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Introduction

The recent development of hepatology revealed the importance of blood circulation of the liver.1) Many measurement methods to calculate the hepatic blood flow were developed2-6), but there were few reports of liver blood volume.7-9) About the space occupied lesions, $^{99m}$Tc labeled RBC was used to distinguish between hemangioma and liver tumor.10,11) But the blood volume of hemangioma was yet calculated. In this study we calculated liver blood volume on liver disease with $^{11}$CO labeled RBC using positron emission tomography.

Method and Materials

Clinical studies were performed to the 3 normal volunteers, 4 patients with liver cirrhosis at compensated stage, 3 patients with caverunus hemangio, and 3 patients with hepatocellular carcinoma. In every cases, the diagnosis was obtained using X-CT, ultrasonic echogram, angiography, biochemical data, cytological findings, and clinical course.

The machine used for this study was ECAT II (ORTEC). The resolution of the system in this study was 15 mm (full width half maximum) using medium resolution shadow shield. The transmission scan using a $^{68}$Ge/$^{68}$Ga ring source was performed before $^{11}$CO inhalation. Twenty mCi of $^{11}$CO was inhaled for about 2 min, and labeled RBC in vitro. Sequential emission scan was performed 5 min after inhalation, and continued until 45 min after starting inhalation.

The blood volume calculation was performed using Phelps's method.12) The equation was as follows.

\[
\text{liver blood volume (LBV)} = \frac{100 \times Ci}{CV \times CF \times d}
\]

Ci: PET count
CV: venous blood count
CF: correction factor for peripheral tissue hematocrit
d: liver density
Everett’s value\textsuperscript{13} were used for correction factor for peripheral tissue hematocrit: liver 0.74, spleen 1.23. Liver density was considered same as dog liver.\textsuperscript{5} We assumed that the correction factor for peripheral tissue hematocrit of space occupied lesion in the liver was same as the liver, because that value were unknown.

Result

Table 1 showed the calculated liver blood volume of liver disease. The liver blood volume of the patients with liver cirrhosis lower than that of normal volunteers. The blood volume of caverunsus hemangioma was three times higher than that of normal liver. The blood volume of HCC was slightly lower than that of the liver with liver cirrhosis.

Figure 1 showed the PET images of the liver disease using \textsuperscript{11}CO 40 min after \textsuperscript{11}CO inhalation. The liver image of Cirrhotic liver represented lower accumulation than that of normal liver. The hemangioma images showed positive images comparing with the surrounding liver.

Segmental filling of labeled RBCs was found in case of hemangioma (Fig. 2), and it took about 30 min to show the homogeneous image. This phenomenon was not obtained on other cases of liver disease.

Discussion

There are many methods to know the hemodynamics of the liver, for example dye-infusion method\textsuperscript{2,3}, \textsuperscript{133}Xe clearance methods\textsuperscript{4,5}, and \textsuperscript{99m}Tc scintigraphic method.\textsuperscript{6} These methods were wide spread and used in a clinical phase. These studies and pathological findings confirmed the concept that the liver cirrhosis is the vascular disease.\textsuperscript{1} Though in vivo volume measurement of the capillary bed in the liver i.e. the measurement of liver blood volume was rarely performed. There were only few reports using organ reflectance spectrophotometry to measure in vivo liver blood volume.\textsuperscript{7-9} Their results revealed the decrease of liver blood volume in the patients with liver cirrhosis but they did not measure the absolute value of liver blood volume and more over their method which used the laparoscopy was not the non-invasive method.

In this study we revealed the decrease of the liver blood volume in patients with liver cirrhosis quantitatively. It was considered that this decrease was caused by the hepatocyte swelling with fatty infiltration, compression and narrowing of sinusoid with fibrosis, and pseudolobales formation. The difference of blood volume between right and left lobe of the liver was unclear because of the small cases of our study. It was well known the difference of the blood flow between right and left lobe in the liver\textsuperscript{4}, though further study was necessary to detect the difference of blood volume between right lobe and left lobe.

Concerning hemangioma, \textsuperscript{99m}Tc labeled RBC was widely used for its specific
accumulation pattern\textsuperscript{10,11}, but quantitative measurement of its blood volume was not performed. Our result of the blood volume of hemangioma shown the over 100 ml/100 g tissue. This result caused by the assumption that the correct factor of peripheral hematocrit in hemangioma was same as the liver. If that correct factor was same as peripheral blood, the blood volume of hemangioma was 84.2 ml/100 g tissue.

The blood volume of hepatoma was lower than that of normal liver and same as the cirrhotic liver. Considering this result and the hypervasculality of hepatoma on angiography, there may be the shunt formation in hepatoma. The measurement of liver blood flow using PET was yet performed. It will be possible to estimate the shunt formation in the hepatoma, which is the topics in hepatology, using PET.

In this report we represent the methods and results to measure the blood volume of the liver. The major problem in this study was the value of correct factor of peripheral hematocrit. Recently Lammertsma reported the peripheral hematocrit of brain using $^{11}$CO and $^{11}$C-methyl albumin.\textsuperscript{14} It will be possible to measure liver blood volume more correctly using their method.

References

1) Galambos J. T., Major Problems in Internal Medicine \textbf{17} (Saunders W. B., Philadelphia 1979).
Table 1. Liver blood volume using C-11 CO

<table>
<thead>
<tr>
<th>Case</th>
<th>Liver</th>
<th>Spleen</th>
<th>Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>45.9 (±5.52)</td>
<td>70.0 (±3.04)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45.5 (±4.81)</td>
<td>69.4 (±1.57)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.7 (±3.37)</td>
<td>70.0 (±1.90)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>47.0 (±2.31)</td>
<td>69.8 (±0.35)</td>
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</tr>
<tr>
<td>Hemangioma</td>
<td>43.4 (±4.89)</td>
<td>68.7 (±1.09)</td>
<td>119.2 (±3.37)</td>
</tr>
<tr>
<td></td>
<td>23.0 (±1.76)</td>
<td>67.6 (±0.98)</td>
<td>98.8 (±11.2)</td>
</tr>
<tr>
<td></td>
<td>32.5 (±1.84)</td>
<td>69.2 (±1.05)</td>
<td>123.4 (±5.20)</td>
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<tr>
<td>Mean</td>
<td>33.2 (±9.82)</td>
<td>68.5 (±0.82)</td>
<td>113.8 (±13.2)</td>
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<tr>
<td>Liver Cirrhosis</td>
<td>18.6 (±3.76)</td>
<td>62.2 (±2.26)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.5 (±6.17)</td>
<td>63.3 (±4.24)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24.3 (±6.91)</td>
<td>86.4 (±2.65)</td>
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<tr>
<td>Mean</td>
<td>21.5 (±3.94)</td>
<td>70.6 (±13.7)</td>
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</tr>
<tr>
<td>Hepatoma</td>
<td>34.1 (±4.11)</td>
<td>59.9 (±4.43)</td>
<td>26.1 (±1.82)</td>
</tr>
<tr>
<td></td>
<td>24.7 (±4.51)</td>
<td>71.54 (±3.81)</td>
<td>18.6 (±1.70)</td>
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<td></td>
<td>47.6 (±6.12)</td>
<td>58.5 (±2.23)</td>
<td>18.9 (±1.14)</td>
</tr>
<tr>
<td>Mean</td>
<td>35.5 (±11.5)</td>
<td>63.3 (±7.14)</td>
<td>21.2 (±4.2)</td>
</tr>
</tbody>
</table>
Fig. 1. Blood volume images of liver disease using $^{11}$CO. Normal liver (upper left), cirrhotic liver (upper right), liver hemangioma (lower left), and hepatoma with normal liver (lower right). All images were calculated according to the Phelp's equation. Cirrhotic liver presented lower accumulation than normal liver. Hemangioma showed clear positive image in normal liver. Concerning the lower right hepatoma image, the necrotic area showed negative image and the viable tumor tissue was localized around the necrotic area.

Fig. 2. Sequential scanning images of hemangioma using $^{11}$CO. Segmental filling of hemangioma with labeled red blood cells was observed.