Is intravascular ultrasound clinically useful or is it just a research tool?

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Coronary angiography has been the gold standard for assessing coronary artery disease and guiding interventions. Because of its reproducibility, quantitative angiography (QCA) has introduced objectivity and consistency into clinical trials. However, angiography is only a lumenogram. Therefore, it has two major limitations: atherosclerosis is a disease of the arterial wall compromising the lumen only in its late stages; and angiography provides only a shadowgraphic representation of complex three dimensional coronary lumen anatomy.

To overcome some of these limitations, new imaging modalities such as intravascular ultrasound (IVUS) have been developed. Unlike angiography, IVUS is a tomographic technique. Normal coronary arterial wall, major components of the atherosclerotic plaque, and qualitative and quantitative changes that occur as part of the atherosclerotic disease process, during interventions, and as a result of restenosis can be studied in vivo in a manner previously not possible. This includes visualisation of relatively radiolucent (but intensely echoreflective) stainless steel stent struts. The early use of IVUS was investigational. More recently, several institutions have emphasised the use of IVUS to guide interventional procedures. This review focuses on some of the clinical uses of IVUS.

Pre-intervention, the interventionalist must decide: whether there is significant lumen compromise; whether there are lesion specific characteristics favouring the selection or avoidance of particular therapeutic strategies; and, once the decision to intervene has been made, the size of the device. Postintervention, before terminating the procedure, the interventionalist must decide: if the result is adequate; and if there are any complications.

Pre-intervention IVUS assessment

LUMEN MEASUREMENTS

IVUS measurement of lumen dimensions (cross sectional areas and diameters) has been validated in vitro.1 When IVUS was compared to QCA, and only lesions with an angiographic minimum lumen diameter larger than the IVUS catheter were included, the correlation between the two was only fair (fig 1). Furthermore, angiographically intermediate or ambiguous lesions were often found to be either very severely or only minimally diseased (fig 2). Therefore, we routinely use IVUS to assess lumen dimensions to determine the need for intervention or, in the case of unprotected left main disease, for surgery.

LESION SPECIFIC CHARACTERISTICS

The IVUS detection of target lesion calcium has been validated in vitro.1 IVUS detects target lesion calcium approximately twice as often as angiography. The sensitivity of angiography does not exceed 80% except in the presence of four quadrant (> 270° of circumferential) calcium. Furthermore, angiography has a false positive rate of 10%.2 Calcium, especially focal calcium, is a major determinant of dissections post-PTCA.3 Angiographically invisible, but IVUS evident, calcium is the major determinant of the success of directional coronary atherectomy.4 Rotational atherectomy may be the preferred treatment strategy for heavily calcified lesions. IVUS can determine the location (superficial v deep) and distribution (target lesion v reference segment) of calcification. Significant calcium in the vessel proximal to the lesion may limit passage of bulky devices such as directional coronary atherectomy catheters or sheath based stent delivery systems.

IVUS measurement of plaque thickness has

**Figure 1** Comparison of minimum lumen diameters measured by intravascular ultrasound (IVUS) and quantitative coronary angiography (QCA) pre-intervention (left), postintervention all devices (middle), and postintervention in the subpopulation of patients treated with stent implantation and high pressure adjunct PTCA (right).
often be clarified by IVUS. Two notable examples are aneurysms \( v \) pseudoaneurysms, and "thrombi" that are, instead, calcified filling defects (fig 3).\(^6\)

**VESSEL SIZE**

We define the IVUS reference segment as the most "normal looking" cross section (largest lumen with the least plaque) within 10 mm proximal to a lesion, but distal to a major side branch. Less than 10% of reference segments are normal; the average reference segment plaque burden (percentage of arterial cross sectional area occupied by plaque) is > 50\(^{\text{a}}\).\(^7\)

Even just using reference segment lumen dimensions, IVUS reference segment measurements are consistently larger than QCA with an average (but not predictable) difference of 0.5 mm (fig 4). This allows more precise sizing of PTCA balloons or new angioplasty devices to achieve larger final lumen dimensions without increased complications. (Importantly, when IVUS reference lumen dimensions are smaller than QCA, vessels are typically calcified. Blindly upsizing balloons and devices in unexpectedly small calcified vessels, will lead to dissections.) The value of this approach has been confirmed by CLOUT (CLinical Outcomes Ultrasound Trial).\(^8\)

**LESION LENGTH**

IVUS length measurements have been validated in vivo.\(^9\) Using motorised transducer pullback through a stationary imaging sheath, lesion lengths and distances from a lesion to a major side branch or coronary ostium can be measured. This allows selection of the appropriate length or number of stents needed to cover a stenosis, anchor the ends in relatively healthy segments, and avoid "jailing" another vessel.

**STENT RESTENOSIS**

There are two main causes of within stent restenosis: inadequate initial stent deployment (which may be reduced, but not eliminated with routine high pressure PTCA); and neointimal tissue proliferation.\(^10\) Although focal within stent restenosis can be treated successfully with repeat PTCA, diffuse restenosis is more problematic with a high recurrence rate after PTCA alone. Debubling strategies (using excimer laser coronary angioplasty or rotational atherectomy) are being tested to treat diffuse with stent restenoses. However, the deleterious effects of atheroablation within underexpanded stents is unknown. Unless we know that a stent was adequately expanded during implantation, we use pre-intervention IVUS to determine whether stent dimensions are adequate for atheroablation device use.

**Postintervention IVUS assessment**

**PREDICTORS OF RESTENOSIS**

The IVUS predictors of restenosis are more sensitive than angiography; in non-stented lesions the strongest predictor is the residual IVUS plaque burden.\(^11\) This is a parameter

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**Figure 2** An ostial left anterior descending lesion with no significant lumen compromise by QCA (minimum lumen diameter = 2.39 mm and diameter stenosis = 39\%, arrow), but with an IVUS minimum lumen diameter < 1.3 mm (< the size of the imaging catheter at the plaque was packed around the catheter). The patient was referred for bypass surgery.

**Figure 3** A patient with unstable angina and a "thrombus" in the mid-right coronary artery (white arrow) was treated with prolonged (> 7 days) heparinisation. When it did not dissolve IVUS imaging showed that this represented a calcified filling defect. Because rotational atherectomy was not available, the patient was referred for bypass surgery.
that is unique to tomographic imaging and, in coronary arteries, unique to IVUS. The residual plaque burden may act as an amplifier of the remodelling process, the major mechanism of restenosis in non-stented lesions.\textsuperscript{12} Thus, it is important to obtain not only the largest possible lumen, but also the lowest residual plaque burden. The predictive value of this parameter has been substantiated in phase II of the GUIDE Trial (blinded postintervention IVUS imaging) and in two IVUS guided coronary atherectomy trials (OARS (Optimal Atherectomy Restenosis Study) and ABACAS (Adjunct Balloon Angioplasty Coronary Atherectomy Study)) in which restenosis rates tracked the residual plaque burdens.\textsuperscript{13 14}

**FINAL DIMENSIONS**

Some patients do have good long term results after conventional PTCA. Unfortunately, angiography does not predictably identify them (fig 5). As with the pre-intervention assessment of lumen dimensions, the correlation between IVUS and QCA is only fair; this also true for patients treated with stents and high pressure PTCA (fig 1).

Our IVUS end points for stent implantation in native coronary arteries are: minimum stent cross sectional area > 80% of the reference lumen cross sectional area or an absolute minimum stent cross sectional area > 7.0 mm\textsuperscript{2}; and complete stent–vessel wall apposition. Even after routine high pressure (>16 atm) adjunct PTCA, 40% of cases require additional balloon inflations (higher pressures or larger sizes) to achieve these end points. If these IVUS end points are met, the clinical restenosis rate is approximately 10%, regardless of patient, lesion, or treatment characteristics (number of stents, pre-stent use of atheroablative devices, etc)\textsuperscript{15}; this is significantly lower than if these end points are not met. For example, aorto-ostial stent placement is often technically challenging. IVUS identifies proper stent placement \textit{v} misplacement (in which the stent does not cover the aorto ostial junction but slips into the proximal vessel).

**COMPLICATIONS**

Complications during interventional procedures are a reality. Dissections are detected by IVUS twice as often as by angiography (fig 5); however, it is important to note that dissections behind calcium are shadowed by the calcium and, therefore, will not be seen by IVUS. Similarly, vessel perforations after directional coronary atherectomy and deep wall haematomas may be detected only by IVUS.

**Conclusions**

Limitations to the routine incorporation of IVUS into interventional procedures are: cost, equipment clumsiness, and image interpretation. Nevertheless, based on the above findings, we have gradually evolved from a strategy of angiographic guidance of interventional procedures to IVUS guided intervention in more than 6000 patients.
Do we have enough evidence to insist we have IVUS?

Ian R Starkey

The use of intravascular ultrasound (IVUS), a method of imaging the wall of the coronary artery, complements the information obtained by coronary angiography, which defines the contour of the vessel lumen. IVUS demonstrates that significant mural disease is almost invariably present in angiographically normal segments of "focally" diseased coronary arteries, and has shown obstructive disease in patients with coronary arteries judged angiographically to be normal or near normal, which might justify its availability, at least as a supraprovincial service.

IVUS has been used to guide selection of the device used for percutaneous interventional treatment of coronary lesions but it has yet to be shown that this approach influences clinical outcome, and few interventional centres offer routine pre-interventional IVUS imaging and a choice of interventional devices that includes three different atherectomy catheters and an excimer laser. The demonstration by IVUS that coronary stents deployed at nominal balloon pressure are usually under expanded was an invaluable contribution. We now appreciate the need for optimal stent deployment, but it is unclear whether the routine use of IVUS guidance is actually essential for optimal stenting. The remarkable results obtained in the Benestent II pilot study, for example, were obtained without the routine use of this technique.

The use of IVUS will continue to help our understanding of coronary artery disease. As it is both time consuming and expensive, widespread clinical use is not justifiable unless and until further information suggests that this significantly improves the clinical outcome of large numbers of patients.
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