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New techniques in medicine

Intracoronary ultrasound

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Summary
Although contrast angiography is important in the diagnosis and treatment of atherosclerotic disease, it does have limitations. Intracoronary ultrasound more accurately assesses the amount of atherosclerosis and has given us new insights into the pathophysiology of coronary plaque accumulation and remodelling. It also allows the monitoring of therapeutic intervention. Intracoronary ultrasound is a new gold standard. It does not obviate the need for angiography but provides complementary information that enables us to perform optimal interventional procedures.

Keywords: intracoronary ultrasound; ultrasound; coronary angioplasty; stents; atherectomy

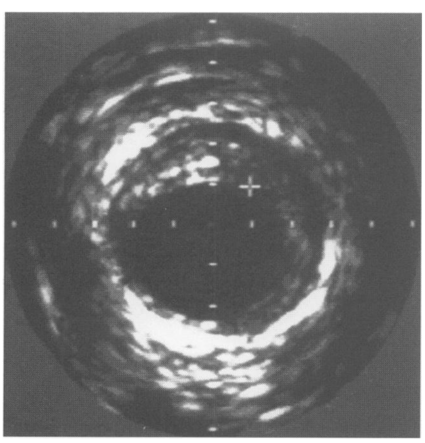

Figure 1 Angiographically normal left anterior descending artery that has a large area of plaque demonstrated by ICUS

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Coronary angiography has been the gold standard for the diagnosis and monitoring of the treatment of atherosclerotic disease for many years.[1] It does have some limitations, however, which has lead to the development of other imaging techniques such as intracoronary ultrasound (ICUS) and coronary angioscopy. Intracardiac ultrasound for imaging the heart valves and chambers was first described in 1971,[2] although it was not until 1989 that the first *in vivo* human coronary images were obtained.[3] Following the validation of the images obtained by further *in vitro* and pathological studies,[4–7] the role of ICUS in the evaluation of coronary atherosclerotic disease and subsequent interventions has become more defined.

Limitations of angiography

For many years it has been suggested that atherosclerosis is more extensive than can be seen angiographically.[8] As plaque accumulates in coronary vessels, the wall expands by 30–40% to accommodate this extra plaque burden prior to any luminal narrowing, thus keeping the artery patent for as long as possible.[9,10] Therefore, as angiography is just a lumenogram, there is frequently atherosclerotic disease in segments that appear to be of normal diameter on the angiographic images but show abnormalities on ICUS (figure 1).[11] This compounds the errors in estimation of the severity of a stenosis, as stenotic segments are being compared to angiographically normal areas that are, in fact, diseased. Problems also occur as the coronary circulation is a three-dimensional (3D) branching structure, often with overlapping vessels that are inadequately demonstrated by two-dimensional (2D) images, especially if the lesions are complex or eccentric. Repeated injections of contrast and prolonged fluoroscopy are not without risk.

Benefits of ICUS

Although angiography provides an overview of the circulation, unlike ICUS, it is unable to visualise the vessel wall and assess the amount, nature and position of plaque. ICUS is better at demonstrating the presence of calcium, which is a risk factor for increased coronary events,[12] and a marker for the atherosclerotic plaque burden.[13] Calcification can be seen in 50–70% of lesions on ICUS, compared to 20–30% on angiography,[14] but the total amount of calcium can still be underestimated by ICUS examination as deep calcium may be hidden by the shadow of any superficial calcium (figure 2). The brightness or depth of the shadow from the calcified areas is not related to the calcium bulk, but is determined by the settings of the machine.

Although angioscopy also produces real-time 3D images of the lumen, it is expensive, time-consuming and requires large boluses of fluid to be injected in the coronary tree to ensure a bloodless field so the vessel wall can be visualised.

Types of ICUS catheters

There are two main types of ICUS catheter. Both types can accommodate a 0.014 inch angioplasty wire and come in a range of operating frequencies from 20–40 MHz. The axial resolution of catheters (the ability to distinguish two neighbouring objects in line with the beam) is 150–200 μm and radial resolution (the ability to distinguish two objects that are side by side) is 200–400 μm.

- *Phased array:* the catheter has 64 transducer elements that are arranged in a cylinder near its distal end. Each of these elements is capable of transmitting and receiving an ultrasound signal independently. There is sequential firing of the elements and the beam is rotated to achieve the image. The 'back scatter' signals received by the individual elements are sent to an image-processing computer where a 2D cross-sectional picture is reconstructed

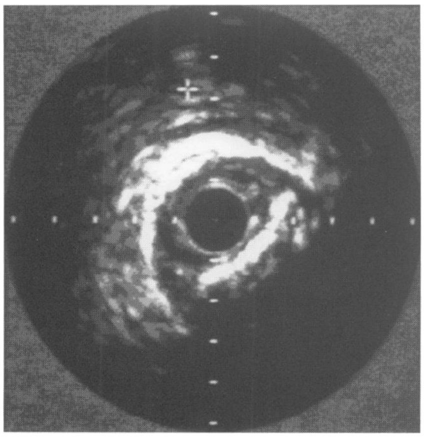

Figure 2 Superficial area of calcium prevents the evaluation of the deeper layers

- *Mechanical:* the images are obtained either by rotating a transducer or by a revolving reflector around a stationary transducer. The catheter has a fluid-filled tip to produce an acoustic pathway from the transducer to its exterior and is connected to an external motor unit to produce the revolutions.

The phased array catheter is more flexible than the mechanical one, although until recently its lateral resolution has been more limited. As the mechanical catheter is connected to an external drive, there can be uneven rotation of the transducer or reflector producing non-uniform rotational distortion. Other difficulties with the mechanical system are that the guidewire is offset and can appear as a ray-like artefact and any bubbles in the fluid-filled tip produce a poor quality image.

Method

During a coronary interventional procedure, the ICUS catheter is positioned in the artery under fluoroscopic guidance, usually via a femoral puncture site and over a guidewire. At present, pre-intervention ICUS is dependent on being able to cross the lesion which may lead to temporary vessel occlusion with consequent pain or ischaemic complications. Images are obtained as the catheter is smoothly withdrawn through the stenosis. Whilst these images are being recorded it is helpful to have a superimposed commentary on the tape. This is useful when reviewing the procedure.

Safety of ICUS

The exact incidence of complications due to ICUS is difficult to assess as it is usually performed in conjunction with other interventional procedures. In the European registry[15] of 718 patients, ICUS had an acute complication rate of 1.1% with no permanent clinical consequences. This compared favourably with the US registry[16] where the overall complications rate with certain or possible relation to ICUS was 3.9% (spasm 2.9%, dissection, acute occlusion or thrombus 0.7%, nonfatal myocardial infarction or emergency coronary artery by-pass grafting 0.3%).

Vessel definition on ICUS

In muscular arteries such as the coronary circulation three layers can be seen when using a 20–30 MHz transducer[17]:
- the bright inner layer of the internal elastic lamina and intima
- the echolucent middle layer of media (echolucent as low collagen and elastin content)
- the outermost echogenic layer of the external elastic lamina and adventitia.

In normal arteries it is unusual to see the intima except for occasional tiny portions as it needs to be ≥175 μm thick to get a clear interface.[18 19] Hence, if it is seen, it is abnormally thick. Intimal thickening has been shown to increase with age.[11]

Types of plaque

With the development of improved technology it is becoming easier to determine the composition of plaque, which, in turn, has implications with respect to the stability of the lesion (box 1).

Rasheed *et al*[20] found that patients with chronic stable angina and crescendo angina (accelerating pattern or prolonged anginal episodes) had a significantly higher frequency of fibrous and calcified plaque than patients with severe rest pain or postinfarct angina, who tended to have soft lesions. This correlates with Davis' theory of the progression of atherosclerosis.[21] He suggested that lesions progress either via slow development to fibrous or calcified lesions, or plaque rupture with thrombus formation. Unfortunately, thrombus is still hard to diagnose accurately on ICUS examination.

Types of plaque

- soft plaque consists of material of which more than 80% is less echodense than the adventitia (figure 3)
- fibrous plaque consists of material of which more than 80% has tissue brightness greater than that of the adventitia without acoustic shadowing
- calcified plaque has an echodensity greater than that of the adventitia with acoustic shadowing
- mixed plaque is composed of soft, fibrous and calcified plaque in varying proportions

Box 1

Uses of ICUS

ICUS examination provides both quantitative and qualitative information. It can aid in the sizing of equipment. Changes in treatment have been reported in up to 40% of patients following ICUS.[22] Of particular benefit is the ability of ICUS to reveal occult disease, especially in the left main stem which may then result in patients being referred for surgery.[23 24] It can also delineate branches that appear to be overlapping despite multiple angiographic images and bifurcation lesions,

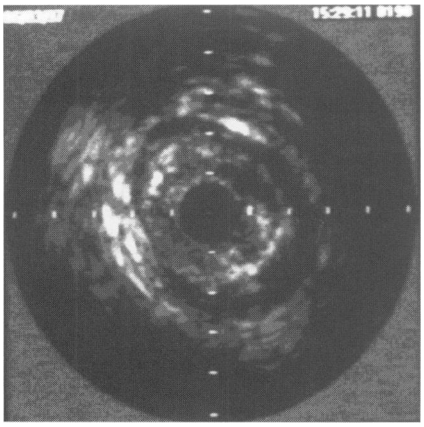

Figure 3 Soft plaque filling the vessel

and allows very proximal lesions to be imaged that may have been crossed by the angiographic catheter.

ICUS has provided the opportunity to assess the results of interventions *in vivo*. It can illustrate the cracking and stretching of vessels following angioplasty and any resulting dissections. This has led to the two main classifications of angioplasty results,[25 26] and studies of risk factors for re-stenosis.[27-29] There is a further role for ICUS in monitoring the progression of disease in cardiac transplant recipients.[30]

Some patients with syndrome X have atherosclerosis when viewed by ICUS.[31] Others that have normal arteries even on ICUS imaging may have an abnormal coronary flow reserve.[32] This has been suggested to correlate with microvascular abnormalities.[33] Hence, ICUS in syndrome X patients may separate different categories of patients and have implications for their management.

ICUS and predictors of re-stenosis following intervention

Vascular injury leads to the immediate release of thrombogenic, vasoactive and mitogenic factors. This results in platelet aggregation, thrombus formation and inflammatory changes in both macrophages and smooth muscle cells and is a self-perpetuating cascade.

Deep tears involving the media are associated with higher rates of intimal proliferation following percutaneous transluminal coronary angioplasty (PTCA), which in turn increases the risk of re-stenosis.[27] Mintz *et al* found that residual cross-sectional narrowing was the most important predictor of re-stenosis.[28] Other factors, such as small reference vessel diameter and decreased acute expansion during the procedure, are also linked to re-stenosis.

ICUS and atherectomy

The use of PTCA is hampered by its re-stenosis rates of 25–30%.[34] Directional coronary atherectomy (DCA) was developed to improve luminal diameter by debulking plaque, especially in eccentric lesions. ICUS has been used to position the atherectomy catheter[35] and has demonstrated that the main method of vessel enlargement in DCA is tissue extraction with a small amount of vessel stretch.[36] However, two large early trials comparing DCA with PTCA did not demonstrate any significant benefits from DCA.[37 38] There was an increased risk of myocardial infarction and death in the DCA group that persisted at one year.[39]

It has been well documented that, post-DCA, there can still be large amounts of plaque on ICUS which is not visible on angiography.[40] Therefore, further trials have been initiated using ICUS to guide the DCA so that optimal results are obtained. The BOAT (Balloon versus Optimal Atherectomy Trial) study demonstrated that more aggressive plaque removal led to an improved luminal diameter post-procedure and decreased re-stenosis rates at 6 months.[41]

ICUS is useful in assessing the proximal vessel to ensure that the atherectomy catheter can reach the lesion; it will also identify any superficial calcium which may influence the success of the atherectomy.[42]

Rotational atherectomy is a newer technique involving a diamond-coated burr that ICUS has demonstrated is effective by selectively abrading plaque to increase luminal area without increasing the vessel size nor harming elastic tissue.[43] Rotational atherectomy is particularly useful in small vessels with calcified lesions,[43] so ICUS can be utilised to identify suitable patients.

ICUS and stenting

ICUS guidance of stent implantation lead to the development of less aggressive anticoagulation regimens[44] using aspirin and ticlopidine rather than warfarin. This has decreased stent complication rates and reduced times spent in hospital. Incomplete expansion increases the likelihood of subacute stent closure because of flow disturbance and the larger amount of metal exposed to the blood, facilitating platelet aggregation and thrombus formation. Recognition of the problems of inadequate stent deployment, has led to the use of high pressure balloon inflation to decrease the rate of subacute thrombosis (figure 4).[45] ICUS is useful to measure the post-stenting luminal diameter, which may be overestimated by angiography as the contrast medium may fill the gap between the stent and the vessel border.[46 47]

ICUS has also demonstrated that the main mechanism of in-stent re-stenosis is uniformly distributed neointimal proliferation[48] with no extra tissue growth at the stent edges.[49]

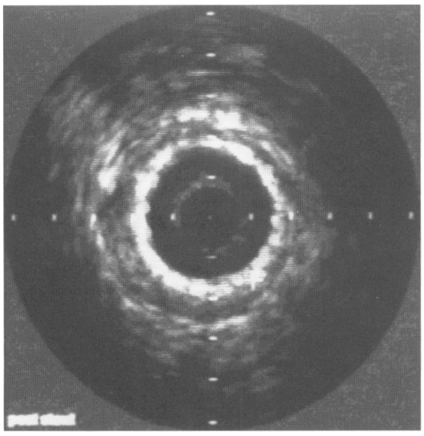

Figure 4 A stent that is well opposed to the vessel wall

Summary points

- atherosclerosis is often more extensive than can be seen angiographically
- ICUS allows visualisation of the vessel wall and the amount, nature and position of plaque
- ICUS is useful in selecting the appropriate equipment for an interventional procedure and assessing its results

Box 2

Recent and future developments

3D RECONSTRUCTION

The development of 3D reconstruction has enhanced the use of ICUS. Initially 2D images are taken with reference to their position in relation to other vessels, often by adjunctive angiography. The images are then analysed by a computer and the reconstruction is performed. This is usually done using the pullback technique, which involves the movement of the ICUS probe back over the lesion at a constant rate to ensure that equally spaced images are obtained. These are then assimilated into a longitudinal reconstruction, which allows the estimation of disease severity and extent. As the catheter follows a complex curve through the artery and there is movement of the catheter on a beat-to-beat basis it can be difficult to obtain exactly spaced images.

Recently, Evans *et al* reported on their technique of spatially correct 3D reconstruction, which involves ICUS recording with biplane digital fluoroscopy triggered by the patient's electrocardiogram whilst the patient holds his/her breath. The fluoroscopy enables accurate positioning of the ICUS catheter. If respiration is suspended and the image borders can be detected on ICUS, then the 3D reconstruction demonstrates all the curves of the vessel as well as the angiogram.[50]

FORWARD ULTRASOUND

As one of the problems with conventional ultrasound is that the lesion has to be crossed prior to imaging, which may compromise flow in the artery, ICUS catheters that can image the lesion without having to cross it are under development.[51] At present these are quite large but further miniaturisation will permit their use in the coronary tree.

COMBINED ULTRASOUND AND INTERVENTIONAL DEVICES

The development of devices that can perform dual tasks will make the interventional procedure cheaper and help to decrease the number of manipulations involved and the time taken in the catheter laboratory. At present, ICUS probes and angioplasty balloons on the same catheters are in common usage; DCA devices with ICUS facilities are also available.

IMPROVED IMAGE RESOLUTION

ICUS image resolution high enough to reliably gauge the thickness of the fibrous cap and the amount of lipid present in a plaque would lead to the ability to assess the risk of plaque rupture and consequently aid in the diagnosis and management of unstable coronary syndromes. The ability to distinguish thrombus from soft plaque would also be desirable.

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Medical Anniversary

Sir ALMROTH WRIGHT, 10 August 1861

(Sir) Almroth Wright (1861–1947) was born in Middleton Tyas, Yorkshire, UK. His father was a rector and his mother was Swedish, with the maiden name Almroth. He was educated at Belfast and Trinity College, Dublin, where he graduated in 1883. He became Professor of Pathology to the Royal Army Medical College, Netley, in 1892, where he developed prophylactic immunisation against typhoid fever. In 1902, he became pathologist to St Mary's Hospital, London. He is commemorated frivolously in George Bernard Shaw's *The doctor's dilemma*, and more importantly by the Wright–Fleming Institute at St Mary's Hospital. He died on 30 April 1947 in Farnham Common, Bucks. — *D G James*