Echocardiographic Tissue Characterization and Range-gated Doppler Ultrasound for the Diagnosis of Pulmonary Embolism

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SUMMARY We evaluated reflection and absorption indexes of ultrasound as well as Doppler estimates of intrapulmonary blood flow for diagnosing pulmonary embolism. The pulmonary reflection coefficient (PRC), coefficient of tissue attenuation (alpha R) and range-gated blood Doppler signals were studied in 25 patients with pulmonary embolism, 19 with pneumonia, nine with atelectasis, 20 with congestive heart failure, 20 with chronic obstructive lung disease and 10 normal subjects. The PRC was significantly diminished in pulmonary embolism, pneumonia and atelectasis, but was not altered by underlying chronic obstructive lung disease or congestive heart failure. The alpha R in pulmonary embolism was 1.03 ± 0.04 db/MHz cm, significantly lower than that for pneumonia, 1.48 ± 0.03 db/MHz cm (p < 0.001), but not significantly different from that for atelectasis, 0.95 ± 0.05 db/MHz cm. Doppler signals indicating blood flow in the affected area of lung were present in only two of 25 patients with pulmonary embolism, compared with seven of nine with atelectasis and 17 of 19 with pneumonia. The combined use of PRC, alpha R and blood Doppler signals correctly diagnosed pulmonary embolism in 23 of 25 patients. Thus, ultrasound offers a reliable noninvasive method for diagnosis of pulmonary embolism.

THE SUCCESS of reflected ultrasound as a noninvasive diagnostic tool relies primarily on imaging tissue boundaries and only secondarily on refined analysis of tissue echoes. Nevertheless, a growing body of refined measurements of tissue echoes provide ultrasonic tissue characterization of various diseases. Mimbs et al.1 showed that measurements of ultrasonic back scatter may detect cardiomyopathy and acute myocardial infarction.2 Other ultrasonic measurements are being developed for diagnosing cirrhosis and malignant tumors of the liver.3, 4

Tissue characterization of the lung has been done only recently.5, 6 The normal lung has been modeled as a random collection of air-containing alveoli at its periphery. These structures are highly reflective of ultrasound because of multiple soft tissue-to-air interfaces. A lung affected at the periphery by pulmonary infiltrative, atelectatic or embolic disease would be expected
to demonstrate reduced ultrasonic reflection due to loss of interfaces between soft tissue and air. In atelectatic disease, air loss is associated with collapse of alveoli and other air-conditioning structures. In pulmonary embolism, although current xenon scanning techniques show preservation of ventilation to regions of lung with interrupted blood flow, our studies\textsuperscript{5, 6} showed loss of soft tissue to air interfaces and reduced ultrasonic reflectance.

The coefficient of lung reflection, a measure of absolute reflection of ultrasound from lung surface, is sensitive for diagnosing pulmonary embolism. This measurement is not influenced by chronic obstructive lung disease when the proper ultrasound frequency is selected.\textsuperscript{5, 6} The key problem in applying this measurement clinically is its inability to distinguish pulmonary embolism from other lung diseases. We developed indexes of ultrasonic absorption by the affected region as well as qualitative Doppler estimation of intrapulmonary blood flow to distinguish pulmonary embolism from pneumonia and atelectasis. We postulated that there may be a characteristic range of reduction of absolute reflection of ultrasound from pulmonary embolism, that various pathologic changes in the lung modify absorption of ultrasound differently, and that blood flow is diminished or absent in pulmonary embolism and preserved in other lung diseases.

\section*{Methods}

\subsection*{Instrumentation}

We constructed a portable research instrument (fig. 1) based on our original ultrasonic measurement system.\textsuperscript{5, 6} The instrument consists of a transmitter-receiver, microprocessor and an oscilloscopic display system mounted on a cart about the size of a commercial M-mode echocardiographic unit. The control and display panel permits us to adjust the ultrasonic signals and view the A-mode echo patterns as in conventional echocardiographic instruments. The transmitter drives the transducer to emit ultrasonic pulses while the receiver amplifies the echoes returned for analog-to-digital conversion and Doppler processing. The instrument differs from conventional echocardiographic units in the precise calibration of the transmitter-receiver circuitry and in the use of a microprocessor to control the operation. Moreover, the microprocessor (Data-General MP-100 with a Dual Disket floppy disk unit) directs complex data-taking procedures and prepares the data for real-time graphic display on the oscilloscope. Data-taking and analysis procedures are initiated by pressing one of the control panel buttons. The data are stored on the floppy disk. The range-gated pulsed Doppler signals are presented aurally and recorded on a conventional cassette recorder. The transducer is a one-fourth-inch unfocused disk unit with calibrated frequency response.

The instrument had the capability of measuring the pulmonary reflection coefficient (PRC), bulk tissue attenuation coefficient (alpha R) and pulsed Doppler signals.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Prototype research instrument. (A) Transmitter and receiver. (B) Hand-held transducer. (C) Recording system for Doppler signals. (D) Microprocessor.}
\end{figure}

\subsection*{Pulmonary Reflection Coefficient}

The measurement of absolute pulmonary reflection compared with a perfectly reflecting surface was defined as the PRC. This was measured at a specific frequency of 5.5 MHz, as at this frequency the angular sensitivity of reflection by the pulmonary surface is minimal. Conditions displacing air in the alveoli reduce pulmonary reflection coefficient. To determine PRC, the amplitude of isolated lung surface echo must be measured using a transmitted constant carrier burst of sufficient duration (5 \textmu sec) so that the combined transducer and radiation filters exhibit their Fourier response. The instantaneous PRC was obtained by forming the ratio of echo voltage to transmitter voltage, which was then corrected for bulk tissue loss, transducer filtering, and radiation filtering. After amplitude correction, the PRC was averaged over several seconds to smooth over respiratory fluctuations in echo magnitude. (More detail is provided in the Appendix and in earlier work.\textsuperscript{5}) The current instrument automated the measurement of PRC by forming the instantaneous PRC for every echo and averaging the root mean square of the instantaneous PRCs over 10 seconds.
Bulk Tissue Attenuation Coefficient

The alpha R is a measurement of loss of energy as ultrasound travels through a tissue. This energy loss depends on the nature of tissue. In the present study, the tissue is abnormal lung parenchyma, i.e., infiltrative, atelectatic or pulmonary embolic disease. We postulate that since these disease entities cause different histopathologic changes, they cause different degrees of energy loss. The alpha R is the rate of loss of ultrasonic energy per centimeter of tissue traveled per megahertz of frequency. We measured this rate of loss of energy from the slope of echo amplitude reduction with tissue depth at a frequency of 5.5 MHz (fig. 2).

Range-gated Doppler

In addition to measurement of PRC and bulk tissue attenuation indices, Doppler signal processing of the echoes from within the abnormal region of the lung was also done. As in conventional Doppler, the processed echoes were presented audibly, with pitch representing the speed of moving blood and the intensity representing quantity of blood sensed. The instrument was optimized to detect small volumes of moving blood in the presence of Doppler artifact induced by respiratory motion and hand tremor. To facilitate detection of the Doppler signal, we used a Doppler gate that could be adjusted for width and depth. Thus, we could detect signals that indicated blood flow over an adjustable volume of tissue at different depths inside the chest wall. By adjusting the volume to enclose the entire affected region, we increased the quantity of signals generated by blood flow, thereby increasing sensitivity. Conversely, by adjusting the range-gate interval to the shortest width, we observed regional flow, as is done with conventional pulsed Doppler units.

Patient Selection

All patients who underwent pulmonary angiograms and ventilation/perfusion (V/Q) scans as part of clinical diagnostic workup were studied. Patients with diagnostic angiograms and high-probability V/Q scans, irrespective of size and location of emboli, were assigned to the pulmonary embolism group. Patients with equivocal (poor distal filling or possible cutoff) and negative angiograms were assigned to other lung disease groups. Ultrasonic examination was performed without the knowledge of results of the angiogram or V/Q scan within 72 hours of the procedure (angiogram or V/Q scan).

Studies were performed in six groups of patients. Group 1 included 25 patients with pulmonary embolism, 18 with diagnostic angiograms and seven with high-probability V/Q lung scans. Group 2 included 19 patients with acute pneumonia, diagnosed by the presence of fever, leukocytosis, and focal consolidation on chest x-ray. Group 3 included nine patients with partial or complete lobar atelectasis due to an obstructive lesion. Atelectasis was diagnosed on chest x-ray. In six of these patients, the pulmonary angiogram was also available and showed only arterial crowding.

Group 4 included 20 patients with chronic left-heart failure, diagnosed by clinical history, physical examination and chest x-ray.

Group 5 included 20 patients with chronic obstructive pulmonary disease documented with pulmonary function tests (forced expiratory volume in the first second of < 0.45 of predicted normal).

Group 6 included 10 normal, healthy subjects.

Markedly obese patients were not included in the study because of difficulty in identifying the intercostal spaces in such patients.

Statistical Analysis

Analysis of variance and t test were used to compare the groups.

Scanning Procedure

The ultrasonic examination was performed at the bedside with the patient lying or sitting comfortably and breathing normally. A hand-held transducer was coupled to the skin with a hydrophilic gel (Aquasonic 100) and was moved along intercostal spaces to scan the underlying lung. The A-mode echographic pattern for the skin, soft tissue and lung was observed on the oscilloscope. The echo from the lung surface was identified by its distinctive temporal modulation with breathing. The range marker (fig. 3A) was positioned on the pulmonary echo (arrow). The echo was sampled automatically and the PRC displayed on the oscilloscope. The PRC identified abnormal regions of lung (i.e., more negative than –26 db) according to limits of normal defined previously.4 In the abnormal regions thus defined, the alpha R was measured and a search was made for presence of absence of Doppler signals. The characteristics of the Doppler signals and the depth at which they were present were noted. Audible Doppler signals with pulsatile modulation at the cardiac rate were recorded on magnetic tape for subsequent analysis.

Figure 2. Measurement of the bulk tissue, attenuation coefficient, i.e., slope of echo magnitude, vs range divided by twice the scanning frequency, i.e., 5.5 MHz \( \times 2 \) (to obtain slope vs distance).
Review. Analysis of alpha R was performed at a later date independently, without knowledge of clinical or angiographic diagnosis. Three types of Doppler signals were detected: pulsatile blood Doppler from within the affected region of the lung; breathing Doppler, i.e., audible microscopic vibration by air movement in the affected region; and Doppler sounds from the heart along the sternal border and occasionally over the cardiac impulse. Cardiac Doppler signals were observed at a depth less than 3.5 cm from the chest wall, whereas Doppler signals from the affected region of lung were observed superficially. Doppler signals from the heart were detected readily in all patients and normal subjects. The total scanning procedure lasted 30–45 minutes. PRC and Doppler signals were obtained instantly, but alpha R was calculated later, although recent improvements in microprocessor software provide the alpha R at the bedside.

Results

Pulmonary Reflection Coefficient

Figure 3 shows echograms of the lung surface from a patient with pulmonary embolism. The modulating echo from the normal lung surface is seen at 1.6 cm in figure 3A. The amplitude of the echo from the corresponding region on the opposite side at 2.1 cm is markedly diminished (fig. 3B). Table 1 is a comparison of the PRCs from each group. The PRCs from the normal lung in all groups are similar, except in the group with chronic obstructive lung disease, in which it is higher ($p < 0.02$). The PRC is significantly diminished in patients with pulmonary embolism, atelectasis and pneumonia; the reduction is most marked in pulmonary embolism and atelectasis. However, a range of reduction of the PRCs in pulmonary embolism characteristically distinctive from other lung diseases was not observed. The PRC is minimally reduced in patients with chronic congestive heart failure.

Bulk Tissue Attenuation

Figure 2 shows an example of the alpha R from a patient with pulmonary embolism. The alpha R is similar in patients with pulmonary embolism and atelectasis, but is higher in those with pneumonia. Figure 4 is a comparison of the alpha R from all patients in each group. The alpha R in pulmonary embolism is significantly lower than that in pneumonia ($p < 0.01$), but is similar to that in atelectasis.

Range-gated Doppler

Pulsatile Doppler signals indicating blood flow in the affected region of lung were heard in only two of 25 patients with pulmonary embolism, and these two patients had radiologic evidence of atelectasis. In the atelectatic group, seven of nine patients had Doppler flow and two had pleural effusion, which accounted for absence of blood flow signals. Presence of pleural effusion made it difficult to position the Doppler gate correctly in the lung tissue, which was displaced deeper. Sixteen of 19 patients with pneumonia had Doppler blood flow; two of the seven without Doppler blood flow had pleural effusion. None of the patients with congestive heart failure or the normal subjects had blood Doppler signals, as there was no deep penetration of ultrasound into the lung.

Diagnostic characteristics of pulmonary embolism

<table>
<thead>
<tr>
<th>Group</th>
<th>Root mean square mean ± SEM control</th>
<th>Abnormal area of lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>−17.5 ± 0.07</td>
<td>−31.7 ± 0.17</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>−18.2 ± 0.08</td>
<td>−28.3 ± 0.06</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>−17.8 ± 0.16</td>
<td>−31.2 ± 0.4</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>−15.8 ± 0.1</td>
<td>—</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>−17.5 ± 0.1</td>
<td>—</td>
</tr>
<tr>
<td>Normal subjects</td>
<td>−17.6 ± 0.01</td>
<td>—</td>
</tr>
</tbody>
</table>

Measurements are in db at 5.5 MHz.
are summarized in Table 2. Pulmonary embolism (one or multiple emboli) was correctly diagnosed in 23 of 25 patients when a diminished PRC, alpha R of 1.03 ± 0.04 and absence of Doppler signals indicating blood flow were used in combination.

**Discussion**

Our results support our postulate that indexes of pulmonary reflection and absorption of ultrasound distinguish pulmonary embolism from other focal lung disease. The present study confirms our previous observations that the PRC is a sensitive measurement to differentiate normal from abnormal lung surface and, unlike the V/Q lung scan, it is not affected by chronic obstructive lung disease and congestive heart failure. However, the PRC alone lacks specificity.

Joyner showed that atelectasis and pneumonia were the most common sources of confusion for ultrasonic diagnosis of pulmonary embolism. Addition of attenuation coefficient and qualitative estimates of intrapulmonary blood flow resolve the problem of distinguishing pulmonary embolism from pneumonia and atelectasis (Table 2).

Measurement of alpha R and detection of pulmonary blood flow exploit the phenomena of penetration of ultrasound into the diseased lung tissue. Normal lung modeled as a random collection of air-containing alveoli at its periphery is reflective of ultrasound because of multiple soft tissue-to-air interfaces. A lung affected at the periphery demonstrates reduced ultrasonic reflection and increased penetration of ultrasound into the diseased lung. This phenomenon permitted us to measure tissue attenuation and use range-gated pulsed Doppler to distinguish pulmonary embolism from other focal lung diseases. We postulated that bulk tissue attenuation would be different in various diseases, because it depends on the nature of lung pathology. This was confirmed by our data, i.e., the alpha R distinguished pulmonary embolism from pneumonia but not from atelectasis. Atelectasis is often associated with pulmonary embolism, so it is not surprising that alpha R was similar in these two conditions.

We also postulated that pulmonary blood flow would be diminished or absent in pulmonary embolism and preserved in atelectasis and pneumonia. We used pulsed Doppler to detect the presence or absence of pulmonary blood flow without any quantitative analysis. We failed to detect pulsatile blood flow in patients with pulmonary embolism, but did detect blood flow in patients with atelectasis. We were aware that blood flow may not be completely interrupted in pulmonary embolism and, conversely, in atelectasis it may be diminished because blood is shunted away from hyperventilated areas. Therefore, the presence or absence of Doppler blood flow may not be a determinant in patients in the chronic phase of pulmonary embolism.

We have demonstrated that measurement of three ultrasonic indexes, i.e., PRC, alpha R and Doppler blood flow, used in combination, reliably diagnose pulmonary embolism. This technique is a unique, simple bedside noninvasive method for not only diagnosing pulmonary embolism, but also in studying the natural history of pulmonary embolism. However, further studies are needed to confirm these results in a larger population of patients and to define the sensitivity and specificity of the technique before lung-surface sonography is offered for widespread clinical application.

**References**


**Appendix**

**Definition of PRC**

The ratio of received echo voltage to the transmitted voltage is a direct...
measure of total energy loss because of the radiofrequency transmission line method used in the design of the instrument. Of the total energy loss, we can correct for bulk tissue loss between transducer and lung surface, transducer filtering, and radiation filtering between transducer and lung surface. The instantaneous PRC was computed pulse by pulse. The PRC used for clinical study is the mean square of many (N) instantaneous PRCs, as given in the equation

\[
P_{RC} = 10 \log \left( \frac{2}{N} \sum_{r=1}^{N} \left( \frac{V_m}{V_r} \right)^2 \right)
\]

where \(V_m\) = the received echo voltage, \(V_r\) = the transmitted voltage, \(G_t\) = bulk tissue fractional loss, \(G_x\) = the transducer filter fractional loss, and \(G_r\) = the radiation filter fractional loss.

The Effect of Variations on Pulsed Doppler Sampling Site on Calculation of Cardiac Output: An Experimental Study in Open-chest Dogs

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**SUMMARY** We measured aortic flow by two-dimensional Doppler echocardiography in an open-chest dog model to examine how variations in Doppler sample volume length and position influence aortic hemodynamic flow calculations. Fourteen dogs underwent right-heart bypass, in which venous return from the vena cavae drained by gravity to a reservoir. A variable-speed roller pump returned the blood to the pulmonary artery, fixing left-sided cardiac input and output.

Echo Doppler measurements were performed using a 3.5-MHz transducer placed directly on the aortic arch to determine internal aortic cross-sectional area. The transducer was then directed to image the aortic arch for Doppler velocity measurements and the various sampling sites were investigated. Doppler cardiac output could then be determined for each of the various sample volumes over a range of known roller pump settings.

Doppler velocity was analyzed using fast Fourier transform spectral analysis. Mean velocity over the cardiac cycle was obtained by planimetry of the area under the Doppler velocity curve with a minicomputer. Doppler-derived determinations of cardiac output achieved a correlation of \(r = 0.98-0.99\) to values obtained by the roller pump over a range of cardiac outputs from 0.75-5 l/min. The standard error of the estimate was 0.2 l/min. In this laminar flow model, there was no difference between the predictive accuracy of any of the sampling sites over the range of roller pump flows.

Our study shows that Doppler velocity measurements can be used to quantify aortic flow over a clinically useful range and that variations of sample length and position did not produce significant differences in calculated flows.

SEVERAL studies suggest that Doppler echocardiography can be used to determine cardiac output noninvasively. Recently, pulsed Doppler two-dimensional echo scanners have been available with quantitative Doppler outputs. The range gate or sample volume obtained in pulsed Doppler echocardiography is a region determined in depth and in location from within a two-dimensional scan over which information is processed for the Doppler shift during the return cycle of an echo pulse. In these new scanners, the Doppler information is calculated by Fourier transform spectral analysis performed rapidly using digital electronics, which provides a linear and quantitative method for determining the Doppler shifts present within the sample volume. An important question for the application of pulsed Doppler technology to flow characterization concerns how sample volume size and location influence the recorded velocities. This question has assumed greater importance because many hemodynamic predictions are being made on the basis of noninvasively derived Doppler flow information from the ascending aorta and other locations. In this study, we examined aortic pulsatile flow in an open-chest dog model using Doppler echocardiography while varying sample volume depth and size.

**Methods**

**Surgical Techniques and Animal Model**

Fourteen mongrel dogs that weighed 20–25 kg were anesthetized with pentobarbital. They were intubated and ventilated after which a midline sternotomy was performed. The aorta and its branch vessel were dis-
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