

## Real-time elastography as a noninvasive technique for quantification of fibrosis in patients with chronic viral liver disease: Preliminary findings<sup>\*</sup>

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KEYWORDS Real-time elastography; Liver fibrosis; Liver disease.	Abstract Introduction: Real-time elastography (RTE) is a novel technique for measuring tissue elasticity. The aims of this study were to prospectively measure liver stiffness with RTE in patients with chronic viral hepatitis and to evaluate the possible correlation between RTE data and the extent of fibrosis based on liver biopsy findings (Ishak score). <i>Material and methods:</i> Between February and October 2011, 26 patients (18M, 8F, mean age 41 $\pm$ 13 [standard deviation], range 22–62) with chronic viral hepatitis were prospectively evaluated with ultrasonography (US) that included RTE. All patients then underwent US-guided percutaneous liver biopsy (right lobe) for evaluation of fibrosis. Examinations were performed with a iU22 scanner (Philips, Bothell, WA, USA); a convex transducer (C5-1) was used for the US examination, and a linear transducer (L12-5) for RTE. In the RTE images, relative tissue stiffness is expressed according to a color scale with soft areas represented in green/red and hard areas in blue. Patients were examined in the supine position in suspended normal respiration; three loops of 20 RTE frames were recorded for each case. For each patient, we calculated the mean strain ratio (MSR) for the 3 loops. The Spearman correlation coefficient was used to assess correlation between the ASR and fibrosis stage (F) reflected by the Ishak score. <i>Results:</i> The Spearman coefficient showed significant correlation between the MSR and F (Rho = 0.470, $p = 0.015$ ).
	(Rho = 0.470, $p$ = 0.015). Conclusions: RTE appears to be a useful tool for noninvasive evaluation of fibrosis in patients with chronic viral hepatitis although these findings need to be confirmed in larger case series.

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**Sommario** Introduzione: L'elastosonografia real-time (ERT) è una nuova tecnologia integrata all'ultrasonografia convenzionale in grado di rappresentare la rigidità dei tessuti. Scopo dello studio è quantificare la rigidità epatica tramite ERT in pazienti con epatopatia cronica virale e ricercare una correlazione con lo staging istologico di malattia.

*Materiali e metodi:* Da Febbraio a Ottobre 2011, 26 pazienti (18M, 8F, età media 41  $\pm$  13 [deviazione standard], range 22–62) sono stati valutati prospetticamente con ecografia addominale (US) ed ERT e sono stati sottoposti a biopsia epatica (lobo destro) secondo indicazione clinica. Gli esami sono stati eseguiti con l'ecografo iU22 (Philips, Bothell, WA, USA) usando per l'US una sonda convex (C5-1) e per l'ERT una lineare (L12-5). L'apparecchiatura rappresenta la rigidità relativa dei tessuti esplorati secondo una scala cromatica, mostrando le porzioni più rigide in blu e quelle più morbide in verde/rosso. Per tutti i pazienti, sono stati registrati 3 loop di 20 frame di ERT; è stata ottenuta la media delle medie degli strain ratio dei 3 loop (MSR) ed è stato calcolato l'indice di correlazione di Spearman (IS) tra la MSR e lo stadio di fibrosi (F) secondo Ishak.

*Risultati:* L'IS è risultato significativo (rho = 0.470, p = 0.015) mostrando una buona correlazione tra F e MSR.

*Conclusioni*: l'ERT potrebbe essere utile per la quantificazione non invasiva della fibrosi nei pazienti con epatopatia cronica su base virale, ma per confermare questa ipotesi è necessaria una casistica più ampia.

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## Introduction

Assessment of hepatic fibrosis is fundamental for staging chronic viral liver disease. The information it provides is indispensable for planning drug therapy and follow-up in these cases, especially when antiviral drugs are prescribed [1,2]. The extent of fibrosis is one of the main predictors of response to drug therapy in patients with HCV-related liver disease [1]. The "gold standard" method for quantifying fibrosis is still percutaneous liver biopsy, although owing to its invasiveness, this procedure is not without risks [3]. Up to 25% of patients experience postprocedural abdominal pain, but the incidence of serious complications is low (1 in 4000-10,000) [4–6]. Other limitations involve sampling errors, which can occur in several types of liver disease, including those caused by HCV [7-10]; operator-dependent variability in the interpretation of the morphological features of the specimen [11], which can lead to under- and overestimates of the actual extent of fibrosis; costs; the limited repeatability of biopsy (which makes it unsuitable for monitoring the evolution of the disease); and contraindications to the procedure (which include coagulation disorders, lack of patient cooperation, refusal to submit to the procedure).

For these reasons, numerous attempts have been made in the past few years to develop noninvasive methods for assessing hepatic fibrosis, some based on laboratory tests, others on instrumental techniques. One of the first ultrasound-based methods investigated for the measurement of liver stiffness (as an indirect index of fibrosis) was transient elastography (FibroScan), which is based on the use of mechanical waves generated by vibration [12]. Its diagnostic reliability has been validated in patients with HCV-related liver disease (in three important multicenter studies) [13-15] and in patients with nonalcoholic fatty liver disease [16]. It is important to recall, however, that in some cases (10–20%), reliable data cannot be obtained due to excess body weight, narrow intercostal spaces, or excessive measurement variability [17,18].

Acoustic radiation force impulse (ARFI) imaging is an elastosonographic technique that furnishes quantitative measurements of hepatic elasticity during conventional abdominal B-mode sonography. It involves the transmission of a high-intensity ultrasound pulse, which causes tissue displacement and thereby produces a new mechanical wave that propagates transversely to the transmitted pulse. The propagation velocity of this wave (referred to as shear wave velocity) can be measured, and it correlates with the stiffness of the hepatic parenchyma. ARFI elastography has proved to be a reliable tool for assessing hepatic fibrosis in patients with chronic liver disease [19,20].

Real-time elastography (RTE) is another new technique that is used during conventional B-mode sonography to evaluate tissue stiffness. It provides qualitative (colorimetric) and quantitative readouts. This method has been used to differentiate benign and malignant lesions of the thyroid, breast, and prostate [21] and to study the liver [22,23]. The aims of this study were to measure hepatic stiffness using RTE in patients with chronic viral liver disease and to assess the possible correlation between these data and the extent of fibrosis assessed with liver biopsy (the reference method).

## Materials and methods

We prospectively enrolled 26 patients with chronic viral liver disease (18 men, 8 women, mean age 41  $\pm$  13 years [standard deviation], range 22–62) with clinical indications for ultrasound-guided percutaneous liver biopsy. The inclusion criteria were as follows: 1) chronic liver disease

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