Point–Counterpoint: The Role of IVUS

Gary Mintz, MD, and Jean Marco, MD, share their thoughts on IVUS, its utility in routine practice, and their positions on the impact that this imaging modality has on procedural outcomes.

***Cardiac Interventions Today*:** How does intravascular ultrasound (IVUS) affect diagnosis and stent placement?

Dr. Mintz: The traditional method of assessing coronary artery disease has been coronary angiography, which is a very imprecise tool. In individual cases, IVUS can affect almost any aspect of diagnosis and treatment—anything from assessing the severity of a lesion to assessing the extent of atherosclerosis to assessing the morphology of the lesion (including calcification and eccentricity) to looking at angiographically unusual lesions (such as filling defects and aneurysms).

With regard to stent placement, IVUS allows for better stent sizing in terms of diameter. It allows for more accurate stent length selection to cover secondary plaques at the edges, which are associated with a higher risk of restenosis. It also allows for better optimization of the acute results, including stent expansion and recognizing and treating complications. Almost every aspect of interventional cardiology can be positively affected by IVUS. That does not mean that IVUS has an impact on every decision in every patient; it just means that in an individual patient, it can affect almost any aspect of the procedure.

Dr. Marco: It is clear that IVUS can improve the diagnostics and improve the precision of the plaque features, as well as the calcification and the morphology of the plaque. It is also capable of accurately determining the diameter of the vessel. There is no question that IVUS positively affects these aspects of diagnosis.

With regard to stent placement, it is also clear that IVUS is superior to angiography when investigating stent deployment after the procedure, as well as stent dimension, stent area, and the completeness of stent apposition.

***Cardiac Interventions Today*:** What effect does IVUS have on determining completeness of treatment?

Dr. Mintz: We have learned repeatedly that the quality of the acute results determines long-term outcome. When it comes to stents, the number one issue is adequate stent expansion, and the number two issue is whether you leave significant inflow or outflow tract disease (eg, a secondary plaque at the edges of the stent or a residual dissection). Those are the two fundamental parameters of stent implantation that determine long-term outcome. IVUS allows you to adequately expand the stent or at least determine whether the stent is adequately expanded and, therefore, if additional work is necessary. It also allows you to better select stent length so that you cover inflow and outflow tract disease; or, if you do not perform preintervention imaging, IVUS imaging after stent implantation can be used to ensure that you have not left behind significant inflow and outflow tract disease.

Expansion and covering significant inflow and outflow disease were the two fundamental observations that were important in the bare-metal stent era; they are also important in the drug-eluting stent era. Expansion and covering significant inflow and outflow disease cannot be well determined angiographically. Similarly, when physicians try to use manufacturer's compliance charts to determine stent size and the inflation pressure that optimizes stent expansion, they achieve an average of only 75% of the predicted lumen diameter and 67% of the predicted stent area.

Regarding follow-up, if a patient is doing well, he or she does not require angiographic or IVUS follow-up, except in specific critical situations. However, the situation is different if a patient is not doing well and returns with in-stent restenosis. There are several reasons for in-stent restenosis, ranging from simple intimal hyperplasia to the stent totally missing the lesion. Although most cases of stent restenosis are a result of intimal hyperplasia, a significant percentage (perhaps as high as 35%–40%) is the result of stent underexpansion that occurred at the time of the initial interventional procedure, was simply missed at the time of the initial

interventional procedure, and was only detected at follow-up. Another cause of restenosis is mechanical problems with the stent; the stent could be crushed, it could have fractured, or it may have embolized during the initial procedure.

All of these issues are easily determined through ultrasound but are difficult to delineate angiographically. The procedural approach to dealing with each of these situations is entirely different.

Dr. Marco: There are two different points. The first concerns the effect that IVUS has on the completeness of treatment after stent placement. It is clear that that by using IVUS we can better appreciate the quality of stent deployment and stent dimension.

With regard to follow-up, I do not believe that IVUS should be a regular part of routine follow-up in any patient.

***Cardiac Interventions Today*:** What are the contraindications to using IVUS?

Dr. Mintz: There are certain anatomic vessel situations that are relative contraindications to using IVUS—for example, in a very tortuous vessel in which catheters tend not to track very well. A tight turn just proximal to a tight stenosis is also a relative contraindication. In these situations, it can be difficult to deliver the IVUS catheter to the target lesion.

Dr. Marco: In my mind, there are no contraindications to using IVUS when used by a properly trained interventionist.

Cardiac Interventions Today: What are the advantages and disadvantages of IVUS in assessing plaque composition?

Dr. Mintz: Grayscale IVUS is not a technique primarily designed to look at plaque composition, with the exception of calcification.

If you extend that question to ask how good IVUS is in looking at lesion morphology, it is good at looking for plaque ruptures in patients with acute coronary syndromes. It is good for determining if a filling defect is thrombus or calcium. It is probably pathognomonic for spontaneous dissection. But, if you are looking at an individual lesion to determine if it contains fibrotic or fibrofatty plaque, grayscale IVUS is not very effective.

When compared to optical coherence tomography (OCT), IVUS can penetrate better than OCT and show the overall plaque burden better, but in terms of looking at the plaque composition, it is not as good.

Dr. Marco: Classical IVUS (grayscale) may be able to distinguish the plaque composition in terms of calcification or spontaneous dissection, but it provides no other information about composition of the core of the plaque itself.

***Cardiac Interventions Today*:** How does IVUS compare to other lesion assessment modalities?

Dr. Mintz: Fractional flow reserve (FFR), which is an excellent technique for assessing the hemodynamic significance of a lesion, provides no information in terms of guiding the interventional procedure. In discussing whether FFR or IVUS is better for assessing intermediate lesions, there are different opinions. IVUS is good as long as it is used appropriately; it cannot be used in small vessels (the vessel must be at least 3 mm in size). The data regarding FFR in left main disease are not nearly as robust as those regarding IVUS in left main disease.

Angioscopy is great for assessing thrombus, and it is pretty good at assessing vulnerable plaque based on the color of the plaque. It can also detect endothelialization of the stent reasonably well. But, it is only a surface technique and has no quantifying ability in the setting of intermediate lesions. It does not tell you anything about the plaque burden, calcification, lumen dimension, remodeling, or stent expansion or coverage.

I think OCT is the new kid on the block. The images are impressive, with resolution far better than IVUS. In terms of assessing plaque burden and overall atherosclerosis (and perhaps stent sizing), it is currently not nearly as good as IVUS because it cannot penetrate the plaque to the vessel wall. The amount of experience concerning IVUS amounts to more than a decade of data, whereas that of OCT is very short. I think time will tell whether OCT will compete with IVUS in terms of routine interventional and diagnostic procedures, or if it will be relegated to the role of a niche application that supplements IVUS.

Dr. Marco: As compared to angiography, IVUS provides more information about the size and diameter of the vessel, the significance of calcification and vessel disease, as well as data in some eccentric lesions.

As compared with FFR, whereas IVUS is an imaging modality, FFR measures the hemodynamic significance of the lesion.

***Cardiac Interventions Today*:** Does using IVUS have an impact on procedure time?

Dr. Mintz: Yes, using IVUS does have an impact on procedure time in that it does take a bit longer. However, that additional time is dependent on how facile one is with the technique and how well you are set up to perform IVUS. If IVUS is part of your routine performance of procedures,

DR. MINTZ'S PATIENT OUTCOME DATA

In BMS era, 10/12 studies supported IVUS-guided PCI

Study	Angio Better	IVUS Better	IVUS Also Cheaper
Choi et al (AHJ 2001;142:112-8)		x	
CRNIC (JACC 2002;39:54A)		x	
CRUISE (Circulation 2000;102:523-30)		x	
SIPS (Circulation 2000;102:2487-502 and AJC 2003;91:143-7)		x	x
AVID (Circulation 1999;100:1-234)		x	
Gaster et al (Scan Cardiovasc J 2001;35:80-5 & Heart 2003;89:1043-9)		x	x
RESIST (JACC 1998;32:320-8 & Int J Cardiovasc Interven 2000;3:207-13)		x	
TULIP (Circulation 2003;107:62-7)		x	
BEST (Circulation2003;107:545-551)		x	
OPTICUS (Circulation. 2001;104:1343-9)	x		
PRESTO (Am Heart J. 2004;148:501-6)	x		
DIPOL (Am Heart J 2007;154:869-75)		x	

Independent predictors of mortality in 805 patients with LM disease treated with DES

	HR	95% CI	P
Previous CHF	2.66	1.03-6.85	0.043
Chronic Renal Failure	4.87	2.10-11.26	<0.001
COPD	2.93	1.00-8.53	0.049
Euroscore ≥ 6	3.24	1.48-7.09	0.003
IVUS guidance	0.43	0.21-0.87	0.019

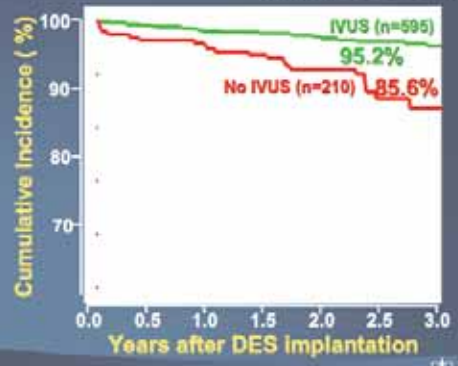
(SJ Park et al. TCT 2007)

1296 IVUS-guided, DES-treated lesions in 884 pts vs 1312 propensity-score-matched, angio-guided, DES-treated lesions in 884 pts

	IVUS-guided	Angio-guided	p
30 day			
MACE	2.8%	5.2%	0.01
Stent thrombosis	0.5%	1.4%	0.045
TLR	0.7%	1.7%	0.045
1 year			
MACE	14.5%	16.2%	0.3
Definite stent thrombosis	0.7%	2.0%	0.014
Probably stent thrombosis	4.0%	5.8%	0.08
TLR	5.1%	7.2%	0.06
Late definite stent thrombosis	0.2%	0.7%	0.3

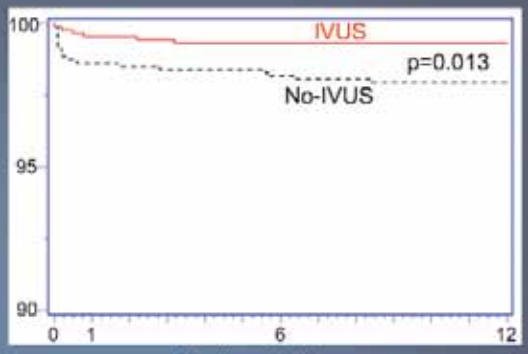
Roy et al. Eur Heart J. 2008;29:1851-7

Impact of IVUS Guidance on All-Cause Mortality After LMCA DES Implantation (n=805)



(SJ Park et al. TCT 2007)

Stent-thrombosis Free Survival (%)



DR. MARCO'S PATIENT OUTCOME DATA

What does robust evidence mean?

- Data derived from:
  - multiple controlled, randomised, adequately powered trials with a *clinical primary endpoint* at an appropriate time interval.(**Level of Evidence A)**

« high priority to the importance of significantly improving patients'outcome as the primary endpoint investigated in an adequately powered sample size »

interval.(**Level of Evidence B)**

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Source: ESC Guideline on PCI; EHJ 2005

Is there robust evidence to support that IVUS guidance improves patient's clinical outcome (hard events)?

DES era

The choice of δ and the number of subjects required for the trial,

"DES + IVUS guidance " vs "DES + Angiographic guidance"

☞ Such a study specifically addressing the clinical utility of IVUS in the DES era does not exist.

δ =	3%	require *N*	# 6000 pts
	4%		# 3500 pts
	5%		# 2500 pts

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Source: JAMA 2006; 295: 1152

Is there robust evidence to support that IVUS guidance improves patient's clinical outcome?

	Nb patients	*Primary end point*	
RESIST	155	Angio	Restenosis: 28.8% / 22.5% **(NS)**
AVID	759	Outcome (@ 12 months)	Death: 0.3% / 0.6%, MI: 8.9% / 5.2%, CABG: 3.1% /. 3.2% **(NS)**
☞ Underpowered (+ shorter FU time) to detect small differences ☞ No consistent trend in the incidence of death or MI			
			(NS)
TULIP *Lesion> 20mm* *Stent > 3.0mm*	144	Combined Angio+ death, MI, TLR	MLD: 1.82 ± 0.53 / vs. 1.51 ± 0.71 mm (p < 0.042)

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Long-term Health Outcome and Mortality Evaluation after Invasive Coronary Treatment Using Drug Eluting Stents With or Without the IVUS guidance.

Results

	DES + IVUS	DES + HP angio	P value
N pts	**105**	**105**	
MACE (%)	**11**	**12**	**NS**
Death (%)	3	2	NS
MI	1	4	NS
Re-PCI	6	6	NS
Underpowered to detect small differences			
Stent Thrombosis	4	6	NS

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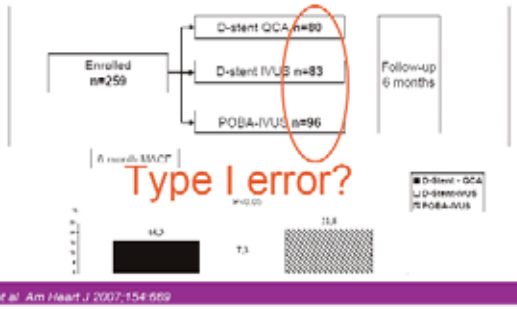
Source: Červinka P et al. Late breaking Trials, EuroPCR 2008

Comparison of angiographic guided direct stenting, direct stenting guided with IVUS or balloon angioplasty with IVUS guiding

Objective: is IVUS guiding > to QCA guiding during stenting or POBA?
Study: Multicenter randomised trial.
Population: pts with stable angina FC 1& 2 de novo lesions in vx ≥ 2.75mm - LL< 25 mm
Primary Endpoint: MACE: death, MI, repeat revascularisation



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Source: Gil et al. Am Heart J 2007;154:669

IVUS may add 5 minutes doing multiple imaging runs. If your facility is not prepared to perform IVUS on a routine basis, then of course, performing IVUS will negatively affect procedure time. It is just like anything else; if you do it often, are comfortable with it, and are good at it, you become very efficient at it, whereas if you perform IVUS once a year, it will become an impediment to your routine procedures.

Dr. Marco: The time required to perform IVUS is not a major issue.

***Cardiac Interventions Today*:** What is the learning curve associated with IVUS?

Dr. Mintz: I think this is a real issue. IVUS images are better than they used to be, but they are still not perfect. The steepness of the learning curve very much depends on the individual. Some people are good at learning how to interpret new images, whereas others are not. The most important thing to understand is that taking an IVUS catheter and placing it down a patient's artery does not affect patient outcomes *unless* you can interpret the images, use the gleaned information appropriately, and then appropriately alter your intervention. It isn't the ultrasound energy, nor is it the resulting images, that are the key to successfully using IVUS—it is correctly interpreting the images, knowing what you are looking at, and using the information appropriately to make the right therapeutic decisions.

If people are not going to learn how to interpret IVUS images, then the utility of IVUS in their hands is going to be minimal. One way around this issue is to train technologists. In many echocardiography labs, the technologists do the primary image interpretation. You can do the same thing with fellows or technologists or nurses in the catheterization lab, where they can help you learn to interpret the images or provide the image interpretation necessary to optimize the procedure.

Another way to reduce the learning curve is to do many cases, to look at lots of images, and perhaps spend time in a lab in which IVUS is routinely performed. It is something that a busy senior interventionist is often not willing to do. It is also the busy senior interventionist who is often the IVUS nihilist. In my opinion, this is simply because he or she refuses to take the time to learn. People who are willing to spend the time and energy to learn how to interpret IVUS images will learn how to do so. But it takes a concerted effort to climb that curve. An appropriate analogy would be if you learned how to read American street signs. Suppose you were placed in a foreign country where nothing is in English. The information on the street signs in that country is still there—it is still valid and important. But, unless you learn that language, you won't understand the street signs. It does not mean the street signs are worthless, it just means you have not made the effort to learn them. Correct interpretation of IVUS images is no different.

DR. MINTZ'S TAKE-HOME POINTS

- With regard to stent placement, IVUS allows for better stent sizing in terms of diameter, more accurate stent length selection, and better optimization of acute results (including stent expansion and recognizing and treating complications).
- The learning curve associated with IVUS depends on the operator's dedication in learning to correctly interpret IVUS images, which can be accomplished by performing a lot of cases, spending time in labs that have a high volume of IVUS cases, as well as modifying practice habits to include fellows, technologists, and nurses in the interpretation of images.
- There is a need for better reimbursement or cheaper catheters.
- Use of IVUS results in improved patient outcomes.

Dr. Marco: Of course, it is a real issue. Like all techniques, there is a learning curve associated with how to perform IVUS and, most importantly, how to correctly interpret the IVUS image. However, I believe that the learning curve of IVUS in routine use in practice is relatively short if a practitioner takes time to learn "how to correctly use IVUS images."

***Cardiac Interventions Today*:** What are the overall advantages and disadvantages of using IVUS?

Dr. Mintz: The bottom line when it comes to IVUS is that patient outcomes are improved, the interventional procedure is made simpler and less mysterious, and ambiguous angiograms are clarified, but most important is that patient outcome is improved. There are now 12 studies in the bare-metal stent era, 10 of which showed that patients treated with IVUS guidance did better, and there are two studies in the drug-eluting stent era, both of which showed that IVUS guidance improved patient outcomes.

Dr. Marco: All of the questions so far have been somewhat in favor of using IVUS. However, the major question is

DR. MARCO'S TAKE-HOME POINTS

- IVUS is a fantastic tool to increase our understanding of percutaneous coronary intervention procedures and for research and teaching.
- In some specific groups of patients (ie, calcified lesions, difficult anatomy, bifurcation lesions), IVUS guidance may improve patient outcomes. As such, IVUS may be considered an optional companion to current clinical practice.
- In routine clinical practice, there is no need to adopt regular use of IVUS because current and future angiographic techniques and technology suffice for providing accurate information during percutaneous coronary intervention.

does all of this information have an impact on clinical outcomes (both short- and long-term outcomes). At the present time, we do not have in the literature clear and robust data to support that routine (in all patients) IVUS guidance improves patient clinical outcomes.

In terms of short-term outcomes (in-hospital major complications), the rate of death after routine angiography is very low (0.25%–1.5%). The risk of myocardial infarction is approximately 1% to 2.5%. To justify using IVUS, we would need to demonstrate a decrease in these rates, which would require a huge randomized trial (involving between 30,000 and 40,000 patients) in order to be correctly powered. It is impossible to perform such a trial.

When looking at the long-term results after the procedure (ie, restenosis or clinical outcomes), there is no robust evidence to support that routine IVUS guidance improves long-term patient clinical outcomes. All of the studies in the literature that do present data on this are underpowered, with a very short follow-up time (between 6 and 12 months). These studies are too underpowered to detect such a small difference. This is a major limitation to proposing the use of IVUS in routine practice.

***Cardiac Interventions Today*:** What is the financial cost associated with implementing IVUS at a facility, and is the cost justified?

Dr. Mintz: That is a hard question to answer. There are two studies that have suggested that if you follow the patients long enough, the reduced cost of long-term patient care offsets the increased cost of using the IVUS catheter. The catheter cost varies among countries and continents. The cost also changes over time.

Also, the overall cost of IVUS is not trivial: you have to buy the box, the catheters, and, if you want dedicated personnel, you have to pay them. In the US, catheter costs can also depend on your volume. I acknowledge that cost can be an issue in an environment in which reimbursement is nonexistent, and cath lab budgets are critically important.

Dr. Marco: The cost of IVUS is a very important point to take into consideration. Cost is a major limitation of IVUS in Europe. In some countries, there is specific reimbursement for IVUS, but in most countries in Europe, there is no major reimbursement. This combination (the lack of robust data to support the use of IVUS and the overall lack of reimbursement of IVUS) is a major limitation to using IVUS in the majority of cath labs.

***Cardiac Interventions Today*:** What are the reimbursement concerns or problems regarding use of IVUS?

Dr. Mintz: In Japan, IVUS is fully reimbursed, and this level of reimbursement has been attributed as one of the reasons for the 70% rate of IVUS usage in Japan. In the US, reimbursement exists, but it is modest and varies by region. In Europe, I do not believe there is any country that has agreed to reimburse for IVUS. In Korea, where there is no reimbursement, IVUS has a 30% rate of use. IVUS reimbursement is an issue, and there is a need for better reimbursement or cheaper catheters. I do believe the lack of reimbursement does hamper its adoption; however, there are other procedures and other diagnostic tests that are not reimbursed that have achieved better traction.

Dr. Marco: If a specific reimbursement for IVUS ever comes to pass or if IVUS is available at a low cost, perhaps there would be justification for using IVUS more frequently in daily practice. However, until it can be proven that IVUS improves clinical patient outcomes, such reimbursement is highly unlikely. ■

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