NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance scope

FibroScan for assessing liver fibrosis and cirrhosis outside secondary and specialist care

1 Technology

1.1 Description of the technology

FibroScan (Echosens) is a non-invasive medical device that assesses liver fibrosis and cirrhosis by measuring the degree of liver stiffness. It can distinguish normal liver or minimal fibrosis from cirrhotic livers. FibroScan uses proprietary vibration controlled transient elastography to quantify liver stiffness which is essentially a measure of the extent of liver scarring. The test takes around 15 minutes to complete and does not require visualisation of the liver or the use of anaesthetics. During the assessment, a probe is placed on the skin over the liver. The probe emits a shear wave that passes through the subcutaneous tissue into the liver. An algorithm analyses the returned wave to determine its speed in meters per sec (m/s) and the equivalent stiffness in kilopascals (kPa). In harder tissue shear waves propagate faster. FibroScan can measure liver stiffness up to 75kPa. The threshold used in clinical practice may depend on the underlying cause of liver disease.

FibroScan results can be combined with other parameters (including blood markers such as AST) to generate FibroScan-based scores.

In addition to fibrosis, FibroScan can also assess levels of fat in the liver using a controlled attenuation parameter (CAP) tool. From 2021, functionality is available to allow continuous measurement of CAP during an examination

using the SmartExam tool. Adding the SmartExam functionality is optional and comes at an extra cost.

Products in the FibroScan range are listed in table 1. Different sizes (small, medium or extra-large) of probes are available. The device comes with a medium probe. Small and extra-large probes are optional extras. The extra-large probe is designed to enhance signal penetration through deeper tissues, reducing device failure rates in obese patients. The company states that the Fibroscan 430 Mini and Fibroscan 430 Mini+ are currently used in primary care, noting that the greater mobility of these systems allows easier movement between different locations within the same primary care network. The company state that there is no restriction on the use of any of the products in primary care.

Table 1. Fibroscan products

Technology	Portable system	Smart Exam	Indications	Battery-powered	Weight (Kg)
FibroScan 230 / FibroScan Go (*The company states that Fibroscan 230 will be launched in the UK in 2022*)	Mobile	Yes	Liver fibrosis and liver steatosis	No	4.4
FibroScan 430 Mini and M probe (*The company states that Fibroscan 430 mini will not be sold form January 2022*)	Mobile	No	Liver fibrosis	Yes	5
FibroScan 430 Mini+ and M probe	Mobile	Yes	Liver fibrosis and liver steatosis	Yes	5

FibroScan 530 Compact and M probe	Transportable	Yes	Liver fibrosis and liver steatosis	Yes	10
FibroScan 630 Expert Spleen Pack and M probe	No	Yes	Liver fibrosis, liver steatosis and portal hypertension	No	46

Transient elastography is mainly used in secondary care but has been used in a primary care setting at some sites. This scope focuses on the use of the technology outside secondary and specialist care. Primary care services are the first point of contact to the NHS and includes general practice, community pharmacy, dental, and optometry (eye health) services. Community health services include district nursing and health visiting. This technology may also be used in community based services such as weight management services for obese people and alcohol support services alongside other community based services.

1.2 Relevant diseases and conditions

Liver fibrosis is a condition of the liver that can progress into cirrhosis if not managed (see further details below). It is estimated that every day in the UK, 40 people die from liver disease, making it the third leading cause of premature death in the UK (British Liver Trust). A common feature of all liver disease is that over time it can cause low grade chronic inflammation and scarring of the liver. Common risk factors for liver disease include excess alcohol intake, diabetes, obesity and hepatitis B and C infection.

Liver fibrosis

Liver fibrosis occurs when persistent inflammation of the liver causes excessive scar tissue to build up in the organ and nearby blood vessels. The presence of scar tissues can impair the overall liver function and limit blood flow which may lead to the death of liver cells. Advanced liver fibrosis can

develop into cirrhosis, liver failure, and portal hypertension and may require liver transplantation. Liver fibrosis is caused by the following liver diseases:

- Hepatitis – this refers to the inflammation of the liver caused by viral infection or excess alcohol consumption. There are several types of viral hepatitis including hepatitis A, B, C, D and E. Other types of hepatitis include alcoholic and autoimmune hepatitis. Hepatitis C is the most common viral hepatitis in the UK, and it is estimated that around 400,000 people are infected and 180,000 people in the UK have hepatitis B (British Liver Trust). Other forms of viral hepatitis are less common in the UK.

- Non-alcoholic fatty liver disease (NAFLD) – this is the most common cause of liver fibrosis. It starts as a simple fatty liver (steatosis) and can then progress to non-alcoholic steatohepatitis (NASH), a more severe form of NAFLD, estimated to affect up 5% of the UK population. Persistent NASH develops into fibrosis.

- Alcohol-related liver disease (ARLD) – this refers to the damage of the liver caused by excess alcohol intake. ARLD occurs in 3 stages, the first being alcoholic fatty liver disease, caused by intake of alcohol over a short period. It is reversible if alcohol intake is stopped. The second stage is alcoholic hepatitis which is caused by excess alcohol intake over a longer period. Cirrhosis is the third stage of ARLD (NHS 2018). ARLD is common in the UK and over the last few decades, the number of people with the condition has increased. Around 7,700 people die from ARLD each year (British Liver Trust).

Cirrhosis

Cirrhosis is a late-stage liver disease that occurs when inflammation and fibrosis has spread throughout the liver and disrupts the shape, repair and function of the liver. It is characterised by the replacement of normal healthy liver tissue with scar tissues and irregular bumps which harden and prevent the liver from functioning as normal. Cirrhosis usually develops silently

following exposure to 1 or more risk factors such as alcohol misuse and hepatitis B or C which cause inflammation within the liver, or in those individuals with non-alcoholic fatty liver disease (NAFLD). However, not everyone with inflammation of the liver will eventually develop cirrhosis. Untreated cirrhosis can cause liver failure, liver cancer or death. It is estimated that over 4,000 people in the UK die from cirrhosis and around 700 people get a liver transplant each year as a result of the condition (British Liver Trust). People with cirrhosis may show no symptoms or signs of liver disease for many years and so do not come to the attention of health services until their disease progresses and they develop major complications such as jaundice or fluid retention which can manifest as swelling of the abdomen or lower limbs, bleeding from their upper gastrointestinal tract or changes in their mental status.

1.3 Diagnostic and care pathway

Currently, transient elastography (FibroScan) is predominantly used in secondary care. The NICE guideline on Cirrhosis in over 16s recommends that transient elastography is offered for initial assessment to diagnose cirrhosis for:

- people with hepatitis C virus infection
- men who drink over 50 units of alcohol per week and women who drink over 35 units of alcohol per week and have done so for several months
- people diagnosed with alcohol-related liver disease.

The guideline further states "Offer either transient elastography or acoustic radiation force impulse imaging (whichever is available) to diagnose cirrhosis for people with NAFLD and advanced liver fibrosis (as diagnosed by a score of 10.51 or above using the enhanced liver fibrosis [ELF] test)." It is not recommended to offer tests to diagnose cirrhosis for people who are obese (BMI of 30 kg/m^2 or higher) or have type 2 diabetes unless they have NAFLD and advanced liver fibrosis (as diagnosed by a score of 10.51 or above using the ELF test). People diagnosed with cirrhosis on transient elastography are

referred to a specialist in hepatology. Retesting for cirrhosis is recommended to be offered every 2 years for:

- people diagnosed with alcohol-related liver disease
- people with hepatitis C virus infection who have not shown a sustained virological response to antiviral therapy
- people with NAFLD and advanced liver fibrosis.

The NICE guideline on Hepatitis B (chronic) recommends transient elastography as an initial test for liver disease in adults newly referred for assessment and for the annual reassessment of liver disease in adults who are not taking antiviral treatment. It is recommended that liver biopsy is considered to confirm the level of fibrosis in adults with a transient elastography score between 6 and 10 kPa. Liver biopsy is also recommended for adults with a transient elastography score less than 6 kPa if they are younger than 30 years and have HBV DNA greater than 2000 IU/ml and abnormal ALT (greater than or equal to 30 IU/L for males and greater than or equal to 19 IU/L for females) on 2 consecutive tests conducted 3 months apart.

The NICE guideline on non-alcoholic fatty liver disease states that use of the enhanced liver fibrosis (ELF) test should be considered in people who have been diagnosed with NAFLD to test for advanced liver fibrosis. However, if this test is not available, FibroScan is used here in current practice. FibroScan is included as a suggested test for use in the context of fibrosis assessment done for people with NAFLD in an algorithm proposed by the British Society of Gastroenterology.

Treatment

NICE's guideline on the assessment and management of non-alcoholic fatty liver disease recommends advice on physical activity and diet to people with NAFLD who are overweight or obese in line with NICE's obesity and preventing excess weight gain guidelines. People with NAFLD who drink

alcohol are also advised of the importance of staying within the national recommended limits for alcohol consumption.

The guideline makes the following recommendations on pharmacological treatment for people with advanced liver fibrosis:

- In secondary or tertiary care settings only, consider pioglitazone or vitamin E for adults with advanced liver fibrosis, whether they have diabetes or not.
- In tertiary care settings only, consider vitamin E for children with advanced liver fibrosis, whether they have diabetes or not.
- In secondary or tertiary care settings only, consider vitamin E for young people with advanced liver fibrosis, whether they have diabetes or not.
- Offer to retest people with advanced liver fibrosis 2 years after they start a new pharmacological therapy to assess whether treatment is effective.
- Consider using the ELF test to assess whether pharmacological therapy is effective.
- If an adult's ELF test score has risen, stop either vitamin E or pioglitazone and consider switching to the other pharmacological therapy.
- If a child or young person's ELF test score has risen, stop vitamin E.

There is no cure for liver cirrhosis. Medicines offered to people with liver cirrhosis depend on the cause of liver damage. NICE's Clinical Knowledge Summary on Cirrhosis highlights that primary care management of cirrhosis includes offering advice on healthy eating, diet and alcohol consumption, medication review, being alert to features of potential complications of cirrhosis and referral to appropriate hepatology specialists. NICE guideline on Cirrhosis in over 16s: assessment and management includes recommendations on monitoring and managing complications of cirrhosis.

1.4 Regulatory status

FibroScan is a CE marked medical device (class IIa).

1.5 Claimed benefits

The benefits to patients claimed by the company are:

- Enables earlier or more accurate diagnosis
- Reduces risks, side effects or complications
- Enables a test, procedure or treatment to be done non-invasively
- Enables behaviour changes or lifestyle interventions

The benefits to the healthcare system claimed by the company are:

- Enables delivery of care in primary care setting (e.g. GP or community services) rather than in secondary care setting.
- Increases compliance
- Requires less time
- Reduce unnecessary referrals to secondary care

Some of the benefits of FibroScan claimed by the company may capture benefits that would only be realised from wider, or earlier, use of the technology. However, this guidance will only consider FibroScan as currently used in the NHS (that is, not in a wider population or extent of use) but used in primary care, rather than secondary or specialist care.

2 Decision problem

Population	People having a FibroScan to assess for liver fibrosis or cirrhosis (as per current NHS practice)
Intervention	FibroScan done outside secondary or specialist care (for example, GP or community services).
Comparator	FibroScan done in secondary or specialist care
Outcomes	The outcome measures to consider include: • Test accuracy • Agreement between measurement made by FibroScan done in primary and secondary/tertiary care

	• Comparative performance between different FibroScan models • Test failure • Uptake of offered FibroScan test • Uptake of behavior/ lifestyle change intervention • Number of referrals to secondary care • Number of people referred to alcohol or weight management services • Severity of liver fibrosis • Device-related adverse events • Use of NHS services (for example, GP or outpatient appointments) • Mortality • Morbidity (such as liver cirrhosis, liver related complications, cardiovascular complications)
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.
Subgroups to be considered	Use of Fibroscan in specific populations, for example for people with: • Non-alcoholic fatty liver disease • Suspected non-alcoholic fatty liver disease (for example, people with metabolic syndrome or type-2 diabetes) • Alcohol-related liver disease • Suspected alcohol-related liver disease (for example, based on hazardous alcohol use) • Hepatitis
Special considerations, including those related to equality	Fibroscan may have higher failure rates in people with higher BMI, particularly for people with central obesity, where possible data reporting failure rates in this group should be extracted. People from Black African, African Caribbean and South Asian (Indian, Pakistani, Bangladeshi) backgrounds are at a higher risk of developing type 2 diabetes from a younger age and therefore have a higher risk of liver disease. People with alcohol or substance misuse are at higher risk of liver disease. Liver cirrhosis may in the long term, prevent a person from performing their normal day-to-day activities. Disability is a protected characteristic under the Equality Act 2010.

Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

3 Related NICE guidance

Published

Non-alcoholic fatty liver disease (NAFLD): assessment and management (2016) NICE guideline (NG49)

Cirrhosis in over 16s: assessment and management (2016) NICE guideline (NG50)

Hepatitis B (chronic): diagnosis and management (Published 2013, updated 2017) NICE Clinical guideline (CG165)

4 External organisations

The following organisations have been invited to register as stakeholders.

4.1 Professional

- British Society of Paediatric Gastroenterology, Hepatology and Nutrition
- Faculty of Public Health
- Royal College of General Practitioners
- Royal College of Physicians
- Royal College of Nursing

- British Society of Gastroenterology
- Royal Society of Medicine
- Royal College of Radiologists
- Royal College of Pathologists
- The Association of Clinical Pathologists
- British Association for the Study Of The Liver
- British Liver Nurses' Association
- British Liver Transplant Group
- The British Viral Hepatitis Group
- Royal Society for Public health UK
- Society for Endocrinology

4.2 Patient

- Black Health Agency
- Equalities National Council
- Muslim Council of Britain
- South Asian Health Foundation
- Liver4Life
- Children's Liver Disease Foundation
- British Liver Trust
- The Hepatitis C Trust
- Guts UK