National Institute for Health and Care Excellence
Medical Technologies Evaluation Programme
MT210 Virtual Touch Quantification to diagnose and monitor liver fibrosis

Consultation Comments table
MTAC date: 19 February 2015

There were 31 consultation comments from 10 consultees: 2 companies, 1 External Assessment Centre, 1 Department of Health, 2 patient organisations, 2 Guideline Development Groups, and 1 professional society. One further comment from a NHS professional was received during the resolution period and had been missed from the original consultation. The comments are reproduced in full.

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1	6. Liver4Life	1.1	**'Gold Standard'?** Although a liver biopsy may be regarded as the 'gold standard' of care when assessing the health of the liver, L4L would dispute that it remains a necessity for patients to undergo. If a liver condition or virus is present and known, then a liver biopsy is superfluous to the on-going management of the condition. A liver biopsy only provides a snapshot of the liver, and can provide samples that could be misinterpreted, due to the location of the disease being different to where the sample area is taken. As such, L4L encourages the development and the use of non-invasive techniques to assess liver damage across all liver conditions, not only hepatitis B and C. L4L believes that this is a major limitation in the use of this technology, as there are other non-invasive tools, such as the Fibroscan, which is used across all forms of liver disease.	Thank you for your comment. The scope of this evaluation specified both liver biopsy and transient elastography as comparators because current guidelines and expert advice indicated that biopsy remained the principal method for some conditions and that it was in common use in the NHS. The Committee's recommendations aim to clarify the role of VTq in settings would otherwise be used. The Committee's considerations on the benefits of avoiding liver biopsy are in sections 3.22, 3.24 and 3.25. The scope of this evaluation considered only hepatitis B and C. This is not intended to preclude the use of the technology in other liver conditions for which non-invasive liver testing may be valuable. The decision to consider only hepatitis B and C was based on the quality and availability of evidence in the timescale of the evaluation.
2	6. Liver4Life	1.2	**Accessibility factors of this technology** L4L believes that further information is required that assesses how accessible this technology could be as well as its feasibility in the community setting. L4L	Thank you for your comment. The Committee's recommendations do not limit the use of VTq to any particular care setting. Sections 4.5 and 4.7 of the

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			would like to better understand what the potential rollout and uptake this technology would be. Furthermore, L4L would like to better understand the optimum patient pathway associated with this technology, for example whether it will be available in clinic at point of contact with a gastroenterologist/hepatologist, or would it require a separate appointment and visit to the hospital. L4L would also like assurances that the manufacturer has developed appropriate patient information to aid patient understanding that allows them to correctly interpret their results and care management plan. L4L is concerned that the VTq will only be available in specialist centres, which would mean that not *all* patients will be able to access this new technology.	consultation document describes the Committee's considerations on the place of VTq in the care pathway. The Committee was advised by clinical experts that there is potential for VTq to be used in primary care settings where ultrasound imaging is offered. NICE's Health Technologies Adoption Programme (HTAP) is planning to publish adoption support tools for the NHS alongside the guidance. These tools include a description of the patient pathway and the impact of adopting the recommended technology.
3	6. Liver4Life	1.3	The patient pathway using this technology We are particularly concerned that this technology requires a number of specialties across the health service to manage the results. This could potentially compromise the timely delivery of results to patients. Liver patients already suffer from a number of health inequalities in the way in which their liver conditions are managed; the lack of robustness in service configuration and expertise in the district general hospital largely compounds the problem. L4L is concerned that the patient pathway has the potential to be a lengthy process when using the VTq, which requires a number of clinicians to feed in. It should be noted that other non-invasive tools are now available and are being used in the community setting, such as drug and alcohol centres, sexual health clinics and also prisons This is critical in the future management of liver disease, as large cohorts of the patient population with liver disease are some	Thank you for your comment. The Committee's considerations on the system impact of adopting VTq are described in section 4 of the guidance. Expert advice to the Committee was that patients being assessed for liver fibrosis usually have an ultrasound scan and so adding a VTq measurement in these cases would not lengthen the pathway. The Committee understood that the use of VTq in different settings was limited by the availability of Siemens ultrasound machines. In section 4.7 the Committee also noted the different staff costs associated with transient elastography and VTq measurements. The recommendations in the guidance do not hinder access to the technology for any specific group. The recommendations in the guidance are not meant to limit use of other relevant technologies which may offer similar advantages.

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			of the most vulnerable and deprived groups in society, but are some most needing of these services. Their access to conventional health systems i.e. hospitals can sometimes be intermittent. Being able to provide non-invasive tools, which can be interpreted by non-specialists, is often essential in managing a patient's liver condition.	
4	6. Liver4Life	1.4	Assessment of other existing non-invasive tools We are minded to remind NICE that a similar evaluation has not been carried out, as far as we are aware, for hepatic elastography using the FibroScan technology. As the Committee repeatedly points out this has become the technology of choice for most institutions to evaluate hepatic fibrosis. Furthermore, NICE HBV guidance suggests that this is the first line investigation for assessment of liver fibrosis assessment.	Thank you for your comment. Transient elastography was specified as a comparator in this evaluation because it is recommended in the NICE hepatitis B clinical guideline. Development of NICE medical technologies guidance is for innovative technologies which are not current standard care. In the development of medical technologies guidance the case for adoption of a single medical technology is evaluated based on the claimed advantages of introducing the specific technology made by the company at notification, compared with current management of the condition. It is not a multiple technology assessment and does not compare evidence for all similar or comparator technologies. These principles are described in further detail in the Medical Technologies Evaluation Programme methods guide.
5	2. Echosens	3.8	This clinical evidence (Kuroda et al. 2010) is based on a study performed on a very small sample size (70 patients only). VTQ performance was evaluated in comparison with liver biopsy taken as a reference in a subgroup of 19 patients only. Diagnostic evaluation of VTQ by the mean of AUROC is not statistically meaningful given this small sample size.	Thank you for your comment. In response to this comment, the External Assessment Centre noted that a small sample size does not always equate to statistically non-meaningful results, and that Kuroda et al (2010) was accepted as it was within the scope – comparing VTq with liver biopsy in a study population of Hepatitis C patients and healthy controls. The evidence presented in the study was synthesised as part of a meta-analysis, which places an appropriate weight on population size, and helps to compensate for any limitations in study size or quality.
6	2. Echosens	3.10	Authors of this study conclude that ARFI	Thank you for your comment.

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			measurements do not correlate either with inflammation levels or with patient BMI. However AST and ALT levels ranges were 31.5-82.0 UI/L and 35-91.5 UI/L respectively in this 108 patient cohort. Very few patients were out the normal range of transaminases and none of them exhibited AST or ALT levels >5 times the Upper Limit of Normal (ULN) Range. Additional studies would be required to rule out the influence of liver inflammation on ARFI results, especially in case of flares occurring in the natural course of chronic hepatitis B. The same comment could be made regarding the potential influence of patient BMI since BMI ranged from 20.5 to 24.6 kg/m2 in the study population. Additional studies performed on obese patients would also be required to evaluate the influence of BMI on ARFI applicability rate and diagnostic performances.	Please note: AST and ALT are taken to denote aspartate transaminase and alanine transaminase respectively. Serum AST and ALT levels, and their ratio, are commonly used as clinical biomarkers for liver health. It is commonly measured in international units / litre (IU/L). The standard UK reference range for AST is 5 – 40 IU/L. The standard UK reference range for ALT is 5-7 to 40-56 IU/L. In section 3.10 of the guidance it is noted that in the Nishikawa et al. (2014) study, ARFI measurements did not correlate with inflammation. Clinical experts advised the Committee that inflammation levels and obesity, among other factors, may influence the accuracy of both VTq and transient elastography. The Committee decided to include an additional consideration (section 3.26) to reflect this discussion. In addition the Committee decided to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove any reference to the unsuitability of transient elastography in people with obesity.
7	2. Echosens	3.12	This evidence is based on the Sporea study that compared performances of ARFI (VTQ) and FibroScan on a subgroup of 400 patients. Authors report a significantly higher reliability of ARFI measurements (98.8%) versus 93.7% for FibroScan (p=0.003). Several study methodology biases should be pointed out: □ First reliability criteria applied for FibroScan examination were quite strict (Minimum of 10 valid measurements, IQR/Median %<30, Success Rate>60%), whereas no apparent reliability criteria were applied for VTQ measurements, leading to an unfair comparison. □ Second, the FibroScan machine was not used in its usual configuration (M probe plus XL probe) and	Thank you for your comment. Please note: The Fibroscan XL probe was introduced for use on obese patients (BMI > 30 kg/m^2), with a similar diagnostic accuracy to that of the standard M probe. In response to this comment the External Assessment Centre noted that: - Sporea et al. (2012a) evaluated liver fibrosis by liver biopsy, ARFI (VTq), and in some patients, by transient elastography (Fibroscan). This study found that VTq still significantly correlated with fibrosis stage when compared to liver biopsy alone. - it is reasonable to assume that the reliability criteria in this study were the same for both VTq and ARFI, because the methods section does not explicitly state that the reliability

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			only utilized the standard “M” probe, thus potentially underestimating the reliability rate of transient elastography.	criteria were only applied for TE. - the study authors acknowledged the limitation of using only the M probe, stating that “the problem of transient elastography may have been partially solved by the recent development of a more sensitive ultrasound probe that allows liver stiffness measurement in overweight and obese patients, but ARFI still might be better in these patients.” A later study by Cassinotto et al. (2014) used the M probe on all patients (mixed patient cohort of chronic liver disease) with a BMI <30 (n=243), and the XL probe only on patients with a BMI of ≥30 (n=106). The Committee decided to include an additional consideration (3.26) to clarify that obesity may impact on the accuracy of readings given by both VTq and transient elastography. In addition the Committee decide to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove references to the unsuitability of transient elastography in people with obesity.
8	2. Echosens	3.13	The clinical evidence provided by the company does not demonstrate any ability of ARFI measurement to correlate with the response to antiviral treatment. There was no correlation between VTQ measurements and patient HCV viral load, thus no ability of ARFI to monitor patient response to PEGinterferon and ribavirin bitherapy. Additional studies would be required to evaluate the possibility for ARFI to differentiate SVR patients versus non responders or relapsers.	Thank you for your comment. Please note: SVR has been taken to mean sustained viral response, which is an efficacy measure of a hepatitis C treatment. The Committee understood that there was no evidence evaluating the effectiveness of VTq for monitoring disease progression, however it considered that the technology was likely to be useful for this purpose as assessment of the extent of liver fibrosis will be done for individual patients over time. The Committee heard clinical expert advice that the use of image-guided assessment of liver fibrosis allowed measurements to be taken from the same part of the liver at different times. Section 3.13 of the guidance describes a study by Yamada et

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				al. (2014), which was previously identified and excluded by the company but subsequently included by the External Assessment Centre. The study found that ARFI could have some benefit in predicting response to antiviral therapy for people with genotype 1 hepatitis C, but not for genotype 2. No evidence was presented demonstrating a correlation between ARFI and response to anti-viral therapy as this was outside the scope of the evaluation. Section 3.21 has been updated to further clarify the usefulness of VTq for monitoring disease progression.
9	2. Echosens	3.23	In studies performed with a significant subgroup of obese patients (cf Cassinotto et al. 2013), ARFI has been demonstrated to exhibit significantly lower performances compared to FibroScan when the latter is used with its dedicated XL probe which has been specifically designed and adapted to scan overweight patients.	Thank you for your comment. The External Assessment Centre noted that Cassinotto et al (2013) was conducted in a mixed patient cohort (chronic liver disease) and was outside the scope of the evaluation. It noted that this study found mixed results when comparing VTq and transient elastography with various stages of liver fibrosis and with different transient elastography probes. It acknowledged that it would be useful for future studies to use the appropriate transient elastography probe based on patient's BMI and according to Fibroscan probe specifications. The Committee decided to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove reference to the unsuitability of transient elastography in people with obesity. It also added an additional consideration noting that it is unclear from the available evidence how factors such as obesity influence the accuracy of transient elastography and VTq measurements.
10	2. Echosens	4.1	The company did not provide any clinical evidences (absence of longitudinal studies) of ability of VTQ measurements to monitor fibrosis progression and/or response to antiviral therapy.	Thank you for your comment. Please see the response to comment 8.
11	2. Echosens	4.3	The 4 mentioned studies report smaller failure rate and higher reliability rate of ARFI versus transient	Thank you for your comment.

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			elastography. However reliability criteria applied to the 2 technologies were not the same (criteria were more strict for transient elastography compared to ARFI), potentially causing some comparison bias. In addition tothis the systematic use of the XL probe (not used in these comparison studies) would likely have caused less unreliable FibroScan measurements. Finally Cassinotto et al. (2013 and 2014) reported that the diagnostic performance of ARFI was quite poor on patients for which transient elastography examination was failed or unreliable (likely on obese patients)."	The External Assessment Centre has summarised the reliability criteria applied in each study: Friedrich-Rust et al (2013): Based on described methods, both ARFI (VTq) and transient elastography measurements appear to have been subjected to the same successful acquisitions criteria. It was unclear to the External Assessment Centre if VTq results were subjected to the same success rate as transient elastography (at least 60%, with an interquartile range of 30%). The External Assessment Centre was unable to contact the authors to obtain further clarity on this point. Rizzo et al (2011): Methodology of the studies is not adequately addressed in this report. Liu et al (2014): In this study, 'transient elastography failure was defined as a success rate of less than 60% or an interquartile range of more than 30%' and 'as with transient elastography, ARFI failure was defined as a success rate of less than 60% or an IQR of more than 30%'. The External Assessment Centre considered that the reported methodology suggested that similar criteria for both ARFI and transient elastography. Sporea et al (2012a): With respect to usage of the correct transient elastography probe, please see the response to comment 7. In addition, the External Assessment Centre made the following comments on the studies specified by the consultee: Friedrich-Rust et al (2013): Used the M mode for Fibroscan, but did not report patient BMI information. Rizzo et al (2011): Did not mention the Fibroscan probe used or aspects of patients BMI.

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				Liu et al (2014): Used the M probe for Fibroscan. The reported mean average BMI scores suggest a majority of the study population were in the healthy BMI range, making use of the M probe appropriate. Sporea et al (2012a): Please see the response to comment 7. Cassinotto et al. (2013) was judged by the External Assessment Centre to be outside the scope of the evaluation. Please see the response to comment 9. Similarly, Cassinotto et al. (2014) was also conducted in a mixed patient cohort, and was also judged to be outside the scope of the evaluation. The Committee decided not to change the guidance.
12	2. Echosens	4.6	Same comment as for 4.3	Thank you for your comment. Please see the response to comment 11.
13	2. Echosens	6.2	Absence of clinical evidence on the usefulness of ARFI examination on children. Absence of clinical evidences of the usefulness of ARFI examination for fibrosis longitudinal follow up and to monitor antiviral therapy.	Thank you for your comment. The Committee considered that although no clinical evidence was presented on the use of VTq in children, its potential benefits were likely to be realised, in particular the avoidance of a liver biopsy. No evidence was presented which indicated that the technology was likely to be less effective in children than in adults. Clinical experts supported this view. The Committee also heard that VTq's instructions for use do not distinguish between adults and children. Please see the response to comment 18. The Committee decided to change the guidance so that references to children were removed from sections 1.2, 6.1 and 6.2 of the guidance. The Committee changed section 3.23 to further describe its considerations on the use of the technology in children.

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				No evidence was presented or identified from longitudinal follow-up studies. The External Assessment Centre identified 1 relevant ongoing clinical trial (observational) involving a paediatric population, with an estimated primary completion date of November 2015.
14	2. Echosens	General	Additional comments: Additionally we would have the the following observations: Bibliography: 1. Bota, S., et al., Intra- and Interoperator Reproducibility of Acoustic Radiation Force Impulse (ARFI) Elastography-Preliminary Results. Ultrasound in Medicine and Biology, 2012. 38(7): p. 1103-8. 2. Cassinotto, C., et al., Liver Fibrosis: Noninvasive Assessment with Acoustic Radiation Force Impulse Elastography--Comparison with FibroScan M and XL Probes and FibroTest in Patients with Chronic Liver Disease. Radiology, 2013. 269(1): p. 283-92. 3. Cassinotto, C., et al., Non-invasive assessment of liver fibrosis with impulse elastography: comparison of Supersonic Shear Imaging with ARFI and FibroScan(R). Journal of Hepatology, 2014. 61(3): p. 550-7. 4. Bota, S., et al., Can ARFI elastography predict the presence of significant esophageal varices in newly diagnosed cirrhotic patients? Annals of Hepatology, 2012. 11(4): p. 519-25.	Thank you for your comment. For ease of reading, this comment has been divided into 8 parts – 14a to 14h. No changes have been made to the text.
14a	2. Echosens	General	1. No Hepatology or Infectious Disease clinicians were part of, or co-opted to, the committee conducting the assessment.	Thank you for your comment. The Medical Technologies Advisory Committee is an

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				independent standing committee consisting of about 25 members with a range of expertise. The Committee includes clinicians who develop and use medical technologies, scientists, people who can provide a lay perspective on the issues affecting patients and the NHS, experts in regulation and the evaluation of healthcare, and people with experience of the medical technologies industry. A list of current members is published on the NICE website (www.nice.org.uk/mt). For each evaluation, the Committee is advised by relevant clinical and technical experts and they are identified in the consultation supporting documents. In the case of VTq, the Committee received expert advice questionnaires from 9 clinical experts, including hepatologists and radiologists. Five of these experts advised on the draft scope and assessment report written by the External Assessment Centre. At both the draft guidance meeting and final guidance meeting, 2 clinical experts gave their views on the technology and answered a variety of questions on technical aspects of VTq, its clinical utility, and the care pathway for people with chronic hepatitis B and C. The MTEP Process Guide (section 3.7) describes the way in which expert advisers are identified and engaged.
14b	2. Echosens	General	2. The assessment only considers the use of ARFI VtQ in chronic HBV and HCV. There is no information on its performance in HIV co-infection, Alcoholic Liver Disease, Non-Alcoholic Fatty Liver Disease, Chronic Cholestatic Disease, cystic fibrosis, patients undergoing methotrexate treatment, haemochromatosis, pediatric liver diseases (biliary atresia)…etc.	Thank you for your comment. The scope of this evaluation defines the population as adults or children with chronic hepatitis B or C in whom assessment of liver fibrosis is indicated.
14c	2. Echosens	General	3. Based on the studies listed in the NICE document, there is no clear clinical evidence of the ability of the ARFI machine to monitor fibrosis progression over the	Thank you for your comment. These limitations in the currently available clinical evidence

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			time. The only reference related to this topic (Yamada et al. 2014) does not demonstrate any ability of the ARFI to differentiate between SVR, non-responders or relapsers to the PEGInterferon and Ribavirin bi therapy.	are noted by the Committee. Please also see the response to comment 8.
14d	2. Echosens	General	4. No evidence is included relating to any post-prandial effect, right heart failure, or prediction of HCV or HBV related portal hypertension and of liver decompensation (ie occurrence of oesophageal varices and/or hepatocellular carcinoma).	Thank you for your comment. These outcomes were not specified in the scope or presented in the company's submission of evidence.
14e	2. Echosens	General	5. Obesity seems to significantly affect the diagnostic performance of the machine [2]. Even if the VTQ ARFI measurement is still feasible on these patients (high percentage of "reliable" measurements), its diagnostic accuracy seems significantly affected. In the context of increasing prevalence of obesity, this limitation should be taken into account.	Thank you for your comment. The Committee was advised that the ARFI used in VTq can travel easily through fat and fluid. This may make VTq an option for people with obesity for whom transient elastography may be unreliable. Some of the clinical evidence which supports this view is referenced in section 4.2. However the Committee was aware that the development of a new probe may help resolve this issue for transient elastography. The Committee decided to include an additional consideration (section 3.26) to clarify that obesity may impact on the accuracy of readings given by both VTq and transient elastography. In addition the Committee decided to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove any reference to the unsuitability of transient elastography in people with obesity. Please also see the response to comment 7.
14f	2. Echosens	General	6. Several parameters seem to affect the reproducibility of the ARFI measurement, such as female gender, obesity, presence of ascites, and absence of cirrhosis [4]. Additional studies should be conducted to confirm these results, and longitudinal studies would be required to evaluate whether this	Thank you for your comment. The External Assessment Centre stated that the available evidence did not allow evaluation of several potential variables that may affect the measurements of VTq or its comparators. It noted that the study referred to by the consultee (Bota et al.

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			ARFI technology is accurate and reproducible enough to monitor fibrosis in patients with chronic liver diseases.	2012) was not included in the assessment because it was outside the scope. It did not adequately address the appropriate comparators and used a mixed patient cohort for which HBV and HCV results were not presented separately. The Committee recognised the limitations of the evidence but considered it was sufficient to demonstrate the VTq has equivalent accuracy to transient elastography for diagnosing liver fibrosis. The Committee decided to include an additional consideration (section 3.26) to reflect the uncertainties associated with a variety of factors which can influence the accuracy of results for both the intervention and comparator technologies. Please see the response to comment 8.
14g	2. Echosens	General	7. ARFI requires an experienced radiographer to conduct the assessment. This significantly impacts the utility of the assessment compared to the immediacy of a FibroScan assessment conducted by a CNS in a liver out-patient setting.	Thank you for your comment. Note: CNS is taken to denote clinical nurse specialist. The Committee was advised by clinical experts that VTq assessments should only be done by staff with specialist training in ultrasound imaging and interpretation. The differing resource usage costs associated with VTq and Fibroscan were included in the company's model (see section 4.7).
14h	2. Echosens	General	8. With the increasing incidence of obesity and NAFLD in the UK population ARFI does not offer any means of assessing the degree of steatosis in these patients, compared to the CAP function available with FibroScan.	Thank you for your comment. The scope of this evaluation was limited to the diagnosis and monitoring of liver fibrosis and did not include assessment of steatosis.
15	3. Hephealth Limited (Echosens)	General	Specifically in response to the observation from Dr Sherman below, and in conjunction with the comments of [redacted] (Consultee 2, details provided to NICE) forwarded earlier, I can advise that there are in fact 120+ FibroScan systems installed in	Thank you for your comment. Please note: The document mentioned in the comment refers to a list provided to NICE of all UK centres where Fibroscan has been installed, as of January 2015.

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			the UK, virtually all major liver centres are equipped and increasingly the larger DGHs where there is either a Hepatologist (or gastroenterologist with interest in hepatology) are equipped also. Dr David Sherman Consultant Physician & Gastroenterologist - Main comparator is liver biopsy - Fibroscan is not widely available enough to be considered a comparator. No other equivalent widely available technology (PLEASE SEE THE DOCUMENT ATTACHED TO THIS EMAIL)	The scope of the evaluation included both liver biopsy and transient elastography. The choice of comparator was based on evidence-based guidelines and expert advice received about current NHS practice.
16	2. Echosens	General	Having reviewed the consultation document Echosens, (manufacturer of FibroScan®) would like to make the following comments: Please note: For ease of reading, the remainder of this comment has been reproduced as Appendix 1. No changes have been made to the consultee's text.	Thank you for your comment. The External Assessment Centre was asked to comment on the additional references supplied by the consultee: Bota et al (2012): This study population is comprised of a mixed liver disease cohort. Study results were not stratified by sub-group, meaning that results could not be presented separately for hepatitis B or C. This placed the results of the study outside the scope of the evaluation. Please also see the response to comment 14f. Cassinotto et al (2013): This study abstract was excluded by both the company and by the External Assessment Centre, as it included a population with mixed liver disease, and separate results were not identified for hepatitis B and C patients. This placed the study outside the scope of the evaluation. Please also see the responses to comments 9 and 11. Cassinotto et al (2014): This study population was comprised of a mixed liver disease cohort. Study results were not stratified by sub-group, meaning that results could not be

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				presented separately for hepatitis B or C. This placed the study outside the scope of the evaluation. Please also see the response to comment 11. The Committee decided not to change the guidance.
17	1. External Assessment Centre (KiTEC)	General	KiTEC has no comments to make on the draft guidance for VTq.	Thank you for your comment.
18	4.Guideline Development Group for NICE Clinical Guideline on non-alcoholic fatty liver disease	General	Interesting technology. We can see the advantages in the clinical setting in particular the cost saving compared to liver biopsies and ease of use in outpatient setting. We think the clinical evidence reviewed is limited but sound. Our reservations however relate to the lack of evidence of its accuracy in paediatric cohorts. We would be reluctant to make any recommendations for its use in a paediatric setting until validation data of VTq accuracy in diagnosing and monitoring of fibrosis in children with HBV/HCV are available. A similar process had to be undertaken when transient elastography was introduced and recommended as a valid tool to replace liver biopsy for diagnosing and monitoring fibrosis. Also in a paediatric setting USS, and thus VTq, would generally be carried out by ultrasonographers/radiologists and not by clinicians (this varies from country to country but is certainly the case in the UK). VTq would therefore not be such an easy 'bedside' assessment tool unless clinicians are trained to use it. In practice transient elastography would therefore be much more accessible as this is generally carried out by a non-ultrasonographer/non-	Thank you for your comment. Please note: This guideline is in development and is expected to be published in July 2016. The Committee noted that no evidence was available on the use of VTq in children but it was advised by clinical experts that there was no reason why the benefits of a non-invasive test in adults (as demonstrated by the clinical evidence) would not be applicable to children. The Committee was advised of the current care pathways for children (outlined in the hepatitis B and C guidelines), which state that children are referred to a paediatric hepatologist, gastroenterologist or infectious disease specialist in a secondary or tertiary care centre, and offered liver biopsy to determine the need for antiviral therapy. The Committee considered that the use of VTq would reduce the need for liver biopsy in children. Please also see the response to comment 13. Sections 1.2, 6.1 and 6.2 of the guidance have been updated to remove specific references to children. Section 3.24 has been updated to further describe the Committee's considerations on the use of the technology in children.

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			radiologist.	Recommendations made by the Committee are now applicable to the entire patient population with chronic hepatitis B or C.
19	4.Guideline Development Group for NICE Clinical Guideline on non-alcoholic fatty liver disease	General	Overview comments as a patient representative. Having undergone two liver biopsies anything that could replace them accurately, must be welcomed. Having to spend time in hospital following the procedure, having to lay still in bed for many hours, preventing a bleed can be uncomfortable and anxiety provoking. The test itself can also be painful. However is it worth it for an accurate result which is not always the case given the size of the liver. Transient elastography is said to be dependent upon the operator. The VTq is clearly non invasive it does not require hospitalisation, has it been proved to be as accurate as biopsies? Is it reliable? Is it based upon operator behaviour? As a lay person I found the research evidence confusing. Have there been longitudinal studies to further test its ability to monitor accurately. Testing patients who are subject to liver biopsy and VTq to make comparisons. Have blood tests and VTq results correlated	Thank you for your comment. NICE welcomes the input of patient representatives. The decision made by the Committee included recognition of the benefits of avoiding invasive liver biopsy for both initial assessment and ongoing monitoring. The Committee concluded that VTq can be considered to be as accurate as transient elastography. The External Assessment Centre stated that it is not possible to exclude the possibility of influence by operator behavior in the evidence presented. This view was supported by clinical experts, who stated that appropriate clinical care and diligence were important aspects of any assessment of liver fibrosis. No evidence from longitudinal studies was considered in the evaluation. The External Assessment Centre noted that because VTq is a relatively new technology, there is a lack of longitudinal data. Please see the response to comment 13. The use of blood tests for the diagnosis and monitoring of fibrosis was outside the scope of this evaluation. No evidence on blood tests was presented or considered. Liver blood tests for cirrhosis will be covered in the ongoing NICE guideline on the assessment and management of cirrhosis (anticipated publication date: June 2016). It is not envisaged that liver biopsy will be used to check the reliability of VTq within a patient pathway. The recommendations in section 1 of the guidance state that VTq

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			positively? Have symptoms correlated positively with VTq results? If it is used to monitor and or diagnose will it be relied on solely? Will there be a need to at some stage have a liver biopsy to check that progress has been accurately defined? Almost as a spot check.	should be considered as an option instead of liver biopsy, not as an adjunct therapy.
20	4.Guideline Development Group for NICE Clinical Guideline on non-alcoholic fatty liver disease	General	It should be noted that the NAFLD GDG is also reviewing the evidence for VTq specifically in a NAFLD population (as part of its review on the diagnostic test accuracy of assessment tools to identify the severity or stage of NAFLD); however, since this NICE MT guidance only covers hepatitis B/hepatitis C our remits do not overlap.	Thank you for your comment.
21	5. British Society of Gastroenterology	General	Overall, the data presented demonstrates that VTq is an effective non-invasive method of fibrosis assessment in patients with hepatitis B and C. Use of this technology has significant advantages to patients, particularly the ability of the technology to combine a fibrosis assessment with standard ultrasound. As the technique is relatively inexpensive and the ultrasound machines are already widely available this offers a good cost effective assessment of fibrosis. However, there are some potential limitations with the data presented for VTq that need to be acknowledged and require further ongoing study. No conflict of interest is declared.	Thank you for your comment. For ease of reading, this comment has been divided into 4 parts – 21a to 21d. No changes have been made to the text.
21a	5. British Society of Gastroenterology	General	The data presented relates only to patients with hepatitis B and C, which represents a minority of patients in the community who may need a fibrosis assessment. Fatty liver due to non-alcoholic fatty liver	Thank you for your comment. The scope of this evaluation defined the population as adults or children with chronic hepatitis B or C in whom assessment

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			disease and alcoholic liver disease is much more common. It needs to be emphasised that further study is needed in those patient groups before this technology can be used in patients with those aetiologies.	of liver fibrosis is indicated. Non-alcoholic fatty liver disease was not considered within the scope of this evaluation NICE is currently developing a guideline on non-alcoholic fatty liver disease (publication date TBC). Please also see the responses to comments 14b and 24.
21b	5. British Society of Gastroenterology	General	Further assessment on the effect on BMI is needed as VTq has not been thoroughly assessed in subjects with obesity and it is likely that obesity will affect VTq results as was seen with transient elastography. The data suggest that VTq might be more effective than transient elastography in obtaining successful fibrosis readings, but this needs to be further assessed in a cohort of obese patients, particularly as relatively few obese patients have been included in current studies.	Thank you for your comment. Please see the responses to comments 6, 7, 9, 11 and 14e. The Committee decided to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove reference to the unsuitability of transient elastography in people with obesity. It also added an additional consideration (section 3.26) noting that it is unclear from the available evidence how factors such as obesity influence the accuracy of transient elastography and VTq measurements.
21c	5. British Society of Gastroenterology	General	The effect of hepatic inflammation has not been thoroughly assessed in the studies, particularly in patients with hepatitis B, who can have “flares” of hepatic inflammation that may artificially elevate VTq readings. This has been seen with transient elastography and as both techniques measure liver elasticity it is likely to occur with VTq.	Thank you for your comment. Section 3.8 of the guidance states that in the Nishikawa et al. (2014) study, VTq readings did not correlate with inflammation. Clinical experts indicated to the Committee that inflammation levels, among other factors, may influence the accuracy of both VTq and transient elastography The Committee decided to include an additional consideration (section 3.26) to reflect this discussion. Please see the response to comment 6.
21d	5. British Society of Gastroenterology	General	Further standardisation of reference ranges for stages of fibrosis is needed as reference ranges may need to be different according to the aetiology of the fibrosis.	Thank you for your comment.
22	10. Guideline Development	4.2–4.3 (and	It is stated that VTq can be carried out in people with obesity, while TE would not be suitable or reliable.	Thank you for your comment.

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	Group for NICE Clinical Guideline on cirrhosis	3.23)	However, it is not stated here whether VTq was being compared in these studies with TE using an 'M' probe or TE using the newer 'XL' probe, which is designed to work better in people with obesity. VTq may or may not still be more effective than TE using an XL probe, but this is not discussed. It is mentioned (in 3.23 and 4.6) that there are other conditions in which TE would not be suitable, but these are not specified and it is not clear if these are common conditions.	The External Assessment Centre informed the Committee that all clinical evidence considered in the evaluation described using the 'M' probe or did not specify any probe. The XL probe is a more recent addition to the Fibroscan system. Several of the studies were conducted before the XL probe was made available. The Committee decided to change the guidance (sections 3.23, 4.2, 4.6 and 6.1) to remove reference to the unsuitability of transient elastography in people with obesity. It also added an additional consideration noting that it is unclear from the available evidence how factors such as obesity influence the accuracy of transient elastography and VTq measurements.
23	10. Guideline Development Group for NICE Clinical Guideline on cirrhosis	6.1–6.3	The Committee concludes that VTq is preferable to TE and liver biopsy. The effectiveness of TE and VTq are compared in 6.1. The effectiveness of liver biopsy and VTq do not appear to have been compared. Liver biopsy is more accurate than VTq, but more expensive (and with some adverse effects). No explanation is given of the balancing of costs and benefits of liver biopsy against VTq, and so why the decreased cost and side effects are felt to justify the decreased accuracy. The economic analysis was a cost analysis not a full economic evaluation of both costs and benefits, and so did not seek to answer this question.	Thank you for your comment. Liver biopsy was used as the reference standard in this evaluation, and the meta-analysis of the clinical evidence compared both VTQ and transient elastography results with liver biopsy results. This was reflected in the cost model, which assumed liver biopsy had 100% sensitivity and specificity. Results from the cost model found that VTq was cost saving compared with liver biopsy (sections 5.19-5.20). The Medical Technologies Evaluation Programme evaluates the cost consequences of introducing novel and innovative technologies to the NHS. Further information is available in the programme's methods guide.
24	10. Guideline Development Group for NICE Clinical Guideline on cirrhosis	Section 3	4.1) Clinical evidence for the diagnostic accuracy of transient elastography was only included from studies which also evaluated the accuracy of VTq. Therefore, the accuracy data in table 1 for transient elastography only represents a small amount of the available evidence in the literature for the accuracy of transient elastography (with liver biopsy as the reference	Thank you for your comment. The comparative clinical evidence assessed by the External Assessment Centre in this evaluation included the intervention and comparators. Studies which do not include the intervention do not fall within the scope of an evaluation.

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			standard). For example, in hepatitis B and hepatitis C, the sensitivity and specificity values for the diagnostic accuracy for each fibrosis stage only come from one study. 4.2) No information is provided on the quality/size of the liver biopsy samples used for the reference standard in the included studies. Liver biopsy has limitations as a reference standard test as it is not 100% accurate. This will in turn influence the diagnostic accuracy of the index tests assessed. These inaccuracies of liver biopsy are accentuated in biopsy samples of inadequate size. Due to differences in the size of biopsy samples between studies, this may introduce heterogeneity and the liver biopsy criteria used in each individual study should be considered and discussed.	The External Assessment Centre noted that although liver biopsy is not 100% accurate in clinical practice, it remains the 'gold' standard. It accepted that details on obtaining liver biopsy samples were not addressed, but noted that 7 of 10 studies in the meta-analysis reported the size of liver biopsy samples: Sporea et al. (2012); Friedrich-Rust et al. (2013); Nishikawa et al. (2014); Chen et al. (2012); Rizzo et al. (2011); Ye et al. (2012), and Liu et al. (2014). The majority of studies also described criteria for obtaining biopsy samples.
25	10. Guideline Development Group for NICE Clinical Guideline on cirrhosis	General	The Cirrhosis GDG expressed concerns that the patient pathway had not been taken into consideration during the assessment of VTq. In the UK, ultrasound and consequently VTq is not embedded in hospital liver clinics but in radiology departments, whereas transient elastrography (e.g. Fibroscan) is co-located in liver clinics. This means the patient journey within the hospital will be substantially longer if VTq is used. It also has implications for the use of these technologies in primary care (GP surgery or Prison setting). The cirrhosis GDG is keen to see the diagnosis of liver disease in general and cirrhosis in particular made earlier in the patient pathway e.g. in primary care. The GDG was of the opinion that transient elastrography (e.g. Fibroscan) or blood tests for fibrosis could in principle be used easily in primary care settings, whereas the GDG did not anticipate	Thank you for your comment. The decision problem specified in the scope of the evaluation included considering the use of VTq in primary care. The company's submission stated that VTq could be requested in primary care or used in an outpatient setting. The External Assessment Centre noted that no evidence was available for VTq in a primary care setting. The Committee considered that there was potential for use in primary care settings when ultrasound imaging is offered (section 4.7 of the guidance). The cost model did not consider the patient journey in hospital. It contained the assumption that VTQ assessments would take up 10% of the ultrasound machine use, with a throughput of 500 patients per year, which the External Assessment Centre considered to be reasonable (section 5.9 of the guidance). This assumption and the cost of VTq testing were varied using sensitivity analysis, but this did not affect

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			that VTq could be performed readily in this setting. The cost effectiveness of VTq assumes a high proportion of examinations with the ultrasound machine will not use VTq therefore in primary care where the ultrasound capability of the machine would not be utilised, the GDG anticipated the cost effectiveness analysis would be substantially different. The assessment also assumes a benefit from being able to carry out ultrasound and VTq at the same time. While patients will sometimes require both, frequently patients require assessment of liver fibrosis without the need for liver ultrasound, especially in subsequent monitoring for progression of fibrosis in people who have been receiving care for hepatitis for some time. This will reduce the benefit of using a method of fibrosis assessment based on ultrasound.	the overall cost-saving conclusions associated with VTq.
26	10. Guideline Development Group for NICE Clinical Guideline on cirrhosis	Section 5	The economic evaluations conducted by both the company and the external assessment centre were cost analyses and did not consider the clinical benefits of diagnosis. (Presumably there are clinical benefits of diagnosis or we would not wish to do it.) As a result, the models [assuming correct costs used – see comment on table 4.2] probably favour tests with high specificity/low FP (since FP incurs additional 'wasted' treatment costs) over tests with high sensitivity/low FN (since one would expect worse clinical outcomes for FN but this is not captured in this analysis). It is hard to be sure how much difference this makes to the conclusions without using a model that takes includes a full clinical pathway, which would be unfeasible in the timescale for this assessment, but	Thank you for your comment. A full clinical pathway model is outside the scope of medical technologies guidance, which is concerned with the development of guidance on a specific technology compared with current clinical practice within the framework of a cost-consequence analysis. Further information is available in the Medical Technologies Evaluation Programme's methods guide. The External Assessment Centre stated that the clinical benefits of diagnosis were considered in the cost model, mainly by assigning anti–viral therapy costs for METAVIR scores of F3 and F4. Economic modelling took into account resource consequences of false-negative and false-positive diagnoses. The clinical impact of these was unclear, but the

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			the limitations of the modelling and potential bias should be noted.	External Assessment Centre considered that treatment delay resulting from false-negative misdiagnosis was unlikely to have a clinical impact because disease progression in hepatitis B and C is relatively slow. The clinical impact of a false-positive diagnosis may involve unnecessary treatment and distress for the patient, which was captured by including the relevant anti-viral therapy cost. The External Assessment Centre stated that it reasonably captured clinical benefits of diagnosis within the scope of the assessment and availability of evidence.
27	10. Guideline Development Group for NICE Clinical Guideline on cirrhosis	General	The GDG commented regarding the available evidence on the technology: • No information is presented on the inter-operative or intra-operative variability both in the selection of the site for undertaking the ARFI when using VTq or in the measurements themselves. • No information is provided on the optimal cut-off values for the diagnosis of each stage of fibrosis. The majority of the studies included in the evidence base were undertaken in East Asia. Only three studies include European populations: Friedrich-Rust et al, 2013; Rizzo et al, 2011; Sporea et al, 2012. Of concern is the fact that Sporea et al, who studied a mixed European and Asian cohort, noted that the cut-off levels to determine fibrosis at stage F≥ 2 and F4 were different for European and Asian people. This is an important distinction particularly considering that the evidence supporting the case for adopting this technology is based largely on Asian studies. • Very little if any information is provided on the potential confounding effects of variables known to affect the diagnostic accuracy of transient	Thank you for your comment. No evidence was presented or identified on inter-operative or intra-operative variability. This is a limitation of the evidence. Clinical experts stated that appropriate clinical care and diligence was an important aspect of any assessment of liver fibrosis. Please see the response to comment 19. Details of optimal cut-off values were not specified in the company's submission or the assessment report. Not all accepted studies detailed cut-off values. Limitations of the patient mix and setting are discussed in section 6 of the assessment report. The External Assessment Centre agreed with the view of the consultee that limited evidence was available on specific factors which may influence the diagnostic accuracy of both VTq and transient elastography. The Committee discussed this and agreed that the lack of evidence leads to uncertainty around the impact of a variety of factors, including obesity and hepatic inflammation. An additional consideration has been added to the guidance (section 3.25) to reflect this discussion. For more information, please see the response to comment 14f.

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			elastography, which may, in turn, affect the performance of VTq e.g. the presence of necroinflammation; ascites; portal hypertension; obesity and ongoing alcohol consumption. Chen *et al* 2012 showed that the presence of necroinflammation increases the VTq score with the potential to provide a false positive result. Some authors e.g. Friedrich-Rust *et al*, 2013; Rizzo *et al*, 2011; Yamada *et al*, 2014 comment in the conclusions of their papers that VTq can be used in people with obesity for whom transient elastography may not be suitable or reliable; however they but do not provide quantitative data. The Committee accepted clinical advice that as the ARFI used in the VTq travels through fat and fluid easily it may be suitable for people with obesity or other conditions for whom transient elastography would not ---this statement is, however, largely unsupported by the evidence. The committee has recommended use of this technology in children yet no information is available on its use in children.	The Committee considered the use of the technology in children, and was advised by clinical experts that there was no reason to believe that VTq would be less effective in children than in adults. Sections 1.2, 6.1 and 6.2 of the guidance have been updated to remove specific references to children and section 3.23 has been updated to fully reflect the Committee's considerations. For more information on the use of the technology in children, please see the responses to comments 13 and 18.
28	6. Liver4Life	general	Liver4Life (L4L) welcomes the opportunity to comment on this medical technology consultation document: Virtual Touch Quantification (VTq) to diagnose and monitor liver fibrosis. With an increasing patient population, liver disease is key public health challenge in the UK, driven mainly by alcohol and obesity, but also viral hepatitis and hereditary/autoimmune conditions. With more people being affected by liver conditions in the UK, it is paramount that new medicines, technologies and services are approved, adapted and established. We are pleased that another non-invasive procedure may	Thank you for your comment. NICE values the input of patient organisations, which offer an important patient perspective. The increasing patient population associated with this disease area means that liver disease will continue to be a health care priority. Engagement with patient organisations is an important way to ensure that NICE achieves the best possible outcomes for patients. The aim of this evaluation was to consider evidence examining VTq compared with transient elastography, which were considered to be the most realistic and appropriate clinical

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			be made available, however we would also like to gain a better understanding of how the VTq compares with other, similar technologies.	comparators.
29	7. Department of Health	general	I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
30	8. British Liver Trust	general	As per our previous submission prior to the full consultation the British Liver Trust fully supports any new technology or treatment that is in the best interests of patient care. We would hope this new technology would be used alongside other technologies, including Fibroscan, pathology etc., to offer bets possible options for the diagnosis and on-going monitoring of liver disease; especially where this can avoid the need for liver biopsy. The British Liver Trust is concerned that this consultation is only for people with viral hepatitis and does not include all with liver disease and questions why the limitation has been made. This could definitely lead to unnecessary discrimination against patients with other causes of liver disease who would equally benefit from this technology.	Thank you for your comment. Please note: the previous submission referred to by the consultee is the patient group questionnaire submitted to NICE at the initial presentation to the Medical Technologies Advisory Committee for topic selection. The development of guidance on VTq is not intended to limit access to other diagnosis and monitoring technologies with similar advantages, particularly non-invasive options which may reduce the need for liver biopsy. The scope of this evaluation defined the population as adults or children with chronic hepatitis B or C in whom assessment of liver fibrosis is indicated. The recommendations made in the guidance are not intended to preclude the use of VTq in other patient populations. Evidence has not been considered in these patient populations at this time. The decision was made to limit the scope of the evaluation to people with chronic hepatitis B or C based on the evidence available within the time frame. Please see the response to comment 1.
31	9. Siemens (company)	general	Thank you for inviting Siemens to comment on the draft guidance. We felt that we had the opportunity to put our views forward during the establishment of the guidance and have no further comments to make at this stage.	Thank you for your comment.

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32	11. NHS professional	General	I was very surprised that NICE has endorsed one of the most biased documents I have ever seen. Most of the statements are very partial and clearly reflect the view of the manifacturer of the instrument (Siemens).	Thank you for your comment. This comment was received after the consultation process had been completed because of an internal error within NICE. It was subsequently handled using the published resolution process.

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or Advisory committees."

Appendix 1: Comment 16 (reproduced as an appendix for ease of reading)

1. We suggest the following additional clinical evidence to be added to the guidance and taken in to account:

Bota et al. (UMB 2012) [1] evaluated the intra and inter operator reproducibility of ARFI (VTQ), on cohorts of 33 and 58 patients, respectively. Overall intra operator agreement of VTQ was very good (ICC=0.90).
However female gender, high BMI (>25 kg/m2), ascites and absence of liver cirrhosis were associated with smaller ICCs.

Inter-operator agreement was also very good (ICC=0.81). However ICC was lower in patients with female gender (ICC of 0.67 vs 0.82 for male gender), high BMI (ICC of 0.82 for BMI<25 vs 0.79 for BMI>25), in those with ascites (ICC of 0.78 vs 0.84 in absence of ascites), in non-cirrhotic ones (ICC of 0.70 on non-cirrhotic versus 0.89 on cirrhotic patients).

Authors conclude that the overall reproducibility of ARFI is very good, but is lower on women, overweight patients, non-cirrhotic patients and in the presence of ascites.

Cassinotto et al. (Radiology RSNA 2013) [2] performed a comparative study between ARFI (VTQ), FibroTest and transient elastography used with its dedicated M or XL probes (FibroScan) in a cohort of 321 patients with chronic liver diseases (including 89 chronic hepatitis C patients and 39 chronic hepatitis B patients), using liver biopsy as a reference.
Unreliable FibroScan LSM (*defined as an interquartile range/LSM greater than 30% and less than 10 valid measurements*) occurred in 17.5% with the FibroScan M probe, and in 22.7% with the FibroScan XL probe whereas unreliable ARFI (*defined as an interquartile range/LSM greater than 30%*) occurred in 23.7% of patients. Unreliable results with ARFI elastography were more frequent in obese patients (those with a body mass index of 30 kg/m2 or more, 42 of 86 patients [48.8%]) vs non obese (34 of 235 patients [14.5%], P<0.0001).

ARFI and FibroScan M probe exhibited similar performances for diagnosing advanced fibrosis F≥3 (AUROCs of 0.85 vs 0.89, respectively, p=0.15) and cirrhosis (0.88 vs 0.91, respectively, p=0.12). FibroScan M probe exhibited significantly better performances than ARFI for diagnosing significant fibrosis F≥2 (0.88 vs 0.81 respectively, p=0.008).

ARFI (VTQ) performances were significantly worse in obese patients compared to non-obese patients, for both diagnosis of severe fibrosis (0.63 vs 0.91, p<0.0001) and cirrhosis (0.63 vs 0.92, p<0.0001) (Figure 1). According to authors, this finding may be due to the fact that in obese patients, the increase of soft tissue and fat led to poorer transmission of the US beam.

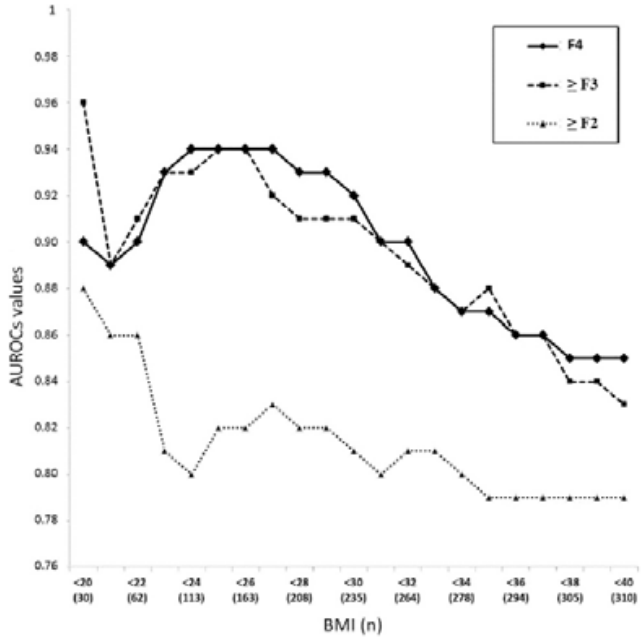

Figure 1 : Diagnostic performances (AUROC) of the ARFI as function of patient BMI [2]

Authors conclude that ARFI seem to be a reliable method to assess fibrosis in non-obese patients with high applicability. Its performance is equivalent to transient elastography (FibroScan®) for diagnosing cirrhosis and advanced fibrosis, but significantly lower for the diagnosis of significant fibrosis. However ARFI cannot be used in its current configuration as a first line examination in obese patients, and FibroScan dedicated XL probe should be preferred in this population.

Cassinotto et al. (JHepatol 2014) [3] performed a comparative study between ARFI (VTQ), Shear Wave elastography (SWE) using the Aixplorer system (SuperSonics Imagine, Aix en Provence, France) and Transient elastography (FibroScan, Echosens, Paris, France) in a cohort of 349 patients, taking histology as a reference for fibrosis evaluation.

LSM failures occurred in 10.4% of cases (35 of 336) with SWE, 2.6% (9 of 341) with FibroScan (6 of 235 patients with BMI<30kg/m² for M probe, and 3 of 106 patients with BMI>30kg/m² for XL probe) and none with ARFI (*0 of 337*). Differences were significant between SWE vs FibroScan (p=0.0002); SWE vs ARFI (p<.0001); and
FibroScan vs ARFI (p=0.003).

Unreliable results were observed in 5.9% of cases with FibroScan (20 of 341 patients, 9 of 235 with the M probe, and 11 of 106 with the XL probe), and in 16% of cases with ARFI (54 of 337 patients) (p=0.0002).

No failure of LSM was observed with ARFI. However, a clear improvement of ARFI performance for the diagnosis of cirrhosis and severe fibrosis was observed after exclusion of patients with failures of LSM by the means of SWE or FibroScan. Therefore, the diagnostic performance of ARFI elastography seems to be poor in patients in whom LSM with SSI or FibroScan failed, i.e. especially obese patients.