A Novel, Simple Method of Functional Spleen Volume Calculation by Liver-Spleen Scan

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Spleen enlargement is commonly associated with portal hypertension from cirrhosis and may cause thrombocytopenia. Thus, accurate assessment of spleen size may be helpful in the clinical evaluation. Spleen length is not a precise estimate of spleen size because of the variation in spleen configuration, and spleen volumes measured by edging techniques can be tedious. We present a new method of measuring the functional spleen volume by liver-spleen scan (LSSs), validation experiments and some clinical data. Methods: The method involves measurement of the total spleen counts by SPECT and dividing by a representative voxel concentration on a single frame to obtain the organ volume. Validation included phantom studies and clinical evaluation in 443 consecutive patients, including 216 with histologic assessments of chronic liver disease (CLD) and 11 healthy volunteers. Results: A calibration factor determined from phantoms was used to convert the calculated volume (CV) to the "true" volume (V): V = CV (0.956) - 66.5 (r = 0.9991; P < 0.001). The volume calculations were validated in a second group of phantoms (r = 0.981; P < 0.0001). Spleen volumes were expressed as volume (cm³) and as volume per pound ideal body weight (IBW) (cm³/lb) (the conversion factor to convert cm³/lb IBW to cm³/kg IBW is 2.2). Clinical studies of reproducibility included demonstration of a significant (P < 0.0001) linear correlation between volumes calculated from repeat LSSs within 9 mo of the initial LSS in 11 healthy volunteers and 32 patients with CLD: y = 1.02x - 25; r = 0.968. The correlation with spleen volumes from autopsy or splenectomy was significant: y = 0.766x + 57; r = 0.845; P < 0.001. The normal spleen volume in 11 patients was 201 ± 77 cm³ and 1.43 ± 0.68 cm³/lb IBW (upper limits of normal: 335 cm³ or 2.5 cm³/lb IBW). In 443 consecutive LSSs over 15 mo, half of the patients had spleen volumes above the upper limits of healthy volunteers, and CLD was present in 90.9% of these patients. In 216 patients with histologically proven liver disease, a progressive increase in the percentage of spleen volumes above the upper limit of normal was noted from no fibrosis (10%) to mild to moderate fibrosis (36.7%) to early cirrhosis (52%) to advanced liver disease (75%). The correlation of spleen volume with platelet count was excellent (r = 0.7635; P < 0.005). Conclusion: This novel spleen volume measurement detects serious liver disease and correlates with splenic hyperfunction. Key Words: liver-spleen scan; spleen volume; chronic liver disease; sulfur colloid; reticuloendothelial cell J Nucl Med 1999; 40:1745–1755

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calculating SVs were noted between these preparations. Total counts were obtained as described (1-3) by summarizing all the frames in the transaxial view, including the object of interest, and expressing it as a two-dimensional image. A region of interest (ROI) was drawn around this image for total counts in the phantom or organ (Fig. 1A). The coefficient of variation in total counts is ±1.1% when the raw data are reconstructed on different days and with ROIs drawn by different technologists.

The key requirement of this technique is to determine a representative voxel concentration (C). The voxel concentration was determined from a single, midorgan frame using a three-voxel square ROI (nine voxels total) over the darker areas of the image on the frame from a peripheral portion of the spleen image (Fig. 1C). It is important for the whole ROI to be within the organ because the mean voxel concentration would be significantly affected by an ROI voxel partially outside the organ. The mean, SD and maximum voxel concentration of this three-voxel square ROI were recorded from ROIs from three different areas of this frame. Four methods of determining a representative voxel concentration were used in combining information from these ROI areas and are described in Appendix 1. The mean of the two greatest maximal voxel concentrations is the only method reported in the text of this article because all of these methods are comparable. In the Figure 1 example, the midframe concentration (C) would be (Cmax1 + Cmax2)/2. Thus, the calculated volume could be determined from the formula below:

\[ CV = V_0 (T/C), \]

where CV = calculated volume, T = total counts, C = voxel count concentration and V0 = voxel volume. The voxel is a small cubic volume that is the basic unit of the SPECT analysis and may be variable between machines. In our machine (Starcam camera), a voxel is approximately 0.64 cm on a side, and the voxel volume is the cube of this value (V0 = 0.26214 cm³). This value may not be precise and even a small error could potentially result in a significant error in the calculated volume. This problem was overcome by external calibration from the phantom studies as discussed in the next section. The settings of this machine, including filters, collimator and radius of rotation, have little impact on the volume calculation because the effect is the same on the numerator (T) and denominator (C). Most machine settings cancel out for this reason. Only the voxel volume is likely to be different between machines. Any effect on attenuation due to differences in body size is likely to affect the numerator and denominator equally. Thus, most machine settings and body habitus factors cancel out.

Spleen length was measured in centimeters as described (1-3) as the greatest length in any orientation from the posterior planar scan.

**Phantom Studies**

Volumes of irregular phantom shapes from 100 to 1300 cm³ were prepared. An experiment consisted of two different volume phantoms of irregular shape assessed at one time in similar placement orientation to the liver and spleen (approximately 4-5 cm apart in the same plane). No more than two experiments were performed on the same day. The first 16 volumes (eight experiments) were used for calibration of the calculated volume by the linear regression equation relating it to the known volume. From these experiments, the subsequent measured volume was adjusted by insertion into the linear regression equation to form a calibrated volume (V): V = CV × (calibration factor). The second 16 phantom volumes (eight experiments) were used to compare with our calculated and calibrated phantom volumes with the true phantom volume.

**Patient Studies**

SVs were calculated prospectively between October 1, 1993, and December 31, 1994, including 443 patients. Eleven healthy volunteers and 35 patients with CLD were studied twice. Healthy volunteers were recruited for fasting and postprandial LSSs. Healthy volunteers had no evidence of active disease of any kind, normal liver tests, normal prothrombin time, normal complete blood cell count and differential and no evidence of liver disease on physical examination. The height in inches and weight of each person were recorded. The ideal body weight (IBW) in pounds was calculated for men [IBW = 106 + (ht - 60) 6] and women

![FIGURE 1](https://example.com/figure1.png)

**FIGURE 1.** Hard copy image was produced of total spleen count (T) measurement (T = 1.8349 × 10⁶) on summed SPECT transaxial image (A), planar scan (B) (spleen length – greatest spleen length in any direction on posterior scan) and placement of three representative ROIs (each containing nine voxels) on single midspleen frame (C). For each ROI on single midspleen frame, mean voxel concentration (Cmax) and maximal voxel concentration (Cmax) are noted for each of three ROIs (Appendix 1). Representative voxel concentration (C) is calculated from average of two greatest Cmax.
[IBW = 100 + (ht - 60) 5], where ht is the height in inches. Volumes were expressed as absolute values in cubic centimeters and as a ratio to the IBW in pounds (the conversion factor to convert cm³/lb IBW to cm³/kg IBW is 2.2).

**Calculated Verses Actual Spleen Volumes.** The SV calculated from the LSS in patients with CLD was compared with spleen weight obtained at autopsy or splenectomy. The SVs by LSS were compared with SVs in 9 patients with recent CT scans.

**Normal Volumes.** Eleven healthy volunteers were studied twice: fasting (12–18 h) and postprandial (meal within 2 h and Ensure [Ross Products Division, Abbott Laboratories, Columbus, OH] within 30 min).

**Reproducibility.** The SVs were calculated from two or more frames in 10 patients to examine whether a representative voxel concentration on a single frame was representative in an individual patient. Thirty-two patients with CLD had SVs determined twice within 9 mo, and these volumes were compared. Three additional patients were studied before and after liver transplant surgery and are reported separately. The 11 healthy volunteers were studied twice and are included in the reproducibility studies.

**Consecutive Volumes in 443 Patients.** The cumulative ratio of patients with a spleen size starting with the smallest to largest size was developed for “normal” volunteers and 443 consecutive patients who had LSSs to determine the frequency of abnormal spleen size that could be expected in a population referred for LSSs. The cumulative ratio is a method of expressing the proportion of patients with a spleen of a given size or smaller. The spleen size at a ratio of 0.5 would be the median spleen size for that population.

Histology was available in 216 patients. Patients were categorized according to criteria described (1–3) as no fibrosis, mild fibrosis (portal expansion with fibrosis), moderate fibrosis (portal-
TABLE 1  
Comparability of Repeat Spleen Volumes in Same Patient

<table>
<thead>
<tr>
<th>Patient method</th>
<th>Patient group</th>
<th>No.</th>
<th>First Spleen volume (cm³)</th>
<th>Second Spleen volume (cm³)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV</td>
<td>Normal</td>
<td>11</td>
<td>201 ± 77</td>
<td>176 ± 65</td>
<td>NS</td>
</tr>
<tr>
<td>CLD</td>
<td></td>
<td>32</td>
<td>677 ± 401</td>
<td>697 ± 433</td>
<td>NS</td>
</tr>
<tr>
<td>CLD + transplant</td>
<td></td>
<td>3</td>
<td>858 ± 254</td>
<td>587 ± 109</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

SV = spleen volume; NS = not significant; CLD = chronic liver disease.

RESULTS

Phantom Studies

Sixteen phantom studies were used for calibration with phantom volumes ranging from 100 to 1300 cm³ (Fig. 2). All subsequent volumes were corrected by these equations. An additional 16 phantom studies compared the calibrated phantom volume with the measured volume: \( y = 1.0566x - 83.47; r = 0.9811; P < 0.0001 \), confirming the ability to accurately determine known volumes.

Clinical Studies

SVs by LSS were calculated as shown in the example in Figure 1 with calculations in Appendix 1.

Comparison with Actual Organ Weights. The spleen weights at autopsy or splenectomy were compared with the measured SV from LSS: \( y = 0.766x + 57; r = 0.845; r^2 = 0.714; P < 0.0001 \) (Fig. 2).

Nine patients had a recent CT comparison with LSS calculations of SV, and these volumes were highly correlated: \( y = 0.856x + 135; r = 0.940; P < 0.05 \) (Appendix 2).

Normal Values. The mean SV in 11 healthy volunteers was 201 ± 77 cm³ (1.43 ± 0.68 cm³/lb IBW or 3.15 ± 1.5 cm³/kg IBW). No difference between males and females was noted (189 ± 82 cm³ versus 214 ± 68 cm³; \( P > 0.05 \)), unless expressed as a ratio to IBW with larger spleens in females (SV/IBW: 1.13 ± 0.50 cm³/lb versus 1.80 ± 0.68 cm³/lb; \( P < 0.05 \)). We found a significant linear regression correlation of SV to age: \( SV = 335 - 4.05 \times \text{age}; r = 0.548; P < 0.05 \), similar to autopsy studies (21, 22). A significant difference was noted between SV per IBW in healthy volunteers <30 and >30 y old: 1.81 ± 0.56 cm³ versus 1.12 ± 0.61 cm³/lb; \( P < 0.05 \). We believe the difference in SV per IBW between males and females was associated with the younger female age (3/5 females were <30 y old compared with 1/6 males).

![Figure 4](https://example.com/fig4.png)

**FIGURE 4.** Spleen volume from initial LSS is compared with second volume from second LSS within 9 mo in 11 healthy volunteers and 32 patients with CLD.

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FIGURE 5. Cumulative ratio of spleens of increasing size in healthy volunteers (■) and 443 consecutive patients (○): spleen length (A), spleen volume (SV) (B) and SV/IBW (C). Upper limit of normal is 15 cm, 375 cm³ and 2.5 cm³/lb IBW, respectively. Half of patients scanned over 15 mo had liver volumes >2.5 cm³/lb IBW (>5.5 cm³/kg IBW) and 90.9% of those with large spleens had CLD.
Reproducibility of Spleen Volume Measurements. The calculated volumes' coefficient of variation (COV) was ≤6% when using different frames from the same LSS to determine a representative voxel concentration. The correlation of volumes using different midorgan frames for calculation was closely correlated: \( y = 0.9823x + 1.5243; r = 0.9996; P < 0.01 \). Volumes calculated from midspleen frames showed a range in the COV from 1% to 6% (COV 3.3% ± 1.7%) in individual patients. The COV increased to as high as 37% in individual patients if end organ frames were included, and these should be avoided. A single midorgan frame could be used to determine a representative voxel concentration.

The initial and repeat SVs in 11 healthy volunteers, 32 nontransplanted liver disease patients and 3 transplant patients are shown in Table 1. No difference in the SV in healthy volunteers or patients with CLD without transplants was found by the paired t test analysis between the first and second volumes. By using both healthy volunteers and the patients with CLD without transplants, the linear regression correlation between the first and second study was highly significant (Fig. 4). A significant decrease in spleen size between the first and second study by the paired t test was noted only in patients with liver transplants (Table 1).

Spleen Volumes in 443 Patients. The cumulative ratio of spleens of a given size in 443 consecutive patients is expressed in Figure 5 for spleen length (cm), SV (cm³) and SV per IBW (cm³/lb). Healthy volunteers are included for comparison. A third of the spleen lengths are above the largest normal compared with 45% for SVs and 50% of volume per IBW. The SV is compared with spleen length in Figure 6. The frequency of abnormal spleen size increases if SVs are used rather than length. This is related to the inconsistent relationship of spleen length to volume related

**FIGURE 6.** Spleen length is compared with spleen volume for healthy volunteers (A) and other patients (B).
primarily to variation in spleen shape (spleen of the same length could be round, oval or crescent shaped). Of this population, 253 patients (53%) had abnormal SVs. CLD was found in 90.9%, noncirrhotic portal vein thrombosis in 0.4%, congestive heart failure in 2%, etiology unclear in 3.2% and lymphoma or leukemia in 3.5%.

The cause and severity of liver disease in 216 patients are shown in Table 2. The SVs in patients with CLD were significantly different from those of healthy volunteers (P < 0.001). Increasing amount of hepatic fibrosis was associated with larger SVs (Table 2 and Fig. 7). SVs were more effective than spleen length in detecting serious liver disease. Only a third of patients with marked fibrosis or early cirrhosis and 60% of patients with advanced cirrhosis had an abnormal spleen length, whereas 50% and 75%, respectively, had abnormal volumes. However, no patient with advanced cirrhosis had a SV < 1.25 cm³/lb IBW because the whole curve was shifted to the right. This indicates that CLD enlarges the spleen in all patients, although the SV may not exceed the normal range in some patients. Nearly all patients with SVs greater than twice the upper limit of normal had cirrhosis. No significant difference in SV was noted between patients with alcoholic and nonalcoholic liver disease by the Student t test.

SV was correlated with WBC (normal: y = 8843 - 702x; r = -0.5027; P < 0.05 and CLD: y = 7285 - 261x; r = -0.2711; P < 0.05), HCT (normal: y = 47.34 - 3.047x; r = -0.4711; P < 0.05 and CLD: y = 43.28 - 1.118x; r = -0.4539; P < 0.05) and platelet count (normal: log y = 5.5138 - 0.06792x; r = -0.5784; P < 0.01 and CLD: log y = 5.435 - 0.06986x; r = -0.7635; P < 0.001) (Fig. 8). Platelet counts >300,000 occurred only in patients with normal SVs, and patients with SVs >7.5 cm³/lb all had a platelet count <150,000. SV is an important determinant of the blood profile in patients with CLD.

**DISCUSSION**

We have shown that volumes calculated by our technique are precise in phantoms and reproducible in patients, and the volume increases with progressive CLD as would be expected. The calculated normal volumes of spleen by this technique are similar to measured volumes by other noninvasive techniques (4–20). Furthermore, the SVs noted at autopsy or transplantation correlated quite well with calculated volumes, as did comparison with CT volumes (Appendix 2). These correlations from autopsy specimens are not exact because removal of these organs may be associated with alterations from the in vivo volume and the terminal changes in an autopsied patient could affect the organ volume as well (14). The only significant in vivo changes occurred after liver transplantation with decrease in SV because of portal decompression (10). We conclude that this voxel method of measuring SVs is accurate as well as simple. We have incorporated this technique as part of the routine LSS evaluation.

The routine determination of SV would add to the value of the LSS. This study shows that spleen size is frequently abnormal in patients referred for LSS and that SV is better than spleen length in detecting abnormal spleen size (Fig. 5) and in assessing the severity of CLD (Fig. 7). An SV above the normal range in patients with CLD is strong evidence of a moderate or greater amount of histologic fibrosis. An SV twice the upper limit of normal is strong evidence for marked fibrosis or cirrhosis. Despite this, some patients with advanced CLD have a normal spleen size, and lack of spleen enlargement alone cannot be used to exclude cirrhosis. Overall, a routine SV measurement appears to add to the detection of serious liver disease and to the value of the LSS.

The pattern of spleen enlargement as liver disease progresses is of interest (Fig. 7 and Table 2). Paying

**TABLE 2**

<table>
<thead>
<tr>
<th>Cause of CLD</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Marked fibrosis or early cirrhosis</th>
<th>Moderate to advanced cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALD 16</td>
<td>0</td>
<td>2.37</td>
<td>0</td>
<td>3.99 ± 2.84†</td>
<td>5.46 ± 3.48†</td>
</tr>
<tr>
<td>HBV 34 (±Delta)</td>
<td>1.25 ± 0.69</td>
<td>2.52 ± 2.21</td>
<td>1.61 ± 0.96</td>
<td>3.05 ± 1.21†‡</td>
<td>6.28 ± 5.16†‡</td>
</tr>
<tr>
<td>HCV 134</td>
<td>1.65 ± 0.98</td>
<td>2.46 ± 2.44</td>
<td>2.44 ± 1.31†</td>
<td>3.37 ± 2.10‡‡</td>
<td>5.37 ± 2.95‡‡</td>
</tr>
<tr>
<td>Other 32</td>
<td>1.63 ± 0.60</td>
<td>1.91 ± 1.41</td>
<td>2.11 ± 1.60</td>
<td>3.31 ± 2.43</td>
<td>4.47 ± 3.13†</td>
</tr>
<tr>
<td>Total 216</td>
<td>1.55 ± 0.79</td>
<td>2.35 ± 2.24†</td>
<td>2.20 ± 1.32‡</td>
<td>3.38 ± 2.14†‡</td>
<td>5.43 ± 3.37†‡</td>
</tr>
</tbody>
</table>

*Times 2.2 to convert to cm³/kg IBW (i.e., in moderate to advanced cirrhosis 5.43 ± 3.37 cm³/lb becomes 11.95 ± 7.41 cm³/kg).
†Compared with normal, P < 0.05.
‡Compared with no fibrosis, P < 0.05.
§Advanced cirrhosis compared with marked fibrosis—early cirrhosis, P < 0.05. CLD = chronic liver disease; ALD = alcoholic liver disease; HBV = hepatitis B virus; HCV = hepatitis C virus. Normal spleen volume = 1.43 ± 0.68 cm³/lb IBW (3.15 ± 1.5 cm³/kg IBW).
particular attention to Figure 7, the distribution of SVs (expressed as the cumulative ratio of spleens of increasing volume) in patients with CLD is similar to normal in the absence of histologic fibrosis. However, in patients with mild to moderate precirrhotic fibrosis the initial portion of the curve is similar to normal but, at cumulative ratios greater than 0.60, a population of patients with large spleens is found. This is consistent with significant portal hypertension in 40% of patients with precirrhotic fibrosis causing early hypersplenism. Presinusoidal portal hypertension is common in nonalcoholic CLD, consistent with this interpretation (2,23). The presence of portal hypertension at an early stage may explain why some patients have massively enlarged spleens later on.

In contrast to patients with precirrhotic fibrosis, the whole cumulative ratio curves for patients with early and well-developed cirrhosis are shifted to the right, consistent with hypersplenism as a result of portal hypertension in the group as whole. Despite some patients with SVs within the normal range, no patients with well-developed cirrhosis had an SV < 1.25 cm³/lb IBW, whereas half the patients with precirrhotic fibrosis had spleens smaller than this. Presumably, cirrhotic patients with SVs within the normal range had very small initial SVs before portal hypertension was present (i.e., <0.6 cm³/lb IBW), which did not exceed the normal range, despite an increase in volumes by three to four times their baseline volume. Conceptually, lack of a large spleen in cirrhotic patients may be associated with a small baseline spleen or lack of portal hypertension at an early stage of fibrosis.

A low platelet count in patients with CLD is often associated with hyperfunction of the spleen as a result of spleen enlargement. The strong inverse correlation of spleen volume with the platelet count suggests the SV can be used to assess whether hypersplenism accounts for the degree of thrombocytopenia. A lower platelet count than typically seen for a given SV suggests the presence of some other factor such as platelet-associated IgG, antiplatelet antibodies, disseminated intravascular coagulation or bone marrow failure. Use of SV to assess parameters related to spleen function is another value of this technique.

The method proposed in this article is the same as indicator dilution measurement of volume. If the total amount of indicator placed in a volume is known, an unknown volume can be determined by dividing this known amount by the measured concentration in the fluid. In this method, the total amount of the ⁹⁹ᵐTc-sulfur colloid in the organ is measured, and the concentration is determined on a

**FIGURE 7.** Cumulative ratios of groups of patients with increasing spleen size at different histologic stages of CLD are given for 216 patients: spleen length (cm) (A), spleen volume (cm³) (B), spleen volume per IBW (cm³/lb) (C). Note shift in whole curve to right from healthy volunteers (•) and patients with no hepatic fibrosis (●) compared with patients with early (○) and advanced cirrhosis (■) compatible with spleen enlargement in nearly all patients in these groups, despite some spleen volumes within normal range in patients with noncirrhotic CLD. Only latter portions of curves in patients with mild fibrosis (□) and moderate fibrosis (●) are different from normal curve, indicating that only a portion of these patients has enlarged spleens.
single midorgan frame by dividing the total counts by the concentration. Many machine-related factors such as filters or body habitus attenuation factors that affect both the numerator and the denominator measurements cancel out in this equation, making volume determination insensitive to machine settings. Therefore, the accuracy of this method is affected primarily by the accuracy of total spleen counts and representative voxel concentration determination. The total count determination is very accurate and reproducible (±1.1%). A representative concentration could be determined from a histogram of all voxel concentrations in all frames or in a single frame rather than by small ROIs within a single midorgan frame. However, the single midorgan frame method seemed equally effective in this preliminary investigation (Appendix 1) and accurate as reported in this article, as long as end organ frames were avoided. Thus, we selected the single midorgan frame method that was simple enough for technologists using routine SV measurement.

This method is applicable to organs other than the spleen, but heterogenous distribution of counts in these organs may require a different method of calculating a representative voxel concentration. Both anatomic and functional volumes can be calculated, depending on how the representative concentration is calculated. Determination of an accurate total organ representative voxel concentration even in a heterogeneous organ should be an accurate determinant of the anatomic volume. Any method of determining the top 10% voxel concentration should produce a clear assessment of the functional volume. Large defects in the spleen not containing reticuloendothelial cells would not be measured as part of the calculated organ volume using the current method. Regardless, an accurate representative voxel concentration will produce an accurate anatomic or functional volume, depending on what is desired. In the spleen, the anatomic and functional volumes are nearly identical but, in the liver (with polycystic disease, for example), these two entities may be quite different. Application to other organs will require specific attention to the pathophysiology of those organs.

Spleen size is estimated by all noninvasive techniques and has been found to be a useful measurement. The edging techniques that have been used to noninvasively determine the anatomic SV by sonography, MRI and LSS are very sensitive to the criteria for edge determination and are sensitive to organ contour problems (4–21). A notable advantage of the proposed method is the lack of effect of shape. The edging technique does not measure functioning volume, which is a disadvantage for physiologic assessment. Measurement of the functional volume by LSS may have some advantages over assessment of volume by edging techniques and can easily be used to determine SVs on large populations and to determine the potential value of routine SV determination.

CONCLUSION

A new method is presented using SPECT LSS that estimates SV without edging techniques, is insensitive to machine settings and can easily be routinely measured. This technique is reproducible and correlates with autopsy assesse-
ment of SV. We believe this method will be a valuable addition to routine LSS assessment.

**APPENDIX 1**

Figure 1 is an example of the processing of the SPECT LLS, where T is the total spleen counts from an ROI around the summed transaxial SPECT scan (Fig. 1A), C mean is the mean count within a nine-voxel ROI from a single midorgan SPECT frame (Fig. 1C) and C max is the maximum voxel concentration for those nine voxels. The three ROIs are labeled 1, 2 and 3, and the values for those ROIs are given below.

<table>
<thead>
<tr>
<th>ROI 1</th>
<th>ROI 2</th>
<th>ROI 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area ROI</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Total counts</td>
<td>4012</td>
<td>4945</td>
</tr>
<tr>
<td>Mean count</td>
<td>445.8 - C mean</td>
<td>551.7 - C mean</td>
</tr>
<tr>
<td>SD</td>
<td>75.0</td>
<td>42.7</td>
</tr>
<tr>
<td>Max count</td>
<td>551 - C max</td>
<td>613 - C max</td>
</tr>
<tr>
<td>Min count</td>
<td>348</td>
<td>492</td>
</tr>
</tbody>
</table>

ROI = region of interest; SD = standard deviation.

The representative voxel concentration was then calculated from a single midorgan frame by the four methods as noted below for Figure 1. The only method reported in the text was C max 2.

**Representative Voxel Concentration Methods**

\[
C_{lg} = C_{\text{mean}}^2 = 552
\]
\[
C_{\text{avg}} = \left( C_{\text{mean}}^1 + C_{\text{mean}}^2 + C_{\text{mean}}^3 \right) / 3 = 501
\]
\[
C_{\text{max}}^3 = \left( C_{\text{max}}^1 + C_{\text{max}}^2 + C_{\text{max}}^3 \right) / 3 = 562
\]
\[
C_{\text{max}}^2 = \left( C_{\text{max}}^1 + C_{\text{max}}^2 \right) / 2 = 582.
\]

The representative voxel concentration was also calculated from an analysis of the spatial resolution and from a histogram of each individual frame in early investigations (data not reported). These techniques were more time-consuming using our equipment and no more effective in calculating SVs. Thus, technologists could be used to select the three ROIs in a single midorgan frame as represented in Figure 1, simplifying processing of routine volumes on the LSS.

The correlation of the calculated volume with external phantoms is shown below, and all P values were < 0.0001. These equations were used as a calibration factor for each technique:

\[
SV_{\text{avg}} = \left( \frac{1.8349 \times 10^6}{552} \right) \times 0.9223 - 67.7 = 736 \text{ cm}^3
\]
\[
SV_{\text{lg}} = \left( \frac{0.26214 \times 1.8349 \times 10^6}{501} \right) \times 0.8763 - 72.5 = 769 \text{ cm}^3
\]
\[
SV_{\text{max}}^3 = \left( \frac{0.26214 \times 1.8349 \times 10^6}{562} \right) \times 0.9186 - 60.1 = 726 \text{ cm}^3
\]
\[
SV_{\text{max}}^2 = \left( \frac{0.26214 \times 1.8349 \times 10^6}{582} \right) \times 0.9562 - 66.5 = 724 \text{ cm}^3
\]

All methods were equally effective in calculating SVs, if properly calibrated with phantoms. SVs by the different methods correlated with one another (r > 0.99). We selected the SV max 2 method as the single best technique and it is the one reported in the text. The calculated SVs in healthy volunteers were similar with the four methods: SV avg 226 ± 82 cm³ (1.56 ± 0.64 cm³/lb IBW); SV lg 214 ± 78 cm³ (1.47 ± 0.62 cm³/lb IBW); SV max 3 214 ± 74 cm³ (1.48 ± 0.63 cm³/lb IBW); and SV max 2 201 ± 77 cm³ (1.43 ± 0.68 cm³/lb IBW).

**APPENDIX 2**

**Spleen Volumes by CT**

A separate cohort of stable patients with LLS within a last 4-mo period were retrospectively evaluated for having CT scans during the same period and whose CT data were still stored on the computer. These CT scans were independently analyzed for SVs. Abdominal CT scans were obtained with CT and CT Advantage scanners (General Electric, Inc.) using helical scans through the upper abdomen with 7-mm collimation and a pitch of 1.3. The studies were obtained in breath-hold and reconstructed with a slice thickness of 7 mm. Most of the studies were performed with intravenous contrast agents, and the regions were drawn on whatever imaging sequence that showed the spleen optimally. The images were reviewed, and sequential images showing the spleen were identified. A manual ROI was drawn closely around the spleen on each slice, and the area of this irregular ROI was computed automatically. The areas of each spleen slice were summed and multiplied by the thickness of each slice (7 mm). This calculated spleen volume by CT scan was compared with the volume by LLS.

The difference in time between the LLS and the CT varied from 0 to 80 d (mean difference of 27 ± 25 d). The SV by LLS (488 ± 221 cm³) correlated with the CT SV (552 ± 202 cm³): y = 0.856x + 135; r = 0.940; P < 0.05. In general, the SVs were slightly larger by the CT scan method, particularly with small spleens.

**REFERENCES**


