In vitro estimation of foetal liver volume using ultrasound, x-ray computed tomography and magnetic resonance imaging

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Abstract. Sixteen formalin-fixed foetal livers were scanned *in vitro* using a new system for estimating volume from a sequence of multiplanar 2D ultrasound images. Three different scan techniques were used (radial, parallel and slanted) and four volume estimation algorithms (ellipsoid, planimetry, tetrahedral and ray tracing). Actual liver volumes were measured by water displacement. Twelve of the sixteen livers also received x-ray computed tomography (CT) and magnetic resonance (MR) scans and the volumes were calculated using voxel counting and planimetry. The percentage accuracy (mean ± SD) was 5.3 ± 4.7%, −3.1 ± 9.6% and −0.03 ± 9.7% for ultrasound (radial scans, ray volumes), MR and CT (voxel counting) respectively. The new system may be useful for accurately estimating foetal liver volume in utero.

Keywords: volume, computed tomography, magnetic resonance, three-dimensional ultrasound

1. Introduction

The volume of a foetal organ can be accurately measured using any tomographic imaging modality such as computed tomography (CT) and magnetic resonance (MR) imaging. For instance, MR has been used to estimate foetal liver, lung and brain volume in foetuses in the third trimester (Mansfield et al 1990, Stehling *et al* 1990, Roberts *et al* 1994, Baker *et al* 1994, 1995). However, for safety reasons, MR is not used to scan foetuses in the first trimester (Saunders 1991), and is too expensive and time consuming for generalized obstetric use beyond the first trimester. CT is never used to scan foetuses because of the well-known risks of x-radiation. Therefore, ultrasound is the modality of choice in obstetrics. Ultrasound is routinely used to estimate foetal dimensions, for example head diameter, abdominal circumference and femur length, from which the total foetal volume is inferred.

The ratio of foetal liver volume to whole-body foetal volume may be important in indicating intrauterine growth retardation. This paper describes the use of a 3D ultrasound system, based on an electromagnetic localizer, for measuring foetal liver volume. Details of the system have been previously described (Hughes *et al* 1996). The purpose of the experiment described here was to assess the accuracy of estimating foetal liver volume using 3D ultrasound (US) compared with CT and MR. Three different US scan orientations were used (radial, parallel and slanted) to simulate how foetal livers might be scanned in utero. Four representative volume estimation algorithms were assessed—the ellipsoid, planimetry, tetrahedral and ray

tracing methods. Voxel counting and planimetry were used to estimate CT and MR liver volumes.

Voxel counting was not carried out on the ultrasound images for three main reasons. Firstly, ultrasound images tend to be much noisier than either CT or MR images and so there are likely to be a significant number of pixels below the count threshold within the margins of the organ. Secondly, as regions of interest (ROIs) have to be drawn to separate the liver from the background before the volume can be estimated by voxel counting, why not outline the edge more carefully and calculate the volume directly from the ROIs? Thirdly, some means would have to be devised for dealing with irregularly shaped voxels.

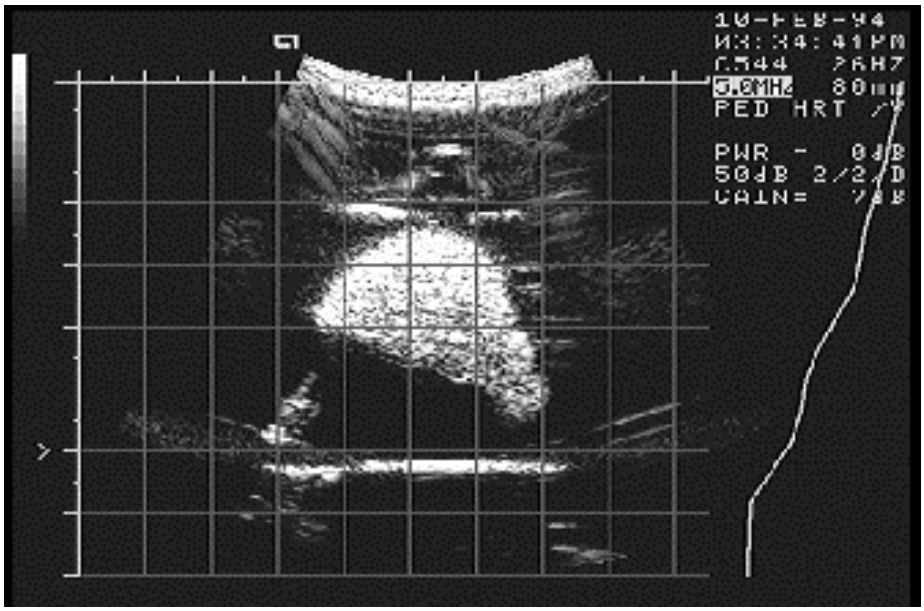
2. Materials and methods

Briefly, the system comprises a video capture card (Win/TV, Hauppauge Computer Works, Inc., Hauppauge, NY, USA), placed inside an IBM compatible 486 personal computer (PC). Captured images are stored on hard disc along with information on the position and orientation of the ultrasound probe acquired using an electromagnetic localization device (3Space Fastrak, Polhemus Inc., Colchester, VT, USA).

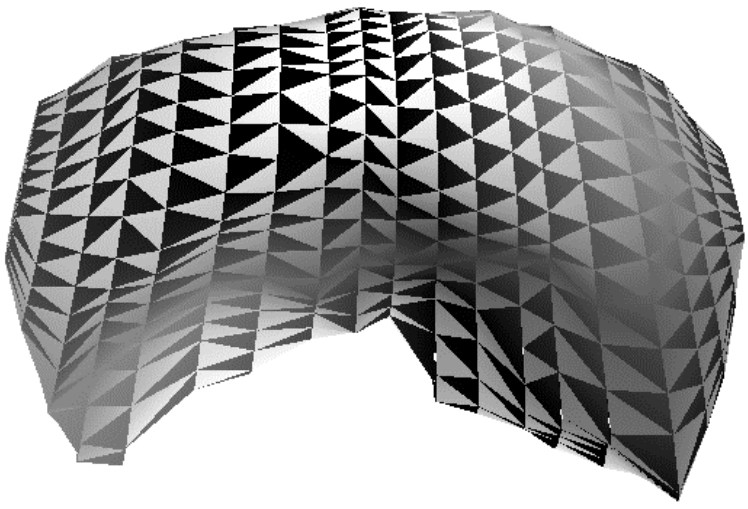
Sixteen cadaveric foetal livers (8–38 ml) were placed on a Perspex plinth in a tank of distilled water. The livers had intact capsules and were fixed in 10% formalin saline. As the livers were denser than water they could be held in place under their own weight. An Acuson 128XP/3 ultrasound scanner (Acuson Corp., Mountain View, CA, USA) with a 5 MHz curvilinear transducer was used to scan the livers. The transducer was held in a gantry running across the top of the tank and between 15 and 20 images, oriented radially, parallel and slanted at 30° to the vertical, were taken through each liver. A 324 × 224 image matrix was used with a pixel size of 0.2 × 0.2 mm and 7-bit resolution (pixel range 0–255 in steps of 2). For the parallel scans, the mean slice separation was around 3 mm (calculated retrospectively). This is comparable to the actual slice thickness in the focal region— estimated at between 3 and 6 mm using the Cardiff resolution test object (Gammex-RMI Ltd, Nottingham, UK). After acquisition, the images (figure 1(a)) were transferred from the PC to a Titan graphics supercomputer (Kubota Pacific Inc., Santa Clara, CA, USA) via a local area network (LAN). The edges of the livers were outlined on the computer monitor using a mouse, and the ROI points transformed into the 3D coordinate system of the Polhemus localization device.

The ROI points were connected into a triangle mesh (figure 1(b)) using a closest neighbour algorithm (Hughes and Brueton 1994). This involves designating a point on the first ROI as the first vertex of the first triangle. The point closest to this vertex on the next ROI becomes the second vertex of the first triangle. The process is repeated, alternating between each set of adjacent ROI points, until the whole surface is filled with triangles. The two end ROIs are filled by connecting the outline points to the ROI centroids. Ultrasound liver volumes were calculated using the ellipsoid, planimetry, tetrahedral and ray tracing methods. The actual volume of the livers was measured by water displacement. The accuracy (mean error ± SD) of the displacement technique was assessed by measuring the volume of seven accurately machined Perspex rods (3–73 ml) and was found to be 0.86 ± 0.65 ml.

To calculate the ellipsoid volume, the long axis (*c*) of each liver was found by calculating the distance between the centroids of the first and last ROIs. The ROI of maximum area was found and the two axes (*ab*) of an ellipse of equivalent area calculated.



(a)



(b)

Figure 1. (a) US image of foetal liver. (b) Surface of a foetal liver reconstructed from multiplanar ROIs.

The volume of the liver was assumed to be equivalent to an ellipsoid of volume $V = \pi abc/6$. The planimetry volume was calculated using the method of Watanabe (1982). This involves multiplying the area of each ROI by a local slice thickness

which takes into account the angle between the image normals and the central axis of the organ (defined by the vectors connecting adjacent ROI centroids).

For the tetrahedral method, the centroid of the whole organ was calculated by calculating the mean of all the vertex *x*, *y* and *z* coordinates respectively. Tetrahedra were constructed by connecting each set of triangle vertices to the organ centroid. The volume of each tetrahedron was calculated from the scalar triple product of three of the edge vectors having a common vertex (Kreyszig 1993). The ray volume was calculated by passing a regular grid of rays through the surface and calculating the intercepts between triangles and rays. The volume of each element was calculated as the length between intercepts multiplied by the area of each grid element. The planimetry, tetrahedral and ray algorithms were tested on a computer-generated ellipsoid with axes in the ratio 60:30:15, with 20 ROIs and 30 points in each ROI (similar to the livers). A 30 × 30 grid was chosen for the RTA. The accuracy for the planimetry, tetrahedral and ray methods on this ellipsoid was −1.1%, −1.4% and −1.6% respectively.

Twelve of the sixteen livers were placed on a Perspex sheet and scanned on a Siemens Somaton DRH CT scanner (Siemens AG, Erlangen, Germany). A slice thickness and separation of 2 mm was used with a pixel size of 0.5 × 0.5 mm. Fifty-five slices were acquired in total. The 12 livers were also scanned on a Siemens Impact Magneton MR scanner (1 T magnet and 15 mT gradient) as a 256 × 256 × 128 volume with pixel size of 0.97 × 0.97 × 1.25 mm (slice separation). Only 12 of the 16 livers were MR scanned due to limitations in fitting all the livers into the scan field at the same time (only one scan session was available). The same 12 livers were also CT scanned, but of these only 11 could be analysed as one liver fell partially outside the field of view.

The CT and MR images were transferred to the Titan computer and the edges outlined using a mouse. Two sets of outlines were produced. One set followed the visible edge of the liver as closely as possible (for the planimetry volumes), and the other was traced a little way out to include all liver pixels not visible in the standard grey-level window. A display window was chosen with a central value close to the mean CT or MR pixel value of the livers, with a width sufficient to display most of the pixels. For example, for CT, the mean pixel value was about 1070 ± 6 and the display window 1000 ± 400.

The CT and MR planimetry volumes were calculated by multiplying the area of each ROI by the scan thickness and summing over the whole volume. For voxel counting, a threshold value midway between the average value of the background pixels and the average value of the object pixels was used, as suggested by Kennedy et al (1989). Software was developed for counting the number of pixels above a given threshold value within a ROI. The volume of the livers was calculated by multiplying the total voxel count by the voxel volume (0.97 mm3 for MR and 0.5 mm^3 for CT).

For graphical purposes, the radial scan technique was arbitrarily chosen for comparing the ultrasound volume estimation algorithms, and ray volume algorithm arbitrarily selected to compare scan techniques. The radial ray ultrasound volumes were then compared with MR and CT planimetry and voxel count volumes. Scatter and Bland–Altman (Bland and Altman 1986) plots were used to assess the agreement between methods.

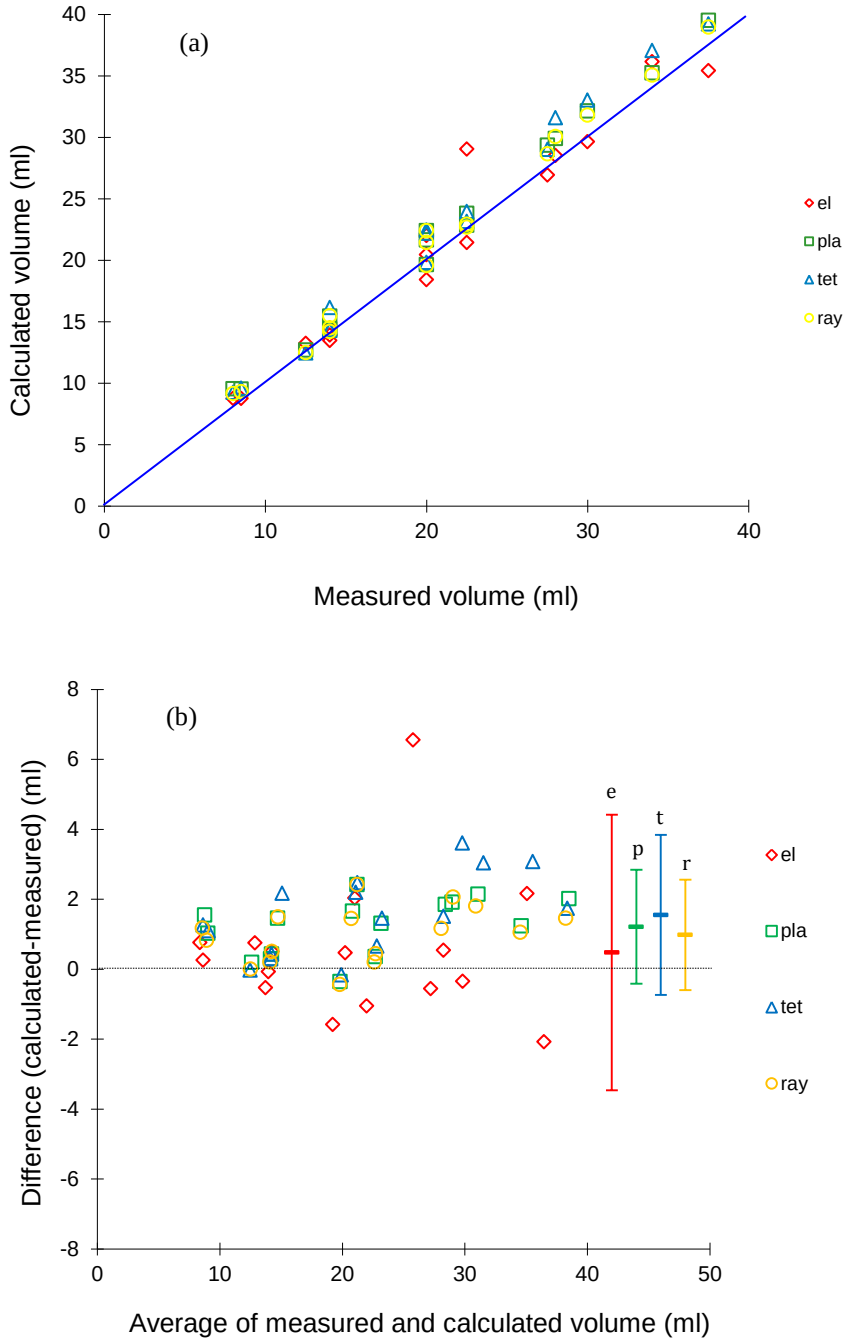


Figure 2. (a) Calculated ellipsoid (el), planimetry (pla), tetrahedral (tet), ray trace (ray) volumes versus measured volume (by water displacement) for radial US liver scans. The line of identity is shown. (b) Bland–Altman plot of the average and difference of the measured and calculated volumes. The error bars represent the 95% limits of agreement (mean difference ± two standard deviations), for each method designated by the first letter of the volume method.

3. Results

All four of the ultrasound volume algorithms produced values close to the line of

identity (figure 2(a)), but tended to slightly overestimate volume (figure 2(b)). The 95% limits of agreement are about twice as wide for the ellipsoid method, although the ellipsoid method has the smallest mean error. Table 1 shows the mean and standard deviation of the absolute and percentage error for the four volume algorithms and three scan techniques.

The radial and parallel scan techniques are very similar with much the same mean difference and limits of agreement. However, the slanted scans tended to underestimate volume with slightly wider limits of agreement compared with the other two methods (figure 3).

Table 1. Mean and standard deviation of the absolute (ml) and percentage error for the four volume estimation algorithms for each ultrasound scan technique on the 16 livers.

Method	Radial		Parallel		Slanted	
	abs. error	% error	abs. error	% error	abs. error	% error
Ellipsoid	0.5 ± 2.0	2.9 ± 8.7	0.4 ± 1.9	1.8 ± 7.6	−0.4 ± 1.8	−1.5 ± 7.2
Planimetry	1.2 ± 0.8	6.5 ± 5.2	0.9 ± 0.9	4.5 ± 4.5	−0.5 ± 1.0	−2.5 ± 5.9
Tetrahedral	1.5 ± 1.1	7.7 ± 5.4	1.7 ± 1.3	8.6 ± 5.6	0.0 ± 1.5	0.2 ± 6.6
Ray tracing	1.0 ± 0.8	5.3 ± 4.7	0.9 ± 0.9	4.7 ± 4.4	−0.7 ± 1.0	−3.1 ± 5.6

Table 2. Mean and standard deviation of the absolute (ml) and percentage error for voxel count and planimetry volumes for 11 CT and 12 MR livers.

Modality	Method	abs. error	% error
CT	Voxel counting	−0.3 ± 1.4	−0.0 ± 9.7
MR		−0.7 ± 1.4	−3.1 ± 9.6
CT	Planimetry	−3.6 ± 2.1	−18.9 ± 8.7
MR		−2.9 ± 1.8	−15.7 ± 8.6

The accuracy of the US radial ray volumes is slightly lower than for CT and MR voxel count volumes, although the precision is slightly better (figure 4). The CT and MR volumes have a very similar mean difference and limits of agreement. Table 2 shows the mean and standard deviation of the absolute and percentage errors for the CT and MR voxel count and planimetry volumes. The variances of the MR and CT volumes are very similar. The MR and CT planimetry volumes on average significantly underestimate volume.

4. Discussion

The results show that under ideal conditions of scanning foetal livers against a high-contrast uniformly low-level background, the accuracy of the 3D US system is lower than CT and MR, although the precision is significantly better ($p < 0.01$). This is corroborated by Gopal et al (1992) who obtained an in vitro standard deviation of 2.27% for US and 8.01% for MR. It is interesting to note that the precision of CT and MR are very similar even although the MR voxels (0.97 mm^3) are about twice the volume of the CT voxels (0.5 mm^3).

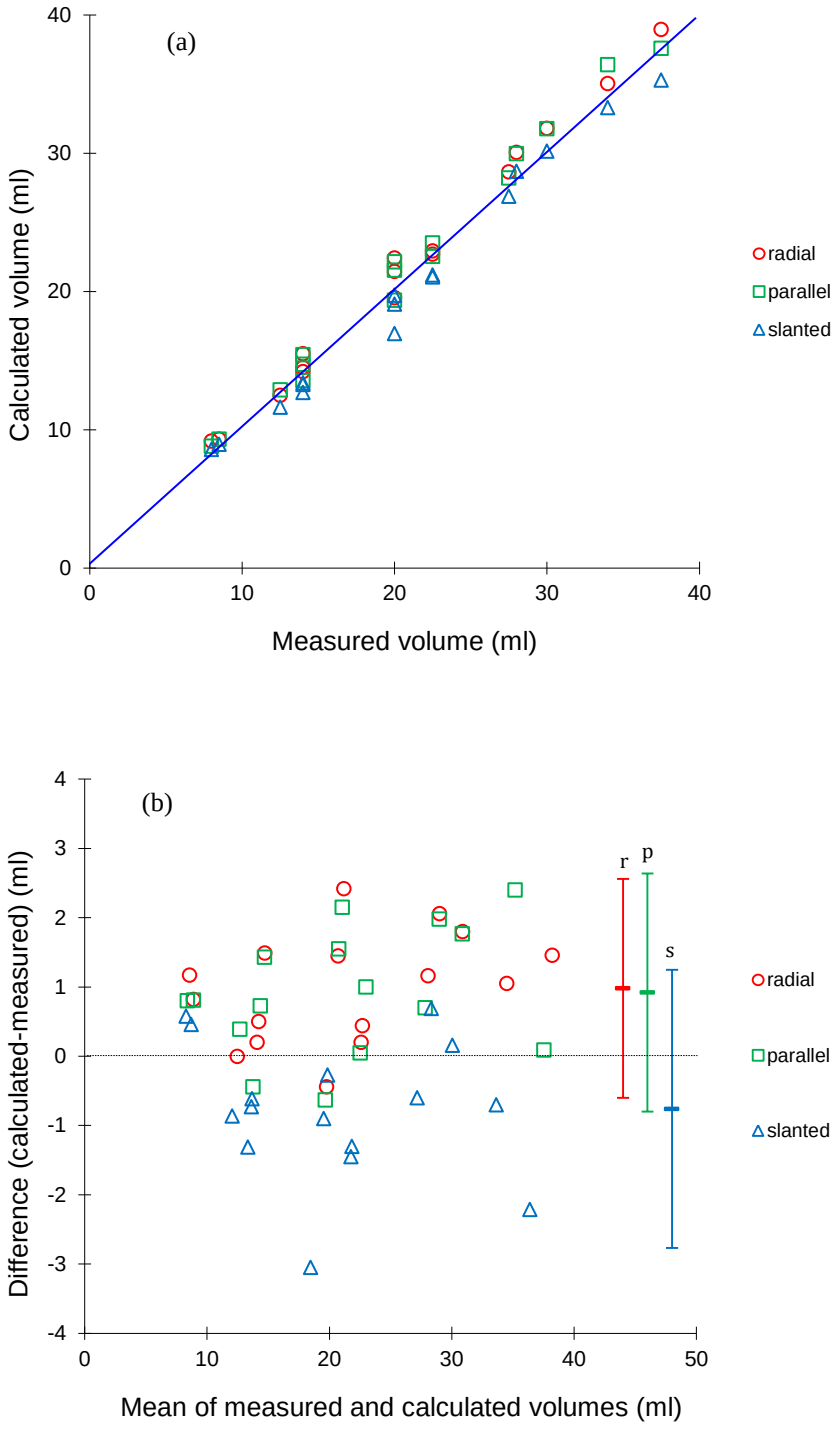


Figure 3. (a) Plot of the ray trace volumes versus scan technique. The line of identity is shown. (b) Bland–Altman plot. Each limit of agreement is designated by the first letter of the scan technique.

In comparison, the US voxels are about 0.12 mm^3 (0.2 × 0.2 × 3 mm) in volume, which may account for the slightly better US precision. The MR and CT results could perhaps be improved by increasing the image resolution. However, it should be borne in mind that CT and MR tend to be used to acquire a section through the whole body rather than a limited region, requiring a lower resolution and therefore a larger pixel size.

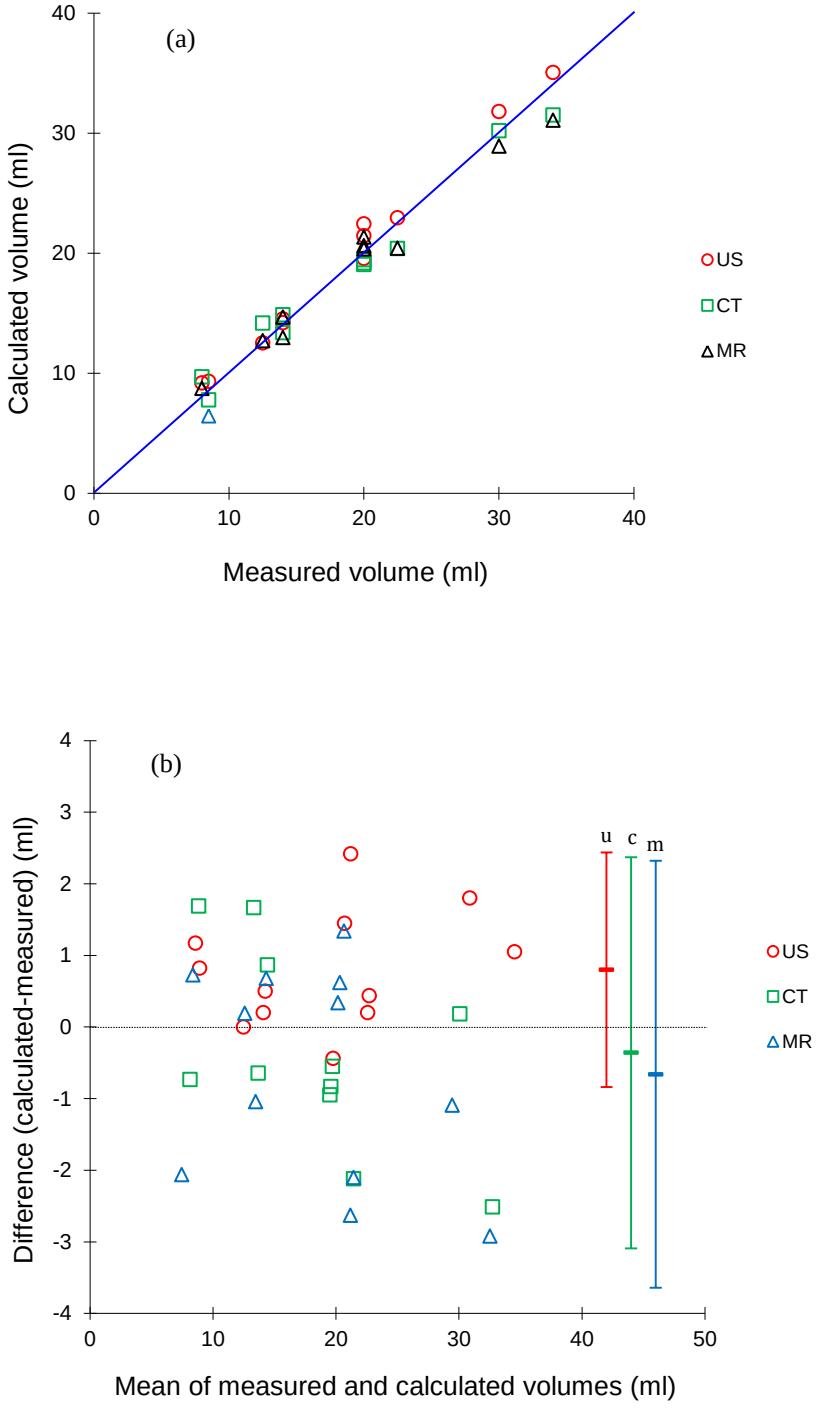


Figure 4. (a) US radial ray volumes and CT and MR pixel count volumes versus displacement volume. (b) The 95% ranges are shown for the three imaging modalities (designated by their first letter).

Ultrasound tends to be used to scan a limited region, enabling higher-resolution images to be acquired. In general, the overall accuracy will be mostly dependent on the ratio between the pixel and object dimensions and on slice thickness and separation.

A number of other factors influence the overall error, for example a difference

between the velocity of sound in the foetal livers and the assumed value for soft tissue (1540 m s^{-1}) will result in distance and refraction errors. Propagation velocity is a function of temperature and the fixing process (Bamber and Hill 1979a, b). At ~22 °C, the temperature at which our experiments were conducted, the data of Bamber and Hill suggest a propagation velocity of about 1590 m s^{-1} in fresh foetal livers, which would lead to a 3.2% *underestimate* of volume. According to Bamber and Hill, formalin fixation results in a *decrease* in propagation velocity of the order of 1% which would result in an *overestimate* of volume of 1%. No data on the propagation velocity in fresh and fixed human foetal livers are reported in the literature, and so more work in this area would be useful. However, the figures quoted above suggest that the effects of temperature and fixation are likely to be small and tend to cancel at temperatures below body temperature. Errors in delineating the margins of liver are likely to be greater.

The results show that the planimetry, tetrahedral and ray volume estimation algorithms are equally as good, although perhaps, as expected, the variance of the ellipsoid method is greater than the other three methods. There is little difference between scan techniques, though the slanted scans have greater variance and on average tend to underestimate volume. This may be due to blurring of the edge at shallower incident angles, leading to increased uncertainty in the true position of the edge.

The CT and MR planimetry volumes significantly overestimate volume because the edge spread function has the effect of extending margins beyond their true position. Hence volume measurements are dependent on window settings (Koehler et al 1979, Baxter and Sorenson 1981, Harris et al 1993). The CT and MR planimetry results demonstrate that the optimal window for viewing is not usually the best for measuring volume.

The system described in this paper could be useful for imaging other organs, for example foetal lungs (D'Arcy et al 1996), neonate brain ventricles, prostate glands etc, and has the potential to complement dedicated 3D scanners (for example the Kretztechnik Combison530). In a dedicated system, the transducer is contained in a housing and is mechanically swept through an angle to image a wedge-shaped volume of interest. While the system is not as compact as dedicated 3D ultrasound machines, it does have other advantages such as being able to collect data over an extended area beyond the range of an all-in-one 3D probe. Our system has flexibility in optimizing the incidence angle of the image plane with respect to the surface of the structure being scanned. Images could in principle be acquired from multiple directions enabling reconstruction of an organ that cannot be viewed from a single scanning window. Another advantage is that the receiver can easily be attached to an intracavity probe (say for imaging the cervix or prostate). In general, 3D US systems are fast enough to enable whole organs to be scanned within a single breath-hold competing with helical CT and echo-planar MR.

Although this in vitro study demonstrates that US volume measurements are comparable with MR and CT, more work needs to be done on assessing *in vivo* errors. Tissue layers interposed between the transducer and organ of interest are known to produce significant image distortion due to velocity and refraction errors. In some cases, these distortions may need removing before accurate *in vivo* volume

measurements can be carried out, for example by the technique proposed by Carpenter *et al* (1995). However, the biggest difference in moving from *in vitro* to *in vivo* will be that the surrounding background will no longer be uniformly low level and so the margin of the foetal liver will not be so clearly defined with such high contrast. This will result in greater variability in the apparent position of the edge.

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