3 (or 4) Dimensional QCA using Coronary Catheter Size Reliably Identifies Severe Occult Stenosis in Diffusely Diseased Vessels: an IQ-CATEGORIZE Hidden Lesions sub-Study

(Intravascular ultrasound Quantitative Coronary Angiography comparison To Effectively Gauge Otherwise under-Recognized Lesions Study)

Dr Charles Laham- LBCT SCAI Las Vegas May 30 2014
Dr. Charles Laham, MD, FACC, FRCPC, FSCAI

Interventional Cardiologist Holy Family Memorial MC
Associate Midwest Cardiovascular Research Foundation
On behalf of the IQ- CATEGORIZE Lesions investigators

No conflicts of interests
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

**BACKGROUND**

Identifying “visibly underwhelming mild-moderate disease” as truly severe in setting of suggestive testing invites both controversy and wide variations in revascularization.

- Cause discrepancies: *physiologic/anatomic/test limitations*:
  - hypertensive stress response, ↑intra-cardiac pressures, small vessel spasm, inadequate testing, reader error.
  - Heavy diffuse moderate disease burden in target vessel.
  - Severe lesions hiding in diseased reference vessels (RefV)
  - Unmasking occult severe symptomatic lesions is difficult, often unrecognized by “>70% angiographic criteria.”
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

BACKGROUND: Technology choices/limitations: 0D-4D testing used!

Lesions = 4D: length; height on angio, depth (not seen); vary in time (change shape with cardiac cycle; vaso-active in time-spasm)

- (0-2D)- typical full speed angiogram very limited: 50% accuracy vs gold-standard IVUS (intravascular coronary ultrasound)

- (2-3D)-QCA: (quantitative coronary angiography): >7-10% reliability of severe lesion detection by single-view QCA vs visualization (reliability still only 60%): ↓ as 20-30% lesions elliptical:
  - using using frame-by-frame stopped image analysis at end diastolic & measure lesion features by calibrated reference diameter of a contrast filled coronary catheter of known outer dimensions.

- (3-4D)-IVUS: cross sectional lesion parameters measured on pullback
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

Summary of all Non-Left main IVUS–Physiologic Comparison Studies

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<td>&gt;72%</td>
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<td>%PAS&gt;88% accur</td>
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<td>IVUS vs MACE w/o PCI</td>
<td>EEM size-calc</td>
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<td>&lt;4 mm2</td>
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<td>80-83%</td>
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MLA <4 mm2 >80-90% accurate: But only in 3.5-4.5 mm vessels: need to adjust MLA for Ref V size: MLA focus undermined IVUS use!

>70%Plaque area stenosis (%PAS) >80-90% physiologically accurate: but ? %PAS neglected as less relevant!?!  
- MLA cutoffs as ↓smaller vessels tested; but %PAS >70% is 75-90% accurate vs FFR at all vessels sizes!!! & >67% PAS similarly accurate across majority Left Mains studies

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<td>CV Revas Med-2012</td>
<td>IVUS vs FFR &lt; 0.8 QCA ref</td>
<td>&gt; 3.5</td>
<td>3.6 mm2</td>
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<td>&gt;75% MLA</td>
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<td>CIRC-1999</td>
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<td>2.9-3.5</td>
<td>&lt;3-3.5 mm2</td>
<td>est &gt;70% (had lum % AS)</td>
<td>&gt;90% with combo MLA and %PAS</td>
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<td>&lt;3.2 mm2</td>
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# 3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

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<td>IVUS vs MACE w &amp; w/o Revasc.</td>
<td>EEM size-calc</td>
<td>4.9-5.6</td>
<td>&lt;7.5 mm²</td>
<td>&gt;67%</td>
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<td>MEDIUM</td>
<td>Leesar</td>
<td>CathCard Intv-2004</td>
<td>IVUS vs FFR &lt; 0.75</td>
<td>EEM size-calc</td>
<td>4.8-5.1</td>
<td>&lt;5.9 mm²</td>
<td>If reeval at FFR &lt;0.8 &lt;7.4 mm²</td>
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<td>If reeval at FFR &lt;0.75 &lt;4.4 mm²</td>
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## IQ-CATEGORIZE Hidden Lesions Sub-Study

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

BACKGROUND

- A prior IQ-CATEGORIZE publication (Int J Angiology, 2012) showed no difference between the in-lesion EEM dimensions & those of Ref Vessels across study. **ie. remodelling not an issue!!!**

- Based on our data, in-lesion external luminal angiographic measures can be approximated= **need use largest Ref V diameter as the “least diseased” estimate of lesion EEM**

- But still 15-60% RefV disease: visualized angiography weakness because: **RefV plaque is a 3D problem: under-recognition errors = squared.** Ex.20% poor visual, 40%s/vQCA, 64%PAS

- Companion poster study shows, need to consider adding a correction factor if > mild RefV, for ↑lesion quantification.
Automatic Reference Obstruction Analysis

Single View QCA Diagonal

- Stenosis Diameter: 0.49 mm
- Minimum Diameter: 0.49 mm
- Maximum Diameter: 2.28 mm
- % Stenosis Diameter: 78%
- Stenosis Length: 5.49 mm
- Expected Diameter: 2.18 mm
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

Angiography: Concentric lesions easy- single view any angle QCA works- limited only by extent of RefV Disease

Lumen dimensions: short & long axes (a & b)

Eccentric is concern for 2D QCA: improve by starting with view of “short axis-a”; try to get closest to 90° b- axis view as possible

Luminal area = (\(\pi \times a \times b\))/4

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3 D QCA with Catheters to Unmasks Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

Angiography: Concentric lesions easy- single view any angle QCA works- limited only by extent of RefV Disease

Eccentric is concern for 2D QCA: improve by starting with view of “short axis-a”; try to get closest to 90° b- axis view as possible

50% in 2 views = 75% Plaque area stenosis

Lumen dimension short & long axis (a&b)

Luminal area = ($\pi \times a \times b$)/4

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

IQ-CATEGORIZE Hypothesis:

Using **tightest short axis view, a** & second orthogonal view 35-90° apart by 2-view 3D-QCA-” should get good **surrogate approximation of true 90° “b- long axis dimensions**

IQ-CATEGORIZE SERIES sub-studies: finds as true and approx. 86%-95% accurate: 15-60% ref vessel disease= part of inaccuracy→ 70% error margins are mildly undercalling lesion severity!!!

Begin with “a” =tightest = View 1

Lumen dimensions: short & long axes (a & b)

Angio view 2: 35- 90° orthogonal to view 1 for “b”
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

**IQ-CATEGORIZE theory & findings:**
Use average of “a” & “b” axes measures at 35-90° to create circular approx. of ellipse dimensions: maths. predicted accuracy ≈ 90-95% even in extremes

**Lumen dimensions:**
short & long axes (a & b)

**Luminal area = (π x a x b)/4**

**Begin with “a” = tightest view!**

**Ex. If a=2 (mm) and b= 4 mm**
**Actual luminal area=**
πx(2x4)/4 = 2π mm²

**Hypothesis:**
ex. if use average of a=2 mm & b= 4mm at 90°
**Estimated luminal area=**
πx((4+2)/2)squared)=
2.25π mm² (vs. 2π mm²)

Diff btwn actual and estimated MLA with b at 90° is (larger by) ≈10% error; 5-20% under at 45-75°; >20% smaller than actual at < 45° diff angles
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study

- 79 symptomatic patients, 131 lesions: some normals,
- real-world study!!! nuclears, stress echos, FFR, etc
- most with +functional evidence of significant disease but only 30-70% lesions by single view QCA;
- all had comparative 2D-angio; 2 view- 3D-QCA & IVUS testing of our hypotheses

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

IQ- CATEGORIZE Lesion Study: Hidden Lesion Substudy
Application: #1) as presented here:

2 view (3D)-QCA is hypothesized to predict extent reduction of lumen area relative to expected true vessel EEM area, using relative luminal diameters reduction in each of 2 views relative to (largest available) size-appropriate RefV segment diameter in each view to gauge range of relative area reduction.

IQ- CATEGORIZE SERIES of substudies: shows this is true and approx. 90% accurate.

Angio View 1

Angio view 2: 35-90° orthogonal to view 1
## IQ-CATEGORIZE Hidden Lesions Sub-Study

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

**THEORY:**

For 3 mm Ref V: if >10% RefV disease, EEM area >2.72 $\pi$ mm$^2$

>70% Plaque area $\rightarrow$ MLA <0.82 $\pi$ mm 2 (ie. MLA < 2.6 mm$^2$ c/w + FFR pred 3mm RefV’s)= **Average Diameter of a & b < 1.8 mm**

**Prediction:**
If average luminal <2 mm = 6Fr catheter- (allowing 5-10% QCA error) will see >70% PSA in 2.6-3.0 mm vessels

**2 view 3D QCA:**
35-90° orthogonal view 2 for “b” vs. tightest view 1 for “a”

2.6-3mm by largest RefV QCA

Est. Aver lumen <2.0 mm if PAS>70%
Figure 1. Small vessel 3D QCA MLD comparison to IVUS Plaque Area stenosis

n = 29, r = -0.710, p < 0.001

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study

**THEORY:**

For 4 mm Ref Vessel; if 10% RefV disease, EEM area > 4 \( \pi \) mm²

>70% Plaque area \( \rightarrow \) MLA < 1.2 \( \pi \) mm² (ie. Approx <4mm², similar to FFR, MACE, SPECT + predicted in 4 mm vessels) Average Diameter of a & b < 2.2 mm

**Prediction:**

If aver luminal diameter of 2 view QCA < 2 mm = 6Fr catheter (allowing 5-10% QCA error) will easily see >70% PSA in 3.1-4.5 mm RefV’s

**2 view 3D QCA:**

35-90° orthogonal view 2 for “b” vs. tightest view 1 for “a”

3.1-4.5 mm by largest RefV QCA

Est. Aver lumen < 2.0 mm if PAS > 70%
Figure 2: Medium vessel 3D-QCA versus IVUS Plaque Area Stenosis

Average MLD by orthogonal 2-view (3D) QCA (mm)

In lesion % plaque area stenosis

n = 71, r = -0.769, p < 0.001

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study

THEORY:

For 5 mm Ref Vessel: if >10% RefV disease, EEM area > 6.25 $\pi$ mm$^2$

>67% (or >70%) Plaque area $\rightarrow$ MLA<2.1 (or <1.9) $\pi$ mm$^2$ (ie. <6mm$^2$ +FFR & MACE studies = 5 mm Left Mains); Aver. Diameter of a & b < 2.9 (or <2.73) mm

Prediction:
If aver luminal diameter of 2 view QCA <2.67 mm = 8Fr catheter (w 5-10%QCA error) will easily see >67 (or >70%) %PSA in 4.6-6 mm Left mains (or large vessels, resp.)

2 view 3D QCA:
35-90° orthogonal view 2 for “b” vs. tightest view 1 for “a”

Est. Aver lumen <2.67 mm if PAS> 67% left main (70% non-LM’s)

4.6-6 mm by largest RefV QCA
Figure 3: Combined large vessel/Left Main 3D - QCA MLD versus IVUS Plaque Area stenosis

- Average MLD by orthogonal 2-view (3D) QCA
- In-lesion plaque area % stenosis

n = 31, r = -0.686, p < 0.001

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Figure 4. Left main 3DMLD versus IVUS plaque area stenosis

Average MLD by orthogonal 2-view (3D) QCA (mm)

Intrusion plaque area % stenosis

n = 18; r = -0.718; p < 0.001

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3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study: Summary

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3D QCA with Catheters to Unmasks Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study

Case methodology examples
65 yo: + troponin, U/S angina, severe anterior hypokinesis, min ECG changes

2 suspicious LAD lesions
“40- 50%” by visual full speed CINE
QCA View 1-
Begin with
tightest view

Use largest available reference

6 Fr = 2 mm

4 mm proximal reference

MLD = 1.7 mm

(RAO 29)
CRAN 24
QCA View 2
Orthogonal views = 36° difference (caudal-cranial)

6 Fr = 2mm

Both MLD’s = 1.5 mm

(RAO 30)
CAUD 12
**IVUS Image Mid LAD Lesion:** 4mm Prox Ref: By FFR-IVUS Verified Criteria

Okay to Use MLA < 3.5 or 4 mm² and/or % Area stenosis > 70%

Mid lesion MLD by 2-view (3D) QCA’s = 1.5 and 1.7 mm; aver MLD=1.6 mm; pred MLA = 2 mm² !!!

MLA = 2.01 mm²
EEM Area = 13.95 mm²
% PAS = 84%
EEM diam = 4.0 x 4.1 mm
MLD = 1.5 x 1.6 mm
3.5 mm Bare Metal Stent INFLATION
AFTER PCI

LVEF = 65% at 1 month; Maintained to 6 months

RAO 29 CRAN 24
55 yo: ↑Rest angina, Neg nuclear images, **cath 6 months ago**: dominant distal CIRC = 2 x “25%” lesions by full speed visual CINE view

Second cath after + ve dobutamine Str. echo: **mod infero/lateral and mid/apical Ant**: suspect balanced ischemia (nuclear)

Mid LAD ? lesion

Suspicious CIRC lesions
Lesion #1 2D-QCA view 1: begin tightest view

Use Largest Reference = 3mm (consider size appropriate IVUS criteria: MLA <3 mm2; % area stenosis >70%)

MLD = 1.6 mm
QCA View 1
Can repeat other lesions: QCA view 1: begin tightest view

6 French 2.0 mm

2nd lesion MLD=1.7 mm

MLD = 1.6 mm

(RAO 30) CRA 35

3rd lesion MLD= 1.8 mm

All lesions <2.0 mm QCA view 1
QCA view 2: Lesion #1,2,& 3 Assessment:

Cran-Caud: 45 deg orthogonal diff by 2-view 3D-QCA

6 French
2.0 mm

QCA View 2 MLD= 1.6 mm

QCA View 2 MLD= 1.7 mm

QCA View 2 MLD = 2.4- 2.5 mm

(RAO 30) CAU 10
QCA view 2: Lesion Assessment:
Cran-Caud: 45 deg orthogonal diff by 2-view 3D-QCA

Suspect 2 CIRC lesions + ve by IVUS as < 2mm, and likely + FFR

Suspect LAD borderline: ie. QCA View 2 > 2.0 mm
% PAS = 75%
EEM Area = 9.7 mm²
MLA = 2.4 mm²
MLD = 1.7 X 1.8
EEM Diameter 3.5 X 3.7 mm

IVUS mid CIRC
2 view 3D QCA; IVUS & FFR CIRC results

Aver 3D-QCA MLD = 1.6 mm & 1.6 mm = 1.6 mm (ie. < 2.0 mm); est. MLA = 2.0 mm²

Dist CIRC FFR = 0.72
IVUS mid %PAS = 75% (MLA = 2.4 mm²)
IVUS distal %PAS = 70% (MLA = 2.5 mm²)
6 French
2.0 mm

aver 3D QCA MLD = 1.8 mm
& 2.5 mm = 2.1 mm (>2.0 mm); est MLA= 3.5 mm^2

RAO 30 CAU 10

LAD FFR= 0.83
IVUS %PAS= 69% (MLA= 3.4 mm^2)
Rx medically: by 3mm vs 3mm2 IVUS-FFR comparison criteria = neg
POST PCI with 3.5 x 28 mm BMS sustained clinical improved at 6 months
3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study: Summary

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IQ-CATEGORIZE: PRECISE Plaque Severity Prediction sub-Study

- Method and case examples from poster session: see abstract # B-0054

Second application of same concept:
- **findings**: % plaque area stenosis by 2-view 3D-QCA within <5% of IVUS = >85% accuracy; (90% within <10%): most under-call errors.
3D QCA with Catheters to Unmask Severe Occult Stenosis: IQ-CATEGORIZE Lesions Study

Angiography: Concentric lesions easy—single view any angle QCA works—limited only by extent of RefV Disease

50% in 2 views = 75% Plaque area stenosis

Eccentric is concern for 2D QCA: improve by starting with view of “short axis-a”; try to get closest to 90° b-axis view as possible

Lumen dimension short & long axis (a&b)

Luminal area = ($\pi \times a \times b$)/4

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IQ-CATEGORIZE: Precision Percent Plaque Area Prediction sub-Study

IQ-CATEGORIZE Lesion Study: Precision % Percent Plaque Area Prediction sub-study:

Applications #2 as per poster session:

Hypothesis: can predict lumen diameter reduction relative to true EEM diameter by 2 view (3D)-QCA: used to estimate cross-sectional minimum luminal area (MLA) and/or a cross-sectional lesion %Plaque area stenosis (%PAS) similar to IVUS.

IQ-CATEGORIZE SERIES of subsudies: use average of a and b-ellipse axes from 2-view QCA 35-90° apart to predict % plaque area: found true >approx. 90% accurate.
**Average 3D-QCA Lesion Luminal Fraction (LLF) methodology:** (Choose most normal reference segment both views)

- **QCA View 1** = 50% lesion; luminal fraction = 0.5
- Ref Vessel QCA = 2.75 mm (2.9 mm IVUS EEM)
- 2 view diff. = 45 degrees
- **RAO 30 CAU 10**
3D (2-view QCA)- Second method
Area % stenosis estimation technique

6 French 2.0 mm

RAO 30 CRA 35

QCA View 2 = 60% lesion with luminal fraction = 1 - 0.6 = 0.4

3mm distal Ref Vessel QCA (3.7 mm IVUS EEM)
**ALTERNATIVE 3DQCA LESION %PAS METHOD**

**Average 3D-QCA Lumen Fraction (LumFr) method**
(Choose most normal reference segment)

QCA - View 1 LumFr = 0.4 = (1 - 0.60) for 60% lesion

QCA - View 2
LumF = 0.50

2 view
diff. = 45 degrees

Estimate IVUS %PAS by largest reference 3D QCA =
100 x (1 - ((1-LumFr view1)(1-LumFr View 2)))
= 100 x (1 - ((0.5)(0.4))) = 80% (compared to 77% IVUS)
% PAS = 77%
EEM Area = 9.7 mm²
MLA = 2.4 mm²
MLD = 1.7 X 1.8
EEM Diameter 3.5 X 3.7 mm
Post 3.5 x 28 mm BMStent x 1: good sustained clinical result to 7 months
3D QCA using Catheter Size to Identify Severe Occult Stenosis: an IQ-CATEGORIZE Hidden Lesions sub-Study: Conclusion Summary

- **IVUS**- great technique: ?improve clinical relevance by using %plaque area- not MLA and/or both combined!

- %Plaque area stenosis >70% in non-left mains & >67% in left mains likely severity cutoffs = + functionally abnormal.

- 2-view 3D(-potentially 4D)-QCA: >90% reliable for severe-lesion identification:
  - either semi-quantitatively as in the “Hidden Lesion”- substudy.
  - or quantitatively as in poster/summarized “Precision Plaque Prediction” substudy.
3D QCA using Catheter Size to Identify Severe Occult Stenosis: an IQ-CATEGORIZE Hidden Lesions sub-Study: Conclusion Summary

- use **largest available peri-lesion RefV** (15-60% Ref Vdisease)
- **begin with tightest view & second view 35-90° apart useful to accurately (>90%) define several lesion severity measures**
- **Qualitatively**: if lumen diameter < 2 mm = 6 Fr catheter in small, medium and large natives and < 2.67 mm = 8 Fr catheter in 2 averaged views 3D- QCA’s will have >70% plaque in huge natives and >67% in left mains c/w severe plaque
- **Quantitatively**: using **formula= 100x (1-(1-lesion fraction QCA view 1)x(1-lesion fraction QCA view 2))** will correctly predict %PAS within <5% (>85%) & within <10% (>90% accuracy) with most under called if adjust Ref V disease by correction factor from poster abstract

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### 3D QCA using Catheter Size to Identify Severe Occult Stenosis: IQ-CATEGORIZE Hidden Lesions sub-Study: Summary

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3 (or 4) Dimensional QCA using Coronary Catheter Size Reliably Identifies Severe Occult Stenosis in Diffusely Diseased Vessels: an IQ-CATEGORIZE Hidden Lesions sub-Study

(Intravascular ultrasound Quantitative Coronary Angiography comparison To Effectively Gauge Otherwise under-RecogniZEd Lesions Study)

Dr Charles Laham- LBCT SCAI Las Vegas May 30 2014
# IQ-CATEGORIZE Hidden Lesions Sub-Study

## Summary of all Vessel IVUS–Physiologic Comparison Studies

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<tr>
<th>Vessel Size</th>
<th>Author</th>
<th>Journal &amp; Year</th>
<th>IVUS Compared to Functional Study</th>
<th>RefV Measured method</th>
<th>Ref V Size (mm)</th>
<th>MLA CRITERIA</th>
<th>% Plaque Area Stenosis Non Left Mains</th>
<th>% Plaque Area Stenosis Left Main</th>
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<td>JACC-2005</td>
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