White paper

Ultrasound Derived Fat Fraction (UDFF)

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Fatty liver occurs when an excess amount of fat builds up in the liver. A liver is considered “fatty” if the amount of fat contained within the hepatocytes is greater than 5%.[1] Fatty liver, or steatosis, is a broad term that encompasses two distinct categories of liver disease; alcoholic fatty liver disease (AFLD), which results from excessive alcohol use, and nonalcoholic fatty liver disease (NAFLD), which stems from factors outside of alcohol use. Of these two categories, nonalcoholic fatty liver disease is considered the most common chronic adult liver disease worldwide affecting over 25% – or 1 billion – people.[2]

There are two disease state classifications of NAFLD. The first, simple steatosis, is the initial and reversible fatty liver state.

The second, nonalcoholic steatohepatitis or NASH, is the more progressive form of NAFLD that can lead to greater health issues over time.[3] Major contributing factors to NASH are thought to be metabolic (i.e., insulin resistance, diabetes), dietary, and obesity (Figure 1).

Simple steatosis has little to no symptoms leaving many patients to go undiagnosed. Left untreated, these patients can progress to a more serious disease state and are only diagnosed when more prominent symptoms arise, such as abdominal pain, bloating, or even jaundice. Early assessment and characterization of liver steatosis while still in the initial reversible stage is key to overall disease management and improved patient outcomes.
While the exact cause of NASH is not truly known, the disease is known to be rooted in fatty infiltration of the liver. Fatty liver, and therefore NASH, has a broad etiological spectrum that can involve metabolic disorders, certain medications, body habitus size, and even lifestyle choices, such as a fatty diet. Metabolic syndrome, which is a combination of several of the above factors, also increases the likelihood of a person developing NASH.

Current methods for the detection of fatty liver disease involves either an invasive liver biopsy or costly noninvasive magnetic resonance imaging (MRI) tests which are not widely available. There is a significant need for a noninvasive and easily performed testing method to help diagnose these patients.

Ultrasound Derived Fat Fraction (UDFF) is a new and innovative advanced application available for use on the ACUSON Sequoia ultrasound system. UDFF can quantify the amount of fat contained within a patient’s liver quickly and painlessly in just seconds* during a routine abdominal ultrasound. UDFF delivers a similar clinical utility to MRI Proton Density Fat Fraction (MRI-PDFF) to aid clinicians in determining hepatic steatosis. MRI-PDFF and UDFF methods classify hepatic steatosis as an index value greater than 5%. With the use of this simple tool, physicians now have a new, noninvasive way to help manage adult patients** with hepatic steatosis.

* Based on 5 UDFF acquisitions when used as a stand-alone feature.
** When used as part of an overall assessment of hepatic steatosis.
What is a fatty liver?

Fatty liver, known as steatosis, is the abnormal and excessive accumulation of fat globules in the hepatocytes of the liver. Histologically, a normal, healthy liver contains up to 5% fat in its hepatocytes. Should this fat level climb beyond the 5% threshold the liver is then classified as being “fatty” (Figure 2).  

Fatty liver occurs when fat molecules are not metabolized efficiently enough by the body and end up stored in the liver. The pathophysiology of insufficient fat metabolism can be linked to many different factors such as metabolic conditions, medications, or even the overconsumption of fat in the diet. In most cases people have no symptoms, as having a simple fatty liver does not cause any immediate harm or prevent the liver from functioning normally. Over time however, there is concern. Prolonged and continuous fat build-up within the hepatocytes creates a cycle of constant injury and repair within the liver. This persistent cycle paves the way to more serious and permanent liver conditions and what was once a reversible state of simple steatosis can progress to inflammation (steatohepatitis), fibrosis (scarring), and eventually, cirrhosis and/or liver failure.
Figure 2: Normal healthy liver tissue compared to fatty liver at a cellular level. Normal liver tissue consists of healthy hepatocytes surrounded by blood vessels and portal triads. In a fatty liver, these hepatocytes become filled with excess fat globules. These globules are stored in the hepatocytes when the body cannot keep up to the metabolic pace that the amount of fat present demands. Histologically, liver fat is graded from 0 to 3 based on hepatocyte fat content. Grade 0 (normal) = < 5%, grade 1 (mild) = 5%–33%, grade 2 (moderate) = 34%–66%, and grade 3 (severe) = ≥ 67%. The liver is considered fatty when more than 5% of hepatocytes contain fat.

Nonalcoholic Fatty Liver Disease (NAFLD)

There are two types of fatty liver disease. Alcoholic fatty liver disease (AFLD), which results from excess alcohol consumption, and Nonalcoholic fatty liver disease (NAFLD), which is not attributed to alcohol use. Of the two conditions, NAFLD is currently the most common cause of chronic liver disease worldwide. The exact cause of NAFLD is not truly known, however it is thought to be associated with a wide range of diseases and conditions that increase the risk of someone developing NAFLD. These include, but are not limited to:

- Metabolic conditions, such as those associated with insulin resistance or high cholesterol
- Those with diabetes and hypothyroidism are also at increased risk
- Certain prescription medications or steroids
- A body habitus that is overweight or obese

Nonalcoholic fatty liver disease is further divided into two categories each with a different associated risk. The first, nonalcoholic fatty liver (NAFL) is a simple and reversible fatty infiltration of the liver. NAFL is considered...
a benign condition, as it is thought to have minimal risk of progression to cirrhosis if diagnosed early and the necessary steps are taken to reverse the condition. Left untreated NAFL can, over time, become the precursor that leads to the second, and more progressive disease state of NAFLD known as Nonalcoholic steatohepatitis, or NASH. When compared to NAFL, NASH is thought to have a significantly increased risk of progression to cirrhosis and/or end stage liver failure (Figure 3). NASH results when there is an even greater accumulation of fat within the liver tissue ultimately resulting in fibrotic changes. It has few or no outward symptoms initially and often goes undiagnosed until it has progressed to a more advanced state. NASH begins when the excess fat acts as a toxin and causes inflammation of the liver.

This inflammatory stage is known as steatohepatitis. Sustained inflammation causes cellular damage within the liver, as the cells are in a constant state of injury and repair. Eventually this constant attempt to repair and replace damaged cells leads to the formation of scar tissue (fibrosis). If the amount of scar tissue becomes severe enough, it begins to impair liver function; when liver function becomes extremely impaired, cirrhosis results. Cirrhosis is an irreversible condition and carries an increased risk of developing liver failure and/or liver cancer. While not every individual will progress to cirrhosis or liver cancer, early assessment and characterization of liver steatosis is essential to help implement treatment or intervention to lower risk and curb advancement of NAFL to NAFLD (Figure 4).

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**Figure 3:** There are two classifications of fatty liver disease based on the causative factors. Alcoholic fatty liver disease (AFLD) is fatty liver disease that results from the excessive use of alcohol. Nonalcoholic fatty liver disease (NAFLD) results from factors outside of alcohol use which include medication use, metabolic disorders, and obesity to name a few. NAFLD has two categories or stages of disease. The initial benign stage, nonalcoholic fatty liver (NAFL), or the more progressive stage of nonalcoholic steatohepatitis (NASH). NAFL can be a precursor to NASH if left untreated.
NAFLD and obesity

In addition to metabolic disorders and certain medications being causative factors, NAFLD is usually seen in people who are overweight or obese.\textsuperscript{10} In a study of more than 8 million people, obesity was present in 51% of patients with NAFLD and 82% of patients with NASH.\textsuperscript{11} This is very worrisome, as the most current statistics from 2016 by the World Health Organization (WHO) state that worldwide, more than 1.9 billion adults 18 years and older are considered overweight, and of that number, 650 million are categorized as obese.\textsuperscript{12} Even more troubling is being overweight or obese has expanded downward in age to include children. The prevalence of obesity and being overweight among children and adolescents aged 5–19 years has risen dramatically from just 4% in 1975 to just over 18% in 2016.\textsuperscript{12} In 2016 WHO statistics put over 340 million children and adolescents in this age group as either being overweight or obese.\textsuperscript{12} While the concentration of NAFLD per country does vary, the worldwide incidence is estimated to be 25%.\textsuperscript{11} Since obesity affects all races, the prevalence of NAFLD will increase at approximately the same rate as obesity.\textsuperscript{11} Even now, nonalcoholic fatty liver disease is becoming so prevalent worldwide that NASH is quickly becoming one of the leading indications for liver transplant.\textsuperscript{3}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
 & NAFL & NASH & & & & \\
\hline
Normal liver & Less than 5% fat\textsuperscript{1} & & & & & \\
\hline
Steatosis (simple) & Accumulation of fat in the liver. Steatosis is defined as intrahepatic fat of at least 5% of liver weight\textsuperscript{1} & & & & & \\
\hline
Inflammation & Excess fat acts as a toxin and damages healthy liver cells. This results in steatohepatitis (NASH)\textsuperscript{4, 5} & & & & & \\
\hline
Early fibrosis & Scar tissue begins to form in the liver as it attempts to repair and replace damaged cells\textsuperscript{7, 9} & & & & & \\
\hline
Significant fibrosis & Repeated and/or continuous liver damage/repair results in widespread and permanent non-functioning scar tissue\textsuperscript{7, 9} & & & & & \\
\hline
Cirrhosis & Extensive scar tissue and regenerated nodules replace most all healthy tissue and inhibits liver function\textsuperscript{7} & & & & & \\
\hline
Cirrhosis with HCC & Patients with NASH have a 2%–20% 5-year cumulative incidence of hepatocellular carcinoma (HCC)\textsuperscript{10} & & & & & \\
\hline
\end{tabular}
\caption{Categories of nonalcoholic fatty liver disease progression from normal liver through to cirrhosis with the potential complication of liver cancer.\textsuperscript{10} While not all individuals will progress to a cirrhotic or cancerous state, early knowledge of the presence of disease can allow intervention or treatment that can work toward lowering that risk.}
\end{table}

\textbf{Figure 4:} Categories of nonalcoholic fatty liver disease progression from normal liver through to cirrhosis with the potential complication of liver cancer.\textsuperscript{10} While not all individuals will progress to a cirrhotic or cancerous state, early knowledge of the presence of disease can allow intervention or treatment that can work toward lowering that risk.
Why is it essential to diagnose fatty liver at an early stage? Early detection of hepatic steatosis improves the chances of managing or reversing the condition before irreversible changes can occur. At present, there are existing medical techniques (imaging and non-imaging) that can diagnose hepatic fat content. These techniques vary in degrees of effectiveness, cost, invasiveness, availability (of equipment) and/or patient suitability.

Liver biopsy

Currently, liver biopsy is the reference standard for diagnosing and grading hepatic steatosis. Liver biopsy is, however, inappropriate for screening or frequent monitoring as it is invasive, prone to sampling errors, observer variability, and the risk of complications.

There is a need to develop less invasive objective quantitative biomarkers for the diagnosis of hepatic steatosis. Currently this need is largely unmet, which causes people to go undiagnosed. Additionally, the lack of noninvasive testing techniques represents a major barrier for drug development in NASH, as treatment response assessment continues to require liver biopsy.

Most recent noninvasive avenues involve magnetic resonance spectroscopy (MRS) and chemical shift-based magnetic resonance imaging (MRI).

Proton Density Fat Fraction (PDFF)

Magnetic resonance spectroscopy (MRS) is considered the most sensitive, noninvasive modality for the detection and quantification of hepatic steatosis. Magnetic resonance spectroscopy exploits the difference in resonance frequencies between water and fat proton signals to quantitatively measure the proton density fat fraction (PDFF). PDFF is defined as the ratio of mobile triglyceride protons to the sum of the mobile triglyceride and water protons. The resultant index is a marker of fat. Several studies have reported that the fat fraction measured by MRS closely correlates with the histologic assessment of liver fat content. Despite the high accuracy of MRS for quantifying the fat fraction, its use is limited as it is time-consuming to perform and analyze, and samples only a small portion of the liver.

Rapid chemical shift-based magnetic resonance imaging (MRI) techniques have been developed that can accurately quantify liver fat across the entire liver. These techniques involve water-fat separation, as MRI is sensitive to the signal from protons in mobile, unbound molecules, such as water and triglycerides. MRI accomplishes this phenomenon by acquiring images at 2 or more echo times after signal excitation. MRI-PDFF then exploits the difference in resonance frequencies of protons in water and fat to provide an estimate of...
tissue fat fraction. This index is calculated by separating the signals from water and fat then calculating the percentage using the individual fat value over the combined value of fat and water. The PDFF index is expressed as a percentage (%) and ranges from 0 to 100%.

\[
\text{PDFF} = \left( \frac{\text{Fat}}{\text{Fat} + \text{Water}} \right) \times 100\%
\]

MRI-PDFF estimation is shown to be accurate and reproducible with good correlation to the histological steatosis grade assigned to specimens obtained from liver biopsies. The MRI-PDFF technique does suffer from some limitations which include high cost, low accessibility, long scan times, sedation of young children, and the exclusion of patients with metal implants.

**Controlled Attenuation Parameter (CAP)**

Controlled Attenuation Parameter (CAP) is another noninvasive method used to evaluate hepatic steatosis. The degree of fat present in the liver is estimated using a non-imaging ultrasound-based device. The piston-like transducer is placed between the ribs on the right side of the patient where it can emit an ultrasound wave that will travel through the liver. The CAP value is an estimate of the attenuation of the emitted ultrasound wave as it propagates through the liver. This value is calculated from data acquired by either the traditional CAP method consisting of several manually-triggered sequential measurements (typically 10), or the subsequent continuous CAP method, where the transducer remains in contact with the skin surface for several seconds while acquiring “continuous” [attenuation] data. CAP is reported in decibels per meter (dB/m) and has a range of 100–400 dB/m. Since fat affects ultrasound propagation through absorption and scattering leading to signal attenuation, a higher fat content within the liver will translate to a higher CAP value. While CAP can be performed rapidly and painlessly, it has several challenges that can prevent use in certain patient populations and/or lend itself to the inability of the operator to avoid certain artifacts. Unlike conventional ultrasound, where the liver and surrounding structures are visualized on the imaging screen, CAP is a non-imaging or “blind” test. The lack of visualization of the liver can result in the inability of the user to avoid fluid-filled vascular structures or unknown ascites in a patient, both of which can affect results. Additionally, in patients with a body mass index (BMI) higher than 30 (obese), the accuracy of the CAP measurement may be decreased. Contra-indications for CAP usage include patients who have an implanted pacemaker, which is thought to make up about 5% of the patient population, and patients who are pregnant.

**Conventional ultrasound**

Conventional ultrasound is the most common imaging modality for assessing hepatic steatosis. In conventional ultrasound, assessment is made based on qualitative features of the B-mode images of the liver. These include:

- Liver parenchymal echogenicity appearance
- Signal loss at depth (penetration)
- Liver texture
- Ability to visualize vessels and the diaphragm clearly
- Presence/absence of focal fatty sparing
- Increased hepatorenal echogenicity

The sensitivity and specificity of conventional ultrasound for the detection of moderate-to-severe fatty liver is high, however the sensitivity decreases markedly in incidents of mild steatosis where less than 30% of hepatocytes are affected. Conventional ultrasound assessment techniques also suffer from operator and machine dependency, which leads to variability in the detection and/or severity of hepatic steatosis.

**Hepatorenal index**

The hepatorenal index was developed to remove subjectivity associated with qualitative interpretations of B-mode images. The hepatorenal index quantifies liver echogenicity relative to the kidney and has a good correlation with the degree of steatosis. The hepatorenal index measurement does have limitations, most notably, the comparison cannot be performed on patients who have renal disease that affects the cortical echogenicity of the kidney. Another limitation is finding proper imaging windows to place 2 regions-of-interest (ROIs) at the same depth within the kidney cortex and the liver parenchyma.
Ultrasound Derived Fat Fraction (UDFF)

What is UDFF?

Ultrasound Derived Fat Fraction (UDFF) is a unique new technology available on the ACUSON Sequoia ultrasound system to noninvasively quantify fat in the liver. The Ultrasound Derived Fat Fraction provides an index of hepatic fat content in a region-of-interest (ROI) positioned within the liver by the user.

The UDFF index is estimated from both the Attenuation Coefficient (AC) and the Backscatter Coefficient (BSC). The resulting UDFF index is displayed in percent (%) and has a range of 0–100%. The UDFF index exhibits a linear relationship with fat content such that the higher the UDFF index value, the higher the fat content level is within the liver.

UDFF delivers a similar clinical utility to Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF) for determining hepatic steatosis. Both methods classify hepatic steatosis as an index value of greater than 5%.

With a total exam time of less than 1 minute*, the Ultrasound Derived Fat Fraction is a measurement tool to aid physicians in managing adult patients as part of an overall assessment of hepatic steatosis.

* Based on 5 UDFF acquisitions when used as a stand-alone feature.
Attenuation Coefficient (AC)

As sound propagates through the body it is absorbed by tissue reducing the amplitude and intensity of the ultrasound wave (Figure 5). The rate of absorption is dependent on frequency, tissue type and depth. Higher frequency sound waves are absorbed by the body more quickly than lower frequencies, which is often a factor in transducer selection. Attenuation rate is also influenced by tissue type, as not all tissues attenuate sound waves at the same rate. Sound propagating through fatty tissue will tend to be more readily absorbed than through non-fatty tissue. We experience the phenomenon of sound absorption constantly during an ultrasound exam and try to accommodate for it by changing to a lower frequency transducer or exam frequency setting to help visualize deeper structures. The Attenuation Coefficient describes the rate of decay of the ultrasound energy as it propagates through a tissue and is a quantitative measure for tissue obscuration as visually assessed from a B-mode image.

Attenuation alone is not sufficient for estimating fat content in the liver. Microscopic tissue properties, such as the size of a fat cell, affect the backscattered echo signals. The addition of the backscatter coefficient provides another piece of information which allows us to estimate the percentage of fat in the liver with improved accuracy.

Figure 5: Tissue attenuation can be determined by estimating the frequency content of the sound at different depths then comparing them to values taken from a known reference. This method allows us to isolate the attenuation of the tissue and estimate its attenuation coefficient. In figure 5, the slope of the orange line is related to the attenuation within tissue; the greater slopes indicate greater attenuation coefficient values. No attenuation or almost no attenuation would be seen when imaging in water (a) whereas moderate to high attenuation (b, c) would be seen in soft tissues (liver, kidney, fat etc.).
**Backscatter Coefficient (BSC)**

The Backscatter Coefficient (BSC) describes the scattering properties of the underlying tissue and can be measured from the strength of the scattered ultrasound signal (brightness) at a particular frequency. The BSC contains information relating to the microstructure of the underlying tissue, in particular, fat globules. While it is normal to have a small amount of fat in the liver, continued deposition causes the fat cells to increase in size. As the fat cells enlarge, they begin to reflect and scatter sound differently than normal sized liver and fat cells. Smaller fat cells have little interference on the sound wave when compared to healthy liver tissue. This results in a small amount of backscatter (Figure 6a–b).

The larger “obstructive” fat cells interfere with the sound wave more intensely. This results in a higher amount of reflection and scattering of the sound back to the transducer (Figure 6c–d). In 2D scanning we see the intensity of the backscatter depicted as a bright “fatty” liver image. We use the backscatter coefficient qualitatively when we visually compare the liver brightness to that of the kidney. This visual brightness assessment based on perceived BSC has morphed into the semi-quantitative hepatorenal index (HRI) measurement. The HRI indirectly compares the BSC of the liver to the BSC of the kidney with a larger value indicative of higher liver fat content.

**Figure 6:** Cell size has a direct influence on the amount of backscatter that occurs. The larger the cell, the greater the degree of sound reflections and scatter that occurs. Figure (a) depicts a small fat particle interacting with the propagating sound wave (orange arrow). When the sound wave interacts with the small fat cell only a small amount of reflection and/or scattering occurs (b, green arrow). Figures (c) and (d) depict the same sound wave interaction but with a larger fat cell. The larger cell produces a greater amount of reflection and/or scattering due to the larger surface area with which the sound wave interacts.
The UDFF index value is calculated from the AC and the BSC values. These values are determined by comparing the frequency content of the backscattered echo signals at different depths within the tissue to the frequency content of a tissue mimicking reference phantom. The AC and BSC values of the reference phantom are pre-characterized. This comparison allows us to isolate the attenuation of the tissue and estimate its AC. Likewise the ratio of the two frequency spectra, along with estimated AC of that phantom, can be used to estimate the BSC of the tissue sample. Following BSC estimation, the value for the UDFF index is finally calculated from the BSC of the tissue sample at 3 MHz using a unique proprietary mathematical algorithm. This mathematical procedure (P) converts BSC into the UDFF index in units of percent (BSC at 3 MHz is linearized to provide the UDFF index).

\[ \text{BSC (3 MHz)} \xrightarrow{P} \text{UDFF} \]

Unlike the AC and BSC values, the UDFF index exhibits a linear relationship with the fat content – as the UDFF index value increases, so does the fat content level. The UDFF index demonstrates similar clinical utility to MRI-PDFF (Figure 7).²

Figure 7: The backscatter coefficient is an acoustic tissue parameter which provides a direct relationship to the microstructure of liver; however, the relationship between BSC and fat content is nonlinear. UDFF is a linearization of the BSC to provide a 1:1 relationship between the UDFF index and the fat content.
Validating UDFF

The UDFF index is calculated from the AC and the BSC of the liver using a reference phantom method. This method is repeatable and reproducible between transducers in adults with known or suspected NAFLD.\(^\text{18}\) Using histologic steatosis grades as reference, the diagnostic accuracy of the UDFF index in detecting the presence of steatosis (>5% hepatocytes) was 0.94 (0.85–0.98), which is comparable to the diagnostic accuracy of MRI-PDFF: 0.94 (0.81–0.98).\(^\text{2}\) The sensitivity and specificity of UDFF were 0.84 (0.76–0.92) and 1.0 (1.0–1.0) respectively compared to 0.80 (0.71–0.87) and 1.0 (1.0–1.0) for MRI-PDFF. Using MRI-PDFF as reference, the diagnostic accuracy of the UDFF index in detecting the presence of steatosis (MRI-PDFF > 5%) was 0.97 (0.93–0.99) with sensitivity of 0.94 (0.87–0.97) and specificity of 1.0 (1.0–1.0).\(^\text{2}\) The mean bias between MRI-PDFF and the UDFF index was close to zero indicating good agreement between UDFF and MRI-PDFF; the limits of agreement were ±8.5%. The Pearson correlation coefficient was 0.87 indicating good correlation between UDFF and MRI-PDFF.\(^\text{2}\)

Comparing UDFF to other fat quantification technologies

At present, the most widely accepted noninvasive imaging modality to characterize fat content in the liver is MRI-PDFF. MRI-PDFF is a quantitative imaging biomarker that enables accurate, repeatable, and reproducible quantitative assessment of liver fat over the entire liver.\(^\text{3}\) MRI-PDFF provides a specific fat content number, in percent, between 1–100%. The cost, exam time and ease of availability makes routine usage of MRI-PDFF challenging, thus other more cost-effective and widely available fat quantifying tools have been developed – but how do they compare?

Controlled attenuation parameter, or CAP, estimates ultrasound energy decay and then analogues it to the attenuation coefficient estimation. The obtained CAP value (displayed in decibels per meter [dB/m]) along with the patient’s proposed etiology, is then charted to determine a steatosis stage corresponding to that of histology. For example, a patient with a CAP value of 305 dB/m with a NAFLD/NASH etiology is classed as being an S1 steatosis grade with a corresponding fat content range of 5–33%.\(^\text{19}\)

Ultrasound imaging techniques have emerged that are based solely on measuring the level of attenuation to determine the liver fat content. These techniques, unlike MRI-PDFF, do not determine a fat percentage but rather the resulting attenuation coefficient that is graded against fat content – the higher the attenuation coefficient, the higher the degree of fat contained within the liver. These techniques provide a result that is like CAP in that the value of the attenuation coefficient is then assigned a grade (S0, S1, etc.) with an associated fat range. Like CAP, these results are not in the same unit (percent) as MRI-PDFF.
UDFF is unique in that it measures both attenuation and backscatter and then uses those results to calculate a UDFF index. The UDFF index is displayed in percent and demonstrates a similar clinical utility to that of MRI-PDFF – the most widely accepted and repeatable fat quantification method. Since UDFF uses the same unit and > 5% classification criteria as MRI-PDFF, there is no need to convert the result or consult a chart to determine the liver fat content. Sufficient agreement between the modalities enables rapid adoption of a less expensive and time-consuming modality enabling better use of health care resources.

For validation, a meta-analysis was done to compare the diagnostic performance of UDFF in detecting the presence of steatosis (> 5% fat content) with that of MRI-PDFF and CAP. The analysis is summarized in a Receiver Operating Characteristic (ROC) curve in Figure 8. The performance of the given technologies is visualized with sensitivity on the Y-axis and specificity on the X-axis. The accuracy of each technology is defined by the area under the curve (AUC).

For this meta-analysis, the diagnostic accuracy was the highest for MRI-PDFF (AUC = 0.91) as denoted by the black dot in Figure 8. The green dot, representing the controlled attenuation parameter (CAP), had an AUC of 0.81. The Ultrasound Derived Fat Fraction (UDFF) identified by the orange dot, demonstrated an AUC of 0.88. The results of this meta-analysis supports the claim that UDFF demonstrates a similar clinical utility to that of MRI-PDFF.20

![Summary Receiver Operating Characteristic (ROC) Curve](siemens-healthineers.com/ultrasound)

**Figure 8:** A meta-analysis comparing MRI-PDFF, CAP and UDFF demonstrates that the Ultrasound Derived Fat Fraction has a similar diagnostic performance to that of MRI-PDFF and CAP in detecting the presence of steatosis.20
To perform a UDFF measurement, the patient should fast for at least 4 hours prior to the exam. Position the patient in a supine or slight (30°) left lateral decubitus position with the right arm raised above their head. This is optimal positioning to improve intercostal access. Place the transducer perpendicular (90°) to the skin surface using ample gel. Transducers that are not perpendicular will have an inadequate transducer angle and can result in artificially low measurement values. Select an artifact-free area within the right lobe of the liver to place the region-of-interest (ROI). An artifact-free area is defined as an area free from vessels, large hepatic ducts, bright reflectors, and rib shadows. Ensure the liver capsule marker is aligned flat/parallel with the echogenic interface of the liver capsule when placing the ROI. Proper placement of the marker ensures that the sample is taken at least 1.5 to 2 cm below the liver capsule (Figure 9). Have the patient breathe normally until you are ready to acquire your measurement. When you wish to activate the measurement, have the patient suspend/pause their breathing/respiration. The patient can resume normal respiration once the audible tone is heard indicating the acquisition is complete. A single UDFF measurement is made within the ROI and will be displayed as a percent (%) within the measurement display area (MDA) (Figure 9). Siemens Healthineers recommends 5 UDFF measurement samples be acquired for a complete exam study. Once all measurements are obtained, the patient report will display each individual measurement with the associated depth as well as the Mean, Median, Standard Deviation, Interquartile range (IQR), and IQR/Median ratio for all acquired measurements (Figure 10). A normal UDFF index liver fat level is less than or equal to 5% (Figure 11) while an abnormal UDFF index value is above that threshold (Figure 12, Figure 13).
Figure 9: To ensure proper ROI positioning and placement, align the “+” marker of the sample line parallel with the liver capsule. Aligning the sample marker places the ROI at the recommended 1.5–2 cm depth below the liver capsule as well as ensures the sample is placed at the proper perpendicular position optimal for acquisition.

Figure 10: The total number of acquisitions and associated data will be displayed in the patient report. Siemens Healthineers recommends 5 separate acquisitions for a complete UDFF exam.

Figure 11: A normal liver contains a small amount of fat – less than or equal to 5%. A normal UDFF index value uses the same threshold.

Figure 12: Abnormal UDFF index measurement is above the 5% threshold.

Figure 13: Since nonalcoholic fatty liver disease is usually seen in people who are overweight or obese, the deep abdominal transducer (DAX) is a useful tool to help penetrate the liver. An abnormal UDFF index measurement of 25% is noted in this high BMI patient.
Conclusion

Nonalcoholic fatty liver disease is currently the most common cause of chronic liver disease worldwide. Fatty liver, or hepatic steatosis, occurs when fat molecules are not metabolized efficiently enough by the body and end up stored in the liver. While a normal liver contains a small amount of fat, the liver is considered “fatty” if the amount of fat within the hepatocytes exceeds 5%.

Early detection of hepatic steatosis improves the chances of managing or reversing the condition before irreversible changes can occur. At present, the existing medical techniques that can diagnose hepatic fat content vary in degrees of effectiveness, cost, invasiveness, availability of equipment, and/or patient suitability. There is a need to develop less invasive and objective quantitative biomarkers for the diagnosis of hepatic steatosis that is cost-effective and widely available.

Ultrasound Derived Fat Fraction (UDFF) is an innovative advanced application available for use on the ACUSON Sequoia ultrasound system that can quantify the amount of fat contained within a patient’s liver. UDFF can quantify fat content in just seconds* during a routine abdominal ultrasound. UDFF delivers a similar clinical utility to MRI Proton Density Fat Fraction (MRI-PDFF) to aid clinicians in determining hepatic steatosis. MRI-PDFF and UDFF methods classify hepatic steatosis as an index value greater than 5%. With the use of this simple tool, physicians now have a new, noninvasive way to help manage adult patients** with hepatic steatosis.

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** When used as part of an overall assessment of hepatic steatosis.
Citations


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