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IS118 Keynote Lecture

## The Use of Intravascular Ultrasound (IVUS) Imaging for Assessment of Coronary Pathology

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The major benefit of intravascular ultrasound (IVUS) is assessment of the coronary anatomy. Additionally, by providing information about the pathology of atherosclerosis, it is complimentary to Doppler flow or pressure measurements, which provide functional assessment of coronary artery disease (CAD). IVUS may identify anatomy that requires stenting, although physiologically an adequate angioplasty result was obtained as assessed by fractional flow reserve (FFR). Quantitative coronary angiography (QCA) is useful but has some limitations. The pathology in the wall of the artery is not distinguishable from the lumen itself and in some cases all aspects of the lumen are not visualized, leading to inaccurate assessments.

The DESTINI randomized trial showed that Doppler flow and QCA-guided angioplasty provided results equivalent to those with stenting, in terms of target lesion revascularization (TLR) and complication rates. Therefore, the use of coronary flow reserve seems to be diminishing, as the interpretation of the DESTINI results by many people is that it is simpler to stent all patients and obtain equivalent results, since QCA is not always reliable. This is similar to higher pressure and larger balloons replacing IVUS-guided stenting, after it was shown that a significant beneficial result and optimization of the lumen could be obtained.

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**Use of IVUS for assessment of intermediate lesion**

FFR has a higher threshold for intervention, compared with anatomic imaging. In a patient with left main narrowing, unclear severity of narrowing, and some lucency in the left main, it was difficult to determine severity despite multiple views. But, by IVUS a plaque was visualized on the wall of the artery and a significant stenosis was found proximal to the bifurcation of the circumflex that was calcified and narrowed the left main lumen. Quantitation by QCA would likely underrepresent the severity of disease in this case; by IVUS the stenosis was 2 mm in diameter. FFR was normal. Based on the anatomic information, the patient should be treated with surgery rather than medical therapy.

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## IVUS optimizes results

IVUS can have a significant impact when used to determine the best interventional technique or balloon size. In a patient with an abnormal thallium study (50-60% right coronary artery stenosis that did not appear to be critical yet) it was not possible to move the US device across the lesion. Very often these lesions are very calcified, preventing the device to cross. Rotational atherectomy (RA) was done and the lesion studied thereafter. The US pullback showed a 360-degree calcium lesion after RA, confirming the lesion was much tighter than appreciated by angiography and more calcified.

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## Tissue characterization

IVUS has contributed significantly to the understanding of the pathophysiology of remodeling and compensatory dilatation following balloon dilatation. IVUS is able to identify the *type* of plaque present. This can be helpful when performing PTCA where a dissection may occur typically at the edge of calcium where the differential in stress is greater causing a tear in the plaque. IVUS imaging helps to explain why the restenosis rate is high after a successful PTCA. Despite an apparently successful QCA angiographic result, an enormous amount of plaque remains that has been remodeled little. IVUS is perhaps not as accurate as angioscopy for detecting thrombus, but it can be very helpful at times. A case study illustrated the ability of IVUS to define vulnerable plaque that had ruptured, as confirmed by directional atherectomy removal and histology study.

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## IVUS-guided stenting

Ultrasound has had the most impact on IVUS-guided stenting. It can identify lumen cross-sectional areas that are still quite small, so higher pressures or the combination of

larger balloons and higher pressure can be used to obtain a wider cross-sectional area, reducing the requirement for anti-coagulation. The problem of sub-acute thrombosis has essentially disappeared using this much more aggressive IVUS-guided, larger balloon size, higher pressure technique.

The CRUISE study in 500 patients with Palmaz-Schatz stents documented improvement with IVUS-guided stenting. The follow-up cross-sectional area was larger in the IVUS-stented group compared to the angiographic-guided stent group. Target vessel revascularization was reduced by nearly 50% with IVUS-guided stenting. However, the use of IVUS-guided stenting is limited since it is expensive and time consuming, despite the documented statistical benefit.

IVUS-guided spot stenting is useful for treating diffuse disease. Placing a long stent alone in the entire vessel provides a good immediate result but the restenosis rate is very high. Using IVUS to place a stent only in those areas with inadequate cross-sectional lumen areas has been shown to reduce the restenosis rate in diffuse disease. Also, larger balloons can be used as the US provides the true size of the vessel, compared to angiography.

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## Selecting approaches to treatment in atherosclerosis

Better identification of the anatomy and the extent of disease can assist with selecting the best treatment approach. In a patient with severe diffuse disease in the right coronary artery, IVUS identified a large, eccentric plaque with calcium. IVUS also identified that the artery was much larger than appreciated (5 mm in diameter). Many mobile echos consistent with thrombus and an echo lucent zone consistent with either necrotic tissue or high lipid density were present. The fibrous cap was mobile, suggesting it may be torn. Based on these observations, the use of a salvage device, was suggested. Since none was available, a balloon angioplasty was performed. The dilatation caused a no-reflow phenomenon, so aggressive treatment with stents, adenosine and verapamil to re-establish adequate blood flow was used. A subsequent US showed an adequate lumen, as well as the residual thrombus and lipid mixture of the plaque.

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## Identifying vulnerable plaques

Most of the plaques that cause an infarction were less than 50% diameter stenosed at baseline angiography. Lipid lowering trials have shown a reduction in clinical events, but the angiographic change in the coronary anatomy is very small. There is some preliminary evidence that cholesterol lowering stabilizes the plaque, independent of changes in individual lesions.

Tobis presented a case in which a donor heart was shown by post-transplant US to have a large eccentric plaque with a preserved lumen and some compensatory dilation. One year later, the plaque had changed significantly in the low cholesterol environment in the

recipient patient who did not have hypercholesterolemia. Tissue characteristics were much more echogenic, and more consistent with fibrous tissue compared to baseline. Quantitation showed no significant change in lumen during the year, but the external elastic membrane had diminished causing a decrease in the atheromatous area.

The concept is that just as plaques progress with compensatory dilation, they may regress with the lumen remaining constant. Thus, the changes are not seen with QCA studies which only analyze the lumen. This will be tested in a multicenter trial (REVERSAL) with high doses of atorvastatin or pravastatin. Importantly, this will be the first study in which IVUS will quantitate the volume of plaque *as* the primary end point of this study.

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## Device assessment

IVUS will continue to be used in coronary interventions to gain insights to new devices and optimize results. The demonstrated ability of IVUS to obtain better views allows for more accurate assessment of results, which can reduce stenosis. For example, in specific lesion subsets such as complicated LAD diagonal bifurcations, treated with RA and two stents, IVUS assessment is more accurate as angiography has so much overlap. IVUS is being used to assess a new atherectomy device designed to remove thrombus and in-stent stenosis. IVUS can assess whether the device actually removes the material and the amount, to determine whether the results obtained are from material removal or the balloon itself.

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## IVUS-guided debulking

There is a great deal of enthusiasm that a much larger cross-sectional luminal area can be obtained by removing the large plaque, optimizing the result and reducing the restenosis rate. This has been demonstrated with an 8-month follow-up showing minimal hyperplasia. The ongoing AMIGO trial is investigating whether debulking with IVUS-guided stenting is better compared to stenting alone.

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## Future of IVUS

A very exciting therapeutic use of IVUS is being pioneered by Steve Osterlie at Massachusetts General Hospital: in situ coronary artery bypass without surgery.

If this technique is successful, it could potentially replace a lot of bypass surgery.

IVUS imaging is performed by going through the vein and the coronary sinus to visualize the disease in the artery. In situ grafting similar to that used in femoral bypasses is then performed: puncture through the vein to the artery, place a pledget to make a hole proximal and distal, and then close off the vein, resulting in an in situ graft going from the artery proximally through the vein and then distally down to the rest of the coronary artery.

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