

Quantitative IntraVascular UltraSound (QCU)

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Introduction:

For decades, contrast angiography has been the predominant method for the assessment of the presence and severity of atherosclerotic disease in the aorta, peripheral arteries, and the coronary vasculature. However, conventional angiography-based measurements on single vessel segments by QCA has a number of inherent limitations: 1) it is not able to assess the severity of diffuse coronary disease in its early stages as we discussed earlier; 2) it cannot visualize eccentric plaque; and 3) it cannot assess plaque composition. Furthermore, angiography may overestimate lumen areas after percutaneous coronary angioplasty (PTCA) due to the presence of fractured plaque and irregular and rough inside wall surfaces, and it cannot predict the location of plaque fracture, which may result from PTCA.

About a decade ago, IntraVascular UltraSound imaging (IVUS) was introduced as a complementary approach to angiography. It is a catheter-based technique, which provides real-time high-resolution tomographic images of both the lumen and the arterial wall. Figure 1 shows a clinical example of an IVUS image and the angiographic image of the same vessel segment.

In current clinical use of IVUS, the lumen and wall of a particular coronary segment are inspected visually by moving the ultrasound catheter through the vessel. The global positioning of the catheter is guided by X-ray angiography. In this way the section with the narrowest lumen can be selected and analyzed quantitatively by using a manual caliper in its simplest approach or by outlining the lumen and vessel wall borders in a more accurate approach. This will result in the calculation of the percent cross-sectional area narrowing at that particular cross-section, and the minimum and maximum diameters. The inter- and intra-observer variability for these measurements have been studied widely and is high. Furthermore, manual analysis of the images is tedious and time consuming. With the continuing improvement in IVUS imaging, it is now feasible to develop and clinically apply automated methods of three-dimensional quantitative analysis of the coronary artery wall and plaque.

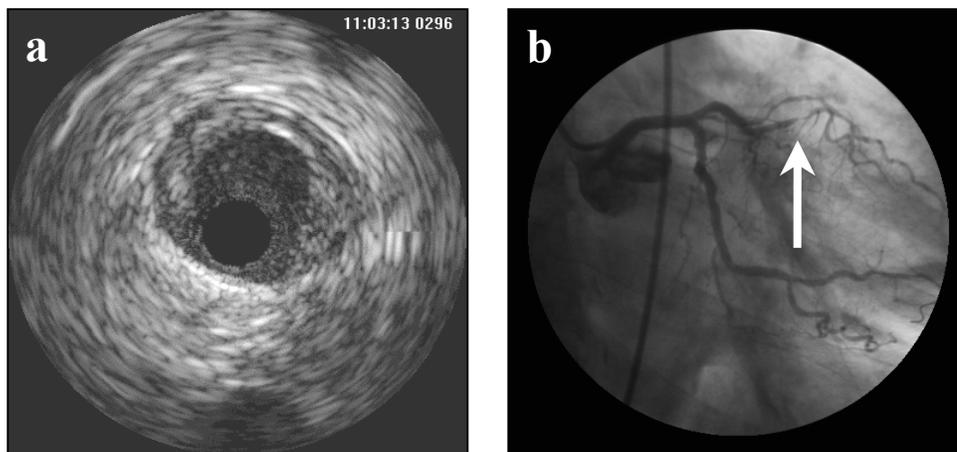


Figure 1: Comparison between an IVUS image (a) and an angiographic image (b) of the same vessel segment.

IVUS technical considerations and image appearance:

IntraVascular UltraSound (IVUS) imaging uses miniaturized transducers at the tip of the catheter to provide real-time cross-sectional images of the coronary and other arteries. In the past few years, the technology for IVUS has moved towards smaller catheters with improved handling in response to the clinical demand. Not only does a smaller catheter offer the opportunity to explore more of the coronary tree, it is also less likely to disturb potentially unstable plaque in a stenosis. Typically clinically catheters now have an outer diameter of 2.9 to 3.5 French (0.97 to 1.17 mm).

The image quality of the IVUS images can be described by two important factors; spatial resolution and contrast resolution. The spatial resolution can be divided into axial resolution (parallel to the beam and depends on the frequency) and the lateral resolution (perpendicular to the beam and depends on the transducer size and focusing system, see Figure 2). For a 20 to 40 MHz transducer, the typical resolution is 80 microns axially and 200 to 250 microns laterally. The lateral resolution closer to the catheter is better than further away. If the catheter is positioned concentrically in the vessel and there are no substantial asymmetries, the morphologic structures in the image are well visible due to the high axial resolution. But as soon as the catheter is positioned non-concentrically in the vessel and/or non-parallel to the vessel axis and/or there is a lot of plaque, the image quality decreases due to the poor lateral resolution. Dissections may disappear, the struts of a stent become vague and the plaque structure is poorly depicted. Also the original circular vessel shape may become an elliptical shape with a larger area.

The contrast resolution is the distribution of the gray scale of the reflected signal and is often referred to as dynamic range. An image of low dynamic range appears as black and white with a few in-between gray scale levels; images at high dynamic range are often softer, with preserved subtleties in the image presentation.

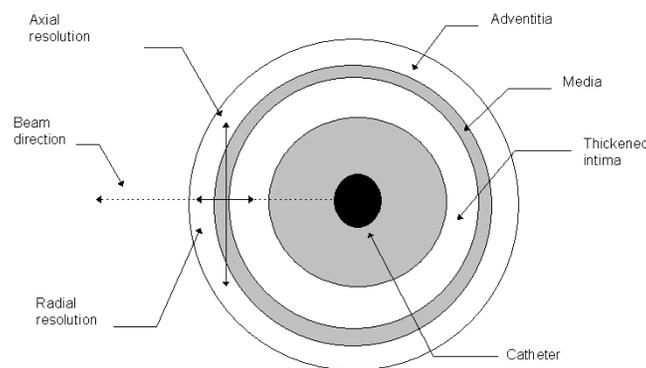


Figure 2: Axial and lateral resolution in an IVUS image.

The ultrasound appearance of normal human arteries in vitro and in-vivo has been studied extensively. The coronary vessel consists of several structures: lumen, intima, media, and adventitia as shown in figure 3. The *lumen* is identified by the region inside the interface between blood and intima. It is typically a dark, relative echo-free region adjacent to the catheter. The *intima* itself is a thin layer, which increases in thickness with age, from a single cell layer at

birth to 250 micron at the age of 40 years. Further adaptive physiological thickening of the intima occurs at the points where the wall tension is increased, such as at arterial bifurcations and on the outer parts of bends, and may be either eccentric or diffuse. With the current generation of ultrasound transducers the intimal thickening becomes visible as soon as it exceeds 178 micron. The *media* is identified by an echo lucent layer, enclosed by the internal and external elastic laminae. Due to the acoustic impedance mismatches, these layers can produce typical bright-dark-bright patterns. The thickness of the media ranges from 125 to 350 micron. The *adventitia* is composed of loose collagen and elastic tissue that merges with the surrounding peri-adventitial tissue and is 300-500 micron thick, and therefore cannot be identified separately.

In all ultrasound techniques, including IVUS, the measurements should be performed based on the leading edge of the boundaries, never on the trailing edge, since the location may be obscured by the scatter response of the tissue in front of the edge. For this reason the media cannot be measured separately and is included in the plaque measurements. In IVUS measurements only two layers are normally distinguished, the lumen border represented by the leading edge of the lumen-intima interface, and the vessel border represented by the leading edge of the media-adventitia interface.

Minimizing the catheter size results in limitations in the spatial resolution that can be achieved; this can only be compensated by increasing the frequency. However an increase in frequency results in a smaller depth of field (less penetration) and in increased influence from the backscatter of the blood, which makes it more difficult to distinguish between blood and tissue. On the other hand, increasing the frequency also increases the spatial resolution, which makes the identification of the small media-adventitia interface easier.

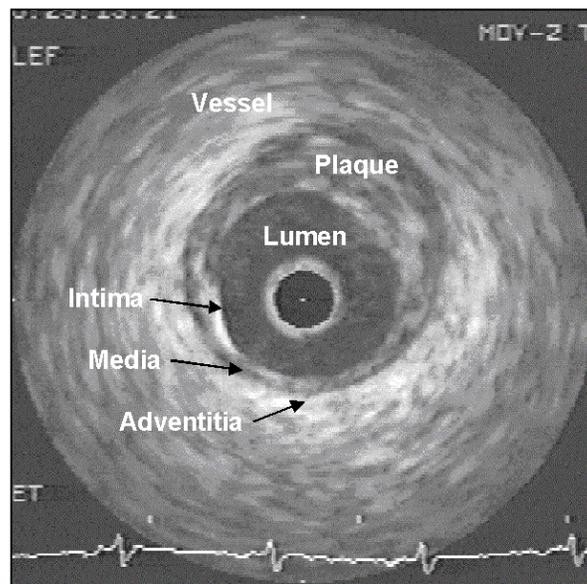


Figure 3: The different layers of a coronary segment in an IVUS image.

Two main technical configurations of IVUS systems are currently in use: the mechanical rotating transducer and the electronically switched multi-element array system.

1. Mechanical system

The mechanical devices rely on a single transducer, which is rotated at 1800 rpm (30 revolutions per second) to generate a 360-degree beam almost perpendicular to the catheter. The distal rotating transducer is housed in an echolucent sheath and is connected to a motor-drive positioned at the end of the catheter outside the patient. The catheter core is inside the sheath and does not have direct contact with the vessel wall, which avoids friction during the pullback of the imaging core. Therefore the pullback trajectory is stabilized by the sheath and it reduces the risk of a non-uniform speed in a continuous pullback. These have been designed for repeated pullbacks and are frequently used for three-dimensional reconstruction. Mechanical transducer catheters require flushing with saline to provide a fluid pathway for the ultrasound beam, because even small air bubbles can degrade image quality. The most common potential artifact with IVUS is the 'ring-down' halo, caused by multiple oscillations around the catheter surface. In mechanical rotating systems, this is reduced by offsetting the transducer by 15° from the surface of the catheter. The Non-Uniform Rotational Distortion (NURD) artifact is unique to mechanical catheter systems and is caused by mechanical binding of the drive cable that rotates the transducer. Especially tortuous vessels and acute bends in the artery may cause NURD artefacts. It should be clear that too much NURD artifact influences the accurate quantitative measurements of the parameters.

2. Electronic system (solid state)

The solid-state devices consist of integrated circuits and an array of transducer elements (64 is quite common today) in a cylindrical pattern at the distal tip. The array can be programmed so that one set of elements transmits echo pulses, while a second set receives the signals simultaneously. The signal acquisition can be manipulated to focus optimally at a broad range of depths, which improves the lateral resolution of the system. In the solid-state system, the transducers are surface mounted, and ring-down is partially reduced by digital subtraction of a reference mask. If this is incorrectly performed, digital subtraction has the potential to remove real information and introduce false targets. Ring-down artifacts are usually seen as bright halos around the catheter and may obscure the area immediately adjacent to the catheter. If the catheter is located against the wall, it is difficult to identify the lumen-intima interface at that point. Since the catheter core is not in a sheath, the trajectory is not stabilized which increases the risk of a non-uniform speed in a continuous pullback. This may be a disadvantage for three-dimensional reconstruction.

Two-dimensional analysis:

Quantification of IVUS images requires segmentation of the images into lumen, plaque, vessel regions, and if present also the stent should be identified. Automated quantification of IVUS images faces several challenges, caused by the low image resolution, the non-uniform luminance and contrast, high noise contents and the image artifacts like guide artifacts, drop-out regions and shadowed regions behind calcified plaque. Fully automated segmentation generally demands a trade-off between accuracy and stability, in which higher algorithm sensitivity increases the risk of segmentation failure.

Most reported successful approaches for (semi-) automated quantitative analysis are based on some kind of contour detection. After the definition of the region of interest, the IVUS images are resampled e.g. into a polar format, which is actually the original IVUS format. In these resampled images, the edge strength of the individual points is determined using Sobel-like filters and the edge direction is determined using Roberts filters. The size of the filters depends on the radial and axial resolution of the images. The boundary points in the resampled image are connected via an optimal path using dynamic programming approaches (for instance the Minimum Cost Algorithm (MCA) or graph searching). This technique ensures that always the most optimal solution is found for a contour, given the fact that the region of interest has been chosen correctly. Dynamic programming methods have been widely used in the field of medical image processing particularly for contour detection in ultrasound images because they are robust in terms of image noise. After the detection of the boundaries in the resampled image, the points on the boundary are mapped back as a contour into the original image space.

Three-dimensional reconstruction:

Three-dimensional reconstruction of IVUS permits a more advanced assessment of the vessel, lumen and plaque morphology. To assess the condition of an arterial segment, a so-called catheter pullback sequence is carried out by starting the acquisition of the images with the ultrasound probe positioned distally in the segment of interest and pulling it back in a controlled manner during continuous image acquisition to the proximal part of the segment of interest. The acquired images are displayed on the monitor in the same sequential order. Experienced IVUS users are able to conceptualize the complex three-dimensional (3D) structure of the morphology and pathology of the arterial segment from this stack of images by reviewing such sequence repeatedly. However, 3D reconstruction and the display by longitudinal images (cross-sections through the entire stack of IVUS images parallel to the IVUS catheter) avoids the difficult mental conceptualization required when using conventional IVUS. Also it facilitates both qualitative and quantitative analysis of the arterial segment and increases the diagnostic value of the IVUS imaging modality.

Another important advantage of 3D quantitative IVUS analysis with respect to 2D analysis is the improved matching capability of target sites for measurements at the same particular position in follow-up studies. Furthermore, 3D IVUS also permits appropriate sizing of stents (diameter and length), and may help to reduce the frequency of procedural complications of high-pressure stenting. The changes in cross-sectional lumen area within a stent in a pullback series are often smooth and gradual and may therefore be more difficult to recognize by visual assessment of 2D IVUS images. To perform 3D reconstruction, the IVUS images need to be acquired during a motorized pullback of the transducer, which can be performed at a uniform speed (typically 0.5 or 1.0 mm/sec) or in an ECG-triggered way. During acquisition side-branches or spots of calcified plaque should be included in the pullback as topographic landmarks to ensure a reliable comparison of the same arterial segment of interest.

Three-dimensional analysis:

It was mentioned before that most successful techniques are based on contour detection techniques using minimal cost algorithm (MCA) approaches in a region of interest defined manually, or by contours found in adjacent slices or in longitudinal images. The latter method is used in several commercially available software packages for the analysis of IVUS images.

The method starts with stacking up the individual slices in the computer memory. The source of the images can be analog from a VCR or IVUS acquisition device, or from a digital storage medium like a hard disc or CD-R. For the analog signal a video acquisition device is needed. It should be recognized that the image quality degrades if the images are stored in an analog format on a video-tape, also in case S-VHS format is used.

Next is the creation of longitudinal cross-sections, resulting in a straight reconstruction of the vessel segment. Since the longitudinal reconstruction may contain a lot of artifacts e.g. due to cardiac motion, the longitudinal images are used for guidance purposes of the contour detection and not for quantitative purposes. To enhance the quantitative analysis, the user is able to identify a segment of interest (e.g. a stent), and a representative proximal and distal segment (e.g. to study vascular remodeling). As a next step, the vessel and lumen contours are detected in the longitudinal images. In the longitudinal cross-sections, the vessel contours are detected *simultaneously* which means that they have knowledge about each other's position. For example, the following situation may occur. At one side of the vessel in the longitudinal image, a clear vessel transition is present which would force the vessel contour detection to the left. On the other side of the vessel, multiple potentially vague vessel transitions in different directions are present. The simultaneous technique will now select the combination of the strong transition at one side, and a transition on the other side that matches best with the morphologic continuity of the vessel and the shape and size of the vessel. This technique is especially useful for regions behind calcified plaque and in side branches where no or sparse image information is available to support the contour detection. If a stent is present, the vessel contour will also be forced outside the already detected stent.

Despite all the additional models and knowledge the detection results still may be influenced by artifacts and speckle noise. Therefore, the results from the contour detection are not always entirely correct and some manual interaction may be needed. An important difference between the available software packages is the handling and flexibility of the user-interaction. In the ideal situation, the user-interaction is used as efficient as possible, reducing the number of corrections and thus required time for the analysis. To overcome image artifacts, additional knowledge is used e.g. removing the ringdown artifact, avoiding guidewire artifacts and using models to overcome the shadowed region behind calcified plaque. As stated before the longitudinal contours are used for guiding purposes only and not for quantitative measurements.

Next the contours are transferred to the transversal slices where they result in support points for the region of interest in the transversal contour detection. The transversal contour detection for the vessel, lumen and stent is based on the same principles as for the longitudinal detection. Based on the contours for each individual slice the vessel, stent and lumen parameters can be determined, e.g. area, average diameter, symmetry, and also the derived parameters e.g. plaque area. The recently published guidelines present an extensive overview of parameters, which should be measured with IVUS.

After the detection of all the contours in the segment of interest, volumetric parameters can be determined using the slice thickness. In general, Simpson's rule is used for volumetric

measurements. Also other length-based measurements can be performed like measurements of stent length. The slice thickness (mm) can easily be calculated by from the pull back speed (mm/sec) and the number of frames per second. Figure 4 shows an overview of an entire analysis with the QCU-CMS software.

Educational Objectives: The attendee will be able to

- 1, Understand the basics of IntraVascular UltraSound.
2. See the difference between the major acquisition systems.
3. Understand the quantification of IVUS images.
3. Learn more about three-dimensional IVUS quantification and the limitations.

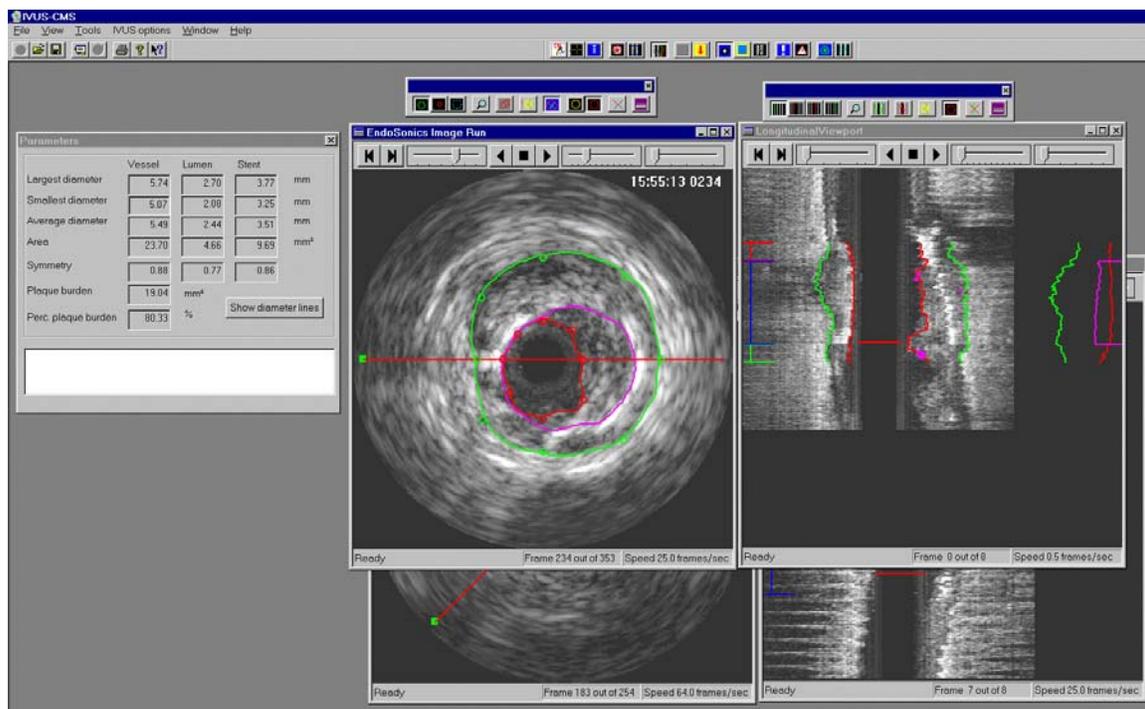


Figure 4: Overview of an IVUS analysis in QCU-CMS when analyzing the distal, proximal and target segment in two pullback runs. The output box on the left displays the parameters for the single frames, however all the parameters can be exported to a separate module for a 3D analysis.