NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

SCOPE

Virtual Touch Quantification to diagnose and monitor liver fibrosis

1 Technology

1.1 Description of the technology

The Virtual Touch Quantification (VTq) (Siemens) software application assesses the stiffness of liver tissue through measurement of shear wave speed. It is used in combination with the Siemens Acuson S2000 or S3000 ultrasound platform. The VTq software uses acoustic radiation force impulse (ARFI) imaging technology to measure the elasticity of tissue. This type of imaging involves the generation of a shear wave by applying an acoustic 'push pulse' lateral to the area of interest identified during a conventional ultrasound scan. The speed of the shear wave is proportional to the stiffness of the tissue. The VTq investigation comprises multiple measurements and is non-invasive and painless. The software generates a report which includes a statistical summary of the median and mean shear wave velocities. The reliability of VTq measurements is usually confirmed by calculating the ratio of the inter-quartile range to median, which should be less than 0.30. A VTq test adds 5-10 minutes to a routine abdominal ultrasound scan or it can be done as a stand-alone test, taking no more than 15 minutes to complete. An ultrasonographer, radiologist or hepatologist will perform the test and interpret the data, enabling reporting to the referring physician on the same day.

1.2 Regulatory status

VTq received a Class II CE mark in 2008 and is reported to be installed in 28 sites in the UK. VTq is indicated for adults or children needing assessment of liver fibrosis.

1.3 Claimed benefits

The benefits to patients claimed by the sponsor are:

- The VTq is painless and may be safer compared to liver biopsy as the standard of care
- No hospital stay or post procedure monitoring is required with VTq because the procedure can be performed in the outpatient setting
- Serial biopsies over several years to monitor fibrosis progression may be avoided, therefore improving a patient's quality of life
- A more complete assessment of the liver is achieved during the VTq procedure as a sonogram provides visualization of the liver parenchyma, portal and hepatic veins, portal and hepatic venous and arterial blood flow measurements, and visualization of the biliary tree for possible obstructions.
- Hepatic cellular carcinoma (HCC) surveillance is included during the sonogram in patients with cirrhosis along with VTq measurements.
- Early identification of fibrosis in patients with viral hepatitis may allow earlier intervention with anti-viral drugs, which can reverse the course of early disease.

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

- Potential for increased capacity because the VTq procedure does not need to be performed by a consultant.
- Reduced procedure costs with fewer biopsies required over several years if fibrosis progression is monitored using VTq.
- Reduced resource costs because no hospital admission or stay is needed for VTq measurements in an outpatient setting.

1.4 Relevant diseases and conditions

Virtual Touch Quantification is intended for use in adults and children in whom assessment of liver fibrosis is indicated. This evaluation is concerned only with people with chronic hepatitis B or C.

Hepatitis refers to the inflammation of the liver. Acute hepatitis may resolve without causing permanent damage to the liver. It can, however, persist for many years (chronic hepatitis) causing scarring of the liver (fibrosis), and in the most serious cases loss of liver function (liver failure), which can be fatal. Hepatitis may be caused by a number of different disease processes including infection of the liver by the hepatitis viruses. Symptoms and signs of liver disease include jaundice, fatigue, itching, pain in the upper abdomen, distention of the abdomen, and intestinal

bleeding. However, liver disease may be silent and only be detected following routine blood tests.

Hepatitis B: NICE clinical guideline (published June 2013) CG165 Hepatitis B (chronic): Diagnosis and management of chronic hepatitis B in children, young people and adults states that approximately 19 people test positive for chronic hepatitis B per 100,000 population. A Foundation for Liver Research report in 2004 stated that around 180,000 people in the UK have chronic hepatitis B; data from the then Health Protection Agency, in 2006, suggested a similar population size.

Hepatitis C: There were 7,834 reported new cases of hepatitis C in England during 2010, but the true incidence is likely to be higher. It is estimated that around 200,000 people in England have hepatitis C. Between 10% and 40% of people with untreated chronic hepatitis C develop cirrhosis, which increases the risk of liver cancer.

1.5 Current management

NICE Hepatitis B (chronic) clinical pathway indicates that assessment of hepatitis B is usually in primary care where blood tests are undertaken; all patients who are hepatitis B surface antigen (HBsAg) positive should be referred to a hepatologist, gastroenterologist or infectious disease specialist with an interest in hepatology (children to a similar paediatric specialist in a secondary or tertiary centre).

In secondary or tertiary care patients are provided with information on disease progress, long term prognosis, HBV transmission and antiviral treatment options. Adult patients are then offered transient elastography as an initial test for chronic liver disease. Transient elastography (for example, FibroScan) is a non-invasive method of assessing liver fibrosis by measuring liver stiffness based on a mechanical wave generated by vibration. Children, young people and their parents or carers are offered liver biopsy to determine the need for anti-viral therapy, with appropriate information on biopsy limitations and risks.

Hepatitis B (chronic; NICE clinical guideline 165) recommends:

- Transient elastography as the initial test for chronic liver disease, offering antiviral treatment (without a liver biopsy) to patients with a transient elastography score ≥11 kPa
- Considering liver biopsy in patients with a transient elastography score between 6 and 10 kPa.

- Offering liver biopsy to patients with a transient elastography score < 6 kPa if they are <30 years and have HBV DNA >2000 IU/ml and abnormal ALT on 2 consecutive tests conducted months apart
- Annual reassessment of patients who are not taking antiviral treatment.

NICE is developing a clinical guideline on hepatitis C which is currently paused. Patients who are hepatitis C RNA positive on a blood test are referred to a hepatology clinic. The degree of fibrosis is assessed and treatment options are discussed depending on specific patient contraindications and degree of liver disease.

Liver biopsy is considered the gold standard for assessing liver fibrosis for both hepatitis B and C. Histological assessment uses the METAVIR score, based on an assessment of fibrosis and the degree of liver architecture disorganisation and classifies the severity of liver disease from none (grade F0) through mild, moderate, severe to cirrhosis (grade F4).

2 Reasons for developing guidance on Virtual Touch Quantification to diagnose and monitor liver fibrosis

The Committee recognised that Virtual Touch Quantification may offer benefits to patients and to the healthcare system. The Committee was advised that the three groups of patients most likely to benefit would be those with (a) viral hepatitis (b) alcoholic liver disease and (c) cystic fibrosis. To enable a comprehensive evaluation of the benefits and costs, using the medical technologies guidance published methods, this evaluation focuses, on pragmatic grounds, on the population with viral hepatitis as this is the largest benefitting population.

The Committee was advised that in addition to liver biopsy, which is the gold standard for the assessment of liver fibrosis, transient elastography should be considered as a comparator for the evaluation because this technology is becoming more widely used.

3 Statement of the decision problem

	Scope issued by NICE
Population	Virtual Touch Quantification is intended for use in adults or children with chronic hepatitis B or C in whom assessment of liver fibrosis is indicated.
Intervention	The Virtual Touch Quantification (VTq) software application used with the Siemens Virtual Touch Tissue Imaging systems (the Acuson S2000 or S3000 ultrasound platforms)
Comparator(s)	• Transient elastography • Liver biopsy
Outcomes	The outcome measures to consider include • Correlation in assessment of stage of liver disease • Sensitivity and specificity (using AUROC) in assessment of liver fibrosis • Correlation in assessment of stage of fibrosis using Metavir score • Use of anti-viral drugs • Quality of life measures • Hospital bed usage and length of stay • Requirement for liver biopsy • Device-related adverse events
Cost analysis	The cost analysis should include both transient elastography and liver biopsy as comparators depending on whether either or both of these represent standard care in the relevant patient population. The use in both primary and secondary care settings should be considered. Scenarios considered in the model should include settings where there is a compatible Siemens ultrasound machine and those without. Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared, for example ongoing fibrosis monitoring. 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	None
Special considerations, including those related to	None

equality		
Special considerations, specifically related to equality issues	None	
	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 characteristics?	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 MTAC will have relevant information to consider equality issues when developing guidance?	No

4 Related NICE guidance

Published

Hepatitis B (chronic): Diagnosis and management of chronic hepatitis B in children, young people and adults NICE clinical guideline 165 (June 2013). Available from http://publications.nice.org.uk/hepatitis-b-chronic-cg165.

SonoVue (sulphur hexafluoride microbubbles) – contrast agent for contrast-enhanced ultrasound imaging of the liver. NICE diagnostics guidance DG5 (August 2012). Available from: http://guidance.nice.org.uk/DG5

Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. NICE public health guidance PH43 (December 2012). Available from: http://guidance.nice.org.uk/PH43

Boceprevir for the treatment of genotype 1 chronic hepatitis C. NICE Technology appraisal guidance TA253 (April 2012). Available from: http://guidance.nice.org.uk/TA253

Extracorporeal albumin dialysis for acute liver failure. NICE Interventional procedure guidance IPG316 (September 2009). Available from: http://www.nice.org.uk/guidance/IPG316

Entecavir for the treatment of chronic hepatitis B. NICE technology appraisal guidance TA153 (August 2008). Available from:

http://www.nice.org.uk/guidance/TA153 Date for review: October 2011 Review decision.

Telaprevir for the treatment of genotype 1 chronic hepatitis C. NICE technology appraisal guidance TA252 (April 2012). Available from: http://guidance.nice.org.uk/TA252

Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B. NICE technology appraisal guidance TA96 (February 2006) Available from: http://www.nice.org.uk/guidance/TA96 Date for review: October 2011 Review decision

Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C. NICE technology appraisal guidance TA106 (August 2006) Available from: http://www.nice.org.uk/guidance/TA106

Tenofovir disoproxil fumarate for the treatment of hepatitis B. NICE technology appraisal guidance TA173 (July 2009) Available from: http://guidance.nice.org.uk/TA173

Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C. NICE technology appraisal guidance TA75 (January 2004). Available from: http://guidance.nice.org.uk/TA75

Telbivudine for the treatment of chronic hepatitis B. NICE Technology appraisal guidance TA154 (August 2008). Available from: http://guidance.nice.org.uk/TA154

Hepatitis C - peginterferon alfa and ribavirin. NICE Technology appraisal guidance TA200 (September 2010). Available from: http://guidance.nice.org.uk/TA200

Subcutaneous implantation of a battery-powered catheter drainage system for managing refractory and recurrent ascites. NICE interventional procedure guidance IPG479 (February 2014). Available from

http://publications.nice.org.uk/subcutaneous-implantation-of-a-battery-powered-catheter-drainage-system-for-managing-refractory-and-ipg479

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

Subcutaneous implantation of the ALFA pump System to manage ascites in patients with cirrhosis of the liver. NICE interventional procedure guidance expected: unknown
http://guidance.nice.org.uk/index.jsp?action=byId&o=13735

5 External organisations

5.1 Professional organisations

5.1.1 Professional organisations contacted for expert advice

At the selection stage, the following societies were contacted for expert clinical and technical advice:

- Association for Clinical Biochemistry
- British Association for the Study of the Liver
- British Medical Ultrasound Society
- British Society of Gastroenterology
- Royal College of Radiologists
- Society and College of Radiographers

5.1.2 Professional organisations invited to comment on the draft scope

The following societies have been alerted to the availability of the draft scope for comment:

- Association for Clinical Biochemistry and Laboratory Medicine
- British Association for the Study of the Liver (BASL)
- British Medical Ultrasound Society (BMUS)
- British Society of Gastroenterology (BSG)
- Royal College of Radiologists (RCR)

- Society and College of Radiographers

5.1.3 Patient organisations

At the selection stage, NICE's Patient and Public Involvement Programme contacted the following organisations for patient commentary and alerted them to the availability of the draft scope for comment:

- Addaction
- British HIV Association
- British Liver Trust
- British Red Cross
- Children's Liver Disease Foundation
- Chinese National Healthy Living Centre
- Equalities National Council
- Expert Patients Programme CIC
- Hepatitis A-Z
- Hepatitis B Foundation
- Hepatitis C Trust
- Hindu Council UK
- Independent Children's Homes Association
- Liver4Life
- Medical Foundation for AIDS and Sexual Health
- MRSA Action UK
- Muslim Council of Britain
- Muslim Health Network
- National AIDS trust
- National Kidney Federation
- National Users Network
- Positively UK
- Sophia Forum
- South Asian Health Foundation
- South Asian Health Foundation
- Specialised Healthcare Alliance
- Sue Ryder
- The Haemophilia Society

- The Hepatitis B Foundation UK
- UK Thalassaemia Society