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● *Original Contribution*

ESTIMATION OF THE HUMAN LIVER VOLUME AND CONFIGURATION USING THREE-DIMENSIONAL ULTRASONOGRAPHY: EFFECT OF A HIGH-CALORIC LIQUID MEAL

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Abstract—The aim of this study was to investigate whether or not a magnetic position sensing system for free-hand acquisition of 3-D ultrasound images could be used to estimate liver volumes, and to study the effect of a high-caloric meal on these volumes in healthy subjects. *In vitro* accuracy was evaluated by scanning porcine and rabbit livers. Ten healthy subjects were examined fasting and 30 min after ingesting a high-caloric liquid meal. Portal and hepatic vein blood flow were measured by 2-D duplex sonography. The 3-D system yielded a strong correlation (r = 0.99) between true and estimated volumes *in vitro*. No significant increase in liver volume in response to the meal was seen. However, portal and hepatic vein flow volume increased significantly. Experience in human subjects suggests that a complete 3-D study of liver volumes can be obtained from multiple acoustic windows. In healthy subjects, no significant increase in liver volume was seen in response to ingestion of a high-caloric liquid meal.

Key Words: **Doppler, Hepatic vein, Liver volume, Portal vein, Postprandial, Three-dimensional, Ultrasonography.**

INTRODUCTION

Quantitative anatomic measurements and knowledge of the size, shape, volume, tissue integrity and perfusion pathways of an individual's liver can be very valuable. Physiologically, it is of interest to know how these measures are affected by various conditions. For example, splanchnic blood flow is known to be altered by fright, stress, exercise, temperature, gravity and digestion; however, the effect of these on liver volume in man is unknown. Furthermore, numerous pathological conditions occur that may affect these liver variables. For example, in surgically treatable tumors, it is advantageous prior to surgery to know the exact location, size and perfusion associated with the affected region of the liver. The surgical plan may, thus, be much more effectively implemented with such definitive knowledge. During and after surgical recovery, it may be of diagnostic and therapeutic value to know whether and how much regeneration occurs after liver resection.

Consequently, liver size assessment is an essential part of clinical examination, and this is usually deduced by palpation and percussion. Despite training and experience, such evaluation can only be crude and is, at times, inaccurate and misleading (Blendis et al. 1970; Meyhoff et al. 1979). Several imaging modalities are available to the clinician for volume measurements. The noninvasive modalities are sonography (Kardel et al. 1971), computerized tomography (CT) (Henderson et al. 1981) and magnetic resonance imaging (MRI) (McNeal et al. 1988).

Using two-dimensional (2-D) ultrasonography, liver volume can be estimated by ultrasonic planimetry (*i.e.*, calculation of liver volume from sagittal or transverse liver slices of 1 cm thickness) (Kardel et al. 1971; Raeth et al. 1984; Van Thiel et al. 1985; Wynne et al. 1989). The techniques have been validated using CT (Van Thiel et al. 1985) with good correlation between methods. Van Thiel et al. (1985) found that the sonographic technique was more accurate than the computed tomography scan

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method because it allowed the use of sagittal scanning of the liver, which is superior to the transverse scanning technique required by the computed tomography scanner. The shortcomings of this method are that it does not use a geometrical model and, thereby, may miss regions of the liver.

Recently, three-dimensional (3-D) ultrasound imaging techniques have been developed by our research group. In one method, the transducer is tilted and swept, by a motor drive, over an angle of 90°, and sequential 2-D image frames are captured. These captured images are then transferred to a graphic workstation for final 3-D processing. This 3-D ultrasound system has been validated both *in vitro* and *in vivo*, and yielded high accuracy and precision in volume estimation of abdominal organs (Gilja et al. 1995b; Thune et al. 1996). The system has been used to measure gallbladder volume (Hausken et al. 1994), to study diseases of the liver (Hokland and Hausken 1994), and for volume computation of the distal stomach (Gilja et al. 1995a). The system, however, is limited by its predetermined, single position of the transducer, which does not provide comparable interrogation of large abdominal organs such as the stomach and the liver for accurate quantitative analysis. In addition, it may result in suboptimal views of some structures.

It is important to have a 3-D ultrasound imaging system that can acquire and combine images from different imaging positions for 3-D liver reconstruction. We have previously built a prototype hardware and software system for quantitative 3-D ultrasound that can acquire and combine images from multiple acoustic windows. A magnetic field system tracks the location and orientation of the ultrasound scanhead to allow rapid freehand scanning, and the software is designed to analyze images acquired using any 3-D tracking system and combination of imaging planes, including rotated, angulated, parallel, or randomly oriented planes; its features include 3-D reconstruction of the organs, and quantitative analysis of volumes (Leotta et al. 1997b). The system has been tested *in vitro* (balloons, animal hearts and pig stomachs) and it yields excellent correlation between true volumes and estimated volumes (Leotta et al. 1997b; Gilja et al. 1997). For pig stomachs, the limits of agreement were −9.1 mL to 70 mL in the volume range 1200–1900 mL, with a mean error of the volume range of 2.11.1% (Gilja et al. 1997).

It is well documented that intestinal blood flow increases markedly in response to a meal (Moneta et al. 1988; Dauzat et al. 1994; Hoost et al. 1996; Sadek et al. 1996). In healthy volunteers, Dauzat et al. (1994) found that the portal vein blood flow markedly increased after a meal. Some data in animals indicate that portal flow exerts a trophic effect that controls liver mass (Greenway and Lautt 1989). The effect of a meal on liver volume in humans has, however, not been investigated in a controlled study.

The objectives of this study were, first, to determine the *in vitro* accuracy of the magnetic tracking system in volume estimation of porcine and rabbit livers of different sizes. Second, we wanted to assess whether or not this system for 3-D imaging was applicable for scanning of the total liver in healthy controls. If a quantifiable volume measure was obtained, we wanted to examine a physiological question that, to our knowledge, has not been answered. This was to measure size of the liver in the fasting state and in response to a standardized meal in healthy subjects. To be sure increased blood flow to the liver occurred after the standard meal, we also wanted to measure blood flow to and from the liver.

MATERIAL AND METHODS

Subjects

Ten healthy men were studied. The median age was 31 y (range 22–37 y), weight 71.3 ± 9.8 kg (mean ± SD), height was 178.5 ± 7.5 cm (mean ± SD), and body surface area was 1.89 ± 0.15 m^2. Before inclusion into the study, a medical history was obtained, and ultrasound examination of the liver, pancreas and biliary tract was performed to rule out diseases of the upper gastrointestinal system. Criteria of exclusion from the study were previous surgery in the upper gastrointestinal tract, previous peptic ulcer disease, alcoholism, or use of any medication. To study intraindividual variability, 1 healthy man, age 28 y, weight 56.7 kg and height 167 cm was examined on 8 consecutive weekdays. He was investigated in the morning after 12 h of fasting.

The study was approved by the International Review Board of the University of Washington and conducted in accordance with the revised Declaration of Helsinki. All volunteers gave written informed consent to participate in the study.

Three-dimensional ultrasound system

Magnetic tracking system. A commercial magnetic position and orientation measurement system (Flock of Birds model 6DFOB, Ascension Technology Corp., Burlington, VT) was used to track the ultrasound scanhead. Three orthogonal coils in a compact receiver, mounted on the scanhead, sense orthogonal magnetic fields sequentially generated by a transmitter. The tracking system can operate over a range of 91 cm. The region of operation must be kept clear of ferromagnetic materials, which introduce inaccuracies in the location measurements through distortion of the magnetic fields.

Calibration is required to define the relationship between the magnetic receiver and the ultrasound imaging plane, so that points in an ultrasound image can be

located in the transmitter's 3-D coordinate system. The magnetic tracking system and calibration procedure have been previously described in detail (Detmer et al. 1995; Leotta et al. 1997a). The precision for the calibrated scanhead/receiver combination was found to be 1.04 mm. Precision was defined as the root-mean–square uncertainty (variation) in locating the same point in space when imaging from any arbitrary position and orientation around the point.

The receiver was attached to a 5–3-MHz phased array sector-scan ultrasound scanhead connected to an HDI 3000 ultrasound platform (Advanced Technology Laboratories, Inc., Bothell, WA). Images were collected using an ImageVue workstation (Nova Microsonics, Mahwah, NJ), under control of a 486 personal computer running custom software designed in the LabView programming environment (National Instruments Corp., Austin, TX). Position data were also digitally recorded on the personal computer under control of LabView software. The ultrasound transducer's distance from the magnetic transmitter ranged from 35–75 cm during imaging. Imaging was performed with the capture system configured for rapid data acquisition. Images and scanhead position information were synchronously recorded every 66 ms (15 frames per s) for a time period specified by the operator. The scanhead was free to be manually manipulated from multiple acoustic windows and imaging positions (tilted, translated and/or rotated) during image capture. The available computer memory established a maximum capture period of 32 s (480 images); the capture period was set to 8 s for the studies described below.

In vitro validation

All *in vitro* tests, performed on 10 pig and rabbit livers of different sizes, were conducted in a plastic tank filled with a hypertonic saline solution (4.6% salinity at 22°C). The speed of sound in this solution is equal to the value typically assumed for the speed of sound in tissue (1540 m/s). The livers were scanned with parallel and slanted scans from different directions to simulate how an organ might be scanned in the clinic. The capture periods were 8 s (120 images), and 2 capture periods were needed for each liver. Immediately after scanning, each liver was placed in a 3000-mL graduated cylinder to measure the volume of water displaced.

Test meal

Two cans of a commercial mixed liquid meal (Ensure-Plus, Ross Laboratories, Columbus, OH) were prewarmed to 37°C and ingested over 3 min. The total volume was 480 mL, and total energy was 710 kcal. The meal contained 26.0 g protein, 25.2 g fat and 94.6 g carbohydrate. The osmolarity was 550 mOsm/L. This mixed meal is appropriate in stimulating portal blood flow and it has its maximal blood flow response 30 min after the meal (Moneta et al. 1988).

Experimental protocol

All participants were investigated after an overnight fast in the morning between 8 and 10 a.m. Imaging was conducted with the subjects lying supine on a custom-built wooden bed.

Liver volume imaging. The ultrasound probe was positioned at the epigastrium and intercostally. Scans were obtained in three separate 8-s periods of suspended midinspiration. Images were captured continuously while freely moving the ultrasound probe in standardized directions (translation and tilting, Fig. 1a,b,c) to cover the entire liver. The three image sets (120 images each) were obtained in a total of 60 s, which included the time between breath holds. Each subject was imaged first fasting and then 30 min after the meal.

Duplex measurements and calculations

Duplex Doppler ultrasonography was used in the measurement of portal and hepatic vein blood flow in the fasting state and 30 min postprandial, with the subject in the supine position. The cross-sectional area (in cm^2) and the mean velocity (in cm/s) were measured during suspended normal expiration. To determine the mean velocity, a caliper was placed at peak systole of one cardiac cycle and a second caliper was placed at peak systole of the third subsequent cardiac cycle. A Doppler angle of less than 60° was chosen. The area and velocity measurements were obtained by using the built-in program of the ATL apparatus, and by averaging three consecutive measurements. The flow volume (in mL/min) was calculated as area $\times$ mean velocity $\times$ 60. A cut-off filter of 100 Hz was used to eliminate possible artefacts from wall motion.

The area of the portal vein was obtained by measuring the diameter of the portal vein at the level of the intersection with the hepatic artery. The velocity of the portal vein blood flow in the portal trunk was scanned longitudinally and the sample volume covering the total vessel was positioned at the level of the intersection with the hepatic artery (Moneta et al. 1988).

Using the right upper quadrant transverse approach, or scanning between the ribs, the right or middle hepatic vein was imaged and utilized for measurements (Zierler et al. 1991). The same location and the same branch were used for measurements before and after the meal.

Volume estimation and surface reconstruction

Using a custom tracing program running on a dedicated Indigo workstation (Silicon graphics, Inc., Moun-

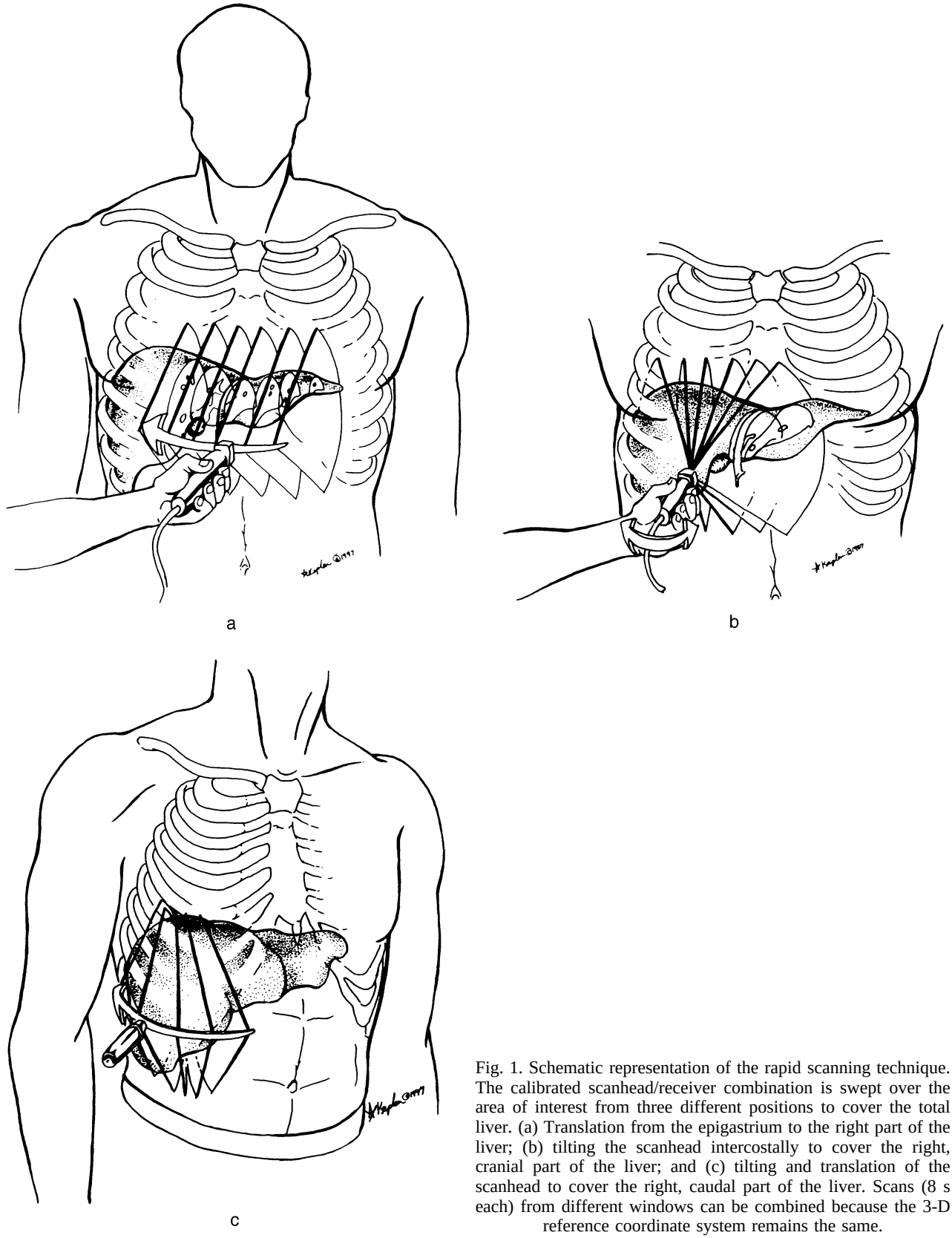

Fig. 1. Schematic representation of the rapid scanning technique. The calibrated scanhead/receiver combination is swept over the area of interest from three different positions to cover the total liver. (a) Translation from the epigastrium to the right part of the liver; (b) tilting the scanhead intercostally to cover the right, cranial part of the liver; and (c) tilting and translation of the scanhead to cover the right, caudal part of the liver. Scans (8 s each) from different windows can be combined because the 3-D reference coordinate system remains the same.

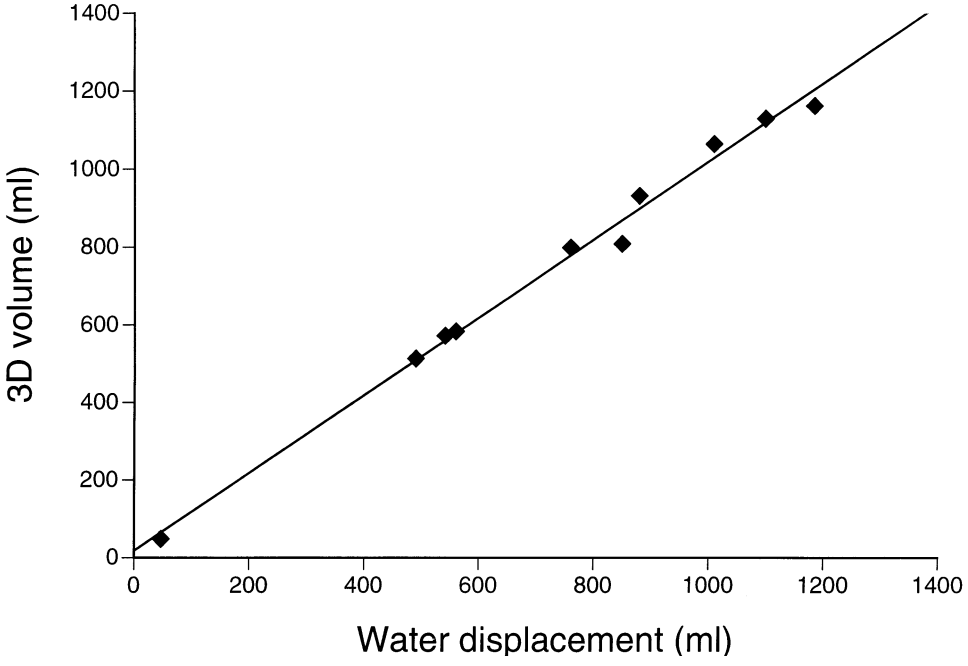

Fig. 2. Calculated volume (3-D volume) plotted against true volume (water displacement) of *in vitro* livers.

tain View, CA), the borders of the liver surface were manually identified. The tracing program was interfaced with the software package AVS (Advanced Visual Systems, Inc., Waltham, MA), providing interactive 3-D visualization and editing of outlines. Border registration could be examined with 3-D stereo viewing glasses (CrystalEyes, Stereographics Corp., San Rafael, CA).

The 3-D reconstruction technique used a piecewise smooth subdivision surface method that fitted the 3-D traced points to a model of a balloon (Bolson et al. 1995). The fitting procedure not only minimizes the distance between the points on the traced borders and the reconstructed surface, but also the lengths of the edges. Points from the different imaging planes that fall in close proximity or in the exact same location are simply included in the minimizing process as individual points. The volumes of the 3-D reconstructed surfaces were computed by summing the volumes of the tetrahedra formed by connecting a point inside the liver with the vertices of each face.

Statistical analysis

The measurements are given as mean values ± SD of each parameter, if not stated otherwise. Pearson's correlation coefficient was determined as an initial measure of association between true and estimated volumes. Linear regression equations were calculated to compare true values for volumes to measurements made from the 3-D reconstructions. Furthermore, limits of agreement were estimated as suggested by Bland and Altman (1986). The percent error of the measurements was defined as mean ((estimated volume − true volume)/true volume) × 100%. The coefficient of variation (C_V) was expressed as the standard deviation divided by the mean multiplied by 100. The distribution of data was evaluated by inspecting a probability plot and by utilizing Kolmogorov–Smirnov test with Lilliefors subanalysis. If the data appeared normally distributed, Student's *t*-test with 2-sided probabilities was used to compare differences between the groups. If not normally distributed, a nonparametric test was applied. A p value < 0.05 was chosen as the level of statistical significance. All calculations and graphic designs were performed using commercially available computer software: Microsoft Excel V5.0 for Windows (Microsoft, Redmond, WA) and SPSS for Windows.

RESULTS

The magnetometer-based system for acquisition and processing of 3-D data proved to be applicable both for *in vitro* and *in vivo* imaging of the liver.

In vitro imaging

The average residual distance from the traced borders to the fitted surface was 2.1 ± 0.8 mm for the *in vitro* livers. The average number of traced borders acquired to reconstruct the livers was 39 ± 16. The 3-D

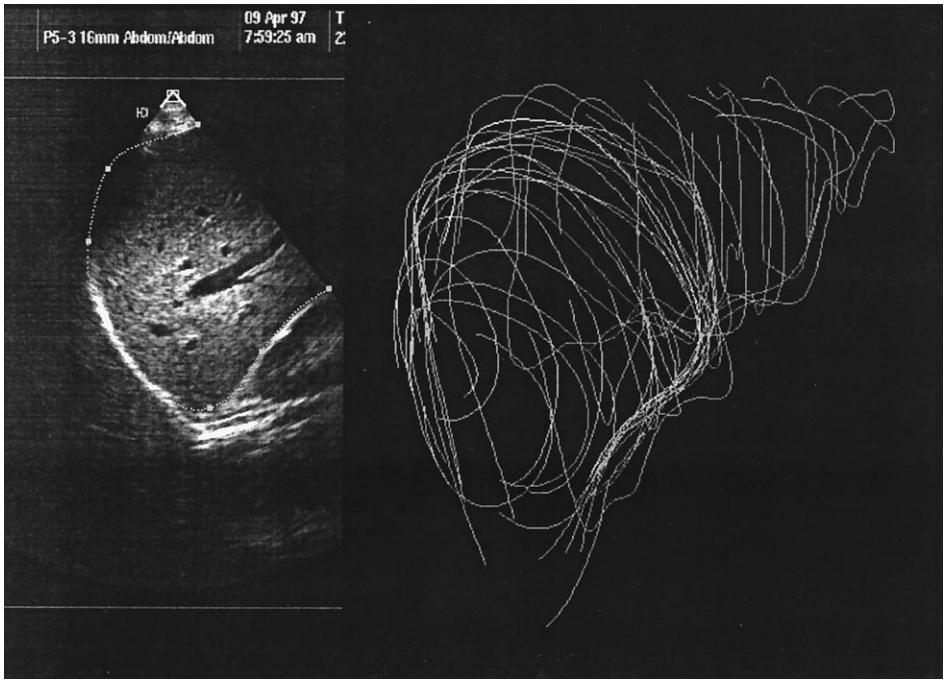

Fig. 3. Left: ultrasound image of the liver with traced borders superimposed. Right: traced borders of the total liver from three different windows.

system yielded an excellent correlation ($r = 0.99$) between true and and estimated volumes (Fig. 2). The liver volumes were overestimated by an average of 19.2 ± 31 mL over the range of 47–1185 mL, giving a mean error of 4.2 ± 1.5%.

In vivo imaging

We acquired 3 image sets (120 images each) from 3 standardized acoustic windows for each liver scan (Figs. 3, 4). The average number of traced borders needed to reconstruct the *in vivo* livers was 34 ± 4. The average residual distance from the traced borders to the fitted surface was 3.4 ± 0.7 mm (including fasting and postprandial measurements). The depth of scanning used to image the liver was 19.9 cm for all acquisitions.

The intraindividual variability of the liver volume measurement was assessed for the fasting liver of 1 healthy volunteer on 8 consecutive days. The measurements varied between 906 mL and 1066 mL, giving a coefficient of variation (V_C) of 4.9% (Fig. 5). In the 10 healthy subjects, the fasting liver volumes ranged between 998 mL and 2067 mL, giving a mean liver volume

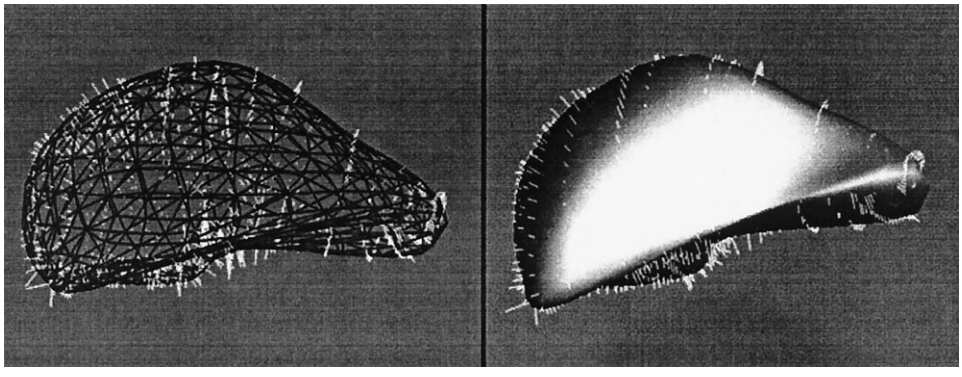

Fig. 4. *In vivo* reconstruction of the total liver. Left: subdivision mesh fit to the traced border points. Right: final reconstructed surface fit to the traced border points. The "hair-like" structures are lines between the fitted surface and the traced points used for the reconstruction. The shorter the "hairs" in a region, the better the fit there.

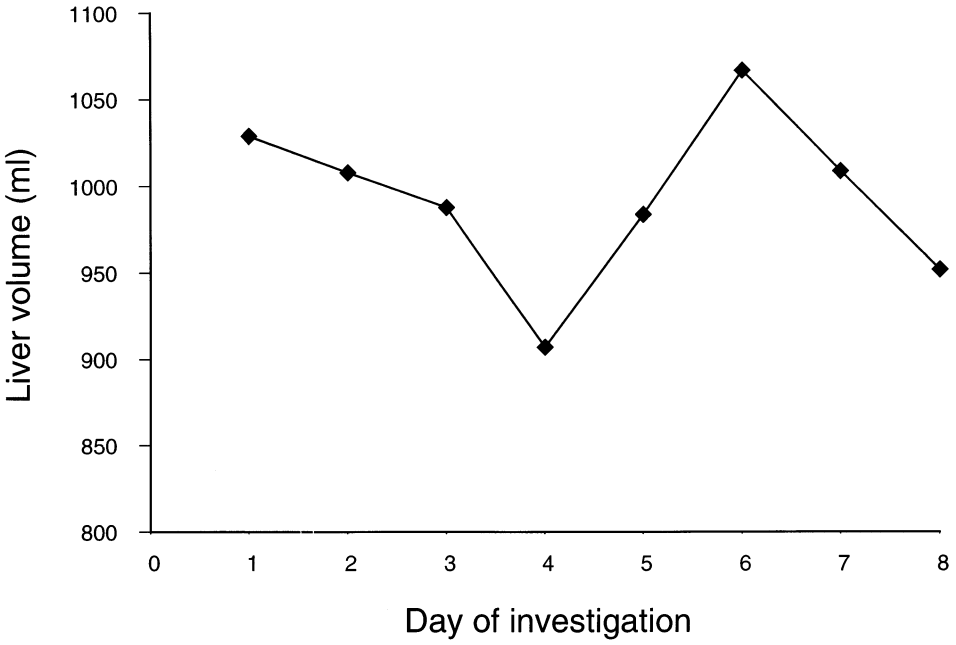

Fig. 5. Fasting liver volume measurement variability of one healthy volunteer on 8 consecutive days.

of 1349 ± 321 mL. Significant positive correlations between liver volume and body surface area and between liver volume and height were found ($r = 0.72$, $p = 0.02$ and $r = 0.74$, respectively, $p = 0.01$) (Fig. 6). The statistical correlation between weight and liver volumes tended to be significant ($r = 0.60$, $p = 0.06$). Thirty minutes after meal ingestion, the liver volumes increased by 3.1 ± 1.4% and the mean volume was 1367 ± 334 mL (Fig. 7). This small increase from fasting to postprandial liver volume was not statistically significant ($p = 0.5$). Of 10 subjects, 8 experienced fullness after the meal. Velocity and flow volume were found to increase after the meal. Portal vein diameter, mean velocity and flow volume increased significantly from fasting to post-

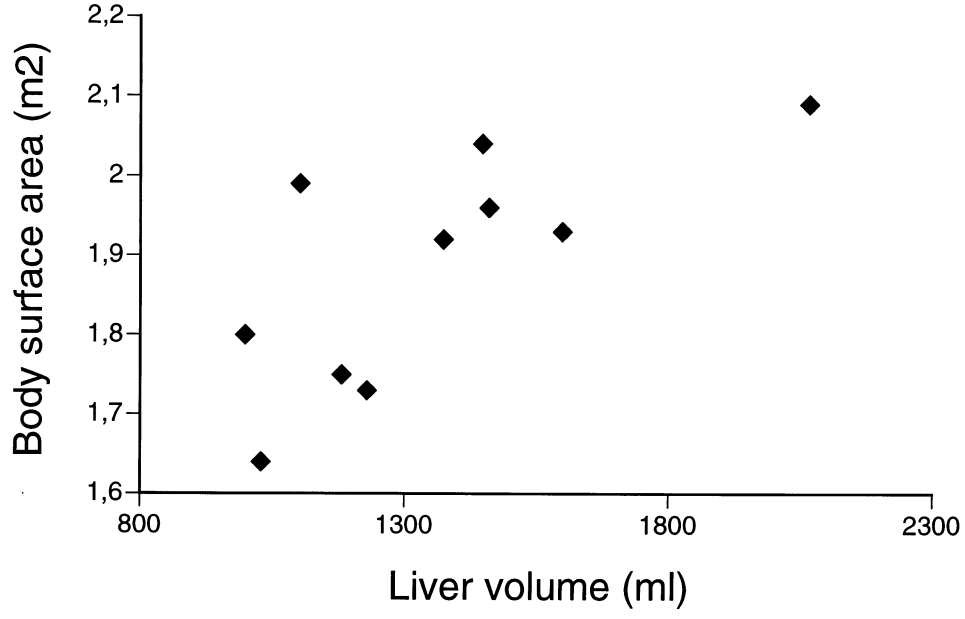

Fig. 6. Body surface area plotted against calculated fasting 3-D liver volume in 10 healthy volunteers.

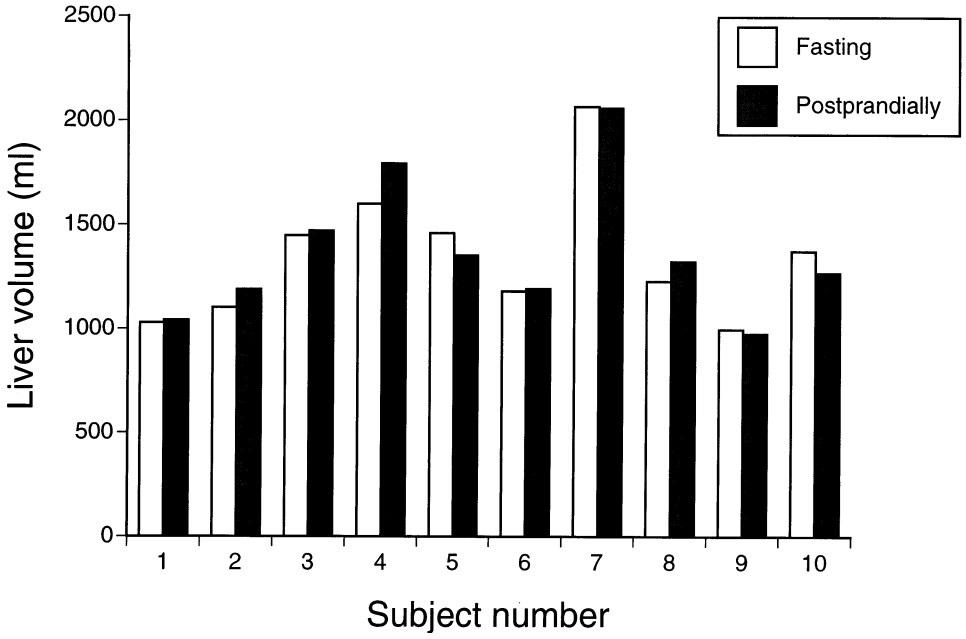

Fig. 7. Calculated 3-D liver volumes fasting and 30 min after a standardized meal in 10 healthy volunteers.

prandial values (diameter: 0.92 ± 0.19 cm to 1.13 ± 0.15 cm, $p = 0.02$, mean velocity: 12.7 ± 4.7 cm/s to 17.3 ± 6.1 cm/s, $p = 0.003$, flow volume: 508 ± 183 mL/min to 1038 ± 369 mL/min, $p = 0.002$). The mean velocity and flow volume in a hepatic vein branch increased significantly from fasting to postprandial values in each subject (mean flow volume 120.2 ± 38 mL/min to 191.9 ± 51 mL/min, $p = 0.003$, and mean velocity 6.2 ± 1.9 cm/s to 10.4 ± 3.3 cm/s, $p = 0.001$). The diameter of the hepatic vein branch did not increase significantly (0.62 ± 0.1 cm to 0.64 ± 0.1 cm, $p = 0.5$).

DISCUSSION

We have described a 3-D imaging system that accurately reproduces volumes of livers *in vitro*; we have also demonstrated the feasibility of the system for use in humans under clinical conditions. This is the first study reconstructing volume and shape of the human liver using 3-D ultrasonography, and the first study quantifying liver blood inflow and outflow together with liver volume in response to a meal. No statistically significant increase in liver volume was seen in response to the standardized meal.

The advantages of this system can be attributed to (a) scanhead tracking, (b) surface reconstruction, and (c) rapid image acquisition. The magnetic tracking system provides views from multiple acoustic windows and imaging positions for volume estimation and evaluation of the configuration of large abdominal organs, such as the human liver. The system allows unrestricted positioning and movement of the transducer during scanning (Gilja et al. 1997). Therefore, three acoustic windows could be chosen for optimal coverage. Mechanical devices (translation, rotation or tilt) provide views from only one acoustic window, which is inappropriate for scans of the total liver.

Improved volume estimation is also attributed to the surface-fitting technique. The process we use results in an average fitting error from 2 mm *in vitro* to 3 mm *in vivo*. This was achieved by the model-based approach, which eliminated the need for assumptions or approximations of liver shape.

Data acquisition time for a liver volume scan was completed in approximately 45 s, which is markedly improved compared to liver volume measurements using the 2-D planimetry ultrasound method (15 min). Liver volume using 2-D planimetry was acquired by a serial longitudinal scans at 1-cm intervals of the whole organ in deep inspiration (Raeth et al. 1984) Rapid image acquisition minimizes artefacts due to subject movement, and reduces patient discomfort.

The 3-D system overestimated the true volumes of the *in vitro* livers with an average of 19 mL in the volume range of 47–1185 mL (error of 4.2%). The pig liver is relatively flat and consists of 3 major lobes. By putting the liver in a tank with hypertonic saline, small amounts of liquid were hidden between the lobes. Our fitting program included these volumes of liquid and was, therefore, the main reason for the overestimation seen. Previously described 2-D ultrasound methods based on

planimetry have an error of 8–13% in reproducing cadaver liver volume (Rasmussen 1972); Raeth et al 1984).

Despite a small overestimation, the present ultrasound system displayed high accuracy *in vitro*. Although we cannot immediately extrapolate these results to *in vivo* conditions, we have reason to believe that the results obtained *in vivo* are of acceptable accuracy. Compared to previous 2-D ultrasound methodological studies of human liver volumes, the variability found in our study is similar. In these studies, the intraindividual day-to–day variation in volume shows a coefficient of variation between 5.4 and 6.5% (Kardel et al. 1971; Raeth et al 1984; Wynne et al. 1989). Because liver volume may change from day to day in relation to exercise, hydration and glycogen content (Leung et al. 1986) , the intraindividual day-to–day variation in volume of 4.9% may be partly accounted for by real changes in liver volume.

Although complete validation of the method is difficult in the living subject, the correlation between liver volume measured by 3-D ultrasound and body surface, as well as with height, is further evidence of the accuracy of the method. The correlation with body surface area and height is in good general agreement with other radiological (ultrasound, CT) studies (Leung et al. 1986; Wynne et al. 1989; Urata et al. 1995).

No significant increase in liver volume in response to the meal was seen. This is the first standardized study investigating the effect of a meal on liver size. Our results are consistent with those found in nonstandardized studies of the effect of a meal on liver volume. Leung et al. (1986), using 2-D ultrasonography, found no effect of food consumption (not standardized), posture, diuresis or circadian rhythm on liver volume in healthy subjects. They, however, found a diurnal variation in liver volume with a minimum between 12 am and 2 pm. The mean liver volume was 1443 $\pm$ 54 mL and the mean fall in volume was 17% (range 9–31%). The effect of a meal on liver volume as measured by 3-D MRI was also investigated in a recent study by Petersen et al. (1996). These investigators measured liver volume in 4 healthy subjects in the evening 1 h after a mixed meal (average of 1430 $\pm$ 90 mL) and again 12 h later before breakfast. No significant changes in liver volume were found between the two times.

We found a significant increase in portal and hepatic vein mean velocity and blood flow volume in response to the meal. Because blood flow was measured in branches of the hepatic veins and no information of hepatic artery flow was obtained, no conclusions from this study regarding total hepatic blood flow can be drawn. Nevertheless, using duplex sonography, changes in liver blood flow can be quantified. The fact that the hepatic vein flow volume and, thereby, the outflow from the liver increased together with the blood inflow from the portal vein may explain why no significant blood pooling and increase in liver size was found. In healthy volunteers, Dauzat et al. (1994) found that the portal blood flow markedly increased after a meal; the hepatic artery however, demonstrated an increase in resistance. These findings suggest that there is an adaptation of hepatic artery to portal vein blood flow after a meal. The interaction between these two vessels suggests further that, if portal flow increases, the hepatic artery flow will decrease, according to the "hepatic arterial buffer response" described by Lautt (1985), thus keeping the total liver blood flow constant.

In the present study, liver volumes were measured 30 min after meal ingestion. We cannot exclude the possibility that significant changes in liver volume might have been found if the measurements had been performed at an earlier time-point after the meal. The portal vein inflow may initially increase more than the hepatic vein outflow and a significant blood pooling in the liver may occur.

A further study with measurements at several timepoints after meal ingestion is necessary. It would also be of interest to study the interaction between liver blood in- and outflow together with liver volumes in response to a meal in circumstances with resistance to hepatic vein outflow, such as in patients with right heart failure.

Several limitations still exist with our current 3-D system. First, the subject must suspend respiration at a fixed point for each set of acquired images. This is important because the position of the liver varies considerably depending upon the level of respiration. We chose to suspend the respiration at the midinspiration to prevent air in the right lung from covering part of the liver. A monitor to standardize the level of respiration may improve the accuracy of the method. Second, in the present study, a sector scanner was used. Liver images would have been improved by using a curved array scanner. Third, the magnetic tracking system is subject to inaccuracies in the presence of ferromagnetic materials. Therefore, it is of major importance that the laboratory environment is evaluated carefully to avoid spatial distortion of the data. The distance from the scanner itself to the sensor on the scanhead should preferably be at least 40–60 cm, and the bed must be made of material that does not influence magnetic fields. Fourth, manual selection and tracing of liver borders is required, a process that takes 30–45 min for each subject. Semiautomatic border detection programs may improve accuracy and reduce the time needed for volume reconstruction and volume estimation.

The ultrasonographic method to reconstruct the human liver in three dimensions and to estimate its volume has a number of potential clinical applications, as well as advantages over liver volume estimates by computerized

tomography. Advantages over CT scan are that the ultrasound method is faster, can be performed at the bedside, is inexpensive and involves no exposure to radiation. The avoidance of radiation is particularly important if repeated measurements are made in humans. In chronic and acute liver disease, the ability to accurately measure liver volume may be of clinical importance in both the management of some patients, as well as in predicting short- and long-term outcome (Leung et al. 1986; Zoli et al. 1990; Brunt et al. 1991).

Patients with cirrhosis and a small liver may have less hepatic reserve than cirrhotics with normal size livers, and the ability to identify these patients might influence therapeutic decisions. For example, patients with small livers are believed to be at risk for liver failure and/or encephalopathy after portal-systemic shunting and are, thus, usually not subjected to operation. Prospective trials are needed in these patients to correlate serial changes in liver volume with other well-established predictors of liver function. Such trials would be much easier and cheaper to perform by employing our technique as opposed to using CT scanning.

Accurate preoperative assessment of liver volume is important prior to liver resection in patients with liver tumors (Kinoshita et al. 1986; Soyer et al. 1992; de Baere et al 1996). Patients with predicted inadequate residual liver volume following liver resection are at substantial risk for postoperative liver failure and death, particularly when estimates of liver volume are combined with functional tests of hepatic reserve (Okamoto et al. 1984; Kinoshita et al. 1986; Yamanaka et al. 1994). Alternatively, preoperative portal vein embolization can be performed to hypertrophy the nonembolized liver lobe. If the nonembolized side of the liver regenerates to a sufficient size, resection can proceed with little risk of postoperative liver failure (Kinoshita et al. 1986). Our 3-D ultrasonic method for estimating liver volume could be used as an alternative to CT scanning to sequentially follow hypertrophy of the nonembolized liver lobe and identify when optimal regeneration has occurred. The ability to accurately monitor liver regeneration on a daily basis with this easy, noninvasive modality would provide a valuable research tool for studying the process of liver regeneration.

Ultrasonic volume estimates could also be used to accurately measure the volume of tumors within the liver over time. Volumetric assessment of tumor volume by CT and MRI in two dimensions, although crude, is currently the "gold standard" method for monitoring objective response to chemotherapy, radiation, and other forms of nonresection ablation (Miller et al. 1981). The 3-D ultrasound method of following tumor volume has the potential to become the preferred method of monitoring response to therapy for many cancers involving the liver.

In conclusion, the results of the present study indicate that the 3-D ultrasonographic reconstructions obtained by the described technique are accurate in reproducing liver volume *in vitro*. Experience in humans suggests that a complete 3-D study of liver volumes, as well as other liver variables, can be obtained from multiple acoustic windows with this method. Finally, in healthy subjects no significant increase in liver volume was seen in response to ingestion of a high-caloric liquid meal.

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