DOI: http://dx.doi.org/10.12775/MBS.2015.025

Medical and Biological Sciences, 2015, 29/3, 27-35

REVIEW / PRACA POGLĄDOWA

Grażyna Rusak, Elżbieta Zawada

MAGNETIC RESONANCE ELASTOGRAPHY: A REWIEV

ELASTOGRAFIA REZONANSU MAGNETYCZNEGO: PRZEGLĄD PIŚMIENNICTWA

Department of Radiology and Diagnostic Imaging, Nicolaus Copernicus University in Toruń
Collegium Medicum Collegium Medicum in Bydgoszcz

S u m m a r y

Magnetic Resonance Elastography (MRE) is a rapidly developing, non-invasive, precise and reproducible imaging technique used for imaging the mechanical properties of tissues and for quantitative evaluation of shear wave propagation in the examined tissues.

Magnetic resonance elastography based on three general steps, which can be described as induction of shear wave with a frequency of 50 - 5000 Hz in the tissue, then imaging of propagation of the waves inside the body (organ) using a special phase-contrast MRI technique and after all processing the acquired data in order to generate images which reveal tissue stiffness.

MRE enables detection and grading of chronic hepatic fibrosis. It can be used to monitor the response to treatment or to evaluate the progress of the disease. Attempts are made to use elastography in the assessment of different organs such as liver, heart, breast, lungs, kidneys, prostate, brain tissue and spinal cord, cartilages, muscles and bones.

S t r e s z c z e n i e

Elastografia rezonansu magnetycznego (MRE) jest szybko rozwijającą się, nieinwazyjną, dokładną i odtwarzalną metoda diagnostyczną, wykorzystywaną dla obrazowania własności mechanicznych tkanek oraz dla ilościowej oceny propagacji fal sprężystych w badanych tkankach. Zasadniczo technika ta składa się z trzech podstawowych kroków. Po pierwsze generowanie w obszarze zainteresowania fal sprężystych o częstotliwości w zakresie 50-5000 Hz. Następnie pozyskiwanie obrazów rezonansu magnetycznego, które przedstawiają rozchodzenie się wyindukowanych fal sprężystych. Ostatecznie przetwarzanie obrazów szerzenia się fal sprężystych na ilościowe mapy sztywności tkanek zwane elastogramami.

MRE umożliwia wykrywanie i stopniowanie przewlekłego włóknienia wątroby. Sekwencja może być wykorzystywana dla monitorowani odpowiedzi na leczenie lub dla oceny progresji choroby.

Trwają badania naukowe z użyciem elastografii rezonansu magnetycznego w ocenie innych organów takich jak serce, piersi, płuca, nerki, prostata, tkanka mózgowa i rdzeń kręgowy, układ mięśniowo-szkieletowy.

Key words: magnetic resonance, elastography, liver, fibrosis and cirrhosis

Słowa kluczowe: rezonans magnetyczny, elastografia, wątroba, włóknienie i marskość

INTRODUCTION

Magnetic Resonance Elastography (MRE) is a rapidly developing, non-invasive, precise and reproducible imaging technique used for imaging the mechanical properties of tissues. To put it simply: this is an imaging technique comparable to palpation – a method that is broadly used by general practitioners.

Palpation, a method that enabled the tactile evaluation of mechanical properties of both healthy and pathological tissues, had remained the only qualitative diagnostic tool in the detection of pathology for a long time. However, this technique can be used only for organs and lesions located superficially. It is used for prophylactic examinations of breasts as it enables detection of stiff, tuberous lesions that may evoke suspicion of a neoplastic lesion. Nevertheless, it lacks objectivism, as it depends on tactile the sensitivity of the examiner [1]. Unfortunately, none of the basic imaging modalities, i.e. neither US, nor CT or MRI, can depict the mechanical properties of tissues – a parameter which can be examined by palpation. The search for new imaging modalities led to the discovery of magnetic resonance elastography. Magnetic resonance elastography, discovered by professor Richard Ehrman and his associates from the Mayo Clinic, is used for quantitative evaluation of shear wave propagation in the examined tissues. The mechanical properties of tissues vary greatly, both in physiological and pathological conditions. Therefore, MRE seems to possess great diagnostic potential. MRE sequences are routinely used in patients of Mayo Clinic who undergo abdominal MR and since February 2007 doctors from Mayo Clinic have performed MRE in over 2400 patients. MRE can be performed using conventional MRI systems with appropriate hardware and software modifications [2, 3, 4]. MRE uses a modified MR imaging technique also known as phase-contrast technique, thanks to which spatial maps of elastic wave propagation can be generated. MRE is non-invasive, well tolerated by patients and does not require administration of contrast agents. MRE enables detection and grading of chronic hepatic fibrosis [2, 5, 6, 7, 8]. It can be used to monitor the response to treatment or to evaluate the progress of the disease. It has been successfully used in the diagnostics of the spread of hepatic fibrosis in the population of children [9] and in patients with HCV infection relapse after liver transplantation [10]. It is also used for identifying non-alcoholic steatohepatitis (NASH) among patients with non-alcoholic fatty liver disease (NAFLD). Research concerning the use of elastography in the determination of hepatic tumours has shown that it can be used as a guide for MRI-guided liver biopsy [11].

Magnetic resonance elastography develops in multiple directions as a non-invasive technique. Attempts are made to use elastography in the assessment of different organs such as liver [8, 12, 13], heart [14], breast [15], lungs [16, 17], kidneys [18], prostate [19, 20], brain tissue [21, 22], spinal cord [23], cartilages [24], muscles [25, 26] and bones [27].

ELASTICITY IMAGING

There are many possible options for imaging mechanical properties of tissues. Most of them use some kind of pressure or mechanical excitation of tissues. Moreover, they measure tissue response to this stimulation and calculate parameters which reflect the mechanical properties of the tissues accordingly.

Imaging of elasticity consists of: application of excitation, measuring tissue response to the stimulus used and estimating mechanical parameters.

Mechanical stress applied to tissue can be caused by internal (heart beat, breathing) [28, 29, 30], and external [21, 22, 31] sources of motion excitation. Stimulation can be classified as static or dynamic according to its temporal characteristics. Palpation can be classified as a static elasticity-measuring method. Static pressure is broadly used in imaging of the elasticity of tissues, and techniques that use it include strain-encoded imaging [32], elastography [33] and stimulated-echo elasticity imaging [34, 35]. Dynamic elicitation technique uses vibrations of 50-500 Hz and depicts the propagation of waves which are excited in the tissues. This is the basis used for ultrasound transient elastography [36, 37] and magnetic resonance elastography [38, 39, 40].

Measuring tissue response, i.e. the deformation of tissue caused by a stimulus is a critical component of tissue elasticity imaging. There are several different methods of measuring this response: optical, mechanical, ultrasonographic and magnetic resonance elastography. One of the first studies concerning tissue elasticity used visible light to measure the propagation of mechanical waves in order to depict elasticity and viscosity of tissues [41]. In the following years, other optical imaging modalities such as optical coherence tomography, and tissue Doppler optical coherence elastography were implemented. [42, 43, 44] Mechanical pressure sensors and accelerometers have also been used for measuring tissue response to stimulation [45, 46]. Ultrasonography is also widely used to visualise tissue elasticity. Tissue stiffness – elasticity acquired after external compression – is measured using ultrasound. This provides a quantitative impression of tissue elasticity. TE – transient elastography is one of the ultrasound methods

of elasticity imaging. In this technique, a special probe excites a single transient shear wave in the tissue, and tracks its propagation with the use of ultrasound [47, 48]. Although ultrasound imaging techniques are fast, inexpensive and widely used, they also have several limitations, such as: an appropriate acoustic window for ultrasound measurements is needed and the depth to which the measurements can be made, is limited and depends on the penetration of the ultrasound wave into tissue [49]. Obesity and ascites prove problematic in evaluating the liver. Moreover, liver elasticity is measured only on the 1 x 4 cm area over the right lobe of liver [50, 51]. The first attempts at measuring tissue movement using MRI technique were performed to evaluate the functioning and pathology of the heart. [52, 53]. Later on, magnetic resonance elastography technique was developed. This technique was based on imaging of propagation of waves of specific frequency induced in tissues, and revealed values that corresponded to mechanical properties of the examined tissues [38, 54].

For quantitative imaging of tissue elasticity it is necessary to process the acquired data and estimate the mechanical properties of tissues. Basically, it is assumed for the purposes of elasticity imaging technique that tissues are linearly elastic, isotropic and possess Hooke's elasticity, which enables implementation of the laws of mechanics concerning the relationship between the deformation of materials and the tension to be applied in such cases. Elastic properties which correspond to what was estimated in palpation can be expressed by Young's modulus (E) or elastic modulus μ. For most soft tissues, E and μ are related in such a way that: E is directly proportional to μ ($E = 3\ \mu$), which means that measuring Young's modulus and elastic modulus gives the same information [49]. Most techniques that use quasi-static excitation calculate the displacement or deformation of the tissues as a qualitative indicator of basic mechanical properties [30, 32, 55]. In order to calculate the quantitative value of elastic modulus, it is necessary to determine the stress applied to the tissue, which is difficult and complicated. However using dynamic wave propagation technique, the quantitative value of tensile modulus (Young's modulus) can be calculated on the basis of elastic wave propagation by using appropriate wave equations [38, 48].

MAGNETIC RESONANCE ELASTOGRAPHY

Magnetic resonance elastography is an imaging modality used to depict tissue elasticity; it uses mechanical waves for quantitative evaluation of the elastic longitudinal modulus of tissue [38]. This technology became available thanks to the upgrading of conventional MR scanners [2, 8, 56]. Magnetic resonance elastography based on three general steps, which can be briefly described:

- induction of shear wave with a frequency of 50-5000 Hz in the tissue,
- imaging of propagation of the waves inside the body (organ) using a special MRI technique
- processing the acquired data in order to generate images which reveal tissue stiffness [49].

Generating mechanical waves in tissue

Usually MRE uses single frequency vibrations ranging in frequency from 50 to 5000 Hz generated by an external appliance. Electric current supplied to these appliances is created by an induced signal generator and synchronised with MR impulse sequences, and is also amplified by an audio amplifier before it reaches the mechanical driver. The amplitude of vibrations which are induced in the tissue is very low and is within the range that is in accordance with the EU directive limiting professional exposure to vibrations of the whole body and extremities [57].

Several propelling mechanisms were developed over the years, each with its own advantages and disadvantages [58]. One of the widely used methods of generating vibrations necessary for MRE uses movement in coils used in acoustic speaker systems. Necessary vibrations are created using Lorentz forces but the static magnetic field comes from the permanent magnet which can be found in an acoustic speaker [8, 12]. The speaker with its permanent magnet must be placed out of the reach of the main MR magnet, and that is why this system requires an additional connecting component that transmits vibrations from the speaker to tissues. So that connecting tubes for pneumatic conduction of harmonic air pressure changes from the speaker to a passive drum acting as a driver kept in contact with the tissue (pressure-activated driver) are used. The components of the driver system that are near the patient are made of materials that do not generate artefacts on MRI scans. Because the driver has two components – the active one which generates vibrations and the passive one, which remains in contact with the tissue, the passive element can be adapted to any organ we are interested

in, such as e.g. liver or breast. This system is used inter alia in clinical liver MR elastography [56].

Imaging of wave propagation

Measuring the motion of tissue induced by the driver in MRE is based on the phase-contrast MRI technique [59]. A dynamic phase-contrast technique was developed in which the propagation of shear waves is visible in MR scans thanks to the use of motion-encoding gradient (MEG) pairs. Conventional MR scanning is performed after continuous harmonic motion is induced in the tissue, and MEG oscillates at the same frequency as the motion induced in the tissue. The MR phase contribution ϕ can be written as an equation of motion but [38] a precise analysis of the equation is beyond the scope of this study.

Since gradients encoding motion, which are necessary for MR elastography, are a component of conventional MR impulse sequences, elastography can be performed using different magnetic resonance sequences. MRE impulse sequences are based on already available techniques such as: SE – spin echo, GRE – gradient-recalled echo, EPI – echo planar imaging, bSSEP – balanced steady-state free precision [60, 61, 62, 63].

Mechanical parameter estimation

If we possess wave images that reflect shear wave propagation in the tissues mathematical inversion algorithms based on motion equations with simplifying assumptions such as homogeneity, isotropy, and incompressibility of the environment can be used. This enables shear modulus to be calculated, which in turn corresponds with the clinical interpretation of acquired images [49]. If the assumption of isotropy of the environment is made, the number of independent quantities is reduced from 21 to two Lame constants, i.e. λ and μ. These constant values are material constants which were introduced in order to simplify Hook's law and which control longitudinal and shear strains. The λ Lame parameter is usually much greater than the shear modulus - μ, which makes the calculation of both these constants at the same time impractical. The lambda effect can be neglected or deleted by filtering out the longitudinal motion wave with the use of a proper filter [64]. Shear modulus, also known as modulus of rigidity, μ (Kirchhoff-G modulus) is a complex quantity and can be expressed as $\mu_r + \mu_i$, where μ_r is the storage modulus and μ_i is the loss modulus which reflects the attenuation in a viscoelastic medium. Shear wave speed and effective shear modulus can be calculated from the complex shear modulus using a simple equation $\mu = \rho Vs2$, where rho indicates the density of the material (usually 1000 kg/m3 in tissue for MRE), and Vs is the wave speed of the shear wave. Using a simple harmonic wave equation wave speed can be written as a product of the wavelength and the frequency. Hence, early MRE analyses based on measuring shear wavelength and were performed manually. Automatically-calculating algorithms were developed, such as phase-gradient (PG), local frequency estimation (LFE) [65] and the direct inversion (DI) algorithm [66]. However, stiffness values are still provided as the product of density and squared wave speed [49].

Before *in vivo* elastography was implemented, research on phantoms with areas of different stiffness was conducted. Mariappan et al. presented a phantom where the background was made up of 2% agarose gelatine and 2 soft inclusions which can be depicted in an MRI image as hyperintense areas made up of much softer 1% agar, and hypointense inclusions made up of stiffer 3% agar. The wavelength decreases in soft tissues and increases in a stiff environment. Shear stiffness was calculated using an inversion algorithm with directional filtering (LFE) and it is shown as an elastogram in kPa. Stiffness difference between inclusions and the background gel is evident and both soft and stiff inclusions can be visualised easily. Representative quantitative stiffness values can be calculated by averaging values presented in the areas of interest from the inside of these areas [49].

LIVER ELASTOGRAPHY

The use of magnetic resonance elastography for the diagnostics of liver diseases has been widely studied [6, 13]. Currently it is used in clinical practice in the assessment of liver fibrosis and cirrhosis in which the stiffness of pathologically changed liver is much higher than normal liver tissue. Liver stiffness is directly connected with the grade of fibrosis and increases along with the development of the disease [49]. Based on ROC, shear stiffness cut-off value of 2.93 kPa is considered optimal for distinguishing between healthy and diseased liver tissue with sensitivity and specificity of 98% and 99%, respectively. The possibilities of other imaging methods such as CT, US and

conventional MR are limited in disclosing the process of fibrosis, and they are effective in irreversible fibrosis only [67, 68].

MRE is considered as a method for early detection of non-alcoholic steatohepatitis (NASH). Non-alcoholic fatty liver disease (NAFLD), associated with obesity and type II diabetes, is a disease that affects 1/3 of the adult population in the US. It has been estimated that almost 25% of NAFLD patients will develop NASH which can induce liver cirrhosis [69]. Currently, the diagnosis of NASH can be confirmed only by liver biopsy. Therefore, there are great opportunities for the development of elastography in this field. MRE can be helpful in distinguishing simple hepatic steatosis from steatohepatitis before fibrosis occurs. MRE as a diagnostic method revealed that in patients with NAFLD and NASH but without liver fibrosis the measured stiffness was greater than in patients with simple hepatic steatosis [70].

Attempts to use liver elastography for the assessment of liver tumours have also been made and it seems to be a promising tool for their determination. Early detection of small tumours is a challenge since it is known that liver cirrhosis is the most important factor predisposing for the development of hepatocellular carcinoma [71]. It was stated that malignant liver tumours exhibit considerably higher shear stiffness values than benign tumours and healthy liver tissue, and a cut-off value of 5 kPa enables one to distinguish malignant tumours from benign lesions [11]. A potential limitation of this method can be cirrhosis of the liver in which the background possesses the same mechanical properties, i.e. stiffness, as the tumour. Hence the use of elastography in the assessment of liver tumours in hepatic cirrhosis requires further research [72].

Clinically, liver elastography is performed using a stationary pneumatic pressure-activated driver that generates low-frequency vibrations of 60 Hz in frequency. The active component of the driver is located outside the main resonance room and the vibrations are transmitted using a flexible tube to the passive driver – a disk of 19 mm in diameter and 1.5 mm in thickness that is located directly over the liver on the anterior wall of the thorax on its right side.

A modified phase gradient echo sequence incorporating a first moment nulled cyclic motion encoding gradients sensitive to through plane motion is used to image propagating sheer waves. Synchronization of the elastography driver system to these gradients is achieved by means of an imager trigger. Trigger time is calibrated in order to sample four different phase offsets of that propagating wave field. A modified direct inversion (DI) algorithm is used to generate quantitative images – elastograms, which enable one to estimate the stiffness of liver tissue. Exemplary MRE sequence parameters are: repetition time (TR) / echo time (TE) – 50.0 / 22.2 ms, flip angle – 25 degrees; bandwidth – 260 Hz/pixel; matrix 256x64; slice thickness – 5 mm; FOV – 390 x 390 mm2. As many as 4 to 8 axial slices are acquired from different anatomical levels of the liver [6, 38, 64, 73].

Images presenting mechanical properties of tissues acquired in MRE are known as elastograms.

In the analysis of MRE images, the regions of interest ROI are placed on elastograms, and an averaged tissue stiffness value is calculated automatically and is provided in Pa. When locating ROIs, one should avoid regions rich in biliary ducts, large hepatic vessels, regions of the liver located directly under the driver and those prone to motion artefacts resulting from the heart, just as the left liver lobe [73].

MRE VERSUS OTHER METHODS OF LIVER FIBROSIS ASSESSMENT

The first transcutaneous liver biopsy was performed in 1923 and until today it remains the only available method of assessing the degree of the destruction of the liver tissue. Liver biopsy is a golden standard in the detection of liver fibrosis and liver cirrhosis [74, 75]. It is an invasive method and poses a higher risk of potential complications. The most frequent complication of liver biopsy is pain with different severity, frequently with accompanying vasovagal reactions and hypotension, and asymptomatic haemorrhages – subcapsular or intracapsular haematomae. Others include: puncture of the lung, pneumothorax, kidney puncture and colon puncture, especially in Chilaiditi syndrome, gallbladder/biliary tract puncture with accompanying jaundice, biliary colic, peritoneal and retroperitoneal haemorrhage. The risk of neoplastic spread along the biopsy canal was also reported on [75]. Liver biopsy is connected with a significant risk of sample size error, from 14 to 25 % when diagnosing liver cirrhosis. It should also be taken into account that histological assessment is subjective

and depends on the experience of the pathologist [76]. So that MRE is interesting due to its non-invasiveness.

MRE has proven a suitable method for the detection and staging of liver fibrosis. Yin et al. comparing 50 patients with liver disease confirmed by biopsy and 35 healthy subjects as a control group revealed 98% sensitivity and 99% specificity in detecting liver fibrosis with a cut-off value for stiffness of 2.93 kPa [8]. The ROC analysis also revealed that MRE could detect patients with moderate to severe liver fibrosis (stage F2 – F4) and those with mild fibrosis (stage F0 – F1) based on the METAVIR system – histopathological system of liver staging [8]. The possibility of distinguishing moderate and severe cirrhosis from mild fibrosis is clinically important as treatment is indicated starting from the F2 stage according to the American Association for the Study of Liver Diseases [77]. The studies by Huwart et al. [5], Kim et al. [78], Rustogi et al. [77] and Wang et al. [7] revealed comparable sensitivity and specificity of this method.

Magnetic resonance elastography was also compared with ultrasound transient elastography (TE). Research by Huwart et al. conducted on a group of 141 patients with chronic liver disease proved that MRE was better than TE – a higher success rate was reported – 94% for MRE and 84% in TE [5]. What is also important, obesity or ascites do not influence MRE measurements, contrary to TE measurements [50]. Moreover, in MRE the whole liver is assessed, whereas TE provides opportunities for the assessment of an area of 1 x 4 cm over the right liver lobe. Although TE exhibits perfect sensitivity and specificity in the detection of liver fibrosis compared to biopsy, its value is limited to 70 % and 80 %, respectively when compared to MRE (86% and 85%, respectively) in the detection of intermediate stages of fibrosis (F2-F4) [51].

Diagnostic magnetic resonance elastography was also compared with diffusion-weighted MRI sequences. In cases of echo planar imaging (EPI) with different diffusion coefficient values we may acquire diffusion-weighted images, and the acquired apparent diffusion coefficient can be depicted as colourful maps comparable to elastograms. In the presence of fibrosis and cirrhosis, tissue diffusion is limited and ADC decreases [79]. ROC analysis revealed that MRE is more precise in staging of fibrosis when compared to DWI when histopathological examination was used as the reference standard. In 76 patients MRE showed greater predictive value in distinguishing the stage of fibrosis than DWI [10]. MRE also showed greater possibilities than DWI for the evaluation of F2, F3 and F4 stages, which proved significant in the AUC analysis. Although liver stiffness in elastography increases along with severity of fibrosis, no consistent relationships between the apparent diffusion coefficient (ADC) and the stage of fibrosis have been stated [79].

REFERENCES

1. T.C. Jacob, N.E.Penn, J.Giebink, R bastein. A comparison of breast self-examination and clinical examination. J Natl Med Assoc. Jan 1994; 86(1): 40–45.
2. Yin M, Chen J, Glaser KJ, Talwalkar JA, Ehman RL. Abdominal magnetic resonance elastograpfy. Topics in magnetic resonance imaging: TMRI 2009;20(2):79-87.
3. http://www.mayoclinic.org/magnetic-resonance-elastography
4. Talwalkar JA, Ehman RL, Salinas A. Needle-free liver assessment with MR elastography and ideal IQ in clinical practice. GE Healthcare MR Application Webinar.
5. Huwart L, Sempoux C, Vicaut E, et al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis. Gastroenterology. 2008;135(1):32-40.
6. Rouviere O, Yin M, Dresner MA, Rossman PJ, Burgart LJ, Fidler JL, Ehman RL. MR Elastography of the Liver: Preliminary Results. Radiology. 2006; 240:440–448. [PubMed: 16864671]
7. Wang Y, Ganger DR, Levitsky J, et al. Assessment of chronic hepatitis and fibrosis: comparison of MR elasrography and diffusion-weighted imaging. American journal of roentgenology AJR. 2011;196(3):553-61.
8. Yin M, Talwalkar JA, Glaser KJ, Manduca A, Grimm RC, Rossman PJ, Fidler JL, Ehman RL. Assessment of hepatic fibrosis with magnetic resonance elastography. Clinical Gastroenterology and Hepatology. 2007; 5(10):1207–1213. [PubMed: 17916548]
9. Binkovitz LA, El-Youssef M, Glaser KJ, Yin M, Binkovitz AK, Ehman RL. Pediatric MR elastography of hepatic fibrosis: principles, technique and early clinical experience. Pediatric radiology. 2011.
10. Lee VS, Miller FH, Omary RA, et al. Magnetic resonance elastography and biomarcers to assess fibrosis from recurrent hepatitis C in liver transplant recipients. Transplantation. 2011;92(5):581-586.
11. Venkatesh SK, Yin M, Glockner JF, et al. MR elastography of liver tumors: preliminary results. American journal of roentgenology AJR. 2008;190(6):1534-1540.
12. Asbach P, Klatt D, Hamhaber U, Braun J, Somasundaram R, Hamm B, Sack I. Assessment of liver viscoelasticity using multifrequency MR elastography. Magn Reson Med. 2008; 60:373–379. [PubMed: 18666132]
13. Huwart L, Sempoux C, Salameh N, Jamart J, Annet L, Sinkus R, Peeters F, ter Beek LC, Horsmans Y, Van Beers BE. Liver fibrosis: noninvasive assessment with MR

elastography versus aspartate aminotransferase-to-platelet ratio index. Radiology. 2007; 245:458–466. [PubMed: 17940304]
14. Kolipaka A, McGee KP, Araoz PA, Glaser KJ, Manduca A, Romano AJ, Ehman RL. MR elastography as a method for the assessment of myocardial stiffness: comparison with an established pressurevolume model in a left ventricular model of the heart. Magn Reson Med. 2009; 62:135–140. [PubMed: 19353657]
15. Sinkus R, Tanter M, Xydeas T, Catheline S, Bercoff J, Fink M. Viscoelastic shear properties of in vivo breast lesions measured by MR elastography. Magn Reson Imaging. 2005B; 23:159–165. [PubMed: 15833607]
16. Goss BC, McGee KP, Ehman EC, Manduca A, Ehman RL. Magnetic resonance elastography of the lung: technical feasibility. Magn Reson Med. 2006; 56:1060–1066. [PubMed: 17036283]
17. McGee KP, Hubmayr RD, Ehman RL. MR elastography of the lung with hyperpolarized 3He. Magnetic Resonance in Medicine. 2008; 59:14–18. [PubMed: 18058936]
18. Shah NS, Kruse SA, Lager DJ, Farell-Baril G, Lieske JC, King BF, Ehman RL. Evaluation of renal parenchymal disease in a rat model with magnetic resonance elastography. Magn Reson Med. 2004; 52:56–64. [PubMed: 15236367]
19. Chopra R, Arani A, Huang Y, Musquera M, Wachsmuth J, Bronskill M, Plewes D. In vivo MR elastography of the prostate gland using a transurethral actuator. Magn Reson Med. 2009; 62:665–671. [PubMed: 19572390]
20. Kemper J, Sinkus R, Lorenzen J, Nolte-Ernsting C, Stork A, Adam G. MR elastography of the prostate: initial in vivo application. RoFo; Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin. 2004; 176:1094–1099.
21. Kruse SA, Rose GH, Glaser KJ, Manduca A, Felmlee JP, Jack CR, Ehman RL. Magnetic resonance elastography of the brain. NeuroImage. 2008; 39:231–237. [PubMed: 17913514]
22. Xu L, Lin Y, Xi ZN, Shen H, Gao PY. Magnetic resonance elastography of the human brain: a preliminary study. Acta Radiol. 2007; 48:112–115. [PubMed: 17325935]
23. Kruse, S.; Kolipaka, A.; Manduca, A.; Ehman, R. Feasibility of Evaluating the Spinal Cord with MR Elastography. Proceedings 17th Scientific Meeting, International Society for Magnetic Resonance in Medicine; Honolulu. 2009. p. 629
24. Lopez O, Amrami KK, Manduca A, Ehman RL. Characterization of the dynamic shear properties of hyaline cartilage using high-frequency dynamic MR elastography. Magnetic Resonance in Medicine. 2008; 59:356–364. [PubMed: 18228594]
25. Dresner MA, Rose GH, Rossman PJ, Muthupillai R, Manduca A, Ehman RL. Magnetic resonance elastography of skeletal muscle. J Magn Reson Imaging. 2001; 13:269–276. [PubMed: 11169834]
26. Ringleb SI, Bensamoun SF, Chen Q, Manduca A, An KN, Ehman RL. Applications of magnetic resonance elastography to healthy and pathologic skeletal muscle. J Magn Reson Imaging. 2007; 25:301–309. [PubMed: 17260391]
27. Chen, J.; McGregor, H.; Glaser, K.; Mariappan, Y.; Kolipaka, A.; Ehman, R. Magnetic Resonance Elastography in Trabecular Bone: Preliminary Results. Proceedings 17th Scientific Meeting, International Society for Magnetic Resonance in Medicine; Honolul. 2009. p. 847
28. Bae U, Dighe M, Dubinsky T, Minoshima S, Shamdasani V, Kim Y. Ultrasound thyroid elastography using carotid artery pulsation: preliminary study. Journal of Ultrasound in Medicine. 2007; 26:797–805. [PubMed: 17526611]
29. Kanai, H. Viscoelasticity measurement of heart wall in in vivo; Ultrasonics Symposium, 2004 IEEE; 2004. p. 482-485.
30. Mai JJ, Insana MF. Strain imaging of internal deformation. Ultrasound in Medicine and Biology. 2002; 28:1475–1484. [PubMed: 12498943]
31. Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. Ultrasonics, Ferroelectrics and Frequency Control, IEEE Transactions on. 2004; 51:396–409.
32. Osman NF. Detecting stiff masses using strain-encoded (SENC) imaging. Magnetic Resonance in Medicine. 2003; 49:605–608. [PubMed: 12594769]
33. Ophir J, cespedes I, Ponnekanti H, Yazdi Y, Li X. Elastography : a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging. 1991; 13(2):111–134. [PubMed: 1858217]
34. Chenevert TL, Skovoroda AR, O'Donnell M, Emelianov SY. Elasticity reconstructive imaging by means of stimulated echo MRI. Magnetic Resonance in Medicine. 1998; 39:482–490. [PubMed:9498605]
35. Steele DD, Chenevert TL, Skovoroda AR, Emelianov SY. Three-dimensional static displacement, stimulated echo NMR elasticity imaging. Physics in Medicine and Biology. 2000; 45:1633–1648. [PubMed: 10870715]
36. Lerner RM, Huang SR, Parker KJ. 'Sonoelasticity' images derived from ultrasound signals in mechanically vibrated tissues. Ultrasound in Medicine and Biology. 1990; 16:231–239. [PubMed:1694603]
37. Levinson SF, Shinagawa M, Sato T. Sonoelastic determination of human skeletal-muscle elasticity. Journal of Biomechanics. 1995; 28:1145–1154. [PubMed: 8550633]
38. Muthupillai R, Lomas DJ, Rossman PJ, Greenleaf JF, Manduca A, Ehman RL. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. Science. 1995; 269:1854–1857. [PubMed: 7569924]
39. Sack I, Mcgowan CK, Samani A, Luginbuhl C, Oakden W, Plewes DB. Observation of nonlinear shear wave propagation using magnetic resonance elastography. Magnetic Resonance in Medicine. 2004; 52:842–850. [PubMed: 15389935]
40. Sinkus, R.; Lorenzen, J.; Schrader, D.; Lorenzen, M.; Dargatz, M.; Holz, D. In vivo tensor Mr-elastography - anisotropy of mamma-carcinoma. Proceedings of the

International Society for Magnetic Resonance in Medicine; Denver, Colorado. 2000. p. 493
41. Gierke HE, Oestreicher HL, Franke EK, Parrack HO, Wittern WW. Physics of vibrations in living tissues. J Appl Physiol. 1952; 4:886–900. [PubMed: 14946086]
42. Rogowska J, Patel NA, Fujimoto JG, Brezinski ME. Optical coherence tomographic elastography technique for measuring deformation and strain of atherosclerotic tissues. Heart. 2004; 90:556–562. [PubMed: 15084558]
43. Ruikang KW, Zhenhe M, Sean JK. Tissue Doppler optical coherence elastography for real time strain rate and strain mapping of soft tissue. Applied Physics Letters. 2006; 89:144103.
44. van Soest G, Mastik F, de Jong N, van der Steen AF. Robust intravascular optical coherence elastography by line correlations. Phys Med Biol. 2007; 52:2445–2458. [PubMed: 17440245]
45. Egorov V, Ayrapetyan S, Sarvazyan AP. Prostate mechanical imaging: 3-D image composition and feature calculations. Medical Imaging, IEEE Transactions on. 2006; 25:1329–1340.
46. Sarvazyan A. Mechanical imaging - a new technology for medical diagnostics. International Journal of Medical Informatics. 1998; 49:195–216. [PubMed: 9741894]
47. de Ledinghen V, Le Bail B, Rebouissoux L, Fournier C, Foucher J, Miette V, Castera L, Sandrin L, Merrouche W, Lavrand F, Lamireau T. Liver stiffness measurement in children using FibroScan: feasibility study and comparison with fibrotest, aspartate transaminase to platelets ratio index, and liver biopsy. Journal of Pediatric Gastroenterology and Nutrition. 2007; 45:443–450. [PubMed: 18030211]
48. Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol. 2003; 29:1705–1713. [PubMed: 14698338]
49. Mariappan YK, Glaser KJ, Ehman RL. Magnetic resonance elastography: a review. Clin Anat. 2010;23(5):497-511.
50. Talwalkar JA. Elastography for detecting hepatic fibrosis: options and considerations. Gastroenterology. 2008;135(1):299-302.
51. Talwalkar JA, Kurtz DM, Schoenleber SJ, West CP, Montori VM. Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. Clinical gastroenterology and hepatology. 2007;5(10):1214-1220.
52. Axel L, Dougherty L. MR imaging of motion with spatial modulation of magnetization. Radiology. 1989; 171:841–845. [PubMed: 2717762]
53. Zerhouni EA, Parish DM, Rogers WJ, Yang A, Shapiro EP. Human heart: tagging with MR imaging - a method for noninvasive assessment of myocardial motion. Radiology. 1988; 169:59–63. [PubMed: 3420283]
54. Muthupillai R, Rossman PJ, Lomas DJ, Greenleaf JF, Riederer SJ, Ehman RL. Magnetic resonance imaging of transverse acoustic strain waves. Magnetic Resonance in Medicine. 1996; 36:266–274. [PubMed: 8843381]
55. O'Donnell M, Skovoroda AR, Shapo BM, Emelianov SY. Internal displacement and strain imaging using ultrasonic speckle tracking. Ultrasonics, Ferroelectrics and Frequency Control, IEEE Transactions on. 1994; 41:314-325.
56. Venkatesh, SK.; Yin, M.; Talwalkar, JA.; Ehman, RL. Application of liver MR elastography in clinical practice. Proceedings of the International Society for Magnetic Resonance in Medicine; Toronto, Ontario, Canada. 2008b. p. 2611
57. Ehman EC, Rossman PJ, Kruse SA, Sahakian AV, Glaser KJ. Vibration safety limits for magnetic resonance elastography. Phys Med Biol. 2008; 53:925–935. [PubMed: 18263949]
58. Tse ZT, Janssen H, Hamed A, Ristic M, Young I, Lamperth M. Magnetic resonance elastography hardware design: a survey. Proc Inst Mech Eng H. 2009; 223:497–514. [PubMed: 19499839]
59. Moran PR. A flow velocity zeugmatographic interlace for NMR imaging in humans. Magn Reson Imaging. 1982; 1:197–203. [PubMed: 6927206]
60. Bieri O, Maderwald S, Ladd ME, Scheffler K. Balanced alternating steady-state elastography. Magnetic Resonance in Medicine. 2006; 55:233–241. [PubMed: 16416431]
61. Kruse, SA.; Grimm, RC.; Lake, DS.; Manduca, A.; Ehman, RL. Fast EPI based 3D MR elastography of the brain. Proceedings of the International Society for Magnetic Resonance in Medicine; Seattle, Washington. 2006. p. 3385
62. Maderwald S, Uffmann K, Galban CJ, de Greiff A, Ladd ME. Accelerating MR elastography: a multiecho phase-contrast gradient-echo sequence. Journal of Magnetic Resonance Imaging. 2006; 23:774–780. [PubMed: 16570244]
63. Rydberg, J.; Grimm, R.; Kruse, S.; Felmlee, J.; McCracken, P.; Ehman, R. Fast spin-echo magnetic resonance elastography of the brain. Proceedings of the International Society for Magnetic Resonance in Medicine; Glasgow, Scotland: International Society for Magnetic Resonance in Medicine; 2001. p. 1647
64. Manduca A, Oliphant TE, Dresner MA, Mahowald JL, Kruse SA, Amromin E, Felmlee JP, Greenleaf JF, Ehman RL. Magnetic resonance elastography: non-invasive mapping of tissue elasticity. Med Image Anal. 2001; 5:237–254. [PubMed: 11731304]
65. Manduca, A.; Muthupillai, R.; Rossman, PJ.; Greenleaf, JF.; Ehman, RL. Local wavelength estimation for magnetic resonance elastography. Image Processing, 1996. Proceedings., International Conference on; 1996. p. 527-530.
66. Oliphant TE, Manduca A, Ehman RL, Greenleaf JF. Complex-valued stiffness reconstruction for magnetic resonance elastography by algebraic inversion of the differential equation. Magn Reson Med. 2001; 45:299–310. [PubMed: 11180438]
67. Faria SC, Ganesan K, Mwangi I, Shiehmorteza M, Viamonte B, Mazhar S, Peterson M, Kono Y, Santillan C,

Casola G, Sirlin CB. MR imaging of liver fibrosis: current state of the art. Radiographics. 2009; 29:1615–1635. [PubMed: 19959511]
68. Talwalkar JA, Yin M, Fidler JL, Sanderson SO, Kamath PS, Ehman RL. Magnetic resonance imaging of hepatic fibrosis: emerging clinical applications. Hepatology. 2008; 47:332–342. [PubMed: 18161879]
69. Fassio E, Alvarez E, Dominguez N, Landeira G, Longo C. Natural history of nonalcoholic steatohepatitis: a longitudinal study of repeat liver biopsies. Hepatology. 2004;40(4):820-826.
70. Salameh N, Larrat B, Abarca-Quinones j, et al. Early detection of steatohepatitis in fatty rat liver by using MR elastography. Radiology 2009;253(1):90-97
71. Willatt JM, Hussain HK, Adusumilli S, Marrero JA. MR imaging of hepatocellular carcinoma in the cirrhotic liver: challenges and controversies. Radiology. 2008;247(2):311-330.
72. Sudharshan Parthasarathy, et al. Magnetic resonance elastography: proven indications, challenges and future considerations. Magnetom Flash. 2012;1:20-27.
73. Taouli B, Ehman RL, Reeder SB. Advanced MRI methods for assessment of chronic liver disease. American journal of roentgenology. 2009;193(1):14-27
74. Bravo AA, Sheth SG, Chora S: Liver biopsy. N Eng J Med, 2001; 344: 495–500.
75. Grant A, Neuberger J: Guidelines on the use of liver biopsy in clinical practice. Gut, 1999; 45(Suppl.IV): IV1–IV11.
76. Regev A, Berho M, Jeffers LJ, et al. Sampling error and intraobserver variation in liver biopsy in patient with chronic HCV infection. The American journal of gastroenterology. 2002;97(10):2614-2618.
77. Rustogi R, Horowitz J, Harmath C, et al. Accuracy of MR elastography and anatomic MR imaging features in the diagnosis of severe hepatic fibrosis and cirrhosis. JMRI. 2012.
78. Kim BH, Lee JM, Lee YJ, et al. MR elastography for noninvasive assessment of hepatic fibrosis: experience from a tertiary center in Asia. JMRI 2011;34(5):1110-1116.
79. Yi Wang, Daniel R.Ganger, Josh Levitsky et al. Assessment of Chronic Hepatitis and Fibrosis: Comparison of Magnetic Resonance Elastography (MRE) and Diffusion-weighted Imaging (DWI). AJR Am J Roentgenol. Mar 2011; 196(3): 553-561.

Address for correspondence:
Grażyna Rusak
Katedra i Zakład Radiologii i Diagnostyki Obrazowej
Uniwersytet Mikołaja Kopernika w Toruniu
Collegium Medicum w Bydgoszczy
ul. M. Skłodowskiej-Curie 9
85-094 Bydgoszcz
g.rusak@cm.umk.pl

Received: 16.02.2015
Accepted for publication: 3.08.2015