Coronary Physiology in 2018

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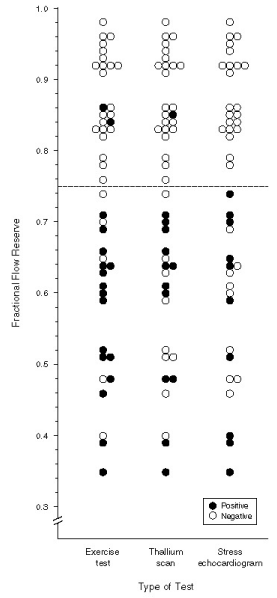
FFR: 20 years ago

FFR

ischaemia diagnosis in the cath lab: one stop shop

- FFR corelates well with Spect and thus can diagnose ischaemia in the cath lab.
- 45 patients



N Engl J Med 1996; 334:1703-1708

How things have evolved afterwards:
FFR in SCAD
Randomized studies and Registries

- Randomized studies
  - DEFER
  - FAME
  - FAME II
  - FUTURE

- Prospective Registry
  - IRIS-FFR

Clinical utility of FFR:

FROM

AN INDEX DIAGNOSING ISCHAEMIA IN CATH LAB AND REPLACING INTO SOME EXTEND THE UTILITY OF MYOCARDIAL FUNCTION TESTS

TO

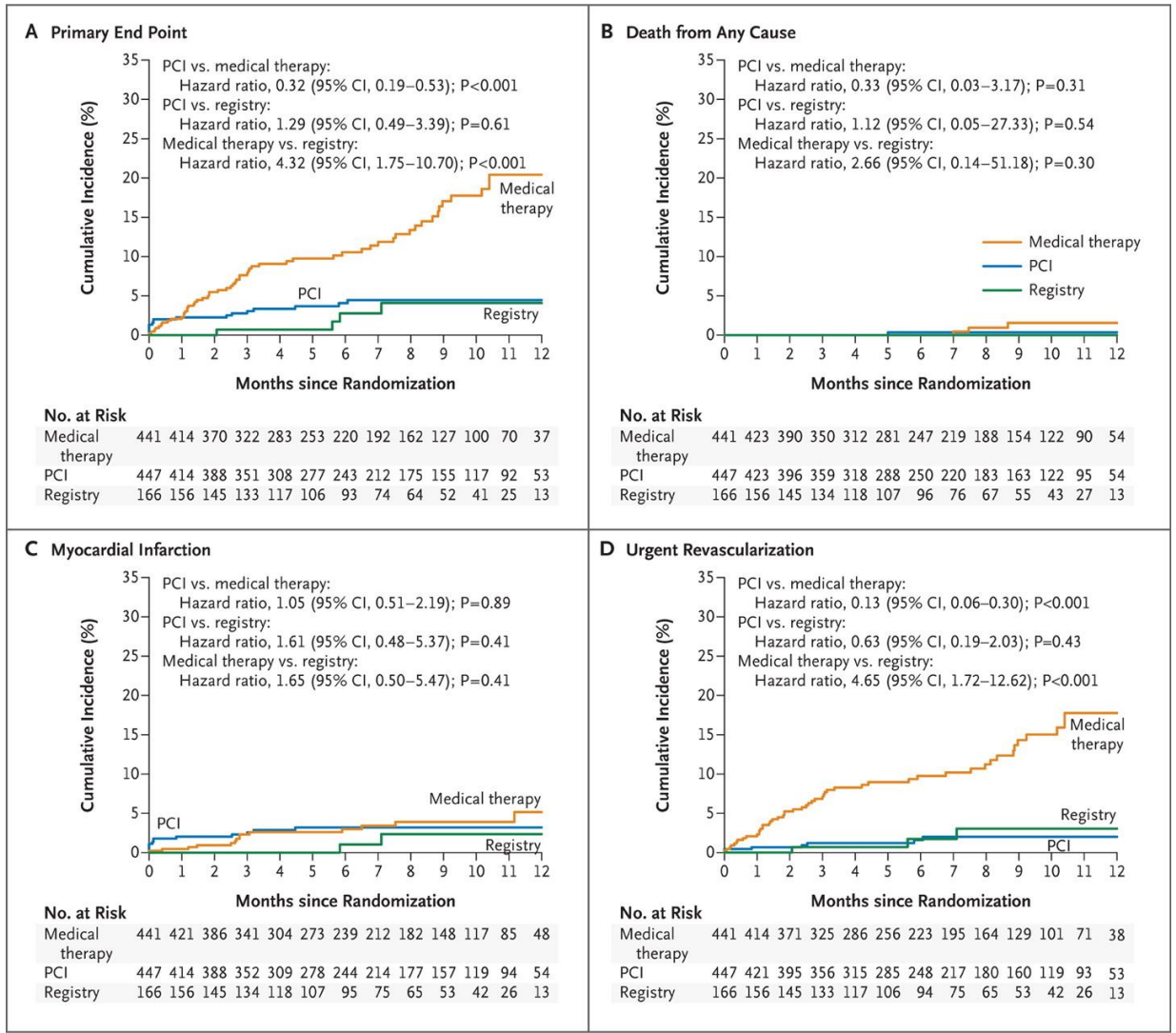
A PREDICTOR OF FUTURE EVENTS

FAME II STUDY: 24 MONTHS FOLLOW-UP:

Can really significant lesions (FFR<0.80) be treated with OMT only?

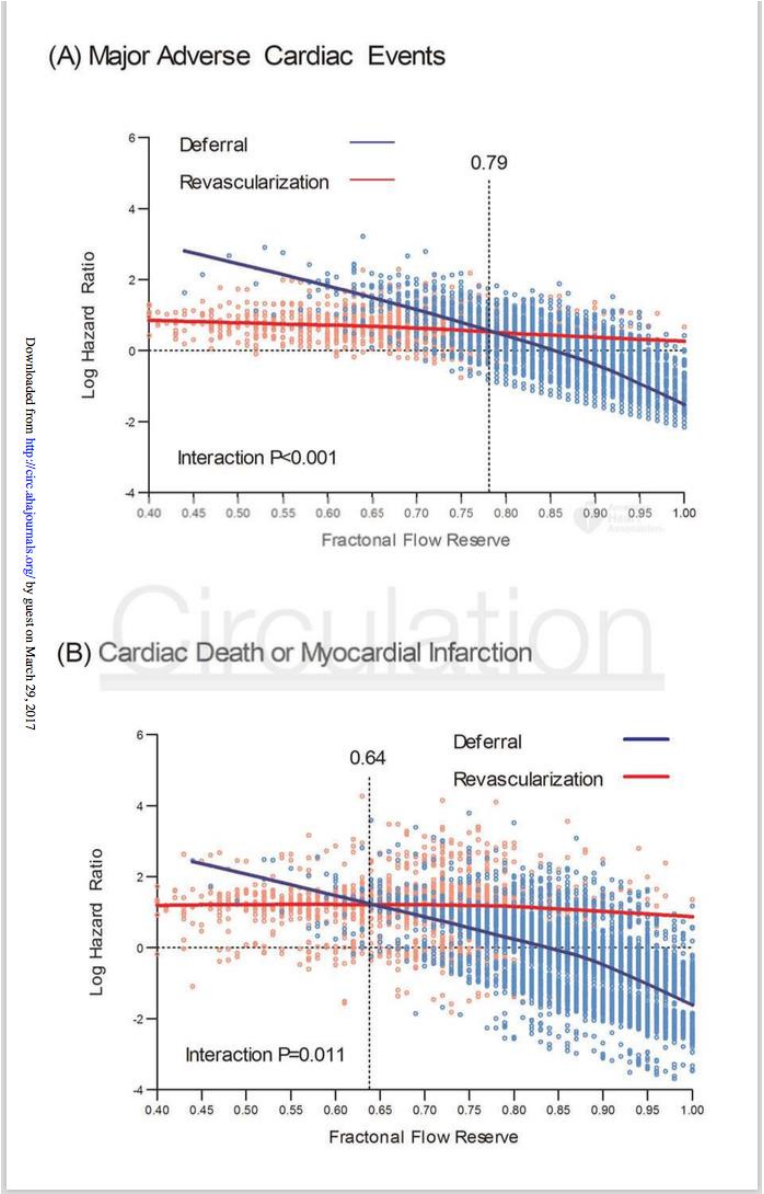
Patients with FFR<0.80 are benefited from PCI due to less urgent ReVasc

Patients with FFR>0.80 do well on OMT



N Engl J Med 2014

IRIS FFR REGISTRY



The largest prospective, multicenter registry of FFR

<u>"risk continuum" for FFR in deferred coronary stenoses.</u>

FFR <0.79 PCI reduces possibility of revasc
FFR <=0.64, PCI reduces possiblility of death of MI
FFR<0.76 reasonable to perform PCI

<u>Independent predictors of clinical events in deferred</u>

FFR,
Imaging characteristics

- thrombus-containing lesion,
- multivessel coronary artery disease, and
- percent diameter stenosis.

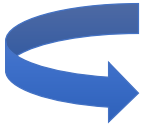
Cicrulation 2017

FFR in SCAD

- FFR can diagnose ischaemia
- FFR can predict future events helping thus clinical decision making in SCAD patients

Clinical use of FFR

- FFR<0.80



PCI with DES reduces the risk of revasc (urgent and non)

- In patients with MVD we can decide which artery should be treated based upon FFR (<0.80)

- FFR<0.64

PCI with DES reduces the risk of death or MI

Use of FFR in the everyday clinical practice

- FFR in <20% of the selective PCIs
  - Possible reasons
    - Financial cost (
    - Prolongation of the procedure
    - Adenosine administration (cost and side effects)

- Alternative to FFR methodologies

  - BASED UPON PHYSIOLOGY
    - iFR
  - STAND ALONE IMAGING
    - Coronary angiography
    - IVUS (virtual histology)
    - OCT
  - IMAGING COUPLED WITH PHYSIOLOGY
    - FFRct
    - vFAI
    - ESS

iFR: Index with similar to FFR philosophy BUT without the need of adenosine

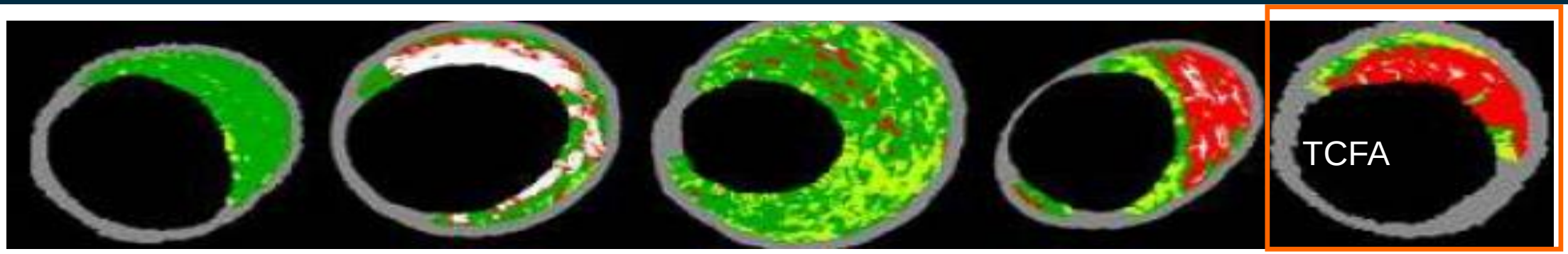
- Deferral of revascularization is equally safe with both iFR and FFR
  - 1 year MACE rate of deferred lesions around 4%
  - 1 year MACE rate of deferred lesions higher in ACS compared to SCA pts (5.91% vs 3.64%)

- Advantages of iFR vs FFR
  - No need of adenosine
    - Cost
    - Side effects
  - ? Better accuracy in predicting severity of tandem lesions

Stand alone imaging

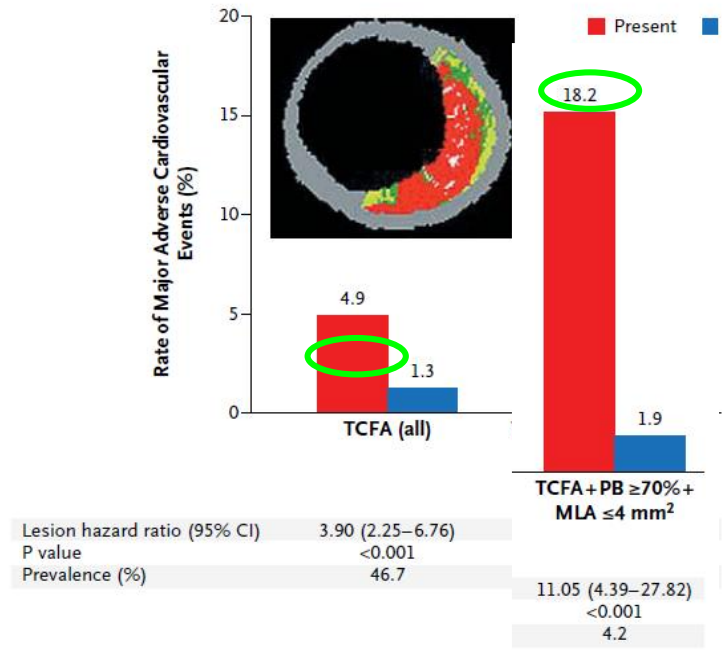
- IVUS and Virtual Histology
- OCT
- 3D coronary angiogram

PROSPECT STUDY



Independent predictors of lesion level events by logistic regression analysis

Variable	OR [95% CI]	P value
PB_{MLA} ≥70%	4.99 [2.54, 9.79]	<0.0001
VH-TCFA	3.00 [1.68, 5.37]	0.0002
MLA ≤4.0 mm^2	2.77 [1.32, 5.81]	0.007
Lesion length ≥11.6 mm	1.97 [0.94, 4.16]	0.07
EEM_{MLA} <14.3 mm^2	1.30 [0.62, 2.75]	0.49



Stone GW et al. N Engl J Med 2011

OCT

- Studies comparing OCT measurements with FFR (FFR been used as the gold standard)

- OCT characteristics of vulnerable plaques

THE MAIN QUESTION REMAINS HOW TO DEAL WITH SENSITIVE PLAQUES OTHER THAN LOWERING CHOLESTEROL LEVELS

3D QCA

- Better assessment of lesion severity compared to 2D QCA (especially eccentric lesions)
- Better correlation with FFR than 2D QCA

ANGIOGRAPHIC ASSESSEMENT OF LESION SEVERITY IS LESS SENSITIVE THAN FFR IN PREDICTING FUTURE EVENTS

- Not always possible to get the views needed

Conclusions

- Only IVUS VH has been proved able to predict future events in a similar manner to FFR
- Both methods have low predictability: ≈ 18%
- FFR is far more easy to use

Imaging coupled with physiology

- FFRct
- vFAI
- Different imaging modalities coupled with ESS

FFRct

- Important advance in the field
- Will continue to be refined
- Increases the cost of CTCA by 4-fold
- Unnecessary ICA and revascularizations can be avoided
- Pts less likely to benefit
  - severe, high risk lesions (80-90% proximal LAD)
  - Unequivocally low-risk lesions (distal, branch vessels)

vFAI: Estimation of coronary stenoses' functional severity by using coronary angiography coupled with physiology?

- The 2nd published study

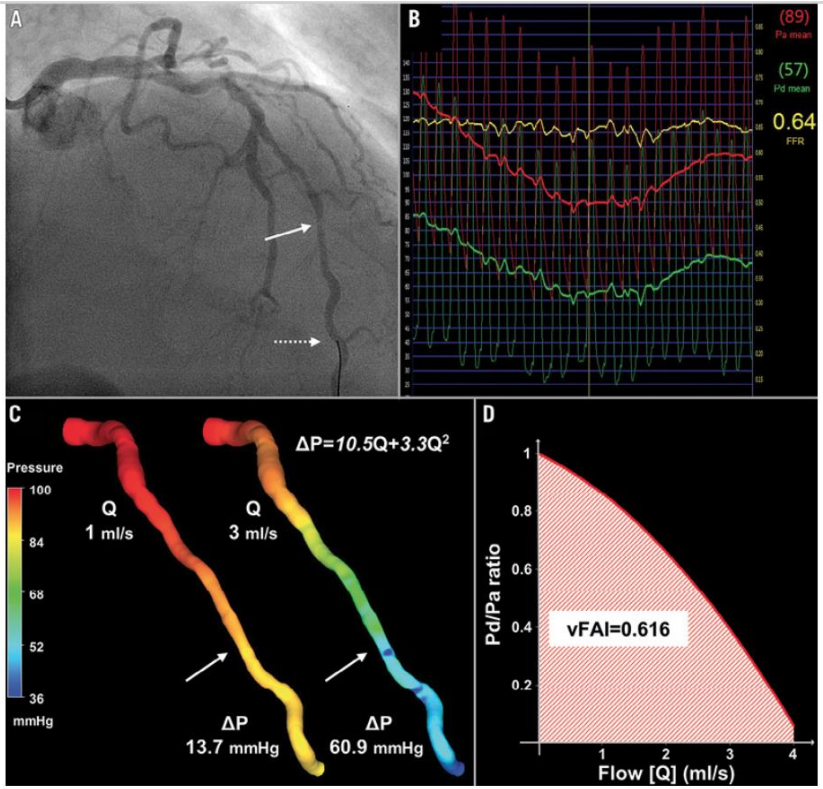


Figure 2. Intermediate lesion with haemodynamic significance. (A) Representative example of a left anterior descending artery (LAD) with a moderate lesion (arrow: maximal stenosis) in angiography (3D-QCA %diameter stenosis: 35%) that had (B) a low fractional flow reserve (FFR=0.64) measured at a distal location (dotted arrow) using the pressure wire. (C) 3D-QCA coronary lumen reconstruction with the pressure distribution in a colour-coded map for two different flow rates (Q), which resulted in a pressure gradient (ΔP) of 13.7 and 60.9 mmHg. The computed artery-specific ΔP–Q relationship is provided. The arrows denote the location of maximal stenosis. (D) Relationship between the ratio of distal to aortic pressure (Pd/Pa) and flow for the studied artery, and calculation of the artery-specific virtual functional assessment index (vFAI: 0.62) shows the good agreement with wire-FFR.

Table 2. Diagnostic performance of the virtual functional assessment index (vFAI) and the anatomic measures from 3D- and 2D-quantitative coronary angiography (QCA) using the optimal cut-points (receiver operator characteristic curve analysis). Fractional flow reserve (≤0.80) measured using the pressure wire was used as the reference standard.

Diagnostic measure	vFAI ≤0.82	3D-QCA %AS >64%	3D-QCA MLA ≤1.66 mm²	3D-QCA %DS >41%	2D-QCA max %DS >51%
Diagnostic accuracy	87.8% (81.1-92.7%)	72.7% (64.5-79.9%)	79.1% (71.4-85.6%)	74.1% (66-81.2%)	73.4% (65.2-80.5%)
Sensitivity	90.4% (79-96.8%)	69.2% (54.9-81.3%)	80.8% (67.5-90.4%)	65.4% (50.9-78%)	44.2% (30.5-58.7%)
Specificity	86.2% (77.2-92.7%)	74.7% (64.3-83.4%)	78.2% (68-86.3%)	79.3% (69.3-87.3%)	90.8% (82.7-96%)
Positive predictive value	79.7% (67.2-89%)	62.1% (48.4-74.5%)	68.9% (55.7-80.1%)	65.4% (50.9-78%)	25.8% (11.9-44.6%)
Negative predictive value	93.8% (86.01-97.9%)	80.3% (69.9-88.3%)	87.2% (77.7-93.7%)	79.3% (69.3-87.3%)	73.2% (63.8-81.2%)

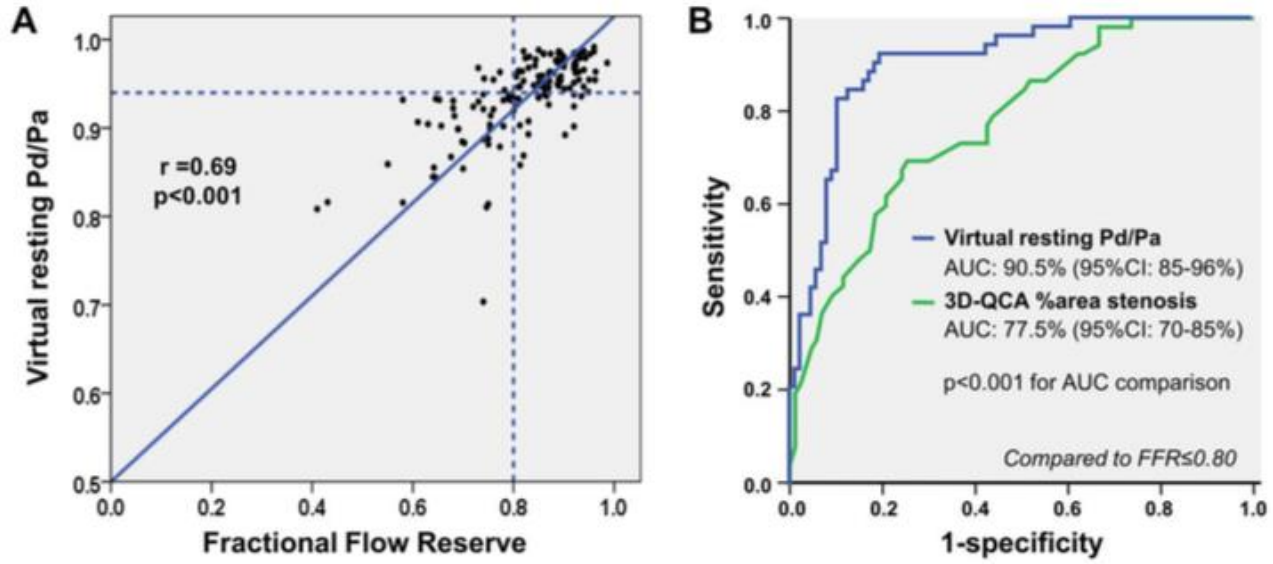
Values are presented as estimates (95% CI); %AS: percent area stenosis; %DS: percent diameter stenosis; MLA: minimum lumen area

EuroIntervention. 2014 Sep;10(5):574-83. doi: 10.4244/EIJY14M07_01.
Fast virtual functional assessment of intermediate coronary lesions using routine angiographic data and blood flow simulation in humans: comparison with pressure wire - fractional flow reserve.
Papafaklis MI[1], Muramatsu T, Ishibashi Y, Lakkas LS, Nakatani S, Bourantas CV, Ligthart J, Onuma Y, Echavarria-Pinto M, Tsirka G, Kotsia A, Nikas DN, Mogabgab O, van Geuns RJ, Naka KK, Fotiadis DI, Brilakis ES, Garcia-Garcia HM, Escaned J, Zijlstra F, Michalis LK, Serruys PW.

How fast virtual FFR can be measured.

Virtual FFR using only coronary angiography in 4 minutes.

Figure 2



Conclusions:
Virtual resting Pd/Pa using routine angiographic data and a simple flow model provides fast and of high diagnostic performance functional assessment of coronary lesions.

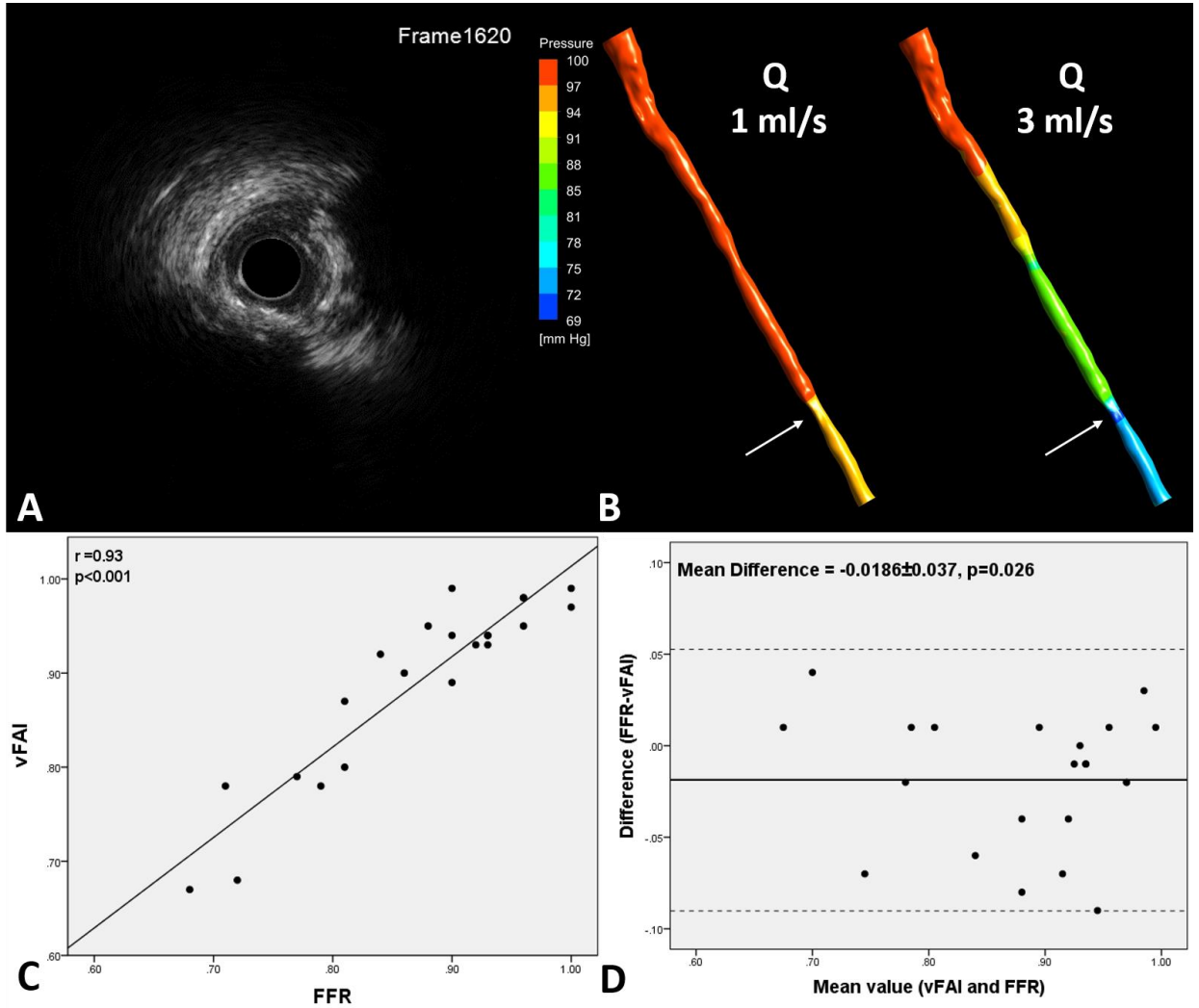
Heart Lung Circ. 2017 May 3. [Epub ahead of print]

Virtual Resting Pd/Pa From Coronary Angiography and Blood Flow Modelling: Diagnostic Performance Against Fractional Flow Reserve.

Papafaklis MI[1], Muramatsu T[2], Ishibashi Y[2], Bourantas CV[2], Fotiadis DI[3], Brilakis ES[4], Garcia-Garcia HM[2], Escaned J[5], Serruys PW[6], Michalis LK[7].

Can we make IVUS an one stop shop

(IVUS and vFFR at the same time). Measuring v FFR from IVUS



Close correlation between the IVUS-based vFAI and fractional flow reserve (FFR; r=0.93).

Virtual Functional Assessment of Coronary Stenoses Using Intravascular Ultrasound Imaging: A Proof-of-Concept Pilot Study

Panagiotis K. Siogkas, PhD,* Michail I. Papafaklis, MD, PhD,† Lampros Lakkas, MD, PhD,† Themis P. Exarchos, PhD,** Ziad A. Ali, MD, PhD, ‡ Dimitri Karmpaliotis, MD, PhD,‡ Gualtiero Pelosi, MD, PhD,*** Oberdan Parodi, MD, PhD,*** Christos S. Katsouras, MD, PhD,† Lampros K. Michalis, MD,† and Dimitrios I. Fotiadis, PhD* (Submitted)

ESS coupled with different imaging modalities

- IVUS & shear stresses
- OCT & shear stresses
- IVUS & VH & shear stresses
- CTCA & shear stresses
- 3D QCA & shear stresses

MAIN PROBLEM: BASED UPON STUDIES

WITH SMALL NUMBER OF EVENTS

NO EVENTS: PROGRESSION OF ATHEROSCLEROSIS

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

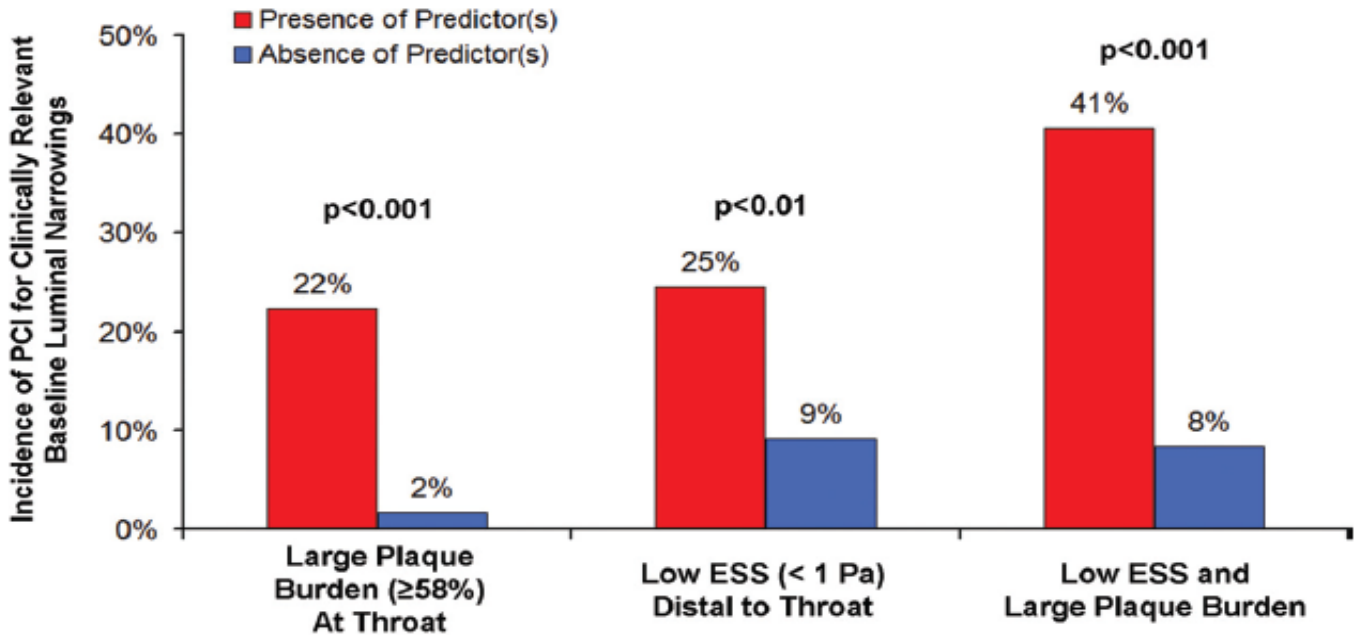
American Heart Association®

Prediction of Progression of Coronary Artery Disease and Clinical Outcomes Using Vascular Profiling of Endothelial Shear Stress and Arterial Plaque Characteristics : The PREDICTION Study

Peter H. Stone, Shigeru Saito, Saeko Takahashi, Yasuhiro Makita, Shigeru Nakamura, Tomohiro Kawasaki, Akihiko Takahashi, Takaaki Katsuki, Sunao Nakamura, Atsuo Namiki, Atsushi Hirohata, Toshiyuki Matsumura, Seiji Yamazaki, Hiroyoshi Yokoi, Shinji Tanaka, Satoru Otsuji, Fuminobu Yoshimachi, Junko Honye, Dawn Harwood, Martha Reitman, Ahmet U. Coskun, Michail I. Papafaklis and Charles L. Feldman

The largest natural history of atherosclerosis study which investigated the effect of ESS on plaque progression in 506 pts with an ACS

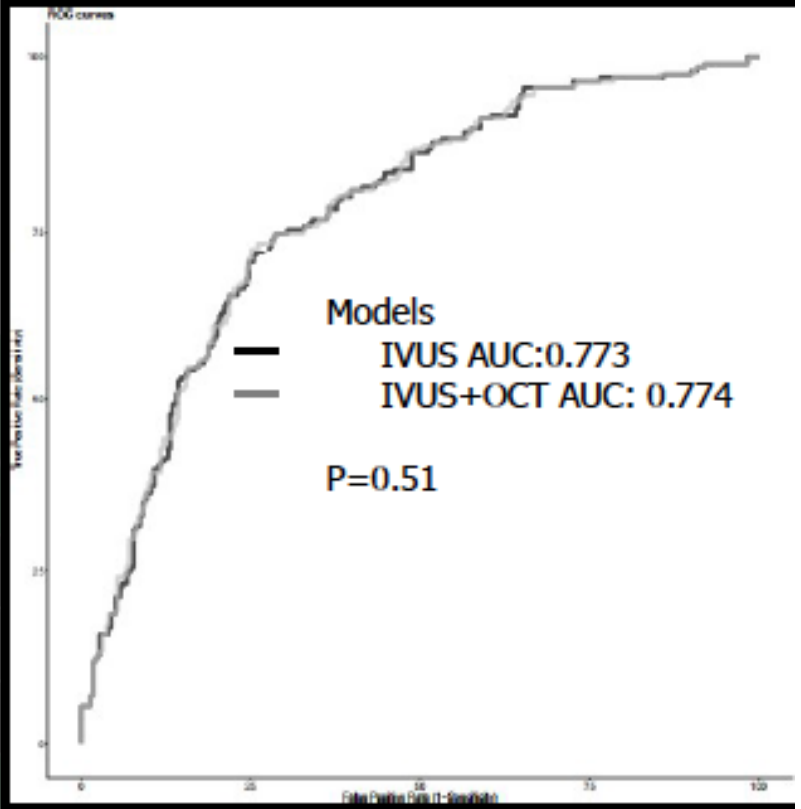
- **Low ESS** was independently associated with disease progression
- Large plaque burden and **low ESS** appeared as independent predictors of plaque progression
- Large plaque burden and low ESS predicted with **41%** accuracy worsening lumen obstruction requiring PCI



IBIS 4 – ESS sub-study

We define as disease progression as an increase in plaque area and reduction in lumen area

IVUS-based MV analysis of disease progression		
	OR	P
BL ESS per 1Pa increase	0.691	0.005
Plaque burden per 10% increase	0.038	0.003
Excessive expanding RM	1.671	0.057
Plaque burden per 10% increase	0.070	<0.001
IVUS and OCT-based MV analysis of disease progression		
	OR	P
BL ESS per 1Pa increase	0.692	0.005
Plaque burden per 10% increase	0.380	0.003
Excessive expanding RM	1.671	0.057
Macrophages	1.011	0.963
Neo-vessels	1.000	0.999



Conclusions: OCT-derived plaque micro-characteristics have little value in predicting more accurately than standalone IVUS and ESS segments that will to exhibit disease progression.

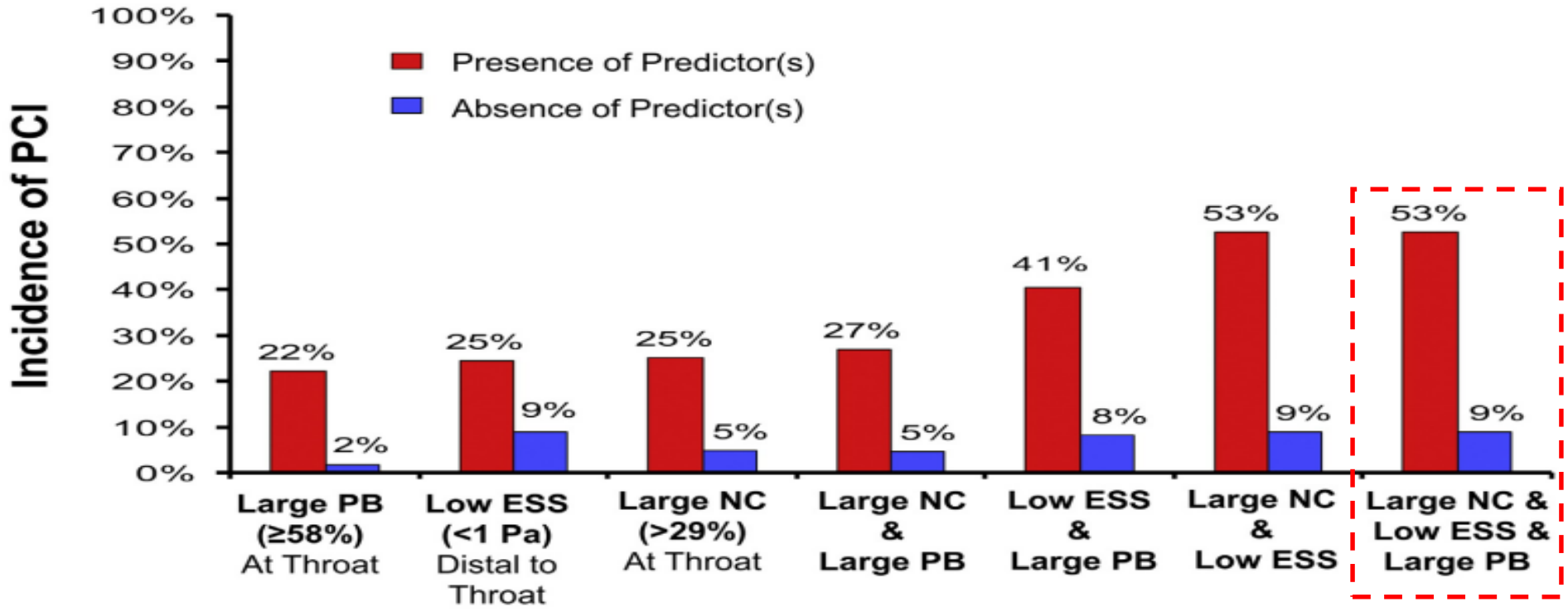
Shear stress analysis in multimodality imaging a sub-analysis of IBIS 4 study

Bourantas CV,[1,2] Raber L,[3] Sakellarios A,[4] Karagiannis A,[3] Kyohei Y,[3] Taniwaki M,[3] Radu M,[5] Moschovitis A,[3] Heg D,[3] Papafaklis MI,[4] Kalatzis F,[4] Naka KK,[4] Fotiadis DI,[4] Michalis LK,[4] Serruys PW,[6] Garcia-Garcia HM,[6] Windecker S[3](submitted)

IVUS-based Tissue Characterization and ESS: PREDICTION of events

combined ESS, necrotic core and plaque burden

prediction of clinically-relevant events

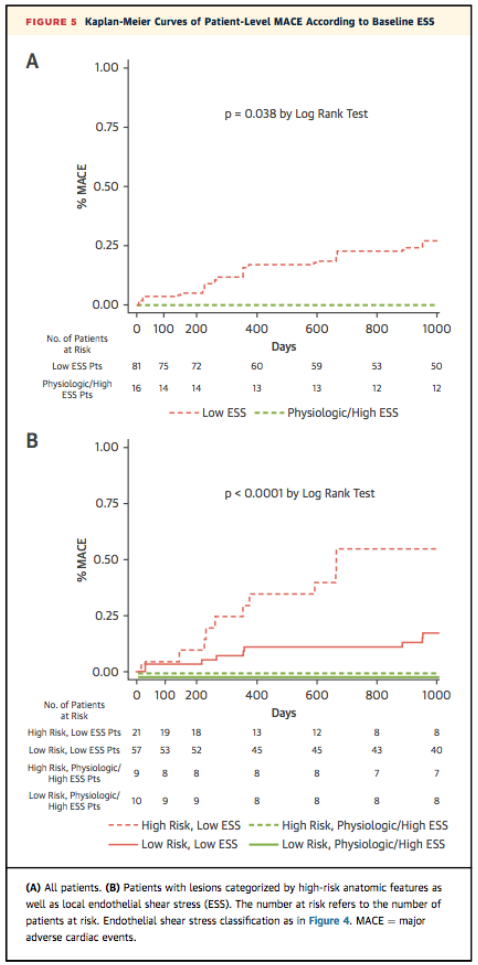


Diagn.Accuracy	59%	77%	70%	72%	85%	88%	88%
Sensitivity	94%	42%	74%	74%	42%	32%	32%
Specificity	54%	82%	69%	72%	91%	96%	96%
Positive PV	22%	25%	25%	27%	41%	53%	53%
Negative PV	98%	91%	95%	95%	92%	91%	91%
Prevalence	22%	10%	16%	15%	6%	4%	4%

Papafaklis et al. Int J Cardiol 2016

PROSPECT Study.

Role of low endothelial shear stress and plaque characteristics in the prediction of nunculprit major adverse cardiac events.



CONCLUSIONS

Local low ESS provides incremental risk stratification of untreated coronary lesions in high-risk patients, beyond measures of PB, MLA, and morphology.

Lesion with normal SS regardless of their characteristis (PB, MLA or lesion phenotype did not develop MACE at follow-up

Low ESS regardless the characteristics of the lesions: 22% possibility of developing MACE

Lesions of high risk and Low ESS: 58% possibility of developing MACE

Role of Low Endothelial Shear Stress and Plaque Characteristics in the Prediction of Nonculprit Major Adverse Cardiac Events The PROSPECT Study

Peter H. Stone, MD, Akiko Maehara, MD, Ahmet Umit Coskun, PHD, Charles C. Maynard, PHD, Marina Zaromitydou, MD, PHD, Gerasimos Siasos, MD, PHD, Ioannis Andreou, MD, PHD, Dimitris Fotiadis, PHD, Kostas Stefanou, PHD, Michail Papafaklis, MD, PHD, Lampros Michalis, MD, PHD, Alexandra J. Lansky, MD, Gary S. Mintz, MD, Patrick W. Serruys, MD, PHD, Charles L. Feldman, SCD, Gregg W. Stone, MD

JACC: CARDIOVASCULAR IMAGING VOL. -, NO. -, 2017

Conclusion

Which is the accuracy of prediction future events:

- FFR: 18%
- IVUS anatomic characteristics + Virtual Histology: 18%
- IVUS anatomic characteristics + ESS: 50%
- IVUS anatomic characteristics + Virtual Histology + ESS: 52% -58%

Intravascular Imaging coupled with physiology vs FFR

Intravascular Imaging coupled with Physiology is a new tool which possibly predicts new events better than FFR

However we need more studies in order to prove it.

We have the tools which can couple Intravascular Imaging with Physiology reliably and quickly enough.

Can we use CTCA in a similar fashion with IVUS + physiology? PROSPECT –MSCT Study.

Summary:

The present analysis for the first time investigated the potential value of MSCT-derived plaque characteristics in identifying lesions that are likely to progress at 3-year follow-up.

We found that:

1) low ESS and increased baseline lumen area were predictors of lumen decrease at follow-up;

2) decreased plaque area and burden were independently associated with an increase in plaque area at follow-up;

3) low ESS and decreased plaque area and burden and increased calcific tissue component were independently related with an increase in plaque burden at follow-up; and

4) a low plaque area and burden and an increased fibrofatty and fibrous tissue component were independently related to an increase in the necrotic core at follow-up.

TABLE 1 Univariate and Multivariate Analysis of the Variables Associated With Atherosclerotic Disease Progression

	Univariate Analysis			Multivariate Model	
	Associated Factor	β (95% CI)	p Value	β (95% CI)	p Value
Increase in lumen area (per 1 mm^2)	Presence of low endothelial shear stress at baseline	−1.06 −(−1.34 to −0.78)	<0.001	−0.47 (−0.78 to −0.16)	<0.001
	Baseline lumen area (per 1-mm^2 increase)	−0.28 (−0.33 to −0.23)	<0.001	−0.22 (−0.28 to −0.16)	<0.001
	Baseline outer vessel wall area (per 1-mm^2 increase)	−0.13 (−0.16 to −0.09)	<0.001	–	–
	Baseline plaque area (per 1-mm^2 increase)	0.08 (0.01 to 0.15)	0.029	–	–
	Baseline plaque burden (per 10% increase)	1.08 (0.88 to 1.28)	<0.001	–	–
	Presence of expanding remodeling at baseline	−1.04 (−1.38 to −0.70)	<0.001	−0.21 (−0.58 to 0.17)	0.277
Increase in plaque area (per 1 mm^2)	Baseline lumen area (per 1-mm^2 increase)	−0.04 (−0.9 to 0.01)	0.083	–	–
	Baseline outer vessel wall area (per 1-mm^2 increase)	−0.14 (−0.17 to −0.10)	<0.001	–	–
	Baseline plaque area (per 1mm^2 increase)	−0.42 (−0.48 to −0.37)	<0.001	−0.40 (−0.46 to 0.33)	<0.001
	Baseline plaque burden (per 10% increase)	−0.66 (−0.84 to 0.48)	<0.001	−0.23 (−0.41 to 0.05)	0.014
	Baseline % fibrofatty tissue (per 10% increase)	0.30 (0.05 to 0.55)	0.017	−0.07 (−0.29 to 0.16)	0.569
	Baseline % calcific tissue (per 10% increase)	−0.21 (−0.44 to 0.03)	0.081	–	–
Increase in plaque burden (per 10%)	Presence of low endothelial shear stress at baseline	0.28 (0.18 to 0.37)	<0.001	0.11 (0.02 to −0.21)	0.018
	Baseline lumen area (per 1-mm^2 increase)	0.05 (0.03 to 0.06)	<0.001	–	–
	Baseline plaque area (per 1-mm^2 increase)	−0.12 (−0.14 to 0.10)	<0.001	−0.10 (−0.12 to −0.07)	<0.001
	Baseline plaque burden (per 10% increase)	−0.46 (−0.53 to −0.40)	<0.001	−0.40 (−0.48 to −0.32)	<0.001
	Baseline % necrotic tissue (per 10% increase)	0.05 (0.01 to 0.09)	0.044	−0.03 (−0.08 to 0.01)	0.154
	Baseline % calcific tissue (per 10% increase)	−0.10 (−0.19 to −0.01)	0.035	0.22 (0.13 to 0.31)	<0.001
	Presence of expanding remodeling at baseline	0.20 (0.09 to 0.31)	<0.001	−0.04 (−0.15 to 0.07)	0.506
Increase in necrotic core (per 1 mm^2)	Presence of low wall shear stress at baseline	0.13 (−0.02 to 0.27)	0.097	0.01 (−0.14 to 0.17)	0.872
	Baseline plaque area (per 1-mm^2 increase)	−0.05 (−0.08 to −0.01)	0.017	−0.08 (−0.12 to −0.04)	<0.001
	Baseline plaque burden (per 10% increase)	−0.17 (−0.27 to −0.07)	0.001	−0.14 (0.25 to 0.03)	0.016
	Baseline % necrotic tissue (per 10% increase)	−0.25 (−0.31 to −0.18)	<0.001	–	–
	Baseline % fibrofatty tissue (per 10% increase)	0.16 (0.02 to 0.31)	0.028	0.17 (0.03 to 0.31)	0.016
	Baseline % fibrous tissue (per 10% increase)	0.22 (0.16 to 0.28)	<0.001	0.29 (0.23 to 0.36)	<0.001

JACC Cardiovasc Imaging. 2016 Aug;9(8):1009-11. doi: 10.1016/j.jcmg.2015.07.005. Epub 2015 Sep 9.

Noninvasive Prediction of Atherosclerotic Progression: The PROSPECT-MSCT Study.

Bourantas CV, Papadopoulou SL, Serruys PW, Sakellarios A, Kitslaar PH, Bizopoulos P, Girasis C, Zhang YJ, de Vries T, Boersma E, Papafaklis MI, Naka KK, Fotiadis DI, Stone GW, Reiber JH, Michalis LK, de Feyter PJ, Garcia-Garcia HM.

Can we measure ESS from 3D QCA reliably?

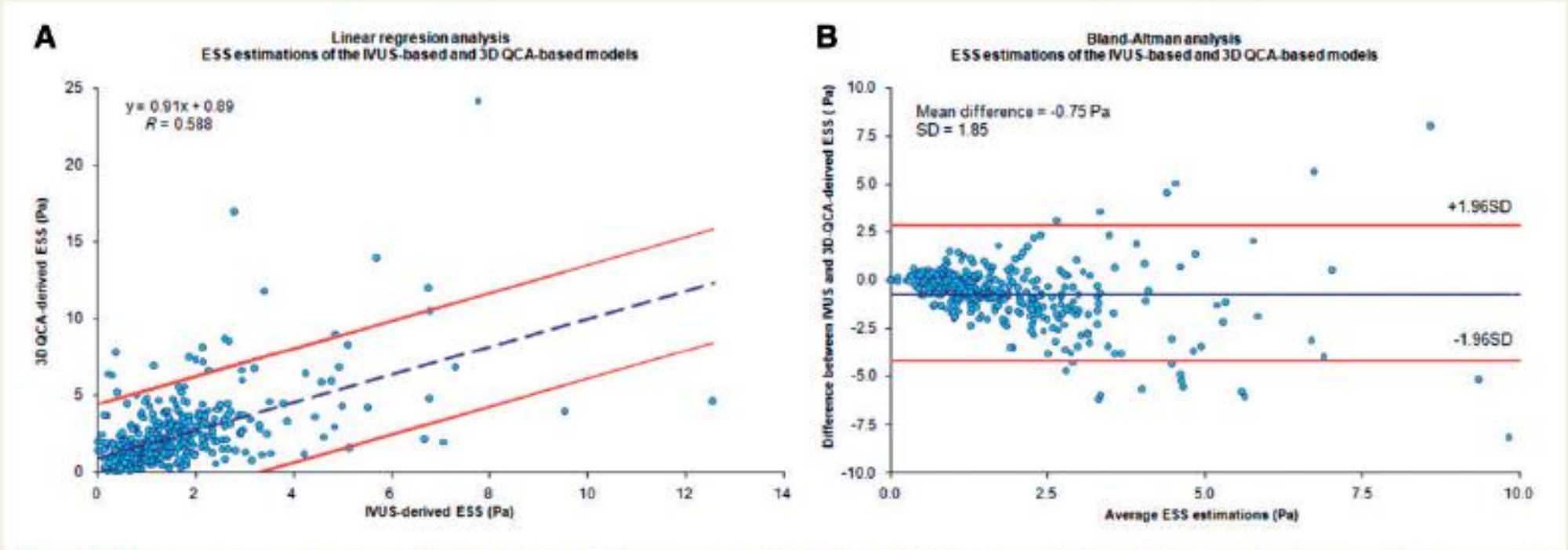


Figure 2 Linear regression analysis (*A*) and Bland and Altman analysis (*B*) of the IVUS-based vs. the 3D QCA-derived minimum predominant ESS values estimated in the 470 3 mm segments included in the present analysis.

Mpourantas, …., Michalis et al: European J CardioVasc Imag, 2018

FINAL CONCLUSION

- We are moving towards a new era

- The whole concept is accurate as possible prediction of new events in order to establish pre-emptive treatments
- It seems that we can predict up to 58% from 18% who is the accepted value till now
- It seems that we will be able to get this results non-invasively

Thank you for your attention