ΚΛΙΝΙΚΗ ΧΡΗΣΗ ΙVUS
Limitations of Angiography

Two dimensional measurements

Under/over estimates lesion extent and severity

Masks Complicated Lesions
Limitations of Angiography

Images the lumen and not the vessel wall

Cannot Account for Coronary Remodeling

Cannot Account for plaque characteristics – Vulnerable plagues
Rationale for intravascular imaging

Advantages of IVUS:

• Images the vessel wall
  ➔ Ability to assess plaque characteristics

• High resolution/360 degree measurement
  ➔ Precise quantification of disease extent and severity
  ➔ Good intra/inter observer correlation
  ➔ Accurate sizing of vessel
Equipment

Mechanical IVUS System:

• single piezoelectric transducer at 1,800 rpm
• operate at frequencies between 30 and 40 MHz
😊 Smaller size compared to solid state systems
😊 Higher resolution
😊 More artifacts - Guidewire, NURD, etc.

Solid State System:

• Annular array of multiple (64) imaging elements providing imaging by sequentially activating the imaging elements
• operate at a centre-frequency of approximately 20 MHz
😊 ability to display blood flow in colour to facilitate distinction between lumen and wall boundaries
😊 Less artifacts
😊 Larger size compared to mechanical systems
😊 Lower resolution
Technique

- 6Fr guide catheter/ Standard 0.014 inch guidewire
- Anticoagulation: bivalirudin or heparin as per routine clinical practice (activated clotting time of >250 sec)
  - Intracoronary nitroglycerin (100-200 μ) to prevent spasm
- Imaging should be acquired starting
  - at least 10 mm distal to the lesion
  - preferably at the site of a branch vessel (as a reference marker)
- Pullback to the proximal vessel
  - Automated pullback device (usually at a rate of 0.5-1.0 mm/s for any length)
  - manual operator pull back
Complications
- transient spasm 2.9%
- acute vessel occlusions, dissections, and/or embolism 0.4%

Risk factors
- unstable angina or acute myocardial infarction
- intervention compared with diagnostic IVUS
- Catheter size
IVUS examination of native atherosclerotic coronary arteries does not accelerate disease progression evaluated after up to 24 months of follow-up.
# Quantitative Image Interpretation

## Table 3: Intracoronary ultrasound measurements of common use

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Abbreviation</th>
<th>Units of measurement</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen area</td>
<td>LA, mm²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total vessel area</td>
<td>VA, mm²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque area</td>
<td>PA, mm²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent plaque area</td>
<td>% PA, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max lumen diameter</td>
<td>MaxLD, mm</td>
<td></td>
<td></td>
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<tr>
<td>Min lumen diameter</td>
<td>MinLD, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean lumen diameter</td>
<td>MeanLD, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumen symmetry index</td>
<td>MinD/MaxD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max plaque thickness</td>
<td>MaxPT, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min plaque thickness</td>
<td>MinPT mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque eccentric. index</td>
<td>Min/max PT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Calculations:
- **Area**:
  - Lumen area: \( \text{LA, mm}^2 \)
  - VA area: \( \text{VA, mm}^2 \)
  - Plaque area: \( \text{PA, mm}^2 \)
  - Percent plaque area: \( \% \text{PA, } \% \)
- **Diameter**:
  - Max lumen diameter: \( \text{MaxLD, mm} \)
  - Min lumen diameter: \( \text{MinLD, mm} \)
  - Mean lumen diameter: \( \text{MeanLD, mm} \)
- **Symmetry index**:
  - Lumen symmetry index: \( \text{MinD/MaxD} \)
- **Plaque thickness**:
  - Max plaque thickness: \( \text{MaxPT, mm} \)
  - Min plaque thickness: \( \text{MinPT mm} \)
  - Plaque eccentricity index: \( \text{Min/max PT} \)

### Comments:
- Lumen area: Area inside leading edge brighter adventitia; do not trace if >90 degrees of vessel circumference not visible (shadowing or attenuation).
- Plaque area: Area included between the two contours indicated above (VA minus LA).
- Percent plaque area: Percentage of VA occupied by plaque, calculated as \( (\text{VA} - \text{LA})/\text{VA} \times 100 \).
- Max lumen diameter: Calculated as: \( \sqrt{\frac{\text{LA}}{\pi}} \times 2 \).
- Lumen symmetry index: 1 indicates circular lumen, <1 indicates increasing elliptical lumen shape.
- Max plaque thickness: 1 indicates concentric plaque, <1 indicates increasing plaque eccentricity.
Tunica intima
• is in direct contact with the blood and is constituted by an endothelial cell monolayer resting upon a basement membrane

Tunica media
• is separated from the tunica intima by the internal elastic membrane (IEM) and is formed by concentric layers of smooth muscle cells

Adventitia
• is the outermost arterial layer, which is separated from the media by the external elastic membrane (EEM), and contains fibroblasts and mast cells, collagen fibrils, vasa vasorum and nerve endings.

Based on histological and ultrasound data, a coronary vessel wall with an intimal thickness ≥0.5 mm is considered to be diseased

Mintz GS et al; JACC, 2001
Plaque Characterization

Soft Plaque

- Hypoechoic compared to adventitia
- High lipid content

Soft Plaque - Concentric

Soft Plaque - Eccentric
Plaque Characterization

**Fibrous Plaque**

- intermediate echogenicity between soft (echolucent or isoechoic) atheromas and highly echogenic calcified plaques;
- Similar/more echogenicity compared with adventitia
- Rarely produce acoustic shadowing
- most common type of plaque
Plaque Characterization

Fibrocalcific Plaque
- Hyperechoic compared to adventitia
- Acoustic shadowing seen
- 180° of calcification must be present before it can be visualized by angiography
Plaque Characterization

**Echo-attenuated plaques**
- have no ultrasound signal behind plaque. This plaque can be either hypoechoic or isoechoic but contained no bright calcium

Pu et al; JACC, 2014
Plaque Characterization

**Echolucent plaque**
- present an intraplaque hypoechoic zone surrounded by tissue of greater echodensity

Pu et al; JACC, 2014
Remodeling interpretation

Reproduced with permission from Dangas, G. et al. Circulation 1999;99:3149-3154
**CONCLUSIONS**

Large eccentric plaque (mean percent plaque area 67 ± 9% Vs. 57 ± 12%\(\text{mm}^2\), \(p < 0.05\)) 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 (6.7 ± 3.0 vs. 7.5 ± 3.7). Compensatory enlargement of vessel wall due to remodeling may contribute to the relatively small degree of stenosis by angiography.

(J Am Coll Cardiol 2000;35:106-11)
Vulnerable plaque on IVUS

Ability of IVUS to predict future coronary events - PROSPECT trial

Three vessel VH-IVUS in 697 ACS patients

Table 3. Independent Correlates of Major Adverse Cardiovascular Events Related to Nonculprit Lesions during Follow-up.  

<table>
<thead>
<tr>
<th>Correlates</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td><strong>Predictors of patient-level events†</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin-requiring diabetes</td>
<td>3.32 (1.43–7.72)</td>
<td>0.005</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>2.03 (1.15–3.59)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Predictors of events at individual lesion sites‡</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque burden ≥70%</td>
<td>5.03 (2.51–10.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thin-cap fibroatheroma</td>
<td>3.35 (1.77–6.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MLA ≤4.0 mm²</td>
<td>3.21 (1.61–6.42)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- Three baseline IVUS characteristics that independently predicted future events
  1. Plaque burden > 70%
  2. TCFA
  3. MLA < 4 mm²

Vulnerable plaque on IVUS

Although no definitive features define a as, a hypoechoic plaque without a well-formed fibrous cap is presumed to represent potentially vulnerable atherosclerotic lesions because this represents a lipid-rich with a thin fibrous cap.

Pu et al; JACC, 2014
Dissection

Classification of Coronary Dissection
♦ Intimal
♦ Medial
♦ Adventitial
♦ Intramural Hematom
♦ Intra-stent

True Lumen (TL): 3-layer appearance (intima, media, adventitia); branches communicating with the lumen
False Lumen (FL): Not all layers are present; branches do not communicate with the lumen
Plaque Rupture

Plaque rupture at the shoulder

Fibrous cap

Lipid core

Ulcerated Plaque

A and B show ulcerated plaque. Follow up IVUS 21 months later shows the same ulcerated plaque (non healed).

Reproduced with permission from Rioufol, G. et al. Circulation 2004;110:2875-2880
Intramural Hematoma

- Accumulation of blood within medial space
- Displacement of internal elastic membrane inwards and EEM outwards
Thrombus

- Echolucent or variable grey scale appearance
- Usually layered, lobulated, or pedunculated
- Micro-channels are occasionally present
- Diagnosis of thrombus by IVUS is always PRESUMPTIVE

Subacute stent thrombosis (IVUS after mechanical thrombus aspiration)
Plaque rupture and ulceration is common in women with myocardial infarction without angiographically demonstrable obstructive coronary artery disease.
Evaluating Intermediate Coronary Lesions

Takagi et al compared IVUS parameters with FFR for determining functional significance of moderate lesions

Using cutoff of $\leq 3\text{mm}^2$ to define abnormal minimum MLA and $< 0.75$ to define abnormal FFR, the investigators found IVUS had a sensitivity of 83% and specificity of 92% for detecting ischemia producing lesions based on FFR.

Circulation, 1999
Evaluating Intermediate Coronary Lesions

Nishioka et al compared IVUS parameter with nuclear perfusion imaging

Minimum LCSA <4mm² had sensitivity of 88% and specificity of 90% for predicting reversible perfusion defect
Other IVUS parameters (eg % area stenosis) performed less well

J Am Coll Cardiol. 1999
Evaluating Intermediate Coronary Lesions

Abizaid et al compared various IVUS parameters with CFR.

Linear relation between CFR and minimum LCSA. They defined minimum LCSA as <4mm² and demonstrated concordance of 89% with CFR (abnormal CFR <2).

Am J Cardiol. 1998
Evaluating Intermediate Coronary Lesions

Briguori et al compared IVUS with FFR only in patients with intermediate lesions

- IVUS minimum LCSA was significantly related to FFR (r=0.41, p<0.004).
- The sensitivity and specificity of minimum IVUS LCSA of <4mm² for predicting FFR <0.75 were 92% and 56%.

Am J Cardiol. 2001
What about the LMS?

Jasti et al examined 55 patients with an angiographically ambiguous LMCS, a pressure guidewire was used to calculate FFR, and IVUS parameters were calculated after automatic pullback.

Best agreement with FFR cut point of 0.75 was found when MLD by IVUS was 2.8 mm (sensitivity, 93%; specificity, 98%). B, Best agreement with FFR cut point of 0.75 was found when MLA by IVUS was 5.9 mm2 (sensitivity, 93%; specificity, 94%)

circulation, 2004
In a prospective multicentre Spanish cohort (LITRO study) involving 354 patients with borderline unprotected left main disease on angiography, the IVUS cut-off criteria of a minimal lumen area > 6 mm² was used to defer revascularisation. The 179 patients eventually not revascularised based on this criterion had a 94% MACE-free survival at 2 years.
Clinical applications: interventional
Preintervention IVUS

- Lesion severity
- Lesion composition
  - lesion calcification/calcium distribution
- Plaque distribution
  - Eccentric plaques / bifurcation carina
- Device selection
  - Stent diameter/length
  - Postdilation balloon diameter/POT-bifurcation lesions
- Saphenous vein grafts
- Unusual lesion morphology
  - preprocedural dissections / coronary artery aneurysms
- Surgical revascularization
Lesion Calcification

• Severe calcification limits stent expansion, and **stent under-expansion** is associated with adverse events

• general agreement that the greater the **arc and length of IVUS-associated lesion calcium** the greater the likelihood of under-expansion

• **localized calcium deposits** or the transition from calcified to non-calcified plaque (or to normal vessel wall) are foci for PCI-associated dissections
STENT SIZING

1) Largest reference lumen whether proximal or distal
2) Midwall
3) Media-to-media (although this is often “discounted” by approximately 0.5 mm)
Post interventional IVUS

Optimal results

• apposition
• expansion
• detection of residual narrowing or proximal/distal stenoses or dissections requiring further treatment
Stent Malapposition

Post-stent implantation

Follow-up

Stent malapposition (white arrows): 1 or more struts clearly separated from vessel wall with evidence of blood speckles behind the strut

MUSIC registry IVUS criteria for optimal stenting

1. complete apposition of the stent over its entire length
2. symmetrical stent expansion defined by the ratio of minimal/ maximal lumen diameter ≥0.7
3. in-stent minimal lumen area ≥90% of the average area of distal and proximal references or ≥100% of the lumen area of the reference segment with the smallest lumen area.

The subgroup of patients who met the criteria had a record 8% rate of restenosis after bare metal stent implantation

😊 However, the criteria are difficult to achieve in real practice

Eur Heart J 1998
AVID trial optimisation criteria

• in-stent lumen CSA cross-sectional area ≥90% of the distal reference area

 مليارات not achieved in >70% of 225 patients
A prospective, randomized trial of intravascular-ultrasound guided compared to angiography guided stent implantation in complex coronary lesions: The AVIO trial

Maide Chieffo, MD, a, b Azeem Latib, MD, a, b, c Christophe Caussin, MD, b, c Patrizia Presbitero, MD, c, d Stefano Galli, MD, a, e Alberto Menozzi, MD, f, g Ferdinando Varbelli, f, h, i Fina Mauri, MD, i, j, k Marco Valgimigli, MD, i, k, l Choroummouzos Arampatzis, MD, a, m Manuel Sabate, MD, a, n, o Andrejs Erzigs, MD, o, p Bernhard Reimers, MD, a, q Madio Airoldi, MD, a, q, r, s, t Mika Lahoe, MD, a, u, v, w Ramon Lopez Pulop, MD, a, v, y Ghada Miqdad, MD, e, y, z, g, h Francesco Romeo, MD, a, v, x, a and Antonio Colombo, MD, FACC, a, v, x, y, z Milan, Parma, Rovoli, Ferrara, Mirandola, and Rome, Italy; Le Plessis Robinson, France; Badalona, Barcelona, and Alicante, Spain; Thessaloniki, Greece; Riga, Latvia; Helsinki, Finland and London, United Kingdom

AVIO study criteria

- Final minimum stent cross sectional area of at least 70% of the hypothetical cross-sectional area of the fully inflated balloon used for post-dilatation
- The optimal balloon size that should be used for post-dilatation is the average of the media to media diameters of the distal and proximal stent segments, as well as at the sites of maximal narrowing within the stent. The value is rounded to the lowest 0.00 or 0.50 mm.
- For values ≥3.5 mm, the operator could downsize the balloon diameter based on clinical judgment

A benefit of IVUS optimized DES implantation was observed in complex lesions in the post-procedure minimal lumen diameter.
No statistically significant difference was found in MACE up to 24 months

American Heart Journal January 2013
The optimal thresholds of post-intervention IVUS MSA that best predicted stent patency at 9 months were **5.7 mm²** for PES and **6.4 mm²** for BMS.
Post-Intervention Optimal Minimal Stent Area

Intravascular Ultrasound Assessment of Optimal Stent Area to Prevent In-Stent Restenosis After Zotarolimus-, Everolimus-, and Sirolimus-Eluting Stent Implantation

Hae-Geun Song, MD, Soo-Jin Kang, MD, PhD, Jung-Min Ahn, MD, Won-Jang Kim, MD, Jong-Young Lee, MD, Duk-Woo Park, MD, PhD, Seung-Whan Lee, MD, PhD, Young-Hak Kim, MD, PhD, Cheol Whan Lee, MD, PhD, Seong-Wook Park, MD, PhD, and Seung-Jung Park, MD, PhD

Catheterization and Cardiovascular Interventions 83:873–878 (2014)
Minimal in-stent lumen area is ≥ 9 mm²

### The Predictive Value of Different Intravascular Ultrasound Criteria for Restenosis After Coronary Stenting

<table>
<thead>
<tr>
<th>Minimum Lumen Cross Sectional Area</th>
<th>Potential Restenosis Rate</th>
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<tbody>
<tr>
<td>&lt;5 mm²</td>
<td>46%</td>
</tr>
<tr>
<td>5.0-5.9 mm²</td>
<td>33%</td>
</tr>
<tr>
<td>6.0-7.9 mm²</td>
<td>27%</td>
</tr>
<tr>
<td>8.0-8.9 mm²</td>
<td>21%</td>
</tr>
<tr>
<td>≥9 mm²</td>
<td>8%</td>
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</tbody>
</table>

The incidence of restenosis has an inverse relationship to post-procedure absolute IVUS lumen CSA.
# IVUS Guiding Coronary Interventions

<table>
<thead>
<tr>
<th>Application</th>
<th>IVUS (MLA)</th>
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<tbody>
<tr>
<td>Ischemia detection (proximal coronaries except Left Main and SVG)</td>
<td>&lt; 2.7 - 4.0 mm²</td>
</tr>
<tr>
<td>Ischemia detection (Left Main)</td>
<td>&lt; 6.0 mm²</td>
</tr>
<tr>
<td>Adequacy of stenting</td>
<td>&gt; 9.0 mm²</td>
</tr>
<tr>
<td></td>
<td>&gt; 80% Reference Area</td>
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</tbody>
</table>

** Pijls et al. Circulation 2002;105:2950–4
Impact of Intravascular Ultrasound-Guided Stenting on Long-Term Clinical Outcome: A Meta-Analysis of Available Studies Comparing Intravascular Ultrasound-Guided and Angiographically Guided Stenting

Gianni Casella,1,2* MD, Volker Klauss,2 MD, Filippo Ottani,3,5 MD, Uwe Siebert,2,4 MD, MPH, MSc, Pietro Sangiorgio,1 MD, and Daniele Bracchetti,1 MD

- IVUS-guided stenting implantation has a neutral effect on long-term death and nonfatal MI compared to an angiographic optimization.

- However, IVUS-guided stenting significantly lowers 6-month angiographic restenosis and target vessel revascularizations.
Meta-Analysis of Randomized Studies Comparing Intravascular Ultrasound Versus Angiographic Guidance of Percutaneous Coronary Intervention in Pre–Drug-Eluting Stent Era

Helen Parise, ScD, Akiko Maehara, MD, Gregg W. Stone, MD, Martin B. Leon, MD, and Gary S. Mintz, MD*

Figure 2. Ratio plots with 95% CIs for rates of 6-month angiographic restenosis among 6 randomized studies reporting restenosis. Combined estimates from both random effects (RE) and fixed effects (FE) models shown. IVUS guidance was associated with significantly lower rate of 6-month angiographic restenosis [heterogeneity $I^2 = 51.5\%$, $p(Q) = 0.07$; $p(\text{Effect}) = 0.016$].

Figure 4. OR plots with 95% CIs for rates of MACE. Combined estimates from both random effects (RE) and fixed effects (FE) models shown. IVUS guidance was associated with significant reduction in overall MACE [heterogeneity $I^2 = 49.2\%$, $p(Q) = 0.07$; $p(\text{Effect}) = 0.044$].

Figure 3. OR plots with 95% CIs for rates of repeat revascularization. Combined estimates from both random effects (RE) and fixed effects (FE) models shown. IVUS guidance was associated with significant reduction in revascularization [heterogeneity $I^2 = 25.6\%$, $p(Q) = 0.23$; $p(\text{Effect}) <0.001$].
• IVUS guided implantation of DES reduced the rate of MACE by about 20% and, within MACE, of MI and death but not of TVR/TLR
• Also, IVUS guidance was shown to decrease the rate of thrombosis and slightly increase post-procedural MLD
• Patients at high risk for thrombosis might be identified as the best candidate for IVUS guidance
Indications

Left main lesions
- IVUS for the evaluation of angiographically indeterminate left main lesions (Class IIa LOE B)
- IVUS may be considered for guidance of coronary stent implantation, particularly in cases of left main coronary artery stenting. (class IIb LOE B)

Non-left main coronary lesions
- Evaluation of angiographically indeterminate (50-70%) non-left main coronary lesions (Class IIb LOE B)

Stent restenosis / thrombosis
- IVUS to evaluate the aetiology of stent restenosis and stent thrombosis (Class IIa Level of Evidence C).

Routine use
- The routine use of IVUS for evaluation of lesions when PCI is not planned was given a Class III recommendation.

Cardiac transplantation
- IVUS and coronary angiography are reasonable 4 to 6 weeks and 1 year after cardiac transplantation to exclude donor CAD, detect rapidly progressive cardiac allograft vasculopathy, and provide prognostic information. (class IIa LOE B)
Take Home Messages

Valuable role
• lesion morphology
• Lesion severity
• Intervention guiding
  • lesion size
  • Determining appropriate stent placement/results
• Critical role in LM PCI