Intravascular Ultrasound Imaging of Pulmonary Arteries*
Methodology, Clinical Applications, and Future Potential

Thomas R. Porter, MD; Pramod K. Mohanty, MD; Natesa G. Pandian, MD

CT=computed tomography; IVUS=intravascular ultrasound; MR=magnetic resonance

Key words: cardiac catheterization; heart failure; intravascular ultrasound imaging; IVUS; pulmonary arteries; pulmonary embolism; pulmonary hypertension

Intravascular ultrasound imaging of the coronary artery has become an accepted standard in the evaluation of atherosclerotic lesions.1-8 It provides more accurate measurements of stenosis areas as well as a qualitative determination of the histologic components of atherosclerotic plaque.9-11 Recently, intravascular ultrasound of the pulmonary artery has been validated as a reliable and rapid method of quantifying proximal and distal pulmonary artery lumen area, pulsatility, and describing vessel wall characteristics.12 These observations have led to the application of intravascular ultrasound (IVUS) in diagnosing acute and chronic pulmonary thromboembolic disease13,14 and evaluating pulmonary artery vessel wall abnormalities in pulmonary artery stenosis,15 primary pulmonary hypertension,16 and chronic heart failure17,18 These investigations delineate the potential value of pulmonary vascular ultrasound in determining anatomic and physiologic responses that have previously not been possible in humans in vivo. The purpose of this review is to outline the current conventional methodology of studying the pulmonary vasculature and then to review the advantages that pulmonary vascular ultrasound has been shown to have in evaluating arterial morphology as well as the pathophysiology of common pulmonary vascular diseases. Finally, future applications of pulmonary vascular ultrasound will be briefly discussed.

Conventional Methods of Studying Pulmonary Artery Anatomy and Physiology

Current methods of evaluating pulmonary artery disease in vivo include pulmonary angiography, magnetic resonance (MR) imaging ultrafast computed tomography, transesophageal echocardiography, and intravascular ultrasound. Each technique has certain advantages and disadvantages.

Pulmonary angiography is an established technique for diagnosing pulmonary emboli and other vascular abnormalities of the pulmonary arteries,19 such as pulmonary artery stenosis, aneurysms, and neoplasms. In chronic pulmonary thromboembolic disease, however, organization of the thrombus may result in no recognizable angiographic abnormalities or nonspecific findings.20 In addition, pulmonary angiography only outlines the vessel lumen, and it cannot assess abnormalities in the vessel wall or flow abnormalities. This technique is also invasive and has a complication rate, especially in pulmonary hypertension, as high as 4%.21 Most of these complications appear to be related to the injection of contrast medium in patients with pulmonary hypertension.

Computed tomography (CT) and MR imaging provide anatomic detail in pulmonary artery disease that cannot be obtained from pulmonary angiography. In pulmonary atresia, MR imaging has shown the presence or absence of pulmonary arteries in regions that are not accessible to catheters.22 In a small study of 21 patients with pulmonary embolism, high resolution CT scanning was shown to be better than angiography in assessing proximal thrombi, examining pulmonary arteries distal to thrombi, and detecting pulmonary infarction.23 Cine MR imaging has also been clinically applied in infants to define accurately the placement of pulmonary artery banding.24 Cardiac and respiratory motion, as well as pulmonary artery pulsatility, limit the application of these imaging techniques in assessing intraluminal abnormalities. Recently, MR angiography has been able to compensate for cardiac motion by using electrocardiographic gating and phase velocity mapping techniques which also may be able to quantify pulmonary blood flow.25 Fast gradient echo-images may be able to semi-quantify the severity of pulmonary hypertension in a wide variety of pulmonary vascular diseases.26

Transesophageal echocardiography has been used to image proximal pulmonary arteries in central pulmonary artery thromboemboli. Wittlich et al.27 showed that transesophageal echocardiography is more than 95% sensitive and more than 85% specific for detecting central pulmonary thromboemboli.

*From the Departments of Medicine, New England Medical Center, Tufts University School of Medicine (Dr. Pandian), Boston; and University of Nebraska School of Medicine (Dr. Porter), Omaha, Neb; and McGuire VAMC and Medical College of Virginia (Dr. Mohanty), Richmond, Va.

Manuscript received March 28, 1994; revision accepted May 26, 1994.

(CHEST 1994; 106:1551-57)
With the advent of multiplane transesophageal echocardiography, more distal portions of the right and left pulmonary arteries can now be visualized with good resolution.28

Direct animal29 and human30 pulmonary artery imaging has also been performed with a small caliber fiberoptic angioscope. The angioscope is typically advanced with the aid of a balloon tip on the scope, or the scope is passed through the central lumen of a balloon-tipped guide catheter. Intraluminal visualization requires balloon inflation and interruption of blood flow. This technique has been used to examine 1.0- to 4.5-mm diameter pulmonary arteries in humans with chronic lung disease.30 It has also accurately detected acute pulmonary emboli31 in dogs. It has been used clinically in patients suspected of having chronic pulmonary emboli where the angiogram is not conclusive.32 In these cases, angioscopy has been useful in excluding other pulmonary vascular disorders, which may mimic thromboemboli, eg, plaque, and has also been used in determining operability.

**IVUS Imaging of the Pulmonary Artery**

IVUS of the pulmonary artery is a new catheter-based imaging modality with high resolution and real-time imaging capabilities. Its advantages over other imaging techniques include significantly better resolution of the pulmonary vessel lumen and wall, detailed description of both proximal and distal pulmonary arterial anatomy, real-time imaging of the pulmonary artery throughout the cardiac cycle, and the ability to rapidly assess the effect of mechanical and pharmacologic interventions. Unlike angioscopy, it is capable of imaging through blood and can describe disease within the vessel wall.

**Pulmonary IVUS Instrumentation**

Currently available intravascular ultrasound imaging devices consist of a mechanical or phased array catheter (3.5-9F) capable of imaging at frequencies ranging from 10 to 40 MHz. Axial resolution with these catheters, therefore, ranges from 150 to 300 μm depending on the transmitted frequency and lateral resolution within the focal point of the transducer is about 150 μm. The catheters can be advanced into the pulmonary artery fluoroscopically using an 0.014-inch guide wire. In some cases, a long sheath that is normally used for transeptal catheterization (Mullins sheath) or endomyocardial biopsy may be necessary to assist in guiding the catheter to a select region in the pulmonary vasculature.

Imaging consoles display ultrasound images at between 15 to 30 frames/s. This is an important feature because it allows the clinician to characterize changes in pulmonary vascular diameter and area throughout the cardiac cycle. This is especially important in the determination of pulmonary artery stiffness.

**Validation of Pulmonary IVUS Imaging**

Using a disposable 6F 20 MHz ultrasound probe in isolated pulmonary artery segments of dogs, it has been shown that IVUS-derived measurements of pulmonary artery area, diameter, and wall thickness correlated very well with anatomic measurements in vitro (Fig 1).12 In this preliminary study, pulmonary IVUS images in humans were also obtained and provided detailed examinations of the changes in pulmonary artery vessel shape and pulsatility from the proximal to the distal pulmonary artery.12 An example of a normal human pulmonary artery using 20 MHz IVUS at end-diastole and end-systole is

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21703/ on 06/26/2017)
shown in Figure 2.

**Clinical Application of Pulmonary Artery IVUS Imaging**

The unique features of pulmonary IVUS described above have been used for diagnostic, interventional, and pathophysiologic assessments in pulmonary vascular diseases (Table 1).

**Diagnostic Applications**

**Acute Pulmonary Thromboembolic Disease:** Recent experimental and clinical studies have delineated the ability of pulmonary IVUS to diagnose acute pulmonary embolus. Kumar et al.\(^\text{[33]}\) injected 2-day-old radiopaque thrombi into the jugular vein of dogs and showed that IVUS was able to identify the location of the pulmonary embolus. In this study, pulmonary emboli were identifiable as bright granular echoes and easily distinguishable from the normal vessel wall. Mechanical disruption of the embolus was also performed in this study, and subsequent destruction of thrombus was verified by IVUS. Tapsin et al.\(^\text{[34]}\) also showed in dogs that pulmonary IVUS was a safe, highly sensitive technique for diagnosing experimental pulmonary emboli.

Hermiller et al.\(^\text{[13]}\) showed in humans that a large acute pulmonary embolus appears as soft echoes within the lumen of an otherwise normal-appearing artery. These investigators also used IVUS (4.8F 20 MHz) to show dissolution of the embolus after intrapulmonary administration of thrombolytic therapy. Gorge et al.\(^\text{[35]}\) also showed that pulmonary intravascular ultrasound could rapidly make the diagnosis of small and large pulmonary emboli, as well as visualize the success of thrombolysis. These preliminary clinical studies suggest that IVUS of the pulmonary artery may be a useful method of rapidly diagnosing pulmonary emboli in critically ill patients who are too unstable for pulmonary angiography. The technique can be rapidly performed in the ICU or emergency department using an internal jugular venous approach with time periods reported to be as short as 10 min.\(^\text{[56]}\)

**Chronic Pulmonary Thromboembolic Disease:** Recent clinical studies have also showed the ability of pulmonary IVUS to diagnose *chronic* pulmonary thromboemboli. Ricou et al.\(^\text{[14]}\) used an 8F 20 MHz IVUS catheter to detect abnormalities in the left and right pulmonary arteries of patients with chronic thromboemboli.\(^\text{[14]}\) These abnormalities were described as either marked thickening of the vessel wall or a crescentic layer of thickening. Using these

---

**Table 1—Clinical Applications of Pulmonary IVUS**

<table>
<thead>
<tr>
<th>Diagnostic Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Pulmonary Embolism</td>
</tr>
<tr>
<td>Chronic Pulmonary Embolism</td>
</tr>
<tr>
<td>Vessel Wall Abnormalities</td>
</tr>
<tr>
<td>Guidance During Therapy</td>
</tr>
<tr>
<td>Assessment of pulmonary artery angioplasty results</td>
</tr>
<tr>
<td>Assessment of response to pharmacologic therapy</td>
</tr>
<tr>
<td>Assessment of Pathophysiology</td>
</tr>
<tr>
<td>Primary and secondary pulmonary hypertension</td>
</tr>
<tr>
<td>Pulmonary artery endothelial function</td>
</tr>
</tbody>
</table>

---

**FIGURE 2.** IVUS image of a pulmonary artery from a normal patient. The end-diastolic (EDA) and end-systolic (ESA) areas have been planimetered. Note the thin intimal surface and vessel pulsatility. Reproduced with permission, from reference 17.
criteria, chronic organized thrombi or tumor were identified at surgery in all of the abnormal segments of the pulmonary artery seen by IVUS. About 90% of the segments that were considered normal by IVUS were free of chronic thromboemboli at surgery.

**Diagnosis of Other Vessel Wall Abnormalities:**
IVUS of the pulmonary artery can also be used to evaluate vessel wall abnormalities in primary and secondary forms of pulmonary hypertension. Although *in vivo* measurements of pulmonary artery wall thickness are not possible since the outer adventitial layer of the vessel is embedded in air-filled lung parenchyma, it is possible to assess qualitatively abnormalities in the pulmonary vascular walls that are not detected by other imaging modalities. In primary pulmonary hypertension, IVUS has shown thickened walls with a granular appearance and reduced lumen area. An intravascular ultrasound of the proximal pulmonary artery of a patient with primary pulmonary hypertension is shown in Figure 3. This was subsequently shown to be severe intimal hyperplasia at autopsy (Fig 3). Responses to vasodilators and prognosis in primary pulmonary hypertension are related to the amount of intimal hyperplasia vs medial hypertrophy. It remains to be determined, however, whether IVUS can distinguish between these two pathologic responses in primary pulmonary hypertension.

Secondary pulmonary hypertension may occur in response to pulmonary parenchymal disease, left-sided heart failure, or mitral valve disease. Intravascular ultrasound has been used to detect abnormalities in vessel wall thickness in pulmonary hypertension secondary to left-sided heart failure, and to determine how this correlates with wall stiffness. Pulmonary IVUS (6F 20 MHz) of vessels from 3 to 7 mm in diameter in patients with chronic congestive heart failure and secondary pulmonary hypertension revealed an increased incidence of plaque in the vessel wall when compared with an age-matched control group, as well as decreased pulsatility and increased vessel stiffness. Although patients with chronic heart failure but normal pulmonary artery pressure had an increased frequency of pulmonary artery plaque by IVUS, they continued to exhibit normal pulmonary artery pulsatility and stiffness. These studies show the usefulness of IVUS in assessing the pulmonary artery dynamics that accompany chronic heart failure. It is unknown whether these IVUS observations can be used to determine reversibility of pulmonary vascular disease with either medical therapy or heart transplantation.

Pulmonary IVUS has also been used to detect pulmonary artery invasion by central bronchogenic carcinoma. In this study, vascular invasion by tumor was shown by IVUS, which was surgically confirmed in two cases. Others have shown the IVUS appearance of a localized fibrous histiocytoma within the pulmonary artery. This exciting new application is an example of the ability of pulmonary IVUS to assess the presence and extent of vascular wall invasion in the evaluation of lung tumors.

![Figure 3](http://journal.publications.chestnet.org/pdfsaccess.ashx?url=/data/journals/chest/21703/)

**Figure 3.** IVUS image of a pulmonary artery *in vivo* in a patient with primary pulmonary hypertension (*left*) and cross section of about the same region obtained at subsequent necropsy (*right*). The patient died during a single-lung transplant surgery within 3 weeks of the IVUS study. Reproduced with permission, from reference 41.
Pulmonary IVUS Guidance in Therapy

Guidance in Pulmonary Artery Angioplasty: Pulmonary artery IVUS has also been used to evaluate surgical, pharmacologic, and other mechanical interventions that involve the pulmonary vasculature. Rein et al.15 used a 5F 30 MHz IVUS catheter in three children with Williams syndrome, a congenital disorder, to evaluate the severity and extent of lumen narrowing in the pulmonary artery before and after balloon angioplasty.15 These pulmonary arteries exhibited regions of severe wall thickening. The focal pulmonary artery stenoses were balloon dilated, resulting in increases in lumen area. The IVUS findings were associated with an improvement in pulmonary artery hemodynamics.

Assessment of Response to Drug Therapy: Pulmonary artery IVUS has been used to detect different pulmonary vascular area responses to dobutamine and nitroglycerin in patients with chronic heart failure undergoing evaluation for orthotopic heart transplantation.18,40 In one case study, despite similar calculated measurements of pulmonary vascular resistance changes to these drugs, pulmonary artery IVUS demonstrated vasoconstriction to dobutamine but vasodilation to nitroglycerin.40 These responses provided additional information on the pulmonary vascular reactivity in patients with heart failure. A subsequent larger study showed a wide variety of pulmonary artery vascular responses to nitroglycerin in patients with chronic heart failure and pulmonary hypertension18 that were not predicted by changes in mean pulmonary artery pressure or calculated pulmonary vascular resistance. Pulmonary IVUS has been useful in showing drug-induced resolution of thromboemboli in patients being treated with thrombolytics for pulmonary emboli.13,35 Resolution of thrombus by IVUS has correlated with improvement in pulmonary artery hemodynamics. The time required for resolution of thrombus with local urokinase, however, requires more than 60 min. Since a prolonged IVUS examination involves minimal additional patient discomfort, it is preferred to other imaging modalities, which could be used to monitor thrombus dissolution such as transesophageal echocardiography.

Pulmonary IVUS to Assess Pathophysiology

Primary and Secondary Pulmonary Hypertension: In addition to delineating the morphologic abnormalities that accompany primary and secondary pulmonary hypertension, pulmonary IVUS has detected that these patients also have increases in pulmonary vascular stiffness.18 This is evident on IVUS examination by the marked decrease in vessel pulsatility.17 Pulmonary vascular stiffness responses are assessed using both pulmonary artery pulse pressure and intravascular ultrasound-derived pulmonary artery area changes in the cardiac cycle.18 The pulmonary artery stiffness responses to nitroglycerin in patients with secondary pulmonary hypertension are variable and not predicted by the change in mean pulmonary artery pressure or pulmonary vascular resistance. These data suggest that IVUS-derived measurements of pulmonary artery stiffness in pulmonary hypertension provide important information regarding functional abnormalities in the vessel wall that are not obtained with conventional measurements.

Pulmonary Artery Endothelial Function: Pulmonary artery IVUS has also been used to determine endothelium-dependent responses in patients with chronic heart failure.40,42 Using IVUS (6F 20 MHz) to observe continuously pulmonary vascular area responses to the endothelium-dependent vasodilator acetylcholine before and after inhibition of endothelium-dependent vasodilation with methylene blue, it has been shown that the endothelial responses of pulmonary arteries in patients with chronic heart failure who maintain normal pulmonary artery pressures inhibit vasoconstriction. These inhibitory effects of the endothelium were defective when pulmonary hypertension developed, suggesting a major role of the pulmonary artery endothelium in attenuating vasoconstriction and thus preventing the development of pulmonary hypertension in treated chronic heart failure.40 Therefore, pulmonary IVUS can rapidly show in vivo the functional status of the endothelium in pulmonary diseases.

Safety of Pulmonary IVUS

Currently, there have been no reported major complications associated with pulmonary IVUS imaging. It has been safely performed in patients with acute and chronic pulmonary emboli as well as severe primary and secondary pulmonary hypertension. The total number of cases, however, has been relatively small. Therefore, although the procedure appears to be safe with minimal patient discomfort, the actual incidence of potential complications is still unknown.

Limitations of Pulmonary IVUS

Despite the advantages of pulmonary IVUS imaging over other currently available techniques, there are limitations with this method that need to be overcome.

First, the proximal pulmonary arteries are large and often beyond the penetration of 12 to 30 MHz ultrasound frequencies: 5 to 20 mm depth penetration depending on the frequency used. Therefore,
lower frequency catheters will be required to provide detailed evaluations of pulmonary vascular responses and wall abnormalities in these more proximal portions. Because these proximal pulmonary arteries are large, it is also difficult to maintain central catheter placement. Eccentric placement of the catheter may distort the measurements of vessel diameter, and methods to improve catheter stability in these larger vessels are needed.

Second, although this technique is the only method of qualitatively determining the severity of vascular wall abnormalities, the ability to characterize the histologic components of the increased wall thickness has not been evaluated. Since the pulmonary arteries are elastic vessels, a three-ringed appearance is not usually seen. Thromboembolism has been described as “soft” echoes, but reflective differences between intimal hyperplasia and medial hypertrophy have not been described. Thus, it is too early to determine whether pulmonary IVUS can detect the components of pulmonary vessel wall disease.

A third limitation with pulmonary IVUS is that it is an invasive technique. It does not, however, require radiographic contrast, and the time period for the subjective evaluation of proximal and distal pulmonary artery structure and function has been shown to take only minutes to perform.

Finally, the cost vs benefit ratio of performing pulmonary IVUS is unclear. Currently, it should still be regarded as an investigational tool. Larger studies assessing the additional clinical value obtained from pulmonary IVUS compared with conventional imaging techniques in pulmonary vascular diseases are necessary to determine its cost effectiveness.

**FUTURE DIRECTIONS IN PULMONARY IVUS**

It is evident that pulmonary artery IVUS has many potential clinical applications. Preliminary studies in pulmonary artery stenosis have shown that it is a useful technique for evaluating the effects of balloon angioplasty. Therefore, it may also be useful in guiding stent placement. Recently, it has been shown that these catheters can be placed into the pulmonary artery with more safety and ease using a balloon-inflation IVUS catheter. By taking advantage of flow, the catheters can reach the pulmonary artery quickly and thus be used more easily in intensive care settings and in interventions.

Since pulmonary IVUS provides high resolution images of the pulmonary artery at high frames sites, it can assess pulmonary artery stiffness and pulsatility as well as rapidly determine responses to pharmacologic interventions. Further work, however, is needed in determining the ability of IVUS to characterize the histologic components of increased pulmonary artery wall thickness in specific diseases such as primary pulmonary hypertension and vascular tumor invasion from bronchogenic carcinoma. Clinical studies are needed to assess how important the determination of pulmonary artery stiffness and endothelial function are in the prognosis of patients with pulmonary hypertension.

It is possible that pulmonary IVUS imaging will supplement many existing diagnostic modalities currently used to diagnose pulmonary embolism and tumors. The high resolution images provided with this technique will allow rapid identification of thrombus, tumor infiltration, and vessel wall abnormalities, and it will enhance the understanding of the pathophysiology and effects of treatment in pulmonary vascular diseases.

**ACKNOWLEDGMENTS** The authors thank Patricia Dunham for secretarial assistance with this manuscript.

**REFERENCES**

12. Pandian NG, Weintraub A, Kreis A, Schwartz SL, Konstam MA, Salem DN. Intracardiac, intravascular, two-dimensional,