Ultrasound measurements of the liver: an intra and inter-rater reliability study

Abstract
Introduction: Ultrasound is an easy and inexpensive method to rapidly assess the size of the adult liver. The literature addressing reliability of liver measurements using ultrasound is poorly reported and inadequate. In this study, intra and inter-rater reliability of multiple measurements of the right lobe, left lobe and entire adult liver were assessed.

Methods: Two examiners acquired ultrasound images of the liver in multiple positions. Fifteen measurements were taken from each set of images by each examiner. One examiner repeated the images and measurements.

Results: Results demonstrated high intra-rater reliability for all measurements (ICC’s 0.67–0.97). Inter-rater reliability also demonstrated high reliability (ICC’s 0.71–0.94) for nine of the fifteen measurements (six representing the right lobe, one representing the left lobe and two representing the entire liver. Further analysis using paired samples t-tests and Bland Altman plots were performed on these nine measurements.

Conclusion: From this study, the most reliable measurements are suggested to be MCL Dome to tip and MCL Max AP for the right lobe and Midline Max AP for the left lobe. The only measurement to truly encompass both lobes (Max Trans) was not shown to be reliable.

Keywords: liver, measurement, reliability, ultrasound.

Introduction
Assessment of the size of the liver aids in the ability to diagnose and track liver disease. It also aids in treatment planning for liver transplantation and resection. Currently the gold standard for assessing liver volume is CT volumetry, while the determination of liver size by clinicians is predominantly performed using a percussion technique. Ultrasound is an easy and inexpensive way to rapidly assess the size of the liver. In addition, ultrasound does not expose the patient to radiation, and as such can be used frequently where necessary. Ultrasound is therefore growing in popularity amongst clinicians, especially with the introduction of cheaper, more portable equipment and increased accessibility.

Multiple methods of assessing the size of the adult liver using 2D ultrasound have been reported in the literature, however, a systematic review of the literature by Childs, Thoirs, & Esterman, et al. (2013) showed that to date, no study has been correctly undertaken in terms of sample size justification, validity, reliability and statistical analysis. Reliability specifically was poorly reported throughout the literature.

The aim of this study was to assess intra and inter-rater reliability of 2D ultrasound liver measurement methods including methods described in the literature.

Methods
Ethics approval was sought and granted from the ethics committee of the University of South Australia prior to commencement of the study.

A sample size calculation was performed using PASS 11 (NCSS, Utah USA) which determined a sample size of 12 participants with two observations per participant to achieve 80% power to detect an alternative hypothesis intra-class correlation coefficient (ICC) of 0.7 against the null hypothesis that the ICC is 0.1 using a t-test with a significance level of 0.05.

A sample of convenience of twelve participants was recruited via email from the staff and students of the University of South Australia. Participants were excluded if they were unable to read and comprehend the information sheet or were under 18 years of age. An information sheet was provided to potential participants. Once they had agreed to take part, written consent was obtained before their ultrasound.

Two qualified sonographers (JC & CP), one of which was the principle investigator performed the ultrasounds. Each participant was asked to
Table 1: Ultrasound Liver Measurements.

| Measurement Name         | Image Measurement Source | Description of Measurement                                                                 | Example of Measurement |
|--------------------------|--------------------------|-------------------------------------------------------------------------------------------|------------------------|
| Measurements of the whole liver: |                          |                                                                                           |                        |
| MaxLong                  | Image 1                  | Maximum longitudinal Diameter seen (right or left lobe whichever greater)                   |                        |
| MaxAP                    | Image 1                  | Maximum anteroposterior diameter seen (right or left lobe whichever greater)                |                        |
| MaxTrans                 | Image 2                  | Maximum transverse diameter                                                                |                        |
| Measurements of the Rt Lobe of the liver |                          |                                                                                           |                        |
| MCL Dome to Tip          | Image 3                  | The diameter of the liver from the dome to the tip                                          |                        |
| MCL Area                 | Image 3                  | The area of the liver seen on the screen in the mid-clavicular line                         |                        |
| MCL Perimeter            | Image 3                  | The distance around the edge of the liver seen on the screen in the mid-clavicular line    |                        |
| MCL Max Long             | Image 3                  | The maximum longitudinal diameter of liver on the screen, measured left to right along the most superior aspect of the screen in the mid-clavicular line |                        |
| MCL Mid AP               | Image 3                  | The midline of measurement 7 was obtained using the machine’s inbuilt callipers and the anteroposterior diameter of the liver measured at this point in the mid-clavicular line |                        |
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**Key:** Image 1: With the transducer in a longitudinal orientation. An image of the liver was taken at its perceived largest longitudinal diameter. **Image 2:** With the transducer in a transverse orientation. A panoramic transverse image of the liver was taken to encompass the maximum transverse diameter. **Image 3:** The right clavicle of each patient was measured with a ruler and the midpoint determined. This was deemed the mid-clavicular line. An image was taken with the transducer orientated longitudinally into the mid-clavicular line. This anatomical position best represented the right lobe of the liver. **Image 4:** The midline of each patient was determined using the xiphisternum as an anatomic marker. An image was taken with the transducer orientated longitudinally along the midline. This anatomical position best represented the left lobe of the liver. **Image 5:** A transverse image of the liver was taken at the confluence of the three hepatic veins with the middle hepatic vein horizontal in the centre of the screen.

| Measurement          | Image   | Description                                                                                                                                 |
|----------------------|---------|---------------------------------------------------------------------------------------------------------------------------------------------|
| MCL Max AP           | Image 3 | The maximum anteroposterior diameter of the liver seen on this image                                                                       |
| **Measurements of the left lobe of the liver** |         |                                                                                                                                              |
| Midline area         | Image 4 | The area of the liver seen on the screen in the midline                                                                                     |
| Midline Perimeter    | Image 4 | The distance around the edge of the liver seen on this screen in the midline                                                               |
| Midline Max Long     | Image 4 | The maximum longitudinal diameter of the liver on the screen, measured left to right along the most superior aspect of the screen            |
| Midline Mid AP       | Image 4 | The midpoint of measurement 12 was obtained using the machine’s inbuilt callipers and the anteroposterior diameter of the liver was measured at this point in the midline |
| Midline Max AP       | Image 4 | The maximum anteroposterior diameter of the liver seen on this image                                                                       |
| MHV AP               | Image 5 | The anteroposterior diameter of the liver through the middle hepatic vein                                                                   |
lay supine on an examination bed with their body rotated 45 degrees to the left away from the examiner. The participant’s abdomen was exposed from the upper hips to the sternum. Three image series were performed for each participant. All images were taken with the participant in a state of inspiration. The first image series was performed by the first examiner, the second image series was performed by the second examiner, and following a short break, the first examiner performed a third repeated image series.

Each image series consisted of five ultrasound images, from which a total of 15 measurements were made (Table 1). Three measurements were representative of the whole liver, 6 measurements were representative of the right lobe of the liver and six measurements were representative of the left lobe of the liver.

Both examiners accessed the saved images at a later date to perform the measurements. Linear measurements were performed using the machine’s inbuilt callipers. Area measurements were performed by tracing the outline of the liver on the screen using the machine’s continuous trace function and track ball which resulted in the machine automatically calculating the area of liver on the screen. The distance around the edge of the liver was calculated using the machine’s continuous trace function and track ball.

The measurements chosen were based both on measurements seen in the literature and measurements developed by the authors. The three measurements of Max Long, Max AP and Max Trans (measurements 1–3) were described in multiple studies. However, none of these studies gave detailed information on the measurement technique.

The measurement of the liver from dome to tip in the right mid-clavicular line (measurement 4) is an adaptation of measurement described by Gosink & Leymaster (2005), Sapira and Williamson (1979) and Kratzer, Fritz and Mason, et al. (2003).

The measurements of maximum longitudinal liver diameter left to right across the most superior portion of the screen and then the anteroposterior diameter in the midline of this measurement in the right mid-clavicular line (measurements 7 and 8) and midline (measurements 12 and 13) were taken from a study by Niderau, Sonnenberg & Muller, et al. (1983).

The maximum anteroposterior measurements of the liver in the right mid-clavicular line and in the midline (measurements 9 and 14) were described in a study by Niderau and Sonnenberg (1984). The remaining measurements of the area and perimeter of the liver in the right mid-clavicular line (measurements 5 and 6) and midline (measurements 10 and 11) and the anteroposterior dimension of the liver at the level of the three hepatic veins (measurement 15) were developed by the authors.

The first examiner performed measurements on the first saved image series that they had taken for each participant and recorded their results. The second examiner performed measurements on the images they had taken, the second saved image series. One week later, the first examiner performed measurements on their repeated image series, the third saved image series.

Intra and inter-rater reliability was initially assessed for each measurement using ICC’s. Values of 0.7 and below were considered as having poor agreement. Values of 0.7–0.8 were considered to have strong agreement, and 0.81 and above very strong agreement. These initial analyses flagged nine measurements as having strong to very strong agreement for both intra and inter-rater reliability. Bland Altman plots were then performed for the nine flagged measurements to assess the limits of agreement, mean bias in the measurements (paired samples t-test) and assess for any patterns in the bias. Analyses were undertaken using Medcalc 12.

Results
There were 11 female participants and one male participant mean age (SD) 36.3 ± 12 years (range 19–56 years). Participants were not asked questions regarding medical history and the liver was not formally assessed for abnormalities during this study.

| Measurement | Mean | SD  |
|-------------|------|-----|
| 1. Max Long | 13.7 cm | 1.42 cm |
| 2. Max AP   | 11.4 cm | 1.94 cm |
| 3. Max Trans| 20.6 cm | 1.91 cm |
| 4. MCL Dome to Tip | 14.1 cm | 1.63 cm |
| 5. MCL Area  | 98.4 cm² | 30.84 cm |
| 6. MCL Perimeter | 40.72 cm | 4.9 cm |
| 7. MCL Max Long | 11.84 cm | 1.32 cm |
| 8. MCL MidAP | 11.27 cm | 1.11 cm |
| 9. MCL Max AP | 11.33 cm | 1.42 cm |
| 10. Midline Area | 43.35 cm² | 9.89 cm |
| 11. Midline Perimeter | 27.47 cm | 2.95 cm |
| 12. Midline Max Long | 9.03 cm | 1.07 cm |
| 13. Midline Mid AP | 6.96 cm | 1.47 cm |
| 14. Midline Max AP | 7.04 cm | 1.36 cm |
| 15. MHV AP | 7.21 cm | 0.96 cm |

*Means and Standard Deviations are based on the first examiners first image series measurements.
Table 3: Results of ICC analysis.

| Measurement                        | Inter-rater ICC | Inter-rater 95% Confidence Interval | Intra-rater ICC | Intra-rater 95% confidence interval |
|------------------------------------|-----------------|-------------------------------------|----------------|-------------------------------------|
| Measurements of the whole liver    |                 |                                     |                |                                     |
| 1. Max Long                        | 0.795           | 0.444 to 0.936                      | 0.875          | 0.626 to 0.962                      |
| 2. Max AP                          | 0.853           | 0.526 to 0.957                      | 0.962          | 0.880 to 0.989                      |
| 3. Max Trans                       | 0.453           | -0.062 to 0.797                    | 0.786          | 0.404 to 0.934                      |
| Measurements of the right lobe     |                 |                                     |                |                                     |
| 4. MCL Dome to Tip                 | 0.930           | 0.785 to 0.979                     | 0.963          | 0.883 to 0.989                      |
| 5. MCL Area                        | 0.954           | 0.853 to 0.987                     | 0.968          | 0.825 to 0.992                      |
| 6. MCL Perimeter                   | 0.943           | 0.818 to 0.984                     | 0.973          | 0.879 to 0.993                      |
| 7. MCL Max Long                    | 0.808           | 0.427 to 0.942                     | 0.901          | 0.691 to 0.970                      |
| 8. MCL MidAP                       | 0.716           | 0.291 to 0.908                     | 0.903          | 0.700 to 0.971                      |
| 9. MCL Max AP                      | 0.834           | 0.520 to 0.949                     | 0.974          | 0.912 to 0.992                      |
| Measurements of the left lobe      |                 |                                     |                |                                     |
| 10. Midline Area                   | 0.611           | 0.119 to 0.868                     | 0.833          | 0.503 to 0.949                      |
| 11. Midline Perimeter              | 0.574           | 0.0326 to 0.856                    | 0.942          | 0.812 to 0.983                      |
| 12. Midline Max Long               | 0.419           | -0.107 to 0.781                    | 0.911          | 0.726 to 0.973                      |
| 13. Midline Mid AP                 | 0.625           | 0.084 to 0.877                     | 0.678          | 0.208 to 0.895                      |
| 14. Midline Max AP                 | 0.865           | 0.593 to 0.959                     | 0.909          | 0.724 to 0.973                      |
| 15. MHV AP                         | 0.412           | -0.154 to 0.783                    | 0.721          | 0.303 to 0.909                      |

An incidental finding of cystic liver lesions was noted in one participant. This participant was retained in the trial but was advised to contact their general practitioner.

The mean measurements can be seen in Table 2.

The results of the intra and inter-rater reliability are demonstrated in Table 3.

Nine measurements had intra and inter-rater ICC results of 0.7 and above. Two of these were representative of the whole liver (Max Long, Max AP), six were representative of the right lobe (MCL Dome to Tip, MCL Area, MCL Perimeter, MCL Max Long, MCL Mid AP, MCL Max AP) and one was representative of the left lobe (Midline Max AP). Further investigation was made of these measurements by way of Bland-Altman plots and t-tests. The results are demonstrated in Table 4.

The limits of agreement for intra-rater reliability for linear measurements ranged from 1.61 cm–3 cm whilst the limits of agreement for inter-rater reliability for linear measurements ranged from 2.7 cm–3.7 cm. The limits of agreement for the area measurement was 34.6 cm². Significance t-tests for both intra and inter rater reliability were performed as a formal test of bias. P values of less than 0.05 demonstrate a statistically significant departure from zero bias. This was demonstrated in two intra-rater measurements of the right lobe, namely MCL area P = 0.021 and MCL Perimeter 0.043.

Discussion
Due to the anatomical position of the liver in the body, measurements taken in the right mid clavicular line were representative of the right lobe of the liver, whilst measurements in the midline were representative of the left lobe of the liver. Measurements of the entire liver were representative of both right and left lobes; however it must be noted that measurements of the maximum anteroposterior and maximum longitudinal diameter of the liver would almost always be found in the right lobe as was the case in all participants in this study. Circumstances in which this was not the case would arguably be the result of obvious liver abnormality. Representative measurements of each lobe of the liver have been included in this study as it is well known that the lobes of the liver can react differently to disease processes. For example, in cirrhosis there is often marked atrophy of the right lobe of the liver; at the same time there is often caudate hypertrophy.19

As expected, measurements of the right lobe of the liver were larger than the left lobe due to normal anatomical configuration of the liver. Measurements of the right lobe were shown to be more reliable than measurements of the left lobe, with all six right lobe measurements showing ICC results of 0.7 and above and only one of the measurements of the left lobe of the liver deemed to have sufficient intra and inter-rater reliability after initial ICC analysis. Two of the three measurements of the entire liver were shown to have sufficient intra and inter-rater reliability and these were both of those measured in the right lobe (Max AP and Max Trans). This is thought to be a reflection of the shape of the liver, with the right lobe being a bulbous rounded shape rather than the often sharply tapering shape seen in the left lobe. As a result, even if measurements were taken in a slightly different plane there would be less variation in right lobe measurements. In contrast, the sharply tapering left lobe may result in wider variations of the measurement values with the same degree of variation in transducer plane.

The intra rater reliability for all measurements (Rt lobe, Lt lobe and entire liver) was good, with the poorest ICC being...
0.68 (Lt lobe Midline mid AP). It is important that inter-rater as well as intra-rater reliability be of sufficient magnitude if these measurements are to be used in a clinical setting by different measurers, and hence only those measurements that had sufficient intra and inter-rater reliability were used for further analysis with Bland Altman testing.

Bland Altman analysis is very important in determining the usefulness and reliability of measurements such as these which are being developed to be used in clinical practice. The reason for this is the determination of the limits of agreement. If the variation in measurements as depicted by the limits of agreement is too high, the measurements would not be useful in a clinical setting.

Liver size has been shown in the literature to change significantly with disease process. Raeth, Johnson & Williams 1984 showed a median normal liver MCL measurement to be 11.3 cm and a median abnormal measurements of 16 cm indicating a median change of 4.7 cm between normal and pathological livers. Similar changes in size were noted in multiple other studies in the literature. Comparatively, a study by Lewis, Philips & Slavotinek 2006 showed the liver volume to reduce by an average of 14% following six weeks of a low calorie diet in patients with fatty infiltration of the liver. As a result of size changes documented in the literature, limits of agreement were determined by the authors to be acceptable. It should be noted then in using these linear measurements, that a change noted in liver size of 3.5 cm or less could be considered operator difference rather than liver change. The p-values for the intra-rater MCL area measurement and MCL perimeter measurements showed a rejection of the null hypothesis of zero bias. The limits of agreement of the MCL area measurement of 25.5 cm² for intra rater and 34.6 cm² inter rater were arguably too high to be useful clinically.

The right lobe measurement with least variability was the MCL dome to tip measurement (limits of agreement up to 2.7 cm between raters), meaning that this measurement could be used to detect differences of dimensional changes in the right lobe of greater than 2.7 cm. For the left lobe midline max AP measurement, based on limits of agreement for inter rater reliability, this measurement could be used to detect differences of dimensional changes in the left lobe of greater than 3.1 cm. Measurements of the entire liver showed the Max AP measure to be the one with the least variable showing limits of agreement of 3.5 cm between raters.

Three measurements showed a pattern of bias in their intra rater reliability (Max AP, MCL dome to tip, MCL perimeter) with all patterns showing the error to increase with increasing liver size. Only one inter-rater measurement (Max Long) showed a pattern of bias which showed the error increasing with decreasing liver size.

### Table 4: Results of Bland Altman plots and t-tests.

| Measurement | Mean Bias Intra-rater | Mean Bias Inter-rater | Significance t-test intra-rater | Significance t-test inter-rater | Limits of agreement intra-rater | Limits of agreement inter-rater | Pattern of bias intra-rater | Pattern of bias inter-rater |
|-------------|-----------------------|-----------------------|--------------------------------|--------------------------------|-------------------------------|-------------------------------|-----------------------------|-----------------------------|
| Measurements of the whole liver | | | | | | | | |
| 1. Max Long | -0.10 cm | 0.40 cm | 0.63 | 0.14 | 3.0 cm | 3.5 cm | None | Increases with decreasing liver size |
| 2. Max AP | -0.17 cm | -0.60 cm | 0.28 | 0.06 | 2.0 cm | 3.5 cm | Error increases with increasing liver size | None |
| Measurements of the right lobe | | | | | | | | |
| 4. MCL Dome to Tip | -0.13 cm | -0.21 cm | 0.32 | 0.31 | 1.6 cm | 2.7 cm | Error increase with increasing liver size | None |
| 5. MCL Area | -5.10 cm² | 3.50 cm² | 0.02 | 0.20 | 25.5 cm² | 34.6 cm² | None | None |
| 6. MCL Perimeter | -0.60 cm | -0.10 cm | 0.04 | 0.86 | 3.7 cm | 6.6 cm | Error increase with increasing liver size | None |
| 7. MCL Max Long | -0.04 cm | -0.50 cm | 0.80 | 0.06 | 2.1 cm | 3.3 cm | None | None |
| 8. MCL Midline AP | -0.07 cm | -0.50 cm | 0.69 | 0.13 | 2.2 cm | 3.7 cm | None | None |
| 9. MCL Max AP | 0.14 cm | 0.10 cm | 0.32 | 0.74 | 1.9 cm | 3.3 cm | None | None |
| Measurements of the left lobe | | | | | | | | |
| 14. Midline Max AP | 0.21 cm | 0.01 cm | 0.21 | 0.89 | 2.1 cm | 3.1 cm | None | None |
Due to the size and location of the liver the MCL dome to tip and MCL maximum long measurements often rely on estimation of the liver borders as the dome and tip are unable to be imaged on the screen. This is amplified as the size of the liver increases. This was the case in multiple images taken during this study. In this instance, the tip of the liver was measured as the point farthest right in the image. The measurement also becomes inaccurate in the presence of a Riedel’s lobe. When the tip of the liver cannot be imaged in the same picture as the dome, the measurements arguably become somewhat reflective of the sector width of the transducer and the ultrasound machine. The implications and impact of this is an area for further research. The MCL Max AP measurements also demonstrate good reliability, without the estimation problems encountered with the MCL dome to tip measurement. In addition, the MCL max AP measurement offers an alternate and orthogonal plane to the MCL dome to tip measurement.

This study was looking at absolute agreement and the sample size of 12 was determined by power calculation. Although adequately powered, the sample size of 12 might be considered small. The study was limited by the use of a sample of convenience. The study was strengthened by the fact that each participant was re-scanned for each set of measurements. This meant that the images as well as the measurements were repeated for each set of data. The biggest source of variation in these measurements is likely to be due to the use of a different scanning plane given that the image achieved and the transducer angle used is very operator dependent.

From this study, the most reliable measurements are suggested to be MCL Dome to tip and MCL max AP for the right lobe and Midline Max AP for the left lobe. Prior to application of these measurements in clinical practice, further research is required into the validity of these measurements, their ability to discriminate between normal and abnormal livers and their ability to detect changes in liver size over time.

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