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Best Practices for Detecting Liver Fibrosis with ARFI

The application of the ultrasound-based technique at The Royal Melbourne Hospital

White Paper | 2015

Overview

Acoustic Radiation Force Impulse imaging (ARFI) is an ultrasound-based quantitative elastography technology that has its major clinical application in the noninvasive assessment of liver fibrosis. A shear wave elastography tool, it relies on the principle that with increasing liver fibrosis there is increasing liver stiffness and decreasing liver elasticity. Liver fibrosis is a key marker of the severity of liver disease. The detection of liver fibrosis and estimation of severity is fundamental in managing chronic liver disease with implications for treatment choices, prognosis, and the need for surveillance for complications of cirrhosis, including hepatocellular carcinoma.

How ARFI Works

To assess liver stiffness, ARFI uses brief high-energy ultrasound "push pulses" to excite a narrow region within the liver parenchyma. This excitation results in minute displacements of tissue, resulting in shear waves that move laterally away from the line of the push pulse. These shear waves can be tracked by lower energy ultrasound beams to allow measurement of their speed. The shear wave velocity is measured within a small region of interest and is expressed in meters per second.

Shear wave velocity increases with liver stiffness and decreasing elasticity. Since the primary determinant (although not the only determinant) of both properties is the degree of fibrosis, an estimate of stage of liver fibrosis can be made.

A number of pathological staging systems for liver fibrosis are used but the most common one is the METAVIR system, which has the following stages:

F0 = no fibrosis

F1 = mild fibrosis

F2 = significant fibrosis

F3 = severe fibrosis

F4 = cirrhosis

If the causative insult that results in liver fibrosis is not removed, there is a tendency for fibrosis to progress from lower stages to higher stages. Once F4 is reached, there is the risk of complications that accompany cirrhosis, including liver failure, hepatocellular carcinoma, and portal hypertension.

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ARFI at The Royal Melbourne Hospital

The Department of Radiology at The Royal Melbourne has used liver ARFI in routine clinical practice since August 2012, with more than 1,200 patients studied. To obtain liver ARFI measurements, The Royal Melbourne uses these parameters:

- Patient preparation—Patient fasts for at least 4 hours.
- Patient positioning—Supine or, if needed, right side slightly raised.

Key Principles for Measurement

ARFI measurements are obtained after performing a liver scan, which usually takes the form of targeted liver ultrasound (TUSL)[1]. As a routine, the measurements are obtained from the right lobe of the liver via an intercostal approach with the probe in the coronal or oblique coronal plane to allow for a good intercostal window.

The key principles in acquiring ARFI measurements are:

- Select a good acoustic window with no shadowing.
- Place ROI at a depth of between approximately 2 and 4 cm deep to the liver capsule.
- Select an area of liver that is free of major veins and portal tracks and appears homogenous and free of focal pathology. The precise segment (i.e., 5-8) does not appear to be as important as achieving a good window.
- Use light pressure only when scanning. Firm pressure may artificially elevate the observed shear wave speed measurement.
- Take measurements during suspended respiration in a way that provides a good window. Avoid prolonged inspiration, expiration, and Valsalva.

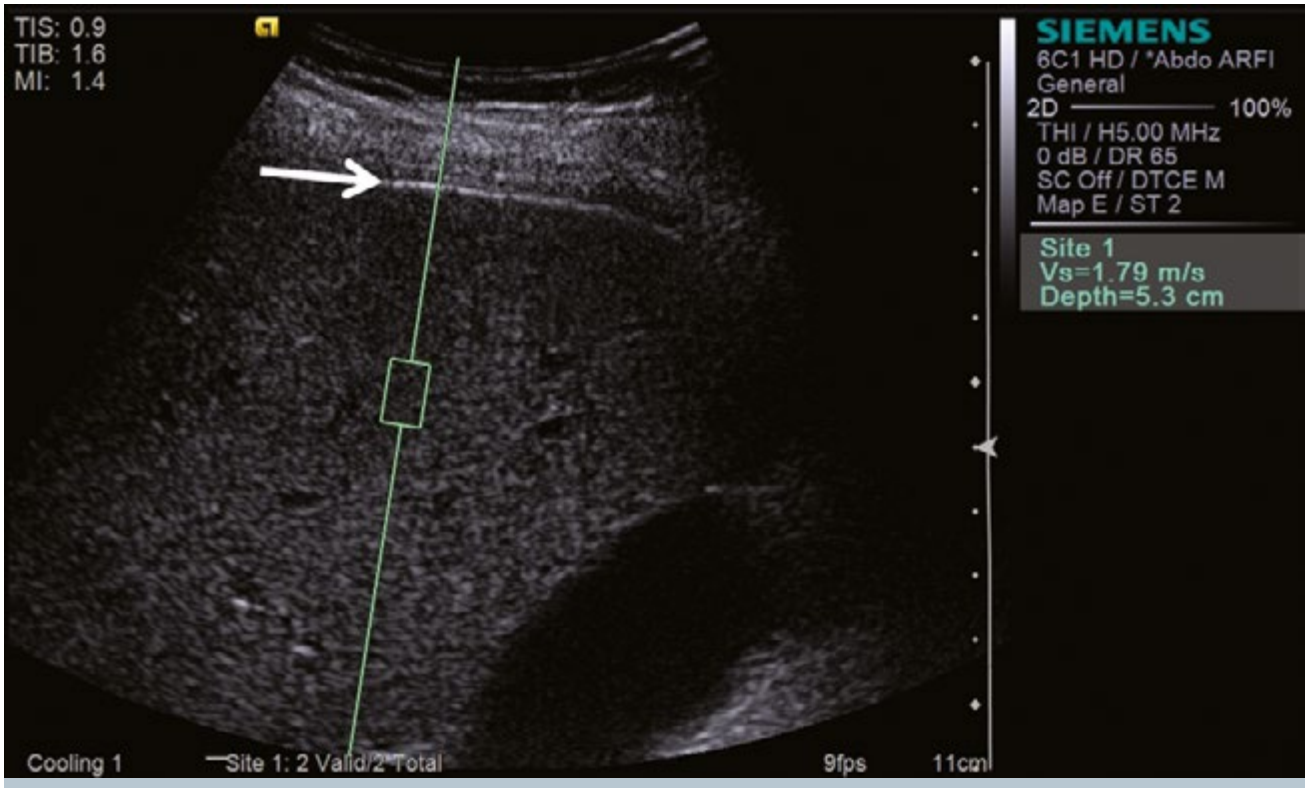


Figure 1. ARFI sample obtained from right lobe of liver where there is a good acoustic window. The ROI is placed 2–4 cm deep to the liver capsule, away from visible portal tracts and veins. The US line of sampling is approximately at right angles to the liver surface in the plane of scanning as well as in the orthogonal plane, which is recognizable by the strong specular reflection (arrow). The measured shear wave speed is displayed on the right. The total of the valid readings is displayed at the bottom. (In this example "2 Valid/2 Total.")

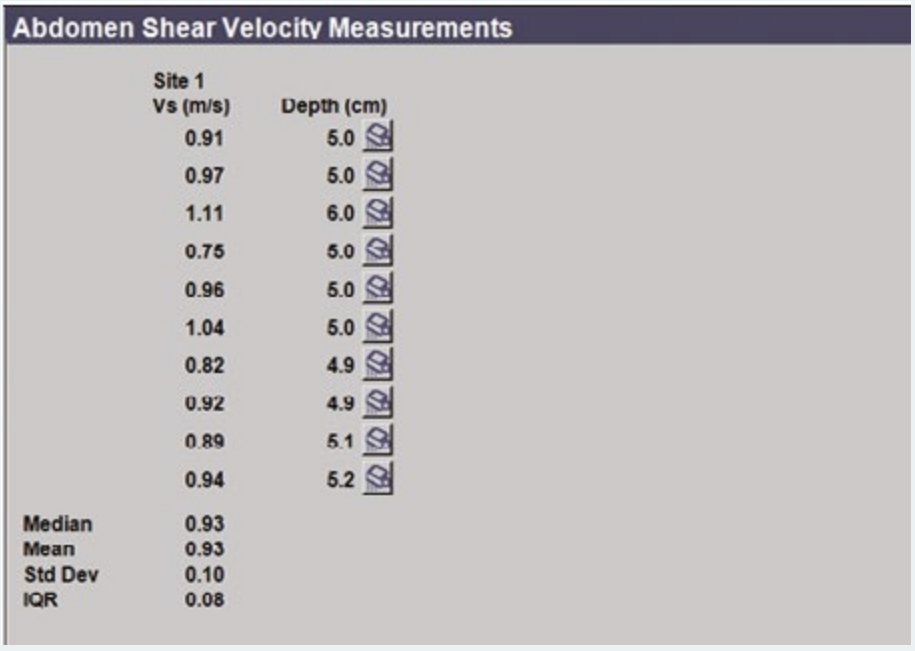


Figure 2. The 10 valid samples are displayed with depth from skin of each measurement, and summary information derived from the 10 measurements namely median speed, mean speed, standard deviation (SD), and interquartile range (IQR).

- Avoid relative movement between the probe and ROI. The probe must be kept still and measurements should only be taken when there is no liver motion. (If motion does occur at the time of pushing the sample button, then this measurement should not be recorded.)
- Obtain one reading per suspended respiration (attempting to take more than one reading tends to result in respiratory motion or a part Valsalva).
- Have the sampling US line cross the liver capsule approximately at right angles in the scanning plane (Figure 1).
- The scanning plane should be approximately at right angles to the liver surface in the orthogonal plane. The latter is achieved by choosing a scanning plane that generates a specular reflection from the liver capsule (Figure 1).

Valid Measurements and Sampling Volumes

Routinely 10 valid ARFI measurements are taken from a relatively small area in the right lobe, which meets the key measurement criteria. The measurements can be separated by a few centimeters provided that these criteria are met. (See the 10 valid samples as shown in Figure 2.)

The value used for reporting is the median speed. The interquartile range (IQR) is included in the report as a measure of the dispersion on shear wave velocity measurements around the median, which helps describe the reliability of the measurement.

If there is reason to suspect a macroscopic variation in the degree of fibrosis (for example, as can occur in primary sclerosing cholangitis), then it may be informative to sample from a wider area of liver. This, however, is not performed routinely.

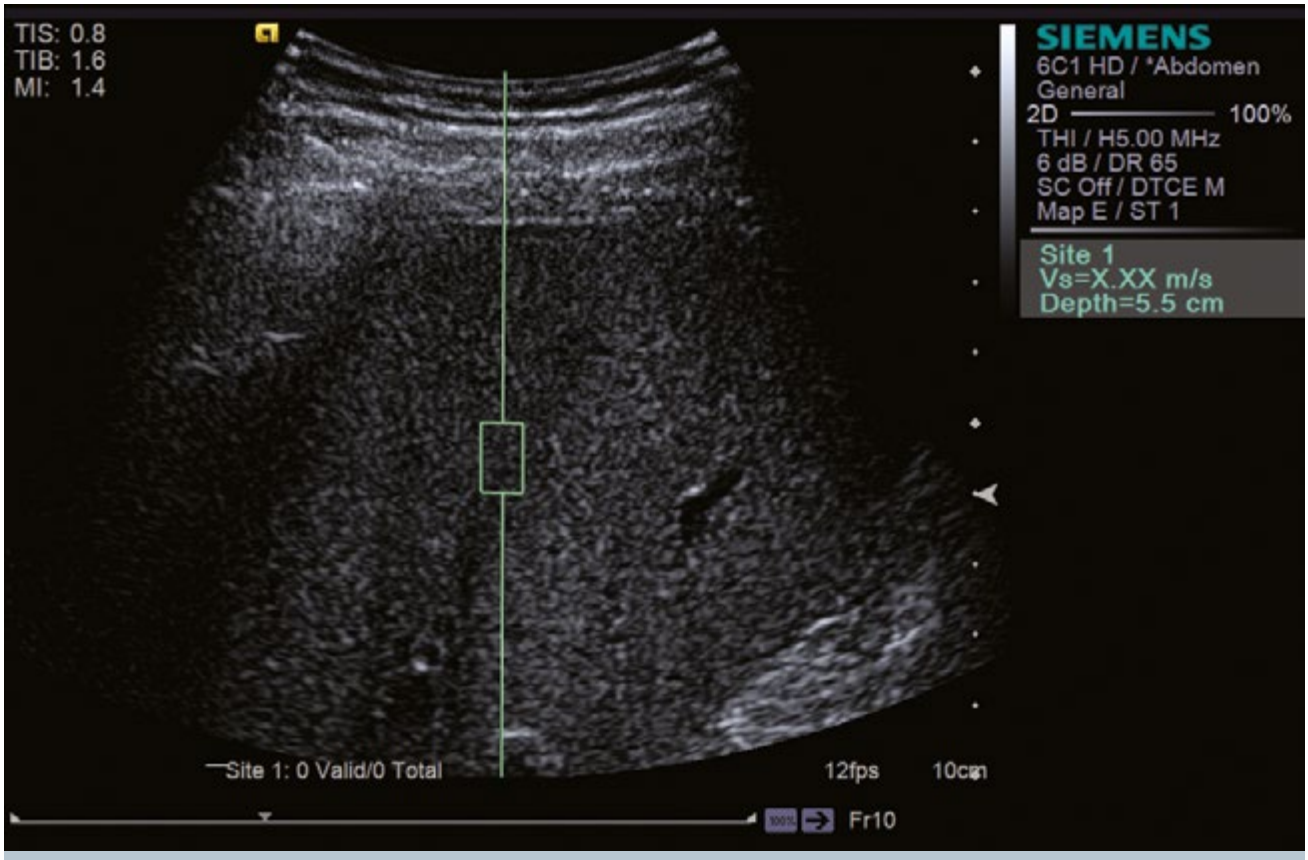
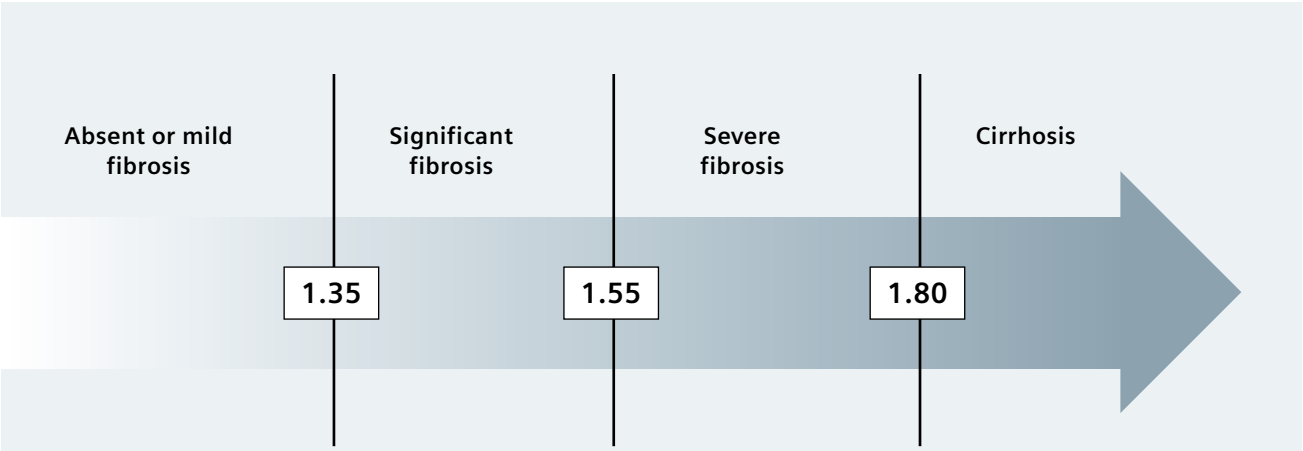


Figure 3. ARFI sample obtained that falls outside of measurable range and is recorded as "XXX m/sec." The tally of measurements at the bottom of the image reflects this as "0 Valid/ 0 Total."

If invalid measurements are obtained, which occur, for example, because of poor signal, movement, or placement of the ROI over a large vessel, this is signified by "XXX m/sec" (See Figure 2). These can be saved but even if not saved, the tally of valid measurements is shown at the bottom of each attempted measurement (Figures 1 & 2). Additional measurements would need to be obtained to achieve the necessary 10 valid measurements.

Assigning Fibrosis Stage Based on ARFI Readings

The threshold values used to assign patients into F0, F1, F2, F3, and F4 vary slightly between organizations. They may also vary slightly depending on the cause of liver disease. The threshold values used in the Department of Radiology at The Royal Melbourne Hospital are those derived from the large meta-analysis of Friedrich-Rust et al[2], which used liver biopsy as a reference in a large cohort comprising mainly patients with hepatitis C-related disease (Figure 4).



after Friedrich-Rust et al J. Viral Hepatitis, 2012, 19, e212-e219[2]

Figure 4. The threshold values used in our department are those derived from the meta-analysis of Friedrich-Rust et al[2]. This approach makes no attempt to separate out F0 and F1 as this is of little clinical importance. The graduated arrow is used to emphasize that the threshold values are not 100% accurate.

Formatting the Report

Since the study is one part of the liver ultrasound examination, the imaging findings and, where appropriate, Doppler findings are first reported. The ARFI findings follow including the median speed and the IQR.

It is important to recognize that the thresholds between fibrosis grades are not absolute and also that factors other than fibrosis may impact ARFI measurements. A footnote in the report is useful to draw this to the attention of those reading the report; Figure 4 is also a useful inclusion in the report. Acute inflammatory activity, in particular, tends to elevate the ARFI values and therefore artificially elevate the fibrosis stage.

The footnote used by the Department of Radiology at The Royal Melbourne Hospital currently reads:

<1.35 - absent or mild fibrosis (F0 or F1)

1.35-1.55 - significant fibrosis (F2)

1.55- 1.80 - severe fibrosis (F3)

>1.80 - cirrhosis (F4)

(Based on meta-analysis of pooled data, which included a predominance of HCV patients - Friedrich-Rust et al J Viral hepatitis 2012, 19 e212-1219.)

- These thresholds are not absolute.
- Results should be interpreted in clinical context. Factors such as inflammatory activity & venous congestion can elevate the ARFI value.
- Values with an IQR of >0.3 x median velocity should be either discounted or interpreted with caution depending on how close they are to this threshold. (i.e., IQR/median velocity should be ideally <0.3)

Identifying Unreliable Measurements[3]

If the interquartile range (IQR) is > 0.3 x median speed (IQR:median > 0.3), then this signifies a wider dispersion of velocities around the median and the median value is less reliable. The options are to reject this set of measurements (and repeat a further set) or, at the very least, exercise caution in interpreting the result.

If the valid measurements (i.e., those that do not appear as XXX) are <60% of total measurements taken, then this makes the overall validity of measurements less reliable. The options are to reject this set of measurements (and consider repeating a further set) or, at the very least, exercise caution in interpreting the result. This situation tends to occur because of patient factors (poor cooperation, high BMI, and/or marked steatohepatosis), and attempts at a second set of measurements often fail.

Author and References

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[2] Friedrich-Rust M, Nierhoff J, Lupsor M, Sporea I, Fierbinteanu-Braticevici C, Strobel D, Takahashi H, Yoneda M, Suda T, Zeumem S, Herrmann E. Performance of Acoustic Radiation Force Impulse imaging for the staging of liver fibrosis: a pooled meta-analysis. J Viral Hepatol. 2012 Feb;19(2):e212-9. doi: 10.1111/j.1365-2893.2011.01537.x. Epub 2011 Oct 30.

[3] Bota S, Sporea I, Sirli R, Popescu A, Danila M, Jurchis A, Gradinaru-Tascau O. Factors associated with the impossibility to obtain reliable liver stiffness measurements by means of Acoustic Radiation Force Impulse (ARFI) elastography—analysis of a cohort of 1,031 subjects. Eur J Radiol. 2014 Feb;83(2):268-72. doi: 10.1016/j.ejrad.2013.11.019. Epub 2013 Dec.

Standalone clinical images may have been cropped to better visualize pathology.

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