

## Clinical applications of intravascular ultrasound (IVUS): experience from an academic high volume centre of Northern Greece

Mantziari A, Ziakas A, Stavropoulos G, Styliadis IH

1<sup>st</sup> Cardiology Department, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

### Abstract

**Background:** Intravascular ultrasound (IVUS) has become a valuable tool adjunctive to coronary angiography due to its ability to directly image atheroma and the vessel wall. We aimed to evaluate the use of IVUS during diagnostic angiography and coronary interventions in a coronary intervention academic high volume center of northern Greece.

**Patients and Methods:** IVUS studies have been retrospectively retrieved from 2005 to 2008 from the archives of the catheterization laboratory of our department. IVUS was performed in 403 patients (294 male) of mean age  $62 \pm 6$  years. Indications for coronary angiography +/- intervention were acute coronary syndromes (49%), stable angina (46%) and previous coronary angioplasty evaluation (5%).

**Results:** Forty eight per cent of the IVUS studies were performed in left anterior descending artery (LAD), 25% in right coronary artery (RCA), 18% in left circumflex artery (LCx), and the rest (9%) in left main coronary artery (LMCA) or in coronary branches. Indications for performing an IVUS study were assessment of intermediate lesions (60%), evaluation of stent placement (36.5%), and determination of stent restenosis aetiology (3.5%). Among studies performed for assessment of intermediate lesions, 63% showed a non critical stenosis. IVUS after coronary stenting revealed a suboptimal stent placement in 77% of the cases, while in cases of stent restenosis, IVUS showed inadequate initial stent deployment in 43% of the patients.

**Conclusions:** The use of IVUS in our department has contributed to the optimization of interventional treatment of coronary lesions by means of evaluating borderline lesions, stenting placement and stent restenosis. Hippokratia 2011; 15 (1): 60-63

**Key words:** intravascular ultrasound, intermediate lesions, coronary angioplasty, optimal stent placement, restenosis

**Corresponding author:** Aglaia-Angeliki Mantziari, 1st Cardiology Department, University General Hospital AHEPA, of Thessaloniki, Aristotle University of Thessaloniki, 1st, St. Kiriakidi Street, 54636, Thessaloniki, Greece, Tel: +306977436678, Fax: +302310994673, e-mail: [lmantziari@yahoo.com](mailto:lmantziari@yahoo.com)

Even though coronary angiography remains the gold standard for the assessment of coronary atherosclerosis, it has several limitations as long as it is a two-dimensional modality depicting a planar silhouette of complex coronary lesions. Post mortem studies have shown that angiography might lead to both under and overestimation of complex and eccentric lesions<sup>1,2</sup>. Moreover, the assessment of stenosis severity relies on comparisons to the adjacent "normal" reference segment, which is often diffusely diseased. Finally, vascular remodeling involves outward displacement of the vessel wall and accumulation of atheroma within the arterial wall without lumen stenosis, resulting in a normal coronary lumen angiography.

Intravascular ultrasound (IVUS) has become a vital adjunctive imaging modality which is performed during coronary angiography and allows both precise quantitative measurements and characterization of plaque<sup>3</sup>. Major diagnostic applications of IVUS are to identify occult atherosclerosis in angiographically normal vessels, to evaluate intermediate lesions, and lesions difficult to assess by angiography, to determine the extent of cardiac allograft vasculopathy

and to assess the result of percutaneous transluminal coronary angioplasty (PTCA)<sup>4,6</sup>. According to the 2005 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) 2005 Guideline Update for percutaneous coronary intervention (PCI), it is reasonable to use IVUS: a) to evaluate coronary obstruction in a patient with a suspected flow-limiting stenosis when angiography is difficult because of location; b) to assess the adequacy of coronary stent deployment, including the extent of apposition and minimum luminal diameter within the stent; c) to assess a suboptimal angiographic result after PTCA; d) to determine the cause of stent restenosis and guide selection of appropriate therapy; and e) to determine the distribution of coronary calcium and the plaque location for guidance for rotational or directional coronary atherectomy respectively<sup>7</sup>.

In the present study we aimed to retrospectively assess the extent of the use of IVUS and the indications for which it was applied during coronary angiography in single academic high volume center of Northern Greece.

## Patients and Methods

### Study population

Coronary angiography +/- percutaneous coronary intervention (PCI) archives from 2005 to 2008 were retrospectively accessed and data were collected from all patients in whom an IVUS study was performed. During this period 7534 coronary angiograms and 3537 PCI were performed. An IVUS study was performed in 403 patients (294 male) of mean age  $62 \pm 6$  years.

### IVUS technique

A hundred to 200 mg of intracoronary nitroglycerin was administered before angiography or IVUS imaging runs. IVUS was performed using a commercially available system (Eagle Eye, Volcano Therapeutics, Rancho Cordova, CA). The ultrasound catheter was advanced 10 mm beyond the lesion/stent, and was pulled back to a point 10 mm proximal to the lesion/stent using motorized transducer pullback device. The device was activated to retract the catheter at a constant speed (at 0.5 to 1 mm/sec) while recording images.

Image interpretation: Intimal thickness was defined as the distance from the intima to the external elastic membrane. Common IVUS measurements were done including the lumen cross-sectional area (LCSA), external elastic membrane cross-sectional area (EEMCSA), maximum intimal thickness (IT-max), minimum intimal thickness (IT-min), vessel diameter and minimum lumen diameter (MLD). IVUS criteria for significant stenosis were: cross sectional area stenosis  $> 60\%$ , and lumen cross sectional area  $< 4.0 \text{ mm}^2$ . Especially for the left main coronary artery a stenosis was considered significant when IVUS showed lumen cross-sectional area  $< 7 \text{ mm}^2$  in symptomatic patients or  $< 6 \text{ mm}^2$  in asymptomatic patients or minimum lumen diameter  $< 2.3 \text{ mm}$ . An optimal post stenting IVUS result was: (1) a minimum lumen area  $\geq 90\%$  of the distal reference lumen area, or  $80\text{-}90\%$  of the average of the proximal and distal reference lumen areas, and (2) no major dissection. A major dissection was (1) a mobile flap, (2) a dissection involving  $> 90\%$  of the vessel circumference, or (3) a dissection causing a suboptimal true lumen area.

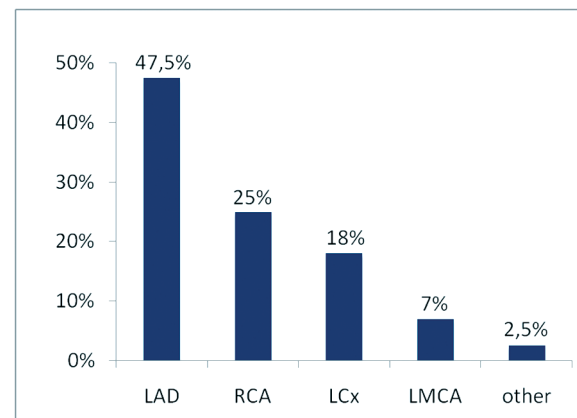
### Statistical analysis

Statistical analysis was performed using SPSS v16 for windows. Categorical variables are expressed as absolute numbers (percentages) and continuous variables are presented as mean  $\pm$  SD.

### Results

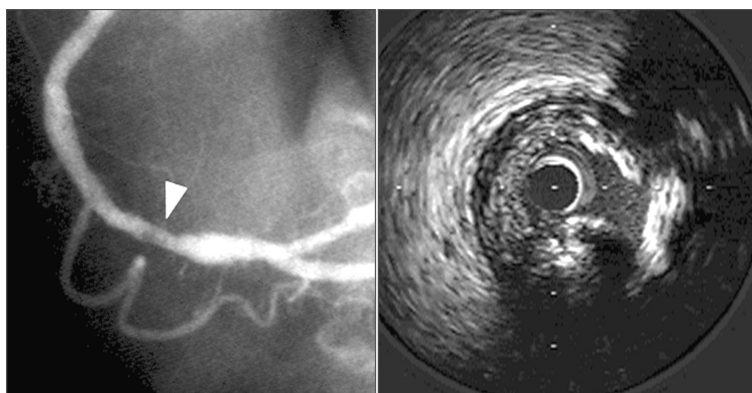
Indications for coronary angiography +/- PCI were acute coronary syndromes in 198 patients (49%), stable angina in 185 patients (46%) and stent restenosis assessment in 20 patients (5%). Almost half of the IVUS studies (48%) were performed in left anterior descend-

ing artery (LAD), 25% in right coronary artery (RCA), 18% in left circumflex artery (LCx), while the rest were performed in left main coronary artery (LMCA) or in coronary branches (Figure 1).



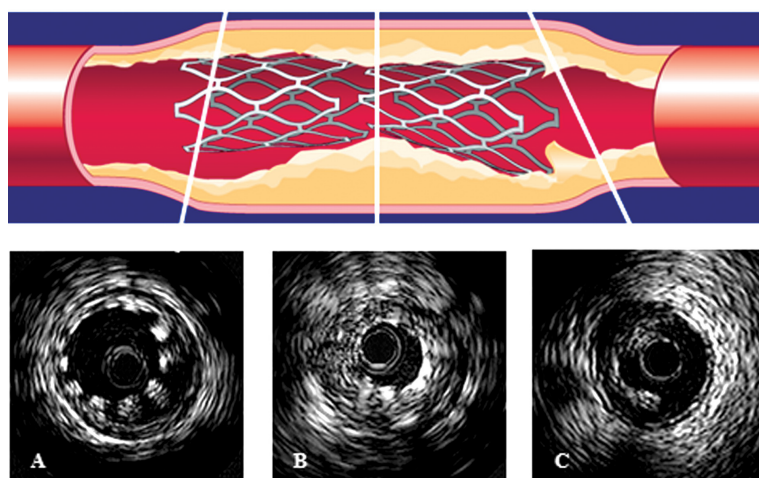
**Figure 1:** Prevalence of IVUS study among different coronary arteries. LAD, left anterior descending artery; RCA, right coronary artery; LCx, left circumflex artery; LMCA, left main coronary artery.

Indications for performing an IVUS study were assessment of intermediate lesions (60%) (Figure 2), evaluation of PTCA result (36.5%) (Figure 3), and determination of stent restenosis aetiology (3.5%). The results are presented in Figure 4. In cases of intermediate lesion assessment IVUS revealed a critical stenosis in 37% of the cases and the patient had further treatment (medical, PCI or aortocoronary bypass grafting), while 63% of the intermediate lesions showed no critical stenosis and no further treatment was needed.



**Figure 2:** Coronary angiography shows a borderline lesion (left panel). Intravascular ultrasound in the same lesion reveals a critical stenosis (right panel).

In cases where IVUS was used in order to evaluate the result of the PTCA, it revealed a suboptimal result in 77% of the cases and further PCI was performed, either stent postdilatation with an angioplasty balloon in cases of stent under-deployment, or placement of a new stent



**Figure 3:** After stent deployment IVUS reveals A, malapposition of the stent at the proximal stent edge, B, malexpansion of the stent in the middle and C, vessel dissection at the distal stent edge.

in cases of major dissection. Finally, in cases of stent restenosis assessment, IVUS showed inadequate initial stent deployment in 43% of the cases and further stent dilatation with larger balloons was performed, and intimal hyperplasia in 57% of the cases, which were treated with cutting balloon angioplasty or drug eluting stenting.

### Discussion

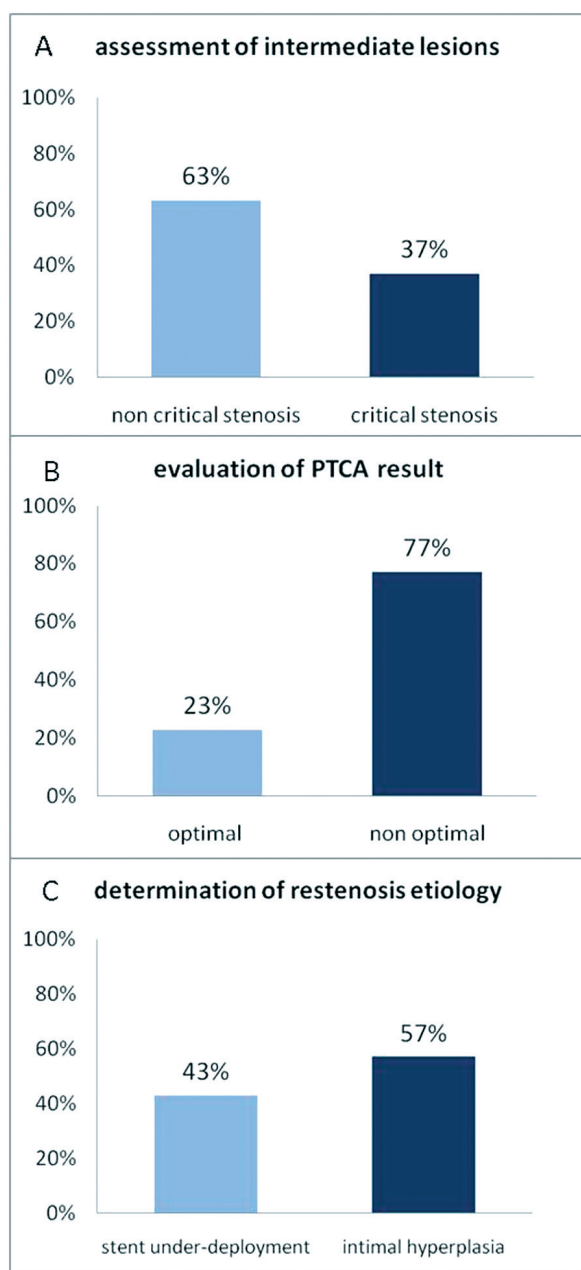
Intravascular ultrasound has been proved a valuable adjunctive tool to coronary angiography. In our department the use of IVUS has largely contributed to the precise evaluation of intermediate coronary lesions, the evaluation of PTCA result and assessment of stent restenosis.

Coronary angiography often underestimates stenosis severity by visual analysis of angiographically “normal” coronary artery reference segments. In one study, IVUS was used to study angiographically normal coronary reference segments in 884 patients and showed that only 6.8% of angiographically normal segments were normal by IVUS<sup>8</sup>. Several prospective studies compared IVUS, stress myocardial perfusion and physiologic lesion assessment to evaluate intermediate lesions. One study showed that a cross-sectional area  $<4.0 \text{ mm}^2$  had a sensitivity of 88% and a specificity of 90% for identifying lesions associated with an abnormal perfusion scan<sup>9</sup>. Takagi et al compared IVUS to fractional flow reserve (FFR) regarding their ability to determine the functional severity of coronary stenosis and showed that the IVUS thresholds that maximized the sensitivity and specificity were MLA  $<3.0 \text{ mm}^2$  (sensitivity, 83.0%; specificity, 92.3%) and area stenosis  $>0.6$  (sensitivity, 92.0%; specificity, 88.5%)<sup>10</sup>. In our study, using the above mentioned criteria 63% of the intermediate lesions assessed by IVUS were found to be no critical and PCI was not performed.

Percutaneous coronary stenting aims to the improvement of lumen dimensions by axial redistribution of atheroma, vessel expansion and plaque compression. Our study demonstrated that IVUS confirmed an optimal stent deployment in only 23% of cases. IVUS has the ability to reveal suboptimal results due to edge dissections, malexpansion, or malapposition even after angiographically successful stent placement. Restenosis after stenting is due to intimal hyperplasia and cross-sectional narrowing<sup>11</sup>. CRUISE (Can Routine Ultrasound Impact Stent Expansion) substudy compared the outcome of ultrasound- and angiographically- guided stenting in 538 procedures and showed that ultrasound guidance of stent implantation resulted in 39% relative reduction in target vessel revascularization<sup>12</sup>. The final in-stent area is a powerful predictor of target vessel revascularization<sup>13</sup>. Ultrasound predictors of restenosis at the stent margins include smaller reference vessel and lumen size, larger plaque burden at the reference segments and smaller final in-stent lumen area at the stent margins<sup>14</sup>. Furthermore, in cases of stent restenosis many operators advocate routine use of IVUS to identify the precise mechanism of restenosis. Stent restenosis could be due to inadequate initial stent deployment, intimal hyperplasia or mechanical problems. In cases of under-deployed stents further stent dilatation with larger balloons is needed as treatment, whereas in cases of intimal hyperplasia dilatation with cutting balloon, implantation of a drug eluting stent, or radiation therapy are advisable. In our study, 43% of the stent restenosis cases were a result of initial stent under-deployment and further balloon dilatation was performed, without need for implantation of a new stent.

In the new era of drug eluting stents (DES) IVUS can aid in confirming the success of stent placement, eliminating the risk of stent thrombosis and improving outcomes<sup>15,16</sup>. Patients at higher risk for DES thrombosis or restenosis may benefit the most from IVUS imaging during DES implantation. High risk patient characteristics are renal failure, limitations to dual antiplatelet therapy use, diabetes mellitus and poor left ventricular ejection fraction<sup>17,18</sup>. In addition high risk lesion features are left main disease, bifurcations, ostial lesions, small vessels, long lesions, treatment of in-stent restenosis<sup>18</sup>.

In conclusion, intravascular ultrasound is a routinely available tool for assessment of coronary lesions, optimal stent placement and stent failure (restenosis or thrombosis). In our department IVUS was performed in cases of angiographically borderline lesions, in order to determine the severity of the lesion, after coronary stenting, in order to confirm optimal stent placement



**Figure 4:** Results of intravascular ultrasound (A) in assessment of intermediate lesions, (B) in evaluation of PTCA result and (C) in determination of stent restenosis etiology.

and in cases of stent restenosis, in order to evaluate the aetiology of restenosis. The use of IVUS has contributed in optimizing the interventional therapy and thus in improving clinical outcomes.

#### Reference

1. Nissen SE, Gurley JC, Grines CL, Booth DC, McClure R, Berk M, et al. Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease. *Circulation*. 1991; 84: 1087-1099.
2. Roberts WC, Jones AA. Quantitation of coronary arterial nar-

- rowing at necropsy in sudden coronary death: analysis of 31 patients and comparison with 25 control subjects. *Am.J Cardiol*. 1979; 44: 39-45.
3. Waller BF, Pinkerton CA, Slack JD. Intravascular ultrasound: a histological study of vessels during life. The new 'gold standard' for vascular imaging. *Circulation*. 1992; 85: 2305-2310.
4. Kimura BJ, Bhargava V, DeMaria AN. Value and limitations of intravascular ultrasound imaging in characterizing coronary atherosclerotic plaque. *Am.Heart J* 1995; 130: 386-396.
5. Nissen SE, De Franco AC, Tuzcu EM, Moliterno DJ. Coronary intravascular ultrasound: diagnostic and interventional applications. *Coron.Artery Dis*. 1995; 6: 355-367.
6. Sipahi I, Nicholls SJ, Tuzcu EM. Intravascular ultrasound in the current percutaneous coronary intervention era. *Cardiol Clin*. 2006; 24: 163-173.
7. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB III, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). *Circulation*. 2006; 113: e166-e286.
8. Mintz GS, Painter JA, Pichard AD, Kent KM, Satler LF, Popma JJ, et al. Atherosclerosis in angiographically «normal» coronary artery reference segments: an intravascular ultrasound study with clinical correlations. *J Am Coll Cardiol*. 1995; 25: 1479-1485.
9. Nishioka T, Amanullah AM, Luo H, Berglund H, Kim CJ, Nagai T, et al. Clinical validation of intravascular ultrasound imaging for assessment of coronary stenosis severity: comparison with stress myocardial perfusion imaging. *J Am.Coll.Cardiol*. 1999; 33: 1870-1878.
10. Takagi A, Tsurumi Y, Ishii Y, Suzuki K, Kawana M, Kasanuki H. Clinical potential of intravascular ultrasound for physiological assessment of coronary stenosis: relationship between quantitative ultrasound tomography and pressure-derived fractional flow reserve. *Circulation*. 1999; 100: 250-255.
11. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Hong MK, et al. Intravascular Ultrasound Assessment of the Mechanisms and Predictors of Restenosis Following Coronary Angioplasty. *J Invasive Cardiol*. 1996; 8: 1-14.
12. Fitzgerald PJ, Oshima A, Hayase M, Metz JA, Bailey SR, Baim DS, et al. Final results of the Can Routine Ultrasound Influence Stent Expansion (CRUISE) study. *Circulation*. 2000; 102: 523-530.
13. Kasaoka S, Tobis JM, Akiyama T, Reimers B, Di Mario C, Wong ND, et al. Angiographic and intravascular ultrasound predictors of in-stent restenosis. *J Am Coll Cardiol*. 1998; 32: 1630-1635.
14. Hoffmann R, Mintz GS, Mehran R, Pichard AD, Kent KM, Satler LF, et al. Intravascular ultrasound predictors of angiographic restenosis in lesions treated with Palmaz-Schatz stents. *J Am Coll Cardiol*. 1998; 31: 43-49.
15. Mintz GS. Features and parameters of drug-eluting stent deployment discoverable by intravascular ultrasound. *Am J Cardiol*. 2007; 100: 26M-35M.
16. Moses JW, Dangas G, Mehran R, Mintz GS. Drug-eluting stents in the real world: how intravascular ultrasound can improve clinical outcome. *Am J Cardiol*. 2008; 102: 24J-28J.
17. Foussas SG, Tsiaousis GZ. Revascularization treatment in patients with coronary artery disease. *Hippokratia*. 2008; 12: 3-10.
18. Mintz GS, Weissman NJ. Intravascular ultrasound in the drug-eluting stent era. *J Am Coll Cardiol*. 2006; 48: 421-429.