

## Transient Elastography (FibroScan)

In people with hepatitis C, determining the level of liver fibrosis is important to monitor disease progression, and assist with treatment decisions.

Liver biopsy has traditionally been considered the “gold standard” test to measure fibrosis, and indeed until 2006, people with hepatitis C could not access government funded treatment unless they had this procedure. However, liver biopsy is an invasive procedure which can be painful, and carries a small risk of complications, it is also costly, and sampling errors have also been a problem.

Non-invasive ways of measuring liver fibrosis are emerging. Hepatology journals and liver conferences frequently discuss the ‘pros’ and ‘cons’ of different tests being trialed. One new test now available at five hospitals around Australia is the FibroScan.

FibroScan (Transient Elastography) is a new device used to measure the elasticity or stiffness of the liver – the stiffer the liver, the more severe the hepatic fibrosis (scarring).

In this article, we will be exploring FibroScans: what they are, how to access them in Australia, how they work and how accurate they are.

With more than 250 FibroScans in use around the world, five are now up and running in Australian hospitals – The Alfred Hospital, Concord Hospital, Liverpool Hospital, St Vincent’s Hospital (Sydney) and Greenslopes Hospital.

We have been talking to Associate Professor Stuart Roberts of the Alfred Hospital in Victoria ...

“It is very likely that FibroScan is going to become fairly standard for most liver centres and probably many private centres to have available for patient assessment. Given the interest we have had in Victoria amongst specialists and GPs, I think demand is only going to grow and grow quite quickly.”

“We conduct an average of 40 scans throughout the week, and are booked up until May, so it is very popular,” he said.

“Fibroscans are a valuable tool that, once people become more aware of, will be very effective in a patient’s clinical management.”

Such a valuable tool should not go unused by those with hepatitis C. Those people who are interested in undergoing FibroScan should be aware that the process may differ depending on their location.

"In Victoria we have FibroScan request pads that GPs can use to refer the patient, that can be patient initiated through their GP," said Professor Roberts.

"In other centres, I think they may have phone numbers you can call."

While many people are familiar with waiting substantial periods of time to learn of their test results, the FibroScan enables a reading to be made at the time of the procedure. Yet further explanation is done by a patient's referring general practitioner after the scan.

"We normally give the patient an indication at the time of the procedure that they have got minimal, moderate, or more marked scarring, but encourage them to go back to their doctor to talk about the results in more formal detail," said Professor Roberts.

"At the Alfred, we get the results back to the referring doctors within two or three days."

While cost may be an issue for many patients, you should again check with the centre closest to you, Professor Roberts explained, as it may cost next to nothing.

"It could vary from centre to centre, but at the Alfred Hospital we do not bill patients so patients are not out of pocket for the test."

"It does not as yet have a Medicare item number but it is hoped that in the future this will occur," he said.

What there is a need for is for people to be aware of what FibroScans do, and how they do it. FibroScans can show the progression, stagnation, or weakening of a person's liver fibrosis when patients are scanned, not unlike an ultrasound, which measures the extent to which their liver is fibrotic.

"FibroScan is an ultrasound- like device that assesses the degree of liver damage, in particular scar tissue, or as clinicians call it, fibrosis, through a measurement of liver stiffness," said Professor Roberts.

"It does this by sending a mechanical vibration wave through the liver. The speed at which that wave travels through the liver is measured via ultrasound as it detects the sound wave reflection. This is then computed into a reading that measures the elasticity of the liver, or conversely, the stiffness of the liver. The more scarred or fibrotic the liver is, the stiffer it is, hence the higher the reading."

However, as Professor Roberts explains, FibroScans are not able to detect the particular cause of the liver fibrosis.

“There is a lot of data in a few specific liver diseases, particularly the most common of fatty liver disease, but also viral hepatitis, in regards to successfully detecting liver fibrosis.”

“In regards to its reliability, there is limited data on other diseases such as hepatitis B, and some less common and more specialised liver diseases, so we don’t know how reliable it is there.”

“There is some suggestion that in liver diseases in which there is impaired bile flow, or cholestasis, the test may not be as reliable. Cholestatic liver diseases are basically diseases in which there is damage to bile ducts, and therefore bile flow through the liver is not as good,” he said.

While FibroScan is unable to accurately detect fibrosis in 100% of cases, Professor Roberts said there are a number of advantages of FibroScan in comparison to liver biopsy.

“Firstly, FibroScan is non-invasive, and for patients, that means a pain free experience when clinicians are assessing their liver disease. It is a simple procedure that can be done in an outpatient setting relatively quickly – a typical test would take no more than ten minutes, 15 minutes in more difficult cases such as those who are overweight.”

“There is also no need for preparation, as patients can have a FibroScan done while fasting or non-fasting,” he said.

“FibroScan can also be performed over time, allowing numerous readings to be done on a yearly basis, for example, in order to track their liver disease and determine whether scarring is increasing. Liver biopsy on the other hand, is not a suitable test in the same sense – it involves a lot of anxiety for patients.”

“FibroScan is a much more patient - friendly option with minimal anxiety attached,” said Professor Roberts.

FibroScans are also of significant benefit to people with haemophilia, providing a welcome alternative to liver biopsies, which are more dangerous to perform due to the risk of bleeding.

In addition to the non-invasive benefits FibroScan provides haemophiliacs, Professor Roberts believes it could also be of benefit for people who have already undergone a liver transplant, but not so much for those *requiring* a transplant.

"In patients requiring liver transplant, FibroScan probably doesn't play a major role, because we already know they have got severe liver disease. They are often in a stage of liver failure, so there is little to add by way of FibroScan," he said.

"Where it might be helpful, is in those patients who have had a liver transplant, and are undergoing regular follow - up appointments. These patients often have a recurring infection. For example, hepatitis C, post-transplant is associated with worsening liver fibrosis or scarring, and this is where FibroScans may be a useful assessment tool, rather than having to have liver biopsies performed post-transplant."

As much as there are real benefits to patients undergoing FibroScan, there is also some limitation to its abilities. Speculation about the accuracy and reliability of FibroScan in assessing the different stages of Fibrosis – stage 0, stage 1, stage 2, stage 3 and stage 4 – have been circulating.

"What we can confidently say with FibroScan is that it's a very good tool for assessing the severity of liver disease at both ends of the spectrum; that is, it's extremely good at picking up mild or minimal disease, and very good at diagnosing cirrhosis, with 90-95% accurate positive predictive value," said Professor Roberts.

"For those with more moderate disease, that being patients who have got stage 2 or stage 3 disease, or possibly even late stage 1, it is not as good at differentiating between the stages in these situations."

"It cannot reliably tell you that this person has stage 2 disease with the same degree of confidence that it can for saying this patient has cirrhosis or minimal fibrosis."

The reason, Professor Roberts explains, stems from the fact that there is considerable overlap in the readings of patients who have moderate fibrosis and have stage 2 disease versus stage 3, whereas there is very minimal overlap for those with stage 1 versus stage 4.

When analysing the reliability of FibroScan, keep in mind the pitfalls of current widely used tools for analysing liver disease, such as liver biopsies and serum markers.

The evidence suggests the FibroScan, in comparison to several other non-invasive tests used to measure the degree of fibrosis, or scarring of the liver, such as biochemical markers, biomarkers and new imaging techniques, is holding its own, explains Professor Roberts.

"The evidence to date supports that FibroScan is better, in the comparisons that have been done. While the other tests are quite good for assessing cirrhosis, FibroScan is right at the top end of the spectrum for assessing fibrosis and cirrhosis."

"The other serum markers are no better, if not worse," he said.

“We also know that liver biopsies aren’t very good at differentiation either, because depending on where the needle is put in the liver, you can get quite different readings on the severity of liver fibrosis.”

“So we can say that FibroScan is reasonably good for those with moderate fibrosis but extremely good for those with minimal or severe fibrosis. We can be very confident at those end points,” said Professor Roberts

There are subsequently implications for both those patients who cannot get a definitive answer as to the stage of their liver disease, and for those who are told they have minimal or severe fibrosis.

“The implications for those patients who we ultimately cannot tell with the same degree of confidence that they have stage 2 or stage 3, as opposed to stage 1 or 4, is that they can only get a guide for their liver disease,” said Professor Roberts.

“On the other hand, for those patients who we can confidently say ‘No, there is no fibrosis’, or ‘Yes, there is advanced fibrosis’; there is not a lot to add by going and doing a biopsy.

However, despite the degree of accuracy that can accompany the reading of a patient with minimal or severe liver disease, some patients still opt to undergo a liver biopsy, explains Professor Roberts.

“For some patients, they may not accept a reading that is suggestive rather than diagnostic, so there may be a role for further assessment via liver biopsy.”

“The biopsy may then influence their decision to undergo treatment, as opposed to FibroScan alone. Whether or not to undergo treatment is one of the main reasons behind patients wanting to assess their liver disease,” he said.

In some situations, liver biopsy is the recommended course of action, rather than relying on the reading given by FibroScan alone.

“Where there is uncertainty about the diagnosis of a patient’s abnormalities, that’s always an issue for liver biopsy, because it can add to the assessment of the patient by picking up other changes such as liver inflammation, where specific changes on the liver that might be alcohol related, fatty liver or viral hepatitis-related may occur. Liver biopsy may be able to clarify this with a more accurate assessment,” said Professor Roberts.

FibroScan also has other limitations that people wanting to undergo a FibroScan should be aware of; its inability to get an effective reading in patients with significant liver inflammation for those who have a pacemaker, or its inability to diagnose moderate fibrosis accurately, and its ineffectiveness in patients who are obese should all be noted. Yet the development of a new probe could overcome the difficulty of assessing patients who are overweight.

“Right at this moment, one of the major limitations of FibroScan is that it is not particularly effective in patients who are obese, or are significantly obese, because it can fail to get a reading. You just won’t get a reading in about 35% of these patients,” said Professor Roberts.

“However, this is about to change. There are probes becoming available for patients who are obese, so readings will now be able to be obtained.”

“Finally, it is not particularly useful for assessing patients who have very significant liver inflammation, be it a flare of their disease, or an acute hepatitis, because it has been shown that in those patients, liver stiffness does increase, and will give a falsely elevated reading at that time. The reading will often settle down as their inflammation settles down, and it is recommended these patients come back and get another reading at a later date.”

All this being said, Professor Roberts does state that FibroScans are not perfect; they should be thought of as a complementary tool, used by clinicians to assess their patients, not as a replacement for liver biopsies.

“It’s not perfect. It certainly does not replace the need for liver biopsy, but it’s a very useful assessment tool that provides important input into a clinician’s assessment of patients with liver disorders.”

“FibroScans can be used to supplement decision making as to whether a biopsy is helpful or not,” he said.

“They are also a tool which can certainly assist greatly in identifying patients with undiagnosed liver disease. We have had a number of cases where we have diagnosed cirrhosis where cirrhosis wasn’t expected.”