 70	(93, 108)	>	(77, 100)	(83, 104)	(70, 8	36)			
Stent expansion at MSA, %	91	85	80	80	69	<(	0.01		
Stort oxparioion at mort, 70	(84, 95)	(78, 93)	(73, 93)	(73, 85)	(60, 7	77)			



## IVUS calcium score predicting stent expansion (as a continuous variable) in lesions with calcium >270°

Test cohort of 97 pts									
		Regression Coeff	95% CI	P-value	Cut-off	Calcium Score			
Length of calcium >270° (per 5mm)		F	-9.7, -1.2	0.01	5.0	≤5mm	0		
		-5.5	-9.7, -1.2	0.01		>5mm	1		
Calcium Nodule		10.2	-16.3 to -4.2	0.0009		absent	0		
		-10.2		0.0009		present	1		
Vessel diameter (per 1mm)		8.6	2.7 to 14.4	0.004	3.5	>3.5mm	0		
						≤3.5mm	1		
Circumferential calcium		-14.3	-25.0 to -3.5	0.009		absent	0		
		-14.5	-23.0 to -3.3	0.009		present	1		
Stent underexpansion (<70%) in the validation cohort of 97 pts									
	Cut-off	C-statistics	Sensitivity	Specificity	PP	V	NPV		
Score	≥2	0.85 [0.77, 0.93]	89%	63%	48°	%	94%		

In 67 lesions without angiographically visible calcium, but with a maximum IVUS angle of superficial calcium >270°, there were none with a calcium score of 4 and only 1 with stent underexpansion.



### STATE-OF-THE-ART REVIEW

### Management of Calcific Coronary Artery Lesions



Is it Time to Change Our Interventional Therapeutic Approach?

Giovanni Luigi De Maria, MD, PnD," Roberto Scarsini, MD," Adrian P. Banning, MD

### ABSTRACT

Patients with obstructive coronary lesions with a high calcium content (LHCC) have an exaggerated clinical risk, because the presence of calcification is associated with more extensive coronary atherona and higher burden of comorbidities. Treatment of LHCC using percutaneous techniques is complex because of an increased risk of incomplete lesion preparation with suboptimal stent deployment and higher rates of acute and chronic stent failure. Rotational atherectomy has been the predominant technology for treatment of high-grade LHCC, but novel devices/technologies have entered clinical practice. It seems likely that combining enhanced intravascular imaging, which allows definition of the patterns of calcification with these new technologies, will herald a change in procedural algorithms for treatment of LHCC. This review provides an overview about LHCC with special focus on existing and emergent technologies. We also provide a proposed procedural algorithm to facilitate optimal use of technology according to specific features of LHCC and coronary anatomy. (J Am Coll Cardiol Intv 2019;12:1465-78) © 2019 by the American College of Cardiology Foundation.

our specific coronary anatomic features are atherectomy (RA) has represented the predominant commonly considered to be markers of interventional procedural complexity: 1) the presence of calcium; 2) severe tortuosity; 3) high

content (LHCC) are probably the most challenging the appropriate patient, and most likely to impact adversely on both the acute and the long-term results of percutaneous coronary intervention (PCI). Obstructive calcium lesion preparation and balloon dilation, making delivery of balloons and stents difficult and by restricting final stent expansion. Rotational of LHCC,

solution for LHCC, but recently new technologies have become available to clinical practices. Understanding the implications of coronary calcification thrombus content; and 4) diffuse atherosclerotic and the clinical and technical challenges related to burden with variable caliber and an absence of a pla- the geographic distribution of calcium, and the que free landing zones, to facilitate safe stent specific mode of action of each technique for the treatment of LHCC, is pivotal to select and adopt Of these features, lesions with high calcium the optimal approach for the relevant anatomy in

This paper provides a contemporary overview about the treatment of LHCC in the catheterization laboratory with a specific focus on the technical increases procedural complexity by interfering with complexities and clinical implications of LHCC, on the role of intravascular imaging, and on the available technologies (old and new) for optimal management

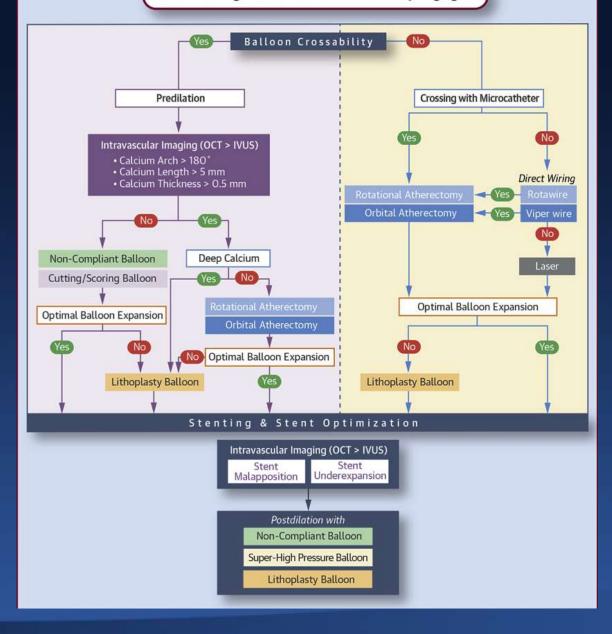
From the Oxford Beart Centre, Oxford University Bospitals, NRS Trust, Coford, United Kingdom, "Drs. De Maria and Scarcini contributed equally to this paper. Dr. De Maria has received a speaker fee from Miracor Medical SA, Dr. Scarnini has received an educational grant from EAPCI. Dr. Burening has received institutional funding for an interventional fieldowship from Ecotom Scientific; has received speaker fees from Boston, Phillips, and Abbott Vasculan and in partially funded by the MHS NBIRI Biomedical Research Centre, Oxford, United Kingdom.

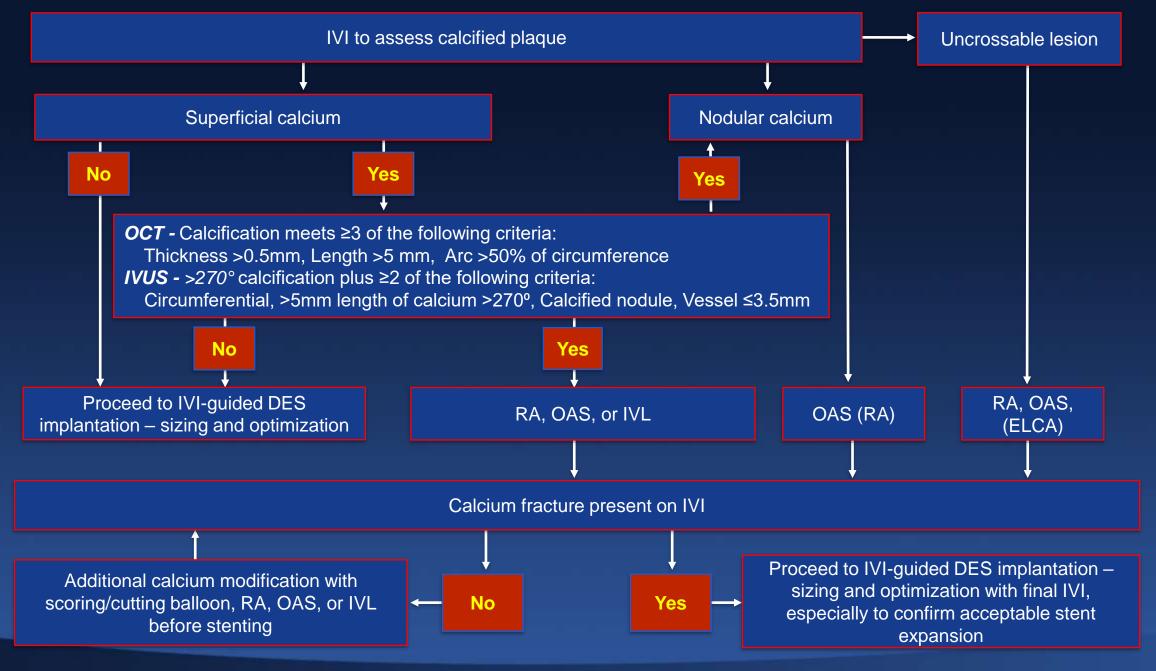
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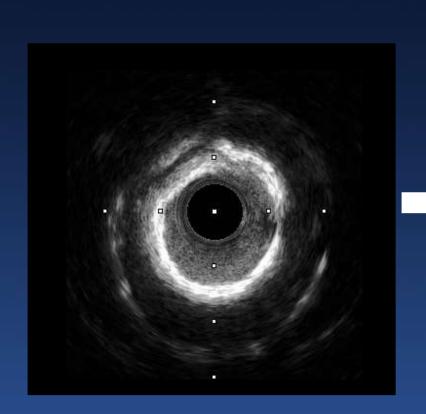
### Lesion with High Calcium Content on Coronary Angiogram



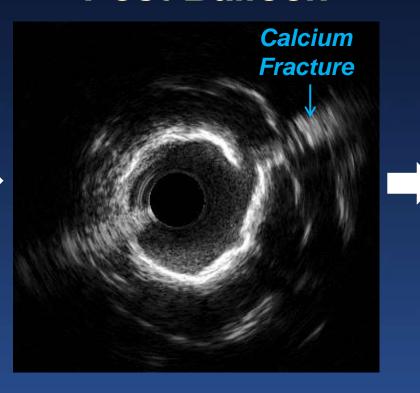




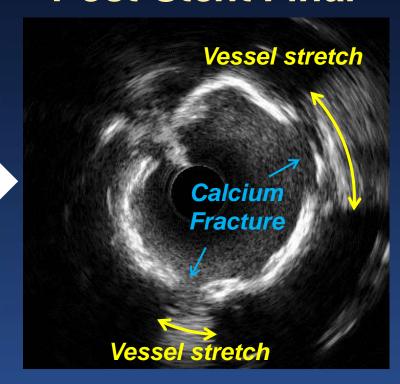
### **Detection of Calcium Fracture**



### Post-Balloon



### Post-Stent Final





### Question

Is the definition of Moderate to Heavy Calcification based on fluoroscopy or intravascular imaging



### Answer

Both. It depends on the situation.

