Chapter 6
Research Utility of Intravascular Ultrasound

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ABSTRACT

Intravascular ultrasound was designed to overcome the limitations of angiography, and in the process it has helped greatly with our understanding of coronary artery disease. There is no doubt that it plays an important role in contemporary interventional cardiology. In this regard, this chapter reviews the most important uses of intravascular ultrasound in current research.

INTRODUCTION / BACKGROUND

Intravascular ultrasound (IVUS) was designed to overcome the limitations of angiographic “luminography”, and was the first intravascular coronary imaging technique to be developed. The technique has made significant contributions to our current understanding of coronary artery disease through its capacity to obtain in vivo images of the vessel wall and its interaction with coronary devices. In addition, IVUS has played a key role in the field of percutaneous coronary interventions (PCI), depicting the pitfalls of stent deployment and improving stenting techniques, a major step
that has dramatically decreased peri-procedural complications, allowing the use of the simpler anti-thrombotic treatments used today. Of note, many modern trials assessing PCI are IVUS based. Knowledge of coronary vessel remodeling during atherogenesis is largely based on IVUS evidence, and many progression/regression studies of atherosclerosis are also IVUS-based. In 20 years of existence, IVUS has undergone major changes. In the last decade backscatter analysis was introduced, facilitating characterization of plaque components and its mechanical properties. Intracoronary multimodality imaging is therefore a promising technique in the study of vulnerable plaques. In complex subsets of PCI, IVUS is an indispensable tool, and new modalities for specific purposes, like forward-looking IVUS for chronic total occlusion recanalisation, are being developed. These trends will be reviewed in this chapter, along with a review of the most important uses of IVUS in current research.

**DRUG EFFECTS ON Atherosclerosis (TABLE 1)**

The initial observations of a positive continuous relationship between coronary heart disease risk and blood cholesterol levels led to the conduction of a number of IVUS-based studies to evaluate the effect of different lipid lowering drugs on atheroma size. Changes in plaque characteristics may be a more relevant endpoint than plaque progression or regression in the prediction of the risk of vascular thrombosis, however imaging tools to accurately evaluate plaque characteristics have only recently become widely available. Other limitations of using conventional grayscale IVUS to assess the natural history of atherosclerosis which should be considered include: 1. catheterization is an invasive procedure and is required for serial imaging; 2. only a segment of the coronary tree can be studied; 3. plaque composition is not obtained; 4. there is no direct evidence linking changes in coronary plaques and clinical events. Figure 1 shows two examples of serial assessment of plaque size changes.

**Lipid Modifying Agents**

The efficacy of lowering low density lipoprotein (LDL)-C with inhibitors of hydroxymethylglutaryl coenzyme A reductase (statins) is unequivocal; however the change in atheroma size by statins is not constant across all IVUS studies. There are many potential explanations for these discrepancies such as different drug properties, dose, and duration of treatment. In early studies, like the German Atorvastatin Intravascular Ultrasound (GAIN) study,(Schartl et al., 2001) atheroma volume was not reduced by atorvastatin despite the reduction in LDL-C (86 vs. 140 mg/dL) at 12 months. In contrast, the Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) (Nissen, Tuzcu, Schoenhagen et al., 2004) study showed that LDL-C levels were lowered by a greater extent with treatment with atorvastatin when compared to pravastatin (110 mg/dL vs. 79 mg/dL), which was subsequently associated with a 2.7% increase in atheroma volume in pravastatin-treated patients, and in a 0.4% reduction in atheroma volume in atorvastatin-treated patients. The clinical significance and the accuracy of IVUS for such measurements are still debated, but these results were “statistically significant”. The Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT) study,(Cannon et al., 2004) showed that the lower the LDL-C and C-reactive proteins (CRP) values, the greater the reduction in clinical events and atheroma progression.

One of the first studies showing regression of plaque size was the ASTEROID trial (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden) (Nissen et al., 2006). At 24 months, treatment with rosvastatin 40 mg daily resulted in a lowering of LDL-C to 60.8 mg/dL and an