ATTENUATION OF ULTRASOUND IN NORMAL LIVER AND DIFFUSE LIVER DISEASE IN VIVO

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Preliminary results of in vivo attenuation measurements of the liver have been obtained in 39 normal patients and in 35 patients with diffuse liver disease. A modified real-time sector scanner incorporating an on-line attenuation measurement method was used. The value of attenuation in normal liver was estimated as 0.52 ± 0.03 dB/cm/MHz, measured at 3 MHz. Significantly higher attenuation values were obtained from patients with alcoholic and cardiac cirrhosis, and following hepatic artery infusion with chemotherapeutic agents. Lower values were obtained from patients with biliary cirrhosis, chronic active hepatitis, and diffuse infiltration by lymphoma or leukemia. Fatty infiltrated livers showed a wide range of values of 0.37 - 0.66 dB/cm/MHz. The results suggest that estimates of attenuation coefficients are useful in detecting the presence of diffuse liver disease.

Key words: Attenuation; diffuse liver disease; liver ultrasound.

I. INTRODUCTION

Ultrasonic imaging of the liver is an established modality in the diagnosis and characterization of focal lesions [1,2]. Diffuse liver disease, however, is often indistinguishable from normal liver on an ultrasonic scan. A diffuse liver abnormality can sometimes be inferred by observing the changes in echogenicity of the liver and the relative difficulty of penetration. Increased echogenicity of liver parenchyma may be seen occasionally in patients with cirrhosis or fatty infiltration [3,4]. In some patients with hepatitis, bright echoes surrounding small portal radicles may be more prominent [5]. However, increase in the receiver gain setting, which directly affects the echo amplitudes may produce similar appearances. Difficulty of penetration of the liver on ultrasonic scanning is sometimes encountered in cirrhotic patients. Technical factors such as incorrect time gain compensation, and effects of the body wall attenuation could be responsible. Often, these qualitative findings are not helpful in diagnosis of diffuse liver disease.

Quantitative methods based on statistical parameters derived from the amplitude of backscattered ultrasonic waveforms have been reported [6]. Cirrhotic livers uniformly exhibited a higher mean amplitude and a broader amplitude distribution than normal liver. In addition, scatterer spacing was found to be greater in cirrhotic livers than in normal livers [6]. A signal processing procedure which estimates the value of the acoustic attenuation coefficient of the liver in vivo from reflected ultrasound signals has shown that inflamed livers produced lower attenuation estimates than cirrhotic livers [7], and that fatty livers produced higher attenuation estimates [8].
In this report we describe preliminary results of *in vivo* attenuation measurements in normal livers and in diffuse liver disease utilizing a modified real-time sector scanner incorporating an on-line attenuation measurement method.

II. MATERIALS AND METHODS

The apparatus used for the measurement of attenuation *in vivo* was a modified real-time sector scanner (Philips Ultrasound Corp., Santa Ana, CA). The scanner was modified for narrowband emission and the attenuation was estimated following the principles outlined by Ophir et al [9,10], and applied to B-mode scanning. The transmitted signals are sinusoid bursts of 4 cycle duration centered at 3.0 MHz. The received echoes are logarithmically amplified and detected. During the time intervals when the echoes originate from the region of interest selected by the user, the time gain compensation voltage is fixed at a constant value, so that it does not interfere with the natural decay of the echo amplitudes due to attenuation. After 8 bit digitization of the A-wave, the software performs averaging of many data points inside the region of interest, each obtained as the difference between two paired and decorrelated echoes separated by a small axial distance. The mean of all data points divided by the axial distance is taken to be the estimate of the attenuation coefficient.

Attenuation estimates were obtained from two groups of patients. Group 1 included 39 patients who had normal liver function tests by serum microanalysis, had no history of liver disease (particularly hepatitis and gall bladder disease) and no history of heavy alcohol intake. Group II included 35 patients, all showing abnormal liver function tests on serum microanalysis and clinical manifestations of diffuse liver disease. Biopsy proof of the etiology of the disease was obtained in 16 of these patients.

Following routine ultrasonic imaging of the upper abdomen, attenuation estimates were obtained in six or seven axially adjacent regions in the right lobe of the liver. Each region covered 30 mm in range and from 30 - 60 mm in cross range, and contained about 2000 data points. The axial separation between any two adjacent regions was 10 mm. The regions were selected to exclude large scattering surfaces such as walls of blood vessels or large branches of the hepatic or portal veins. Ten measurements were obtained for each region, and the mean attenuation as well as the standard deviation were computed. The global attenuation of the liver was calculated as the average of the mean estimates of all the regions. A typical patient attenuation measurement session lasted 10 - 15 minutes.

The attenuation coefficient was calculated by the instrument as the total attenuation (go and return paths) at 3.0 MHz. Assuming linear frequency dependence of attenuation [11], the one way attenuation coefficient per unit frequency was derived by dividing the value obtained from the instrument by six, to account for the center frequency (3 MHz) and the round trip nature of the measurement.

RESULTS

A. Normal liver (Fig. 1)

The observed range of attenuation values in 39 patients was 0.48 - 0.55 dB/cm/MHz. The mean and standard deviation of the attenuation in normal liver was computed as 0.52 ± 0.03 dB/cm/MHz.
ULTRASOUND ATTENUATION IN LIVER

Fig. 1 (a) Sector scan of normal liver. The area of interest was centered at 100 mm from the skin surface and contained 1920 data points (SMPLS). $\alpha$ = attenuation coefficient (go and return paths) at 3 MHz. (b) Results of ten measurements obtained at the same region. The mean attenuation coefficient (mean $\alpha$) and the standard deviation (SD) are computed and displayed.

B. Abnormal liver (Fig. 2)

Thirty-five patients with abnormal livers encompassing a wide variety of diffuse liver diseases with biopsy proof in 16 patients yielded the following results:

1. Alcoholic cirrhosis (5 patients)

The attenuation values measured in alcoholic cirrhosis ranged from 0.72 to 0.92 dB/cm/MHz. The mean and standard deviation

Fig. 2 (a) Sector scan of alcoholic cirrhosis of liver. (b) Results of ten measurements with mean attenuation and standard deviation computed.
of the attenuation in cirrhotic livers was $0.83 \pm 0.09 \text{ dB/cm/MHz}$. The diagnosis was confirmed by biopsy in four patients, while the fifth patient showed the clinical manifestations characteristic of the disease.

2. Other types of cirrhosis (8 patients)

Two patients with biopsy proved biliary cirrhosis showed mean attenuation values of 0.40 and 0.41 dB/cm/MHz. Two patients with biopsy proved postnecrotic cirrhosis showed mean attenuation values of 0.56 and 0.57 dB/cm/MHz. In four patients with the clinical and laboratory findings of cardiac cirrhosis, the mean attenuation value of the liver was computed at $0.66 \pm 0.07 \text{ dB/cm/MHz}$.

3. Hepatitis (13 patients)

In five patients with viral hepatitis (positive serological tests) the mean attenuation value was $0.52 \pm 0.04 \text{ dB/cm/MHz}$. Two patients with biopsy proved chronic persistent hepatitis showed mean attenuation values of 0.49 and 0.53 dB/cm/MHz. In two patients with biopsy proved chronic active hepatitis the attenuation values were 0.40 and 0.43 dB/cm/MHz. Four patients with the clinical and laboratory findings of alcoholic hepatitis showed a mean attenuation value of $0.42 \pm 0.05 \text{ dB/cm/MHz}$.

4. Fatty infiltration of the liver (5 patients)

The range of attenuation values in fatty infiltrated livers was $0.37 - 0.66 \text{ dB/cm/MHz}$. The mean attenuation value in fatty liver was computed as $0.49 \pm 0.11$. Two patients had biopsy proof of the infiltration, two patients showed the characteristics of fatty liver on computed tomography, and the fifth patient had the clinical and laboratory manifestations consistent with fatty infiltration of the liver.

5. Diffuse infiltration (2 patients)

Diffuse infiltration of the liver by lymphocytic lymphoma and leukemia showed mean attenuation values of 0.39 dB/cm/MHz and 0.44 dB/cm/MHz respectively. Both patients had the diagnosis confirmed by biopsy.

6. Hepatic artery infusion with chemotherapeutic agents (2 patients)

The attenuation value in the liver of two patients who underwent hepatic artery infusions was measured at 0.58 and 0.60 dB/cm/MHz.

The results obtained in diffuse liver disease are summarized in Table I.

IV. DISCUSSION

The measurement of attenuation by the technique described involves several assumptions. Present measurements were not corrected for errors due to the far field depth dependent beam diffraction effects [12]. However, the measurement of attenuation in all normal patients shows a stable value with depth (Table II). Moreover, this value is in agreement with other results in the literature [7,8,12]. It is evident that the effect
ULTRASOUND ATTENUATION IN LIVER

Table I. Ultrasonic Attenuation Measurements in Diffuse Liver Disease (35 patients)

<table>
<thead>
<tr>
<th>Diffuse Liver Disease</th>
<th>No. of Patients</th>
<th>Ultrasonic Attenuation dB/cm/MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcoholic Cirrhosis</td>
<td>5</td>
<td>Range 0.72 - 0.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean 0.83 ± 0.09</td>
</tr>
<tr>
<td>Biliary Cirrhosis</td>
<td>2</td>
<td>0.40 &amp; 0.41</td>
</tr>
<tr>
<td>Postnecrotic Cirrhosis</td>
<td>2</td>
<td>0.56 &amp; 0.57</td>
</tr>
<tr>
<td>Cardiac Cirrhosis</td>
<td>4</td>
<td>Mean 0.66 ± 0.07</td>
</tr>
<tr>
<td>Hepatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral</td>
<td>5</td>
<td>Mean 0.52 ± 0.04</td>
</tr>
<tr>
<td>Chronic active</td>
<td>2</td>
<td>0.40 &amp; 0.43</td>
</tr>
<tr>
<td>Chronic persistent</td>
<td>2</td>
<td>0.49 &amp; 0.53</td>
</tr>
<tr>
<td>Alcoholic</td>
<td>4</td>
<td>Mean 0.42 ± 0.05</td>
</tr>
<tr>
<td>Fatty Infiltration</td>
<td>5</td>
<td>Range 0.37 - 0.66</td>
</tr>
<tr>
<td>Diffuse Infiltration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
<td>0.39</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1</td>
<td>0.44</td>
</tr>
<tr>
<td>Hepatic Artery Infusion</td>
<td>2</td>
<td>0.58 &amp; 0.60</td>
</tr>
</tbody>
</table>

of beam profile was negligible and was therefore ignored. The effect of
body wall on amplitude based attenuation has not been thoroughly inves-
tigated. Wells et al [13] postulated that the characteristics of the body
wall muscle and fat layers might exert a significant influence on the
amplitude of intrahepatic echoes. However, their later work [14,15] has
failed to confirm this concern. In addition, since the technique de-
scribed relies on differential amplitude measurements, no significant
effects due to the body wall are expected. This is borne out in the
results of the normal patients, who varied in body weight from 90 - 320
lbs. No significant effect on the results could be attributed to these
variations. The measurement of attenuation using the technique described
relies on the assumption that the second order statistics from multiple
depths remain essentially unchanged. For this reason, areas in the liver
which contain either large blood vessel walls or biliary structures were
excluded from the regions of interest.

Table II. Ultrasonic attenuation measurements in different depths
(39 subjects)

<table>
<thead>
<tr>
<th>Range in cm</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dB/cm/MHz</td>
<td>0.48</td>
<td>0.52</td>
<td>0.52</td>
<td>0.54</td>
<td>0.54</td>
<td>0.53</td>
<td>0.51</td>
</tr>
<tr>
<td>S. D.</td>
<td>0.10</td>
<td>0.10</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.08</td>
<td>0.08</td>
</tr>
</tbody>
</table>
The attenuation coefficient in normal liver has been established in a group of 39 patients at 0.52 ± 0.03 dB/cm/MHz. The values are in agreement with previously reported in vitro and in vivo measurements [16,17]. Kuc [7,8], utilizing a spectral difference method, reported attenuation coefficients of the liver of 0.44 ± 0.07 dB/cm/MHz. Jones [18] utilizing a similar technique reported attenuation in normal liver at 0.47 ± 0.06 dB/cm/MHz measured at 2.25 MHz. Determination of the range of attenuation coefficients in normal liver allows detection of diffuse abnormalities in cases where the attenuation coefficient differs from the established normal range. It is encouraging that the range of attenuation values in normal liver in the present study is very narrow. Thus, attenuation values falling outside the normal range are indicative of likely presence of diffuse disease. This was confirmed by the results obtained (Table I). However, in some cases of diffuse liver disease (i.e., viral and chronic persistent hepatitis) the attenuation values fall within the normal range.

The higher values of attenuation exhibited by patients with alcoholic cirrhosis have been reported [7,17]. The mechanism for the increase of ultrasonic attenuation in alcoholic cirrhosis is not known. Alcoholic cirrhosis is characterized by an increased amount of fibrotic repair tissue within the liver. The increased ultrasonic attenuation in alcoholic cirrhosis has been attributed to the increase in the amount of fibrous tissue [7]. However, the attenuation values were not significantly higher in the two patients with postnecrotic cirrhosis, a condition which also exhibits a large amount of fibrotic repair tissue. An increase in the collagen content of necrotic tissue has been suggested as an explanation for the increased attenuation in myocardial infarction [19]. Hepatic necrosis is one of the main pathologic features of chronic active hepatitis, yet in this condition, the attenuation values were lower than normal in the two patients studied as well as in the patients studied by Kuc [7]. Thus it appears that the collagen content in the fibrotic repair tissue are not major contributors to the increased attenuation that is observed in alcoholic cirrhosis. Bamber et al [20] found no correlation between the attenuation coefficient and the collagen content of normal and cancerous human liver in vitro. These investigators found a strong negative correlation between the attenuation coefficient and the water content of the liver. The results obtained in the present study for alcoholic cirrhosis and other types of cirrhosis may be explained by the variation in water content, although this was not measured. The higher attenuation values obtained in alcoholic cirrhosis and in postnecrotic cirrhosis may be due to a lower water content in these livers than in normal liver. On the other hand, biliary cirrhosis which is characterized by bile lakes within the liver, would lead to lower attenuation values because of the increase of water (fluid) content within these livers. Active inflammation with edema would increase the water content within livers affected by chronic active hepatitis or alcoholic hepatitis, and thus these two conditions would lead to lower attenuation values, which were in fact observed in the present study.

The attenuation values measured in patients with fatty infiltration of the liver varied from below normal to above normal values, and are difficult to explain. Bamber et al [20] have found that increasing the fat content in livers they studied appears to be associated with an increase in the attenuation coefficient. However, when the attenuation coefficients were corrected for variations in water content, there was no correlation between the attenuation and the fat content. Kuc [8] showed increased attenuation slope estimates in patients with fatty infiltration of the liver, ranging from 0.54 dB/cm/MHz for mild infiltration, to 0.7 dB/cm/MHz in massive infiltration. Somewhat similar results were obtained by Narayana and Ophir [21]. A possible mechanism responsible for the variation
of attenuation values in fatty liver is the effect of the fat on the absorption and scattering in the liver. In mild to moderate fatty infiltrations of the liver, the increased number and size of fat globules contributes to the scattering of the sound energy. This increased scatter, when added to the absorption of the liver can result in increased attenuation. On the other hand, when the liver is massively infiltrated by fat, the low absorption due to the fat [16] may become the dominant mechanism resulting in lower attenuation values.

The lower than normal attenuation values obtained in diffuse infiltration of the liver by lymphoma and leukemia are consistent with the characteristic appearance of lymph nodes affected by these conditions. The affected nodes tend to be very homogeneous on B-mode ultrasonic scanning and may show echogenic enhancement along their posterior borders, denoting decreased attenuation.

The values of attenuation coefficients obtained in patients with alcoholic cirrhosis and those in other types of cirrhosis such as postnecrotic and biliary cirrhosis indicate that measurement of attenuation coefficients may be useful in differentiating the various types of cirrhosis. Differentiating alcoholic from postnecrotic cirrhosis is often important. Patients with alcoholic cirrhosis have a five year survival rate of 60% especially if abstinence from alcohol is encouraged. On the other hand, postnecrotic cirrhosis is usually a progressive disease and is fatal in more than 35% of cases within 1 - 5 years. The finding that the attenuation coefficient in alcoholic cirrhosis is much higher than in postnecrotic cirrhosis suggests that this differentiation may be made utilizing the present technique.

Differentiation between chronic active hepatitis and chronic persistent hepatitis is often difficult. This differentiation is important because chronic persistent hepatitis is not a progressive disorder, rarely results in cirrhosis and requires no therapy. On the other hand, chronic active hepatitis is characterized by continuing hepatic necrosis, active inflammation and fibrosis which may lead to or be accompanied by cirrhosis. The differentiation between these two types of chronic hepatitis cannot be made by clinical and biochemical criteria. Liver biopsy can establish this differentiation in many cases. The finding that attenuation coefficient is within the normal range in chronic persistent hepatitis and is reduced by approximately 20% in livers affected by chronic active hepatitis indicates that this differentiation may be possible utilizing attenuation coefficient measurements.

All cases of hepatitis (chronic active, chronic persistent, viral) presented normal appearances of the liver parenchyma on ultrasonic scanning. The evaluation of the ultrasonic images revealed that a diagnosis of diffuse liver disease could be inferred on the basis of increased echogenicity and/or difficulty in penetration of the liver in only two of the five patients with alcoholic cirrhosis, and in three of the five patients with fatty liver. In none of the patients with biliary, cardiac or post-necrotic cirrhosis could the diagnosis be made on the basis of B-mode ultrasonic images. Thus, attenuation coefficient measurements appear to be more sensitive in detecting diffuse liver disease than conventional B-scan ultrasonic imaging.

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