Published in final edited form as:

Top Magn Reson Imaging. 2018 October ; 27(5): 335–352. doi:10.1097/RMR.0000000000000182.

New and Emerging Applications of Magnetic Resonance Elastography of Other Abdominal Organs

Jin Wang, MD^{*}, Ying Deng, MD^{*}, Danielle Jondal, MD[†], David M. Woodrum, MD[†], Yu Shi, MD[‡], Meng Yin, PhD[†], Sudhakar K. Venkatesh, MD[†]

^{*}Department of Radiology, The Third Affiliated Hospital, Sun Yat-sen University (SYSU), Guangzhou, Guangdong, P.R. China

[†]Department of Radiology, Mayo Clinic, Rochester, MN

[‡]Department of Radiology, Sheng Jing Hospital, China Medical University, Heping District, Shenyang, P.R. China.

Abstract

Increasing clinical experience and ongoing research in the field of magnetic resonance elastography (MRE) is leading to exploration of its applications in other abdominal organs. In this review, the current research progress of MRE in prostate, uterus, pancreas, spleen, and kidney will be discussed. The article will describe patient preparation, modified technical approach including development of passive drivers, modification of sequences, and inversion. The potential clinical application of MRE in the evaluation of several disease processes affecting these organs will be discussed. In an era of increasing adoption of multiparametric magnetic resonance imaging approaches for solving complex abdominal problems, abdominal MRE as a biomarker may be seamlessly incorporated into a standard magnetic resonance imaging examination to provide a rapid, reliable, and comprehensive imaging evaluation at a single patient appointment in the future.

Keywords

kidney; magnetic resonance elastography; other organs; pancreas; prostate; spleen; uterus

Prostate cancer (PCa) is the most frequently diagnosed cancer in men worldwide and accounts for 19% of the total new PCa cases in 2017.¹ PCa is also the third most common cause of cancer-related deaths in Western countries.¹ In the last decade, East Asia has undergone tremendous economic growth and cultural globalization, which has resulted in increased life expectancy, changes in dietary patterns, and a westernized lifestyle. Once considered a disease that is commonly diagnosed in western countries, PCa is currently becoming an emerging health problem in East Asia.² The detection of clinically significant PCa is a major challenge. The prostate-specific antigen (PSA) level has been one of the most routinely used methods in PCa screening. According to the research, the level of PSA relates

Address correspondence to Jin Wang, MD, Department of Radiology, Third Affiliated Hospital of Sun Yat-Sen University, No. 600, Tianhe Road, Guangzhou, Guangdong 510630, China (wangjin3@mail.sysu.edu.cn).

The authors report no conflicts of interest.

to the risk of PCa. Approximately 30% to 35% of men with a serum PSA between 4 and 10 ng/mL were found to have PCa, whereas PCa was found in 67% of men with total PSA levels >10 ng/mL.³ PSA screening, however, leads to overdiagnosis and overtreatment due to its poor specificity and high false-positive rate.^{3,4}

PCa tissue is stiffer than normal prostate tissue, so a digital rectal examination (DRE) is one of the most commonly used screening methods in clinical practice.^{5–7} With palpation, urologists can assess the stiffness of prostatic tubercles qualitatively and detect PCa from benign tissue. The combination of an abnormal DRE and an elevated PSA level is the indication for a prostate biopsy.^{4,8} Nevertheless, DRE is subjective and depends considerably on the experience of the operator. Clinically significant PCa is defined as a Gleason score ≥ 7 and/or a volume ≥ 0.5 cm³, and/or extraprostatic extension.⁹ In addition, DRE has low sensitivity in the detection of small or deep lesions in the prostate gland.^{4,7} Transrectal ultrasound (TRUS)-guided systematic biopsy results remain the mainstay in PCa diagnosis. Because of the inaccuracy of TRUS and the limitations of systematic biopsy, several imaging-based noninvasive elastography methods have been developed to quantitatively evaluate the mechanical properties of prostate tissue and have potential in diagnosing PCa. The 2 most commonly used elastography techniques in clinical radiology are magnetic resonance elastography (MRE) and ultrasound elastography (USE).⁸

In prostate elastography, several applications of USE have been reported. USE is applied widely because of its real-time imaging capability, and TRUS elastography has shown its superiority early in clinical practice.^{7,10} No specific preparation is required for TRUS elastography, which is conducted after a complete, high-quality TRUS examination. USE was comparable to power Doppler USE and had significantly higher sensitivity than B-mode USE.¹¹ USE is, however, operator-dependent, and USE imaging is based on a 2-dimensional (2D) ultrasound, which creates a difference of stiffness in PCa among the imaging planes.⁷ The availability of detection of PCa in the transitional zone with USE is uncertain.¹⁰

Similar to USE, MRE can generate shear waves, create an image of the propagation of these waves in tissue, and assess the stiff properties of tissue quantitatively. For clinical diagnosis, the MRE technique has the following steps, which are similar to the steps for a liver MRE. First, a “passive driver” is placed on the body wall and is activated with acoustic pressure waves that are conducted through a plastic tube that is connected to the wave actuator to deliver shear waves to the tissue. Second, the MRE acquisition is a modified phase-contrast sequence. Special motion encoding gradients are used to sensitize the sequence to the cyclic tissue motion that is caused by the shear waves. Third, the magnetic resonance imaging (MRI) system processes the wave images to calculate corresponding elastograms. In research studies, many types of processing algorithms have been evaluated including local spatial frequency, phase gradient, direct inversion of the wave equation, and finite element-based iterative methods. Then, the stiffness maps depict the tissue stiffness across the cross-section that is studied. Regions of interest can be drawn to obtain the shear stiffness of the organ.^{12,13} 2D and 3-dimensional (3D) elastograms can be generated in MRE. As a noninvasive technique, MRE is more accurate than USE. Since MRE technology was reported by Muthupillai et al¹² in 1995, MRE has been performed in different organs, such as the liver,¹⁴ breast,¹⁵ brain,¹⁶ pancreas,¹⁷ and uterus.¹⁸ The most common clinical

application of MRE in the abdomen is assessing chronic liver disease. Recently, prostate MRE has become a research topic based on the application of multiparametric MRI in PCa diagnosis. In this review, we present the applications and development of MRE in the prostate (Figs. 1–6).

Preliminary Application of Prostate MRE

Cancerous tissue has a higher stiffness compared with benign tissue due to the pathological course and the structural changes of cancerous tissue. PCa tissue becomes stiffer than the surrounding healthy prostate tissue because of the following changes: an increase in cellular density and microvascularization; the destruction of the glandular architecture; and the triggering of wound repair. This process is characterized by the stromal reaction and collagen deposition that surrounds the cancer.^{5–7,19} The deposition of collagen increases significantly with the Gleason grade and is linked to a significant reduction in the acinar area in the PCa stroma. All of these changes contribute to the increased stiffness of the tissue that is affected by PCa. Elastography may have the potential to provide the improved characterization of prostate lesions and to increase the detection of PCa.^{7,20} Therefore, many researchers are exploring elastography in the prostate.

MRI has emerged as a promising technique for the identification and localization of PCa due to its excellent spatial resolution and tissue contrast. MRE for PCa diagnosis, spatial localization, and disease staging is an emerging application because MRE may provide the prostate stiffness. An advantage of MRE over USE is that MRE can acquire the full 3D wave field, which enables the full inversion of the wave equation and potentially improves accuracy.²¹ Significant progress has been made in the development of various techniques for the generation of mechanical waves in the prostate gland.²⁰

Conventional MRE uses an external actuator to transmit shear waves into the prostate gland. Because the prostate lies in the depth of the pelvis in the human body, shear waves need to pass through thick soft tissue before reaching the prostate. High-frequency shear waves would attenuate rapidly in soft tissue. Lower-frequency shear waves may attenuate much less rapidly; therefore, only low frequencies can reach the prostate gland by using an external driver in MRE.^{20,22} At low frequency, the corresponding wavelength is on the scale of the entire prostate, which limits the spatial resolution of the elastogram and makes it difficult to resolve small localized regions of increased stiffness that correspond to cancer.²⁰ Prostate MRE has many significant technical challenges that relate to the transmission of shear waves with an adequate amplitude and wavelengths to resolve localized increase in stiffness.

Many studies are exploring the approaches of MRE to generate shear waves in the prostate with adequate spatial resolution at a reasonable frequency. Many approaches for introducing shear waves into the prostate have been proposed, including transpubic, transperineal, transurethral, and endorectal drivers.²⁰

The transpubic method is the initial application for PCa. An external actuator is placed against the pelvic bone to generate the shear waves in the prostate gland. The transpubic

method is widely applied due to its accessibility and convenience.^{22,23} Li et al²³ used a transpubic driver to generate shear waves at a frequency of 100 Hz. In addition, to increase the frequencies and achieve a great spatial resolution, Wang²⁴ demonstrated the feasibility of a prostate MRE by using a modified transurethral driver, which could provide higher frequencies. The modified transurethral driver was combined with a silica gel urethral catheter, and the transducer was placed above the pelvic bones. They reported that the images of a prostate MRE with the modified transurethral driver have a 100% success rate at 60 to 150 Hz.

The transperineal method is another external method. Transperineal excitation is achieved by using a hydraulic system that is positioned between the legs over the undergarment and exerting a small compression on the perineum.²⁰ To balance the shear wave attenuation at high frequencies and poor spatial resolution at long wavelengths, the study used a second harmonic acquisition where the frequency of the motion encoding gradients was twice the frequency of mechanical excitation (100 and 150Hz, respectively).²⁵ In the transperineal method gravity plays no role in the “patient friendliness” so that even when a larger vibration amplitude is required in a larger subject, this did not cause discomfort.^{20,25,26}

The transurethral method is designed to produce shear waves in the prostate with adequate propagation at a high frequency by using an intracavity driver. A flexible tube is inserted into the urethra, and suction is used to create a mechanical fixation of the tissue to the driver. Initial experiments were performed in a phantom at frequencies of 150, 175, 200, and 250 Hz.²⁷ The results of the phantom experiment demonstrated excellent performance and reproducibility with clearly visible radial waves that propagated away from the transurethral driver. A transurethral actuator provides many advantages over external drivers due to the proximity of the vibration source to the tissue of interest. Shear waves that are generated from the transurethral driver have a shorter penetration depth, which allow for higher frequencies of applied motion that results in higher spatial resolution.^{20,27,28}

The endorectal method is an alternative approach that uses an internal actuator to generate shear waves in closer proximity to the prostate. An endorectal coil has been used to both generate shear waves in and acquire images of the prostate. Shear waves were generated in the prostate by using a rigid or an inflatable endorectal coil at frequencies of 100, 200, and 300 Hz. The endorectal coil was coupled with a piezoceramic actuator. The use of the endorectal coil was motivated by the current clinical use of the coil for mpMRIs of the prostate, which may facilitate the incorporation of elasticity information into the mpMRI. Some studies have demonstrated uniform shear waves with no adverse effects on signal-to-noise ratio (SNR) due to the simultaneous acquisition; uniform shear wave propagation across the entire prostate was achieved in all volunteers, and the vibrations were well tolerated.^{20,29–31}

Phantom Experiments

Some feasibility experiments were performed in a gel model that simulated a medium with prostate tissue-like stiffness. MRE with transurethral, endorectal, and transperineal devices has been reported in some phantom experimental studies.

To evaluate the feasibility of generating shear wave propagation in the prostate gland, Chopra et al²⁷ used a transurethral device in gelatin phantoms. Shear wave propagation was measured at frequencies of 150, 175, 200, and 250 Hz. MRI of shear wave propagation were acquired in a plane that was transverse and parallel to the rod to visualize the wave propagation in both dimensions. The results showed that excellent performance and repeatability were observed with this transurethral approach in the gelatin model. They also demonstrated the capability to detect localized inclusions of increased stiffness in agar gel phantom experiments. In all cases, the size and location of the inclusions of the phantom, as well as the stiffness of the background supporting gel, were accurately estimated. Arani et al²⁸ performed gel experiments to determine the wavelengths and frequencies that are required to visualize localized regions of stiffness within a homogeneous background. The frequencies of vibration were 65, 200, and 400 Hz. They found that the inclusions (with diameters of 1.5, 1.0, 0.64, and 0.48 cm) become more apparent both in the wave images and in the elastograms with increasing frequency. They also found that accurate stiffness measurements of 10-mm diameter (with a volume of 0.5 cm³) inclusions can be detected at a frequency of 400 Hz. Concerning detection over the background, inclusions with 5 mm diameters were apparent on the elastograms at 200 Hz or greater. Transurethral MRE places the source of vibration at the center of the prostate gland and reduces the required shear wave propagation to <3 cm. This action enables the acquisition of stiffness images with improved spatial resolution, which may have an application in detecting localized stiffness changes that are associated with PCa. In addition, there is potentially less distortion and compression of the gland compared with endorectal approaches. However, transurethral MRE is more invasive and unacceptable for patients. More studies are needed, especially in human experiments.

An endorectal actuator has greater potential for adoption into clinical use by utilizing the same endorectal coil that is inserted into the body for both imaging and actuation. Arani et al³¹ reported that the endorectal coil showed equivalent SNR values, within the margin of error, in the presence and absence of vibration in the ± 8 - to ± 38 - μ m amplitude range. Thus, endorectal MRE did not affect the SNR of the coil, and in their study, the 1-cm diameter (0.5 cm³ volume) inclusions could easily be identified, whereas the 6-mm diameter (0.1 cm³ volume) inclusion that was closer to the actuator could be identified in prostate-mimicking phantoms. Shear waves that are generated with endorectal MRE must travel 2 cm R to reach the furthest boundary of the prostate, which may lead to reduced shear wave amplitudes in the anterior region of the prostate. Therefore, endorectal MRE may have the potential to provide better resolution images in the peripheral zone of the prostate than in the anterior region of the gland.

Sahebjavaher et al²⁶ proposed that transperineal excitation could be applied to a prostate MRE to ensure good shear wave penetration into the prostate in a noninvasive manner. By using the transperineal mechanical excitation in the phantom, they demonstrated that it is possible to resolve lesions of 0.5 cm³. The mean elasticity of the background and the lesion in the phantom was 12.9 and 19.6 kPa, respectively, which yielded a ratio of 1.5.

Prostate MRE in Animals

Based on the success of the phantom experiments, some studies have been performed in animal models to evaluate the feasibility of prostate MRE by using intracavitary actuators, including transurethral and endorectal actuators.

Chopra et al²⁷ demonstrated for the first time the feasibility of performing transurethral MRE in vivo in the prostate tissue of canines. In their study, a flexible tube with small holes (-1 mm) was inserted in to the urethra, and suction was used to create a mechanical fixation of the urethra to the device. The results showed that the propagation of shear waves was evident in the wave images of the prostates of 3 canines at a frequency of 100 Hz. The mean shear stiffness in the prostate gland at 100 Hz for these 3 dogs was 5.3 ± 1.4 , 5.7 ± 2.0 , and 6.3 ± 1.7 kPa. The decrease in wavelength and reduced penetration depth was apparent with increasing vibration frequency.

Thormer et al³⁰ proved that endorectal MRE was feasible in a porcine model. In this porcine cadaver trial, shear waves could be generated at frequencies between 50 and 150 Hz with increments of 25 Hz. The mean shear moduli were 7.1 ± 2.0 kPa in muscle tissue, 3.0 ± 1.4 kPa in prostate tissue and 5.6 ± 1.9 kPa in the bulbourethral gland at frequencies of 150 Hz.

Prostate MRE in Humans

Conventional MRE uses an external actuator to transmit shear waves into the prostate gland. The transpubic method is applied widely due to its accessibility. Kemper et al²² used an external actuator that was attached to the pubic bone to generate shear waves in the prostate gland of 7 healthy volunteers. In vivo MRE of the prostate gland was proved to be technically feasible. The elasticity of the central gland (2.2 ± 0.3 kPa) appeared to be lower than the elasticity of the peripheral zone (3.3 ± 0.5 kPa) at a frequency of 65 Hz. This finding agreed with the findings of the canine experiment that was performed by Kallel et al.³² The elastic phenomenon could be explained by the morphologic architecture within each zone of the prostate gland: the decreased elasticity of the central portion of the organ might be caused by the larger and more prominent lumens of the gland within this area. The taller, more prominent epithelial cells and the smaller lumens of the glands of the peripheral portion may account for the increased elasticity values.

Li et al²³ investigated the elasticity and viscosity of PCa and benign prostatic disease, and MRE was implemented by transmitting low-frequency longitudinal mechanical waves of 100 Hz into the prostate with a transducer placed above the pubic bones on a 3.0T MR scanner. The mean elasticity and viscosity were significantly higher in the lesions with PCa than in the regions with prostatitis and a normal peripheral zone, and there was a positive correlation between the Gleason scores and elasticity of PCa. Dittmann et al³³ used 3 pressurized-air drivers to excite shear waves within the prostate at frequencies of 60, 70, and 80 Hz. Using externally placed pressurized-air drivers, they demonstrated the technical feasibility of prostate MRE. In the studies of a small number of patients (5 patients total: 2 patients with proven benign prostate hyperplasia (BPH) and the other 3 patients with proven

PCa), the areas with proven cancer tended to present with high stiffness, but benign alterations such as BPH may also have an elevated stiffness.

A prostate MRE that uses external drivers allows only the application of mechanical vibrations at low frequencies (<100 Hz).²³ Wang²⁴ reported a modified transurethral approach that combined a urinary catheter in place with a transducer that was placed above the pelvic bones. This modified transurethral actuator could generate shear waves in the prostate gland at a high frequency of 150 Hz. The results showed that the mean stiffness values of the lesions in patients with PCa and in the peripheral zone and in the central gland of healthy persons were 6.10 ± 1.72 , 3.11 ± 0.69 , and 4.28 ± 0.79 kPa, respectively. There was no significant difference between PCa and the central gland of healthy persons, but a substantial difference existed between patients with PCa and the peripheral zone of healthy persons. MRE may be a new method with the potential to diagnose PCa.

The transperineal approach is another external actuator method that generates shear waves in the prostate gland. Sahebjavaheer et al²⁶ first reported an approach to prostate MRE by using transperineal mechanical excitation in vivo in the prostate glands of 6 healthy volunteers. Mechanical waves were transmitted effectively from perineum to prostate. There were, however, 2 main issues in this study. First, the mechanical excitation method was limited to relatively low excitation frequencies (45 Hz) and amplitudes, and it required an extended setup and adjustment time. Second, the acquisition method proved to be too long for the given resolution and coverage, which rendered the method unsuitable for a clinical mpMRI study. Sahebjavaheer et al²⁵ then developed a new actively shielded electromagnetic transducer and employed a new rapid pulse sequence to shorten the acquisition time to a clinically acceptable 8 to 10 minutes. The methods were tested in 7 human subjects (6 volunteers and 1 patient with PCa). The sequence also encoded the 3D displacement field in the prostate gland. In this study, they increased the frequencies to 70 Hz. Unlike the transpubic method, gravity plays no role in the transperineal method, which would not render the transpubic method being unbearable for the patient with increased pressure on the driver to provide a larger vibration amplitude, and no pain or discomfort was reported.^{25,26}

Although the use of an external actuator is well tolerated by patients, the primary challenge of external actuation is that only very low-frequency shear waves can be resolved inside the prostate because of SNR limitations and the increased attenuation that is associated with high-frequency shear waves. Low frequencies generate shear waves with wavelengths in the order of the entire length of the prostate, which makes it difficult to resolve small localized regions of increased stiffness within the gland.

An alternative approach is to use an intracavitary or internal actuator to generate shear waves in closer proximity to the prostate, which enables the use of higher-frequency shear waves due to the reduced propagation distance from the source of vibration. Arani et al²⁹ first investigated the technical feasibility and tolerability of endorectal MRE in human volunteers, and an inflatable balloon type endorectal coil was demonstrated to produce similar shear wave propagation as a rigid endorectal coil. The flexible actuators may be comfortable for patients, which makes it more accessible. The study showed that all volunteers could tolerate the continuous vibrations for all amplitudes (range: ± 1 –50 μm) and

frequencies (range: 100–300 Hz). The mean stiffness values in the peripheral zone and central gland of the prostate were 2.7 ± 0.6 and 2.5 ± 0.7 kPa at 100 Hz, 9 ± 2 and 9 ± 2 kPa at 200 Hz, and 17 ± 3 and 19 ± 5 kPa at 300 Hz, respectively. The elastogram that was acquired from a volunteer with diagnosed PCa showed a region of elevated stiffness that corresponded to a low signal in a T2-weighted image, which provides a potential method to detect PCa with the endorectal MRE.

The transurethral actuator is another intracavitary actuator that is similar to the endorectal device that is mentioned above. However, due to its invasiveness, the transurethral approach has never been reported in vivo in human prostate tissue.

MRE of Ex Vivo Prostates

Sahebjavaheer et al³⁴ first discussed the setup and driver mechanism of a transducer that is suitable for small-bore 7T MRE in the ex vivo study. The ex vivo prostate specimens (postfixation) of 14 patients who underwent radical prostatectomy were imaged with MRE [9 cases had diffusion-weighted imaging (DWI)]. An electromagnetic driver was designed especially for MRE studies in small-bore MR scanners. In 6 patients, the MRE examination was performed at 3 frequencies (600, 800, and 1000 Hz) to extract the power-law exponent Gamma. The images were registered to whole-mount pathology slides that were marked with the Gleason score. Waves were clearly visible in all directions at multifrequencies in the ex vivo prostate glands with amplitudes between 1 and 100 μm for the frequencies between 600 and 1000 Hz. The cancerous tissue with a Gleason score of at least 3 ± 3 was distinguished from normal tissue in the peripheral zone with an area under the curve (AUC) of 0.75 (G_d), 0.75 (G_1), and 0.70 (Gamma- G_d). The differentiation between peripheral zone of the prostate gland and central gland of the prostate gland was modest for G_d ($P < 0.07$) and G_1 ($P < 0.06$) but was not significant for Gamma ($P < 0.2$). A correlation of 0.4 kPa/h was found between the fixation time of the prostate specimen and the stiffness of the tissue, which could affect the diagnostic power results.

McGrath et al³⁵ then used MRE to measure the distribution of Young's modulus (E) in ex vivo prostates before and after fixation and to determine the effects of fixation and variations due to anatomy and disease. All MRI were carried out in a 7T preclinical MRI scanner. Whole prostatectomy specimens ($n = 4$) and canine prostate specimens ($n = 5$) were imaged before and after a long interval fixation. In this study, it was demonstrated that the biomechanics of the clinical prostate specimens varied greatly with fixation and to a lesser extent, with disease and anatomy. E increased consistently with formalin fixation for all tissue types, normal, and diseased, as a function of the exposure time to fixation and the distance from the tissue edge. The fixation increased the overall E substantially and reduced the differences between healthy tissue and tumors. The change in E was likely associated with the structural alterations in the tissue that resulted from protein cross-linking. This study could improve the precision of prostate pathology correlation and lead to more accurate disease detection and targeting.

Prostate MRE Compared With Other MR Imaging Parameters for PCa Diagnosis

Sahebjavaher et al.³⁴ assessed the diagnostic power of monofrequency and multifrequency MRE and DWI alone and combined, correlated with the histopathology in a patient study. The cancer detection rate based on G_d and G_l was modest but comparable to the cancer detection rate of apparent diffusion coefficient values (ADC) with an approximate AUC of 0.62 to 0.75. The combined MRE + DWI method improved the AUC to 0.78 to 0.82, which suggests that complementary information from MRE and DWI may improve the results for in vivo case, which remains to be proven. ADC and shear moduli may provide complementary information. In fact, in some cases, MRE may perform better in detecting cancerous tissue. This research also demonstrated the potential to detect tumors that could be visualized in the elasticity images, even the tumors that were not obvious on the ADC maps.

MRE is a potential emerging application to improve PCa diagnosis, spatial localization, and disease staging because MRE may provide the prostate stiffness. MRE can successfully use both external transperineal and transperineal drivers to transmit low-frequency shear waves (45, 50, 60, and 70 Hz) into the prostate gland. The reconstructed elasticity distributions correlated well with the zonal anatomy of the normal prostate gland and show promising results in diagnosing PCa,^{21,22,25} but MRE is less effective in resolving smaller lesions in the prostate. The transurethral or endorectal drivers with high frequency provide many advantages over external drivers due to their higher spatial resolution in the prostate gland. The results of the phantom and canine experiments demonstrated excellent performance and reproducibility with clearly visible radial waves that propagated away from the transurethral driver at frequencies between 100 and 250 Hz.²⁷ The preliminary studies demonstrated an endorectal MRE at vibration frequencies of 100, 200, and 300 Hz and showed encouraging results in phantom and human prostates.^{28,29} Another approach for performing a prostate MRE also showed that the commercially available liver MRE driver that is used in combination with a urinary catheter can improve MRE image quality at high frequencies (90 and 120 Hz); this approach also showed the technical feasibility and potential diagnostic value of MRE in distinguishing between PCa and benign prostatic disease.²⁴ These studies also provide motivation for the development of better MRE techniques to improve the repeatability and spatial resolution for the further detection of PCa in the future.

Although mpMRI has become an important technique in PCa diagnosis, prostate MRE is expected to add a new method to routine clinical practice. Additional studies are needed in the advancement of MRE to meet these challenges.

MRE OF UTERUS AND UTERINE FIBROIDS

MRE has been proven to be a valuable tool in the diagnosis of liver fibrosis and breast and cervical cancer, but its application in the uterus and uterine fibroids is relatively new and needs further characterization. Expanding the knowledge base of the mechanical properties of normal uterus and cervix may be useful in differentiation of focal lesions arising from these organs. Uterus 3D MRE in healthy female volunteers showed that the uterine corpus

had a higher elasticity but similar viscosity compared to cervix and that stiffness of both endometrium and myometrium decreased during the menstrual cycle.³⁶ Studies have been published showing the feasibility and quantitation of MRE for uterine fibroids suggesting that characterization of other uterine tumors may be possible.^{18,37} More studies are needed to investigate these findings further.

MRE of Fibroids

Leiomyomas, or fibroids, are benign, monoclonal tumors of the myometrium that are prevalent in approximately 70% of Caucasian women and symptomatic in 1 of 4 with an even higher burden among women of African American descent with an estimated prevalence of 80% or higher.^{38,39} Although benign, these neoplasms can cause serious symptoms such as prolonged or heavy menses, dysmenorrhea, increased urinary frequency, dyspareunia, infertility, and remain the leading reason for women to undergo hysterectomy.^{40–42} Although hysterectomy remains the most common treatment method, other treatments such as pharmacologic therapies, myomectomy, uterine artery embolization, or magnetic resonance-guided focused ultrasound ablation have also become viable treatment options.⁴³ This increases the interest in how the fibroid mechanical properties can differentially affect treatment responsiveness and whether a better means of fibroid characterization would serve to predict best treatment response.

Leiomyomas are characterized by an altered state of mechanical homeostasis and are significantly stiffer upon surgical palpation than adjacent matched myometrium.⁴⁴ The increased firmness (stiffness) compared to the myometrium is thought to be secondary to excess of extracellular matrix in addition to irregular collagen structure and organization.^{45,46} MRE presents a noninvasive imaging technique to recapitulate surgical palpation with quantitative measurement of the tissue elastic properties through inducing harmonic vibrations of acoustic-range frequencies in the tissue of interest, whereas simultaneously imaging the propagation of those vibrations through the tissue. These propagations are used to generate a stiffness map, elastogram, and quantitative values for the tissue's mechanical properties.^{12,47,48}

MRE for uterine fibroids has been accomplished using a 19-cm-diameter passive driver placed on the abdomen above the uterus in a supine patient. Acoustic vibrations conveyed through tubing transmit shear waves into the uterus. Wave images were collected using a modified 2D gradient-recalled echo-based elastography pulse sequence or 3D-MRE was acquired using an MRE multislice spin-echo-based echo planar imaging sequence.³⁷

The largest study examined 102 patients where mean participant age was 44 ± 8.8 years, and 95% were either pre- or perimenopausal. Mean fibroid volume and stiffness were $283.0 \pm 398.0 \text{ cm}^3$ and $4.81 \pm 2.12 \text{ kPa}$, respectively. Analysis of T2 signal characterization versus stiffness demonstrated that fibroids of bright (high) T2 signal intensity fibroids had average stiffness of $2.88 \pm 0.98 \text{ kPa}$ (Fig. 7), whereas dark, minimally heterogenous fibroids had an average stiffness of $5.27 \pm 2.16 \text{ kPa}$ (Fig. 8). Analysis of mean fibroid stiffness compared with fibroid MRI T1 appearance and gadolinium contrast enhancement separately did not show a significant correlation. Furthermore, analysis of stiffness (kPa) by ethnicity showed

no significant differences in fibroid stiffness between Caucasian and African American women.³⁷

Utilizing these techniques, fibroid MRE can visualize and quantitate the uterine fibroid and myometrial stiffness. Comparison of MRI characteristics and MRE measurements demonstrated an inverse correlation between high T2 signal intensity fibroids and stiffness, such that higher-intensity fibroids have lower stiffness values compared to fibroids with low and homogenous signal intensity.³⁷ These findings are consistent with clinical studies in which fibroids of high T2 signal intensity tend to be less stiff, and typically respond less favorably to focused ultrasound ablation than those with low T2 signal.^{12,37,49} Inherent variability in fibroid stiffness can be attributed to differences in fibroid cellularity, collagen content, water content, and presence of degenerative or necrotic tissue. In T2 images, fibroids of high T2 signal intensity can suggest greater water content, lower collagen content, increased cellularity, degeneration, or potential malignancy.^{50–53} Because of the overlap in imaging characteristics between benign high T2-signal fibroids and uterine sarcoma, lesions of high T2-signal are assessed with more scrutiny and additional diagnostic imaging techniques are needed.

The utility of MRE in diagnosis of uterine abnormalities may lend compelling data regarding predicted treatment success, specifically for fibroids of high T2 signal intensity and lower stiffness values.³⁷ In addition, with further characterization of cellular fibroids and future characterization of leiomyosarcoma, MRE may provide valuable insight into the suspected mechanical differences between the 2 lesions.³⁷ The differentiation of leiomyoma versus leiomyosarcoma is difficult at best. Various articles have, however, proposed sarcoma differentiation based on T2 imaging characteristics, gadolinium enhancement characteristics, or diffusion imaging characteristics may be useful, but no single metric is good enough. Furthermore, another article proposed sarcoma differentiation using multiple parametric analysis coupled with some clinical information for a potential classification scheme. Given the overall difficulty with this imaging distinction, a multiparametric approach will likely be the best answer. MRE may be another possible imaging parameter to add into the analysis. Finally, fibroid stiffness may affect how easily a fibroid can be surgically removed. A recent study on brain lesions showed that preoperative tumor MRE may be able to find firm tumors that may require special care in surgical planning or tumor removal, suggesting a role for fibroid MRE in surgical planning as well.⁵⁴ Taken together, MRE has expansive potential for clinical use in the characterization of uterine fibroids in conjunction with typical imaging sequences and contrast enhancement characteristics which are normally obtained in imaging evaluation. With further refinement and study, MRE could become a valuable companion in the diagnosis of gynecologic lesions, selection of appropriate treatment, and potential to aid in the prediction of treatment success.

MR ELASTOGRAPHY OF PANCREAS

The human pancreas is a long, narrow, and relatively small retroperitoneal organ that is located behind the stomach. Pancreatic MRE has been considered challenging because it is difficult to propagate shear waves that can reach the entire pancreas and the patterns of wave propagation in pancreas are extremely complex. The establishment of normative values for

pancreatic stiffness and validation of the reproducibility of pancreatic MRE are critical first steps for incorporating MRE in the evaluation of pancreatic disease. Multislice spin-echo echo planar imaging MRE with a 3D direct inversion algorithm has been designed for application to small and geometrically complex organs, for example, pancreas. It can image the pattern of wave propagation in 3 dimensions and obtain data from all 3 polarizations of motion. Pancreatic MRE has been reported at frequencies ranging from 40 to 60 Hz using either a single flexible rectangular driver that was placed against the upper abdomen or multiple small round drivers that were placed against both the upper abdomen and the back.^{55,56} In a recent study of 20 healthy volunteers,⁵⁵ pancreatic MRE at 40 Hz provided more reliable stiffness values across different subregions of the pancreas than imaging at 60 Hz, and showed less intersubject and intrasubject variation. Overall mean pancreatic stiffness was 1.15 ± 0.17 kPa at 40 Hz and 2.09 ± 0.33 kPa at 60 Hz (Fig. 9). In another test-retest study that included both healthy volunteers and patients with pancreatic disease, inter-rater agreement, and intertime point agreement were also excellent, with intraclass correlation coefficients of >0.95 for both.⁵⁷ MRE was suggested to be performed with an empty stomach to reduce the distance between the driver and the pancreas, and to minimize the compression of the pancreas by a full stomach.

Inflammation, fibrosis, cellularity, and perfusion can all affect the mechanical properties of the tissues.⁵⁸ Pancreatic MRE has the potential to differentiate normal pancreas from diseased pancreas based on these properties, and may be useful for monitoring the progression of pancreatic fibrosis and chronic pancreatitis (CP), differentiating between benign and malignant pancreatic tumors, and predicting the risk postoperative pancreatic fistula (POPF).

Evaluation of Pancreatic Tumors

MRE may be useful in the evaluation of focal solid pancreatic lesions (Fig. 10). In a recent prospective study that included 85 patients with pathologically proven solid pancreatic masses,⁵⁹ pancreatic ductal adenocarcinoma (PDAC) and metastatic tumors had the highest stiffness, followed by mass-forming pancreatitis (MFP), normal pancreas, and finally, lipoma. The stiffness of solid pseudopapillary neoplasms and neuroendocrine pancreatic tumors ranged broadly from low (similar to normal pancreas) to high (comparable to PDAC). The stiffness ratio, calculated as the ratio of mass stiffness to non-mass-bearing parenchymal stiffness, outperformed mass stiffness and serum CA19-9 for differentiation of benign and malignant tumors, and particularly for differentiation between PDAC and MFP. Although PDAC and MFP are both characterized by fibrosis, the former shows dense fibrosis that can make up to 90% of the overall tumor volume and the latter shows loose perilobular and interlobular fibrosis, which may explain the higher stiffness of PDAC compared to MFP. On the contrary, solid pseudopapillary neoplasm and neuroendocrine pancreatic tumor have variable cell distributions and tumor components, which is consistent with the wider ranges of stiffness. The tumors <10 mm were not reported because of the low spatial resolution at 40 Hz,⁵⁹ and the experimental protocol needs to be evaluated to determine if the spatial resolution is adequate to show small tumors.

Chronic Pancreatitis

CP is characterized by progressive inflammation, fibrosis, and impairment of both pancreatic exocrine and endocrine function. CP has various etiologies, but pancreatic fibrosis, which can be detected and quantified by MRE (Fig. 11), is a common histological finding in CP. In a very recent study,⁶⁰ pancreatic stiffness differed significantly among control (1.21 ± 0.13 kPa), mild CP (1.50 ± 0.15 kPa), and moderate/severe CP (1.90 ± 0.16 kPa) groups. Pancreatic stiffness had good performance in differentiation of mild CP from healthy pancreas (>1.34 kPa) and in differentiation of moderate/severe CP from healthy pancreas and mild CP (>1.61 kPa). Patients with severe pancreatic atrophy were excluded from the study because of difficulties in stiffness measurement. This limitation is, however, mitigated in clinical work because the diagnosis of CP with severe atrophy is easily established based on conventional imaging.

Acute Pancreatitis

As with hepatic stiffness, which is known to increase markedly in patients with simple acute hepatitis without biopsy evidence of fibrosis, pancreatic stiffness can be significantly increased in patients with acute pancreatitis (AP), and pancreatic MRE can provide quantitative estimates of the severity of AP (Fig. 12). In a 2017 study, Shi et al⁶¹ compared the diagnostic performance of MRE with that of contrast-enhanced computed tomography (CE-CT) for the early diagnosis of AP and for prediction of the severity of AP within 24 hours of admission. The median pancreatic stiffness in patients with AP was 1.99 kPa, which was notably higher than the pancreatic stiffness in both non-AP patients (median = 1.24 kPa) and healthy volunteers (median = 1.17 kPa). Pancreatic stiffness >1.47 kPa showed significantly greater sensitivity (96.4% vs 78.6%) and accuracy (96.1% vs 81.6%) versus CE-CT for the diagnosis of AP. The accuracy of pancreatic stiffness >2.47 kPa for predicting severe AP within 24 hours was comparable to that of CT severity index, acute physiology and chronic health evaluation-II, and bedside index for severity in AP scores. Thus, MRE within 24 hours of hospital admission appears to be a promising method for early diagnosis and severity assessment of AP.

Prediction of Postoperative Pancreatic Fistula

POPF is one of the most common and serious complications of pancreatectomy, and it remains a leading risk factor for postoperative morbidity and mortality. Pancreatico-enteric anastomoses tend to be more successful in patients with hard and fibrotic pancreatic stumps and more difficult in those with softer, nonfibrotic stumps that are rich in exocrine gland tissue. As such, the latter group is at higher risk of POPF. Pancreatic consistency has traditionally been evaluated by intraoperative palpation to give surgeons a rough prediction of the POPF risk. Now, preoperative MRE at the pancreatic stump can provide objective and quantitative stiffness assessments with the potential to supersede risk prediction based on surgical palpation alone (Fig. 13).

Autoimmune Pancreatitis

Autoimmune pancreatitis (AIP) is a subset of CP that is characterized by lymphoplasmacytic infiltration and storiform fibrosis. Because AIP responds dramatically to steroid therapy, the

diagnosis of AIP is of great importance to obviate the need for unnecessary surgical resection. The stiffness of AIP is similar to that of PDAC, but AIP might be differentiated from PDAC by the shape and distribution of the high-stiffness lesions (Fig. 14). Specifically, AIP may appear as multiple, diffuse, longitudinal lesions, whereas PDAC is more frequently solitary with a nodular/irregular shape. Further study of the usefulness of MRE for differentiation of AIP and PDAC and for follow-up after steroid therapy is needed.

In conclusion, pancreatic MRE is promising to provide valuable information to clinicians and researches interested in distinguishing normal and diseased pancreas, improving the diagnosis of various pancreatic diseases, and showing potentials to monitor the progression of diseases. Preliminary studies have proved that pancreatic MRE is fast and easy to perform, providing robust stiffness estimations for pancreas. Further studies are needed on its clinical applications and mechanisms.

MR ELASTOGRAPHY OF SPLEEN

The current focus of elastography studies of spleen is in the evaluation of portal hypertension (PH) and its complications particularly gastroesophageal varices. PH is one of the leading causes of morbidity and mortality in chronic liver diseases mainly due to bleeding gastroesophageal varices. Portal venous flow congestion from increased vascular resistance due to liver fibrosis leads to splenomegaly initially. The development of hyperdynamic circulation contributes to increase in spleen size and formation of portosystemic collaterals. The splenoportal venous axis exposes spleen to increased portal pressure and it is thought that splenic stiffness (SS) correlates with PH. The bulk stiffness of the spleen is affected by the poroelasticity of the splenic tissue.

Several studies on MRE of spleen are published following the initial feasibility study by Talwalkar et al.⁶² In this preliminary study with 38 patients, they found SS significantly higher in patients with liver fibrosis as compared to normal volunteers, and the liver stiffness was significantly correlated with SS ($r^2 = 0.75$, $P < 0.001$). The spleen volume, platelet count, and splenomegaly predicted SS. A mean SS > 10.5 kPa identified all patients with esophageal varices.

The normal spleen stiffness is not significantly correlated with age, body mass index, arterial mean blood pressure, spleen volume, or liver stiffness.⁶³ The reported normal SS varies from 2.35 to 5 kPa with a mean value of 3.6 kPa.^{62,63} The measured spleen stiffness may vary if it is measured with passive driver placed over the liver versus driver placement directly above the spleen and this is probably due to nonplanar propagation of shear waves. Simultaneous measurement of hepatic and SS is possible using 2 drivers and SS obtained is comparable to a single driver placed over liver and spleen.⁶⁴ SS with MRE is also reproducible across different vendor platforms and is observer independent.^{65,66}

The SS as a noninvasive method of assessment of PH is currently of interest (Fig. 15). Gastroesophageal varices observed at endoscopy are strongly associated with SS^{66,67} and comparable to prediction with dynamic CE MRI.⁶⁸

Future studies are required to explore the utility of SS measurement with MRE for noninvasive assessment of PH, predictor of bleeding esophageal varices. As spleen is a smaller organ, ovoid in shape, and obliquely oriented to axial plane, 3D MRE may be more suitable. 3D MRE of both liver and spleen stiffness by placing a passive driver each over liver and spleen will likely produce accurate and reproducible stiffness measurements.

MR ELASTOGRAPHY OF KIDNEY

There is a great interest in assessment of tissue stiffness of the kidneys for evaluation of many disease processes affecting kidneys; however, the retroperitoneal location and small size of the native kidneys make it challenging to perform MRE of the kidneys. Because the kidneys lie on either side of the spine, modifications in driver technology is needed to deliver shear waves into both kidneys for good quality MRE.

In a preliminary study with normal volunteers, feasibility of MRE of the kidneys in healthy volunteers was demonstrated with subjects lying supine on top of a single large disc shaped driver at the level of kidneys placed in contact with posterior abdominal wall.⁶⁹ In another study, single kidney MRE of the kidney was performed and showed excellent reproducibility of stiffness with an intrasubject variability of 6%.⁷⁰ In both studies, MRE was performed with 45 to 90 Hz frequency. A higher frequency (90 Hz) may be more suitable as kidneys are smaller in size and a 3D technique to evaluate shear wave propagation in a complex tissue structure in the kidney. Kidney MRE with smaller drivers placed in contact with the back closer to the kidneys and a 3D MRE at 90 Hz may be suitable and is under evaluation. MRE obtained in the coronal plane including both kidneys would be useful for comparison (Fig. 16).

Renal tissue stiffness is dependent on several components of the parenchyma. Approximately 25% of renal volume may be attributable to blood pressure, blood content, filtrate, and urine in the kidney.⁷¹ Changes in renal blood flow has been shown to affect renal stiffness, independent of the presence of fibrosis.⁷² Atrophy of the renal parenchyma accompanied by reduced renal blood flow may reduce tissue stiffness in the absence of significant amount of fibrotic tissue (Fig. 17).

Studies on MRE for evaluation of renal parenchymal disease in both animals and humans including renal allografts are reported.^{69,70,72-76} These studies have demonstrated feasibility and shown regional differences in the viscoelastic properties. A recent study⁷⁷ has shown that higher resolution MRE of native kidneys is possible and renal medulla has higher stiffness than cortex. This remains to be confirmed in other studies. Kline et al⁷⁸ studied 10 young patients with early renal parenchymal disease due to autosomal dominant polycystic kidney disease and 10 normal and healthy young adults with matched age and sex, and found that mean stiffness of renal parenchyma of patients were significantly lower than matched normal subjects. These results demonstrate that measured tissue stiffness of diseased kidneys is determined by complex and ongoing processes within the kidneys.

Renal allografts are much more easily accessible for shear wave propagation as they as usually placed in iliac fossa and less likely to move with respiration. Anterior abdominal

wall provides better contact with kidney and high frequency MRE would also be easier. Interstitial fibrosis and tubular atrophy (IFTA) is the most common cause of renal allograft failure. Studies with MRE in renal allografts are few. A MRE study on renal allografts showed a trend of increased stiffness in patients with mild and moderate fibrosis,⁷⁶ no significant differences were found between the different grades of fibrosis. Although another study demonstrated higher stiffness in patients without IFTA (2 patients) as compared to those with IFTA (16 patients).⁷⁹ The results from these studies demonstrate complex relationship between renal graft tissue stiffness and IFTA. Future studies are required for studying these changes.

MRE of the kidneys is challenging with promise for useful application in the evaluation of chronic renal disease and renal allografts.

CONCLUSIONS

MRE is a powerful technology which is capable of imaging propagating mechanical waves within the living human body. Therefore, it has shown a capability to quantify the mechanical properties of tissue. The first well-established clinical application of MRE is the assessment of liver fibrosis. Now that MRE technology is in the hands of clinical and scientific community worldwide, it will be an exciting field with scope for new clinical applications.

In this article, we introduced the new and emerging applications of MRE in prostate, uterus, pancreas, kidney, and spleen. We learned that (1) prostate MRE is a potential emerging application to improve PCa diagnosis, spatial localization, and disease staging; (2) the utility of MRE in diagnosis of uterine abnormalities may lend the compelling data regarding predicted treatment success; (3) pancreatic MRE shows potential to distinguish normal and diseased pancreas, improve the diagnosis of various pancreatic diseases, and monitor the progression of diseases; (4) MRE of spleen as a noninvasive method to assess PH is currently the subject of interest; (5) MRE of kidney is challenging with promise for useful application in the evaluation of chronic renal disease and renal allografts.

MRE has proven to be a noninvasive technology in assessing the stiffness of various organs. Continuing technology improvement and further studies are needed on clinical application of MRE of these new areas.

ACKNOWLEDGMENTS

We gratefully thank Professor Neil Roberts for his writing support.

This research was supported by National Natural Science Foundation of China grant 81271562 (J.W.) and Science and Technology Program of Guangzhou, China 201704020016 (J.W.).

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin.* 2017;67:7–30. [PubMed: 28055103]
2. Zhu Y, Wang HK, Qu YY, et al. Prostate cancer in East Asia: evolving trend over the last decade. *Asian J Androl.* 2015;17:48–57. [PubMed: 25080928]

3. Carroll PR, Parsons JK, Andriole G, et al. NCCN guidelines insights: prostate cancer early detection, Version 2.2016. *J Natl Compr Canc Netw*. 2016;14:509–519. [PubMed: 27160230]
4. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. *Eur Urol*. 2017;71:618–629. [PubMed: 27568654]
5. Phipps S, Yang TH, Habib FK, et al. Measurement of the mechanical characteristics of benign prostatic tissue: a novel method for assessing benign prostatic disease. *Urology*. 2005;65:1024–1028. [PubMed: 15882757]
6. Phipps S, Yang TH, Habib FK, et al. Measurement of tissue mechanical characteristics to distinguish between benign and malignant prostatic disease. *Urology*. 2005;66:447–450. [PubMed: 16098374]
7. Barr RG, Cosgrove D, Brock M, et al. WFUMB guidelines and recommendations on the clinical use of ultrasound elastography: part 5. Prostate. *Ultrasound Med Biol*. 2017;43:27–48. [PubMed: 27567060]
8. Loeb S, Vellekoop A, Ahmed HU, et al. Systematic review of complications of prostate biopsy. *Eur Urol*. 2013;64:876–892. [PubMed: 23787356]
9. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS prostate imaging—reporting and data system: 2015, Version 2. *Eur Urol*. 2016;69:16–40. [PubMed: 26427566]
10. Rouviere O, Melodelima C, Hoang Dinh A, et al. Stiffness of benign and malignant prostate tissue measured by shear-wave elastography: a preliminary study. *Eur Radiol*. 2017;27:1858–1866. [PubMed: 27553936]
11. Kamoi K, Okihara K, Ochiai A, et al. The utility of transrectal real-time elastography in the diagnosis of prostate cancer. *Ultrasound Med Biol*. 2008;34:1025–1032. [PubMed: 18255215]
12. Muthupillai R, Lomas DJ, Rossman PJ, et al. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science*. 1995;269:1854–1857. [PubMed: 7569924]
13. Venkatesh SK, Ehman RL. Magnetic resonance elastography of abdomen. *Abdom Imaging*. 2015;40:745–759. [PubMed: 25488346]
14. Thompson SM, Wang J, Chandan VS, et al. MR elastography of hepatocellular carcinoma: correlation of tumor stiffness with histopathology features—preliminary findings. *Magn Reson Imaging*. 2017;37:41–45. [PubMed: 27845245]
15. Siegmann KC, Xydeas T, Sinkus R, et al. Diagnostic value of MR elastography in addition to contrast-enhanced MR imaging of the breast—initial clinical results. *Eur Radiol*. 2010;20:318–325. [PubMed: 19727753]
16. Reiss-Zimmermann M, Streitberger KJ, Sack I, et al. High resolution imaging of viscoelastic properties of intracranial tumours by multi-frequency magnetic resonance elastography. *Clin Neuroradiol*. 2015;25:371–378. [PubMed: 24916129]
17. Itoh Y, Takehara Y, Kawase T, et al. Feasibility of magnetic resonance elastography for the pancreas at 3T. *J Magn Reson Imaging*. 2016;43:384–390. [PubMed: 26149267]
18. Stewart EA, Taran FA, Chen J, et al. Magnetic resonance elastography of uterine leiomyomas: a feasibility study. *Fertil Steril*. 2011;95:281–284. [PubMed: 20633880]
19. Dvorak HF. Tumors: wounds that do not heal. Similarities between tumor stroma generation and wound healing. *N Engl J Med*. 1986;315:1650–1659. [PubMed: 3537791]
20. Pepin KM, Ehman RL, McGee KP. Magnetic resonance elastography (MRE) in cancer: technique, analysis, and applications. *Prog Nucl Magn Reson Spectrosc*. 2015;90–91:32–48.
21. Sahebjavaher RS, Nir G, Honarvar M, et al. MR elastography of prostate cancer: quantitative comparison with histopathology and repeatability of methods. *NMR Biomed*. 2015;28:124–139. [PubMed: 25395244]
22. Kemper J, Sinkus R, Lorenzen J, et al. MR elastography of the prostate: initial in-vivo application. *Rofo*. 2004;176:1094–1099. [PubMed: 15346284]
23. Li S, Chen M, Wang W, et al. A feasibility study of MR elastography in the diagnosis of prostate cancer at 3.0T. *Acta Radiol*. 2011;52:354–358. [PubMed: 21498375]
24. Wang JGK. MR elastography of the prostate with a modeconversion endourethral driver feasibility at 3.0 T. Singapore: ISMRM 2016.

25. Sahebjavaher RS, Frew S, Bylinskii A, et al. Prostate MR elastography with transperineal electromagnetic actuation and a fast fractionally encoded steady-state gradient echo sequence. *NMR Biomed.* 2014;27:784–794. [PubMed: 24764278]
26. Sahebjavaher RS, Baghani A, Honarvar M, et al. Transperineal prostate MR elastography: initial in vivo results. *Magn Reson Med.* 2013;69:411–420. [PubMed: 22505273]
27. Chopra R, Arani A, Huang Y, et al. In vivo MR elastography of the prostate gland using a transurethral actuator. *Magn Reson Med.* 2009;62:665–671. [PubMed: 19572390]
28. Arani A, Plewes D, Chopra R. Transurethral prostate magnetic resonance elastography: prospective imaging requirements. *Magn Reson Med.* 2011;65:340–349. [PubMed: 20882673]
29. Arani A, Da Rosa M, Ramsay E, et al. Incorporating endorectal MR elastography into multi-parametric MRI for prostate cancer imaging: initial feasibility in volunteers. *J Magn Reson Imaging.* 2013;38:1251–1260. [PubMed: 23408516]
30. Thormer G, Reiss-Zimmermann M, Otto J, et al. Novel technique for MR elastography of the prostate using a modified standard endorectal coil as actuator. *J Magn Reson Imaging.* 2013;37:1480–1485. [PubMed: 23055397]
31. Arani A, Plewes D, Krieger A, et al. The feasibility of endorectal MR elastography for prostate cancer localization. *Magn Reson Med.* 2011;66:1649–1657. [PubMed: 21574182]
32. Kallel F, Price RE, Konofagou E, et al. Elastographic imaging of the normal canine prostate in vitro. *Ultrason Imaging.* 1999;21:201–215. [PubMed: 10604801]
33. Dittmann F, Reiter R, Guo J, et al. Tomoelastography of the prostate using multifrequency MR elastography and externally placed pressurized-air drivers. *Magn Reson Med.* 2018;79:1325–1333. [PubMed: 28585229]
34. Sahebjavaher RS, Nir G, Gagnon LO, et al. MR elastography and diffusion-weighted imaging of ex vivo prostate cancer: quantitative comparison to histopathology. *NMR Biomed.* 2015;28:89–100. [PubMed: 25382459]
35. McGrath DM, Lee J, Foltz WD, et al. MR elastography to measure the effects of cancer and pathology fixation on prostate biomechanics, and comparison with T 1, T 2 and ADC. *Phys Med Biol.* 2017;62:1126–1148. [PubMed: 28092638]
36. Jiang X, Asbach P, Streitberger KJ, et al. In vivo high-resolution magnetic resonance elastography of the uterine corpus and cervix. *Eur Radiol.* 2014;24:3025–3033. [PubMed: 25038856]
37. Jondal DE, Wang J, Chen J, et al. Uterine fibroids: correlations between MRI appearance and stiffness via magnetic resonance elastography. *Abdom Radiol (NY).* 2018;43:1456–1463. [PubMed: 28952003]
38. Baird DD, Dunson DB, Hill MC, et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol.* 2003;188:100–107. [PubMed: 12548202]
39. Dixon D, Parrott EC, Segars JH, et al. The second National Institutes of Health International Congress on advances in uterine leiomyoma research: conference summary and future recommendations. *Fertil Steril.* 2006;86:800–806. [PubMed: 17027353]
40. Incidence Okolo S., aetiology and epidemiology of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol.* 2008;22:571–588. [PubMed: 18534913]
41. Stewart EA. Clinical practice. Uterine fibroids. *N Engl J Med.* 2015;372:1646–1655. [PubMed: 25901428]
42. Walker CL, Stewart EA. Uterine fibroids: the elephant in the room. *Science.* 2005;308:1589–1592. [PubMed: 15947177]
43. Bachmann G Expanding treatment options for women with symptomatic uterine leiomyomas: timely medical breakthroughs. *Fertil Steril.* 2006;85:46–47. [PubMed: 16412726]
44. Rogers R, Norian J, Malik M, et al. Mechanical homeostasis is altered in uterine leiomyoma. *Am J Obstet Gynecol.* 2008;198:474.e1–474.e11. [PubMed: 18395046]
45. Leppert PC, Baginski T, Prupas C, et al. Comparative ultrastructure of collagen fibrils in uterine leiomyomas and normal myometrium. *Fertil Steril.* 2004;82(suppl 3):1182–1187. [PubMed: 15474093]
46. Norian JM, Owen CM, Taboas J, et al. Characterization of tissue biomechanics and mechanical signaling in uterine leiomyoma. *Matrix Biol.* 2012;31:57–65. [PubMed: 21983114]

47. Godfrey EM, Mannelli L, Griffin N, et al. Magnetic resonance elastography in the diagnosis of hepatic fibrosis. *Semin Ultrasound CT MR*. 2013;34:81–88. [PubMed: 23395320]
48. Mariappan YK, Glaser KJ, Ehman RL. Magnetic resonance elastography: a review. *Clin Anat*. 2010;23:497–511. [PubMed: 20544947]
49. Gorny KR, Borah BJ, Brown DL, et al. Incidence of additional treatments in women treated with MR-guided focused US for symptomatic uterine fibroids: review of 138 patients with an average follow-up of 2.8 years. *J Vasc Interv Radiol*. 2014;25:1506–1512. [PubMed: 24998103]
50. Sudderuddin S, Helbren E, Telesca M, et al. MRI appearances of benign uterine disease. *Clin Radiol*. 2014;69:1095–1104. [PubMed: 25017452]
51. Tamai K, Koyama T, Saga T, et al. The utility of diffusion-weighted MR imaging for differentiating uterine sarcomas from benign leiomyomas. *Eur Radiol*. 2008;18:723–730. [PubMed: 17929022]
52. Tanaka YO, Nishida M, Tsunoda H, et al. Smooth muscle tumors of uncertain malignant potential and leiomyosarcomas of the uterus: MR findings. *J Magn Reson Imaging*. 2004;20:998–1007. [PubMed: 15558559]
53. Ueda H, Togashi K, Konishi I, et al. Unusual appearances of uterine leiomyomas: MR imaging findings and their histopathologic backgrounds. *Radiographics*. 1999;19:S131–S145. [PubMed: 10517450]
54. Sakai N, Takehara Y, Yamashita S, et al. Shear stiffness of 4 common intracranial tumors measured using MR elastography: comparison with intraoperative consistency grading. *AJNR Am J Neuroradiol*. 2016;37:1851–1859. [PubMed: 27339950]
55. Shi Y, Glaser KJ, Venkatesh SK, et al. Feasibility of using 3D MR elastography to determine pancreatic stiffness in healthy volunteers. *J Magn Reson Imaging*. 2015;41:369–375. [PubMed: 24497052]
56. Dittmann F, Tzschatzsch H, Hirsch S, et al. Tomoelastography of the abdomen: tissue mechanical properties of the liver, spleen, kidney, and pancreas from single MR elastography scans at different hydration states. *Magn Reson Med*. 2017;78:976–983. [PubMed: 27699875]
57. An H, Shi Y, Guo Q, et al. Test-retest reliability of 3D EPI MR elastography of the pancreas. *Clin Radiol*. 2016;71:1068.e7–1068.e12.
58. Glaser KJ, Manduca A, Ehman RL. Review of MR elastography applications and recent developments. *J Magn Reson Imaging*. 2012;36:757–774. [PubMed: 22987755]
59. Shi Y, Gao F, Li Y, et al. Differentiation of benign and malignant solid pancreatic masses using magnetic resonance elastography with spin-echo echo planar imaging and three-dimensional inversion reconstruction: a prospective study. *Eur Radiol*. 2018;28:936–945. [PubMed: 28986646]
60. Wang M, Gao F, Wang X, et al. Magnetic resonance elastography and T1 mapping for early diagnosis and classification of chronic pancreatitis. *J Magn Reson Imaging*. 2018.
61. Shi Y, Liu Y, Liu YQ, et al. Early diagnosis and severity assessment of acute pancreatitis (AP) using MR elastography (MRE) with spin-echo echo-planar imaging. *J Magn Reson Imaging*. 2017;46:1311–1319. [PubMed: 28252868]
62. Talwalkar JA, Yin M, Venkatesh S, et al. Feasibility of in vivo MR elastographic splenic stiffness measurements in the assessment of portal hypertension. *AJR Am J Roentgenol*. 2009;193:122–127. [PubMed: 19542403]
63. Mannelli L, Godfrey E, Joubert I, et al. MR elastography: spleen stiffness measurements in healthy volunteers—preliminary experience. *AJR Am J Roentgenol*. 2010;195:387–392. [PubMed: 20651194]
64. Dyvorne HA, Jajamovich GH, Besa C, et al. Simultaneous measurement of hepatic and splenic stiffness using MR elastography: preliminary experience. *Abdom Imaging*. 2015;40:803–809. [PubMed: 25294006]
65. Yasar TK, Wagner M, Bane O, et al. Interplatform reproducibility of liver and spleen stiffness measured with MR elastography. *J Magn Reson Imaging*. 2016;43:1064–1072. [PubMed: 26469708]
66. Morisaka H, Motosugi U, Ichikawa S, et al. Association of splenic MR elastographic findings with gastroesophageal varices in patients with chronic liver disease. *J Magn Reson Imaging*. 2015;41:117–124. [PubMed: 24243628]

67. Ronot M, Lambert S, Elkrief L, et al. Assessment of portal hypertension and high-risk oesophageal varices with liver and spleen three-dimensional multifrequency MR elastography in liver cirrhosis. *Eur Radiol.* 2014;24:1394–1402. [PubMed: 24626745]
68. Shin SU, Lee JM, Yu MH, et al. Prediction of esophageal varices in patients with cirrhosis: usefulness of three-dimensional MR elastography with echo-planar imaging technique. *Radiology.* 2014;272:143–153. [PubMed: 24620910]
69. Venkatesh SK, Yin M, Grimm RC, et al. MR elastography of the kidneys: preliminary results. Paper Presented at 16th Annual Meeting ISMRM, 2008; Toronto, Canada.
70. Rouviere O, Souchon R, Pagnoux G, et al. Magnetic resonance elastography of the kidneys: feasibility and reproducibility in young healthy adults. *J Magn Reson Imaging.* 2011;34:880–886. [PubMed: 21769970]
71. Lerman LO, Bentley MD, Bell MR, et al. Quantitation of the in vivo kidney volume with cine computed tomography. *Invest Radiol.* 1990;25:1206–1211. [PubMed: 2254054]
72. Warner L, Yin M, Glaser KJ, et al. Noninvasive in vivo assessment of renal tissue elasticity during graded renal ischemia using MR elastography. *Invest Radiol.* 2011;46:509–514. [PubMed: 21467945]
73. Shah N, Kruse S, Lager D, et al. Evaluation of renal parenchymal disease in a rat model with magnetic resonance elastography. *Magn Reson Med.* 2004;52:56–64. [PubMed: 15236367]
74. Bensamoun SF, Robert L, Leclerc GE, et al. Stiffness imaging of the kidney and adjacent abdominal tissues measured simultaneously using magnetic resonance elastography. *Clin Imaging.* 2011;35:284–287. [PubMed: 21724121]
75. Korsmo MJ, Ebrahimi B, Eirin A, et al. Magnetic resonance elastography noninvasively detects in vivo renal medullary fibrosis secondary to swine renal artery stenosis. *Invest Radiol.* 2013;48:61–68. [PubMed: 23262789]
76. Lee CU, Glockner JF, Glaser KJ, et al. MR elastography in renal transplant patients and correlation with renal allograft biopsy: a feasibility study. *Acad Radiol.* 2012;19:834–841. [PubMed: 22503893]
77. Streitberger KJ, Guo J, Tzschätzsch H, et al. High-resolution mechanical imaging of the kidney. *J Biomech.* 2014;47:639–644. [PubMed: 24355382]
78. Kline TL, Edwards ME, Garg I, et al. Quantitative MRI of kidneys in renal disease. *Abdom Radiol (NY).* 2018;43:629–638. [PubMed: 28660330]
79. Marticorena Garcia SR, Guo J, Durr M, et al. Comparison of ultrasound shear wave elastography with magnetic resonance elastography and renal microvascular flow in the assessment of chronic renal allograft dysfunction. *Acta Radiol.* 2018;59:1139–1145. [PubMed: 29249167]

FIGURE 1.

MRE of the prostate performed using pelvic wall actuator (or the so-called transpubic method) in a 58-year-old man with BPH. It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images at frequencies of 60 to 120 Hz. BPH, benign prostate hyperplasia; DWI, diffusion-weighted imaging; T1WI, T1-weighted imaging, T2WI; T2-weighted imaging.

FIGURE 2.

MRE of the prostate performed using pelvic wall actuator (or the so-called transpubic method) in a 68-year-old man with PCa (Gleason score $4 + 4 = 8$). It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images at frequencies of 60 to 120 Hz. DWI, diffusion-weighted imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.

FIGURE 3.

MRE of the prostate performed using a pelvic wall actuator (or so-called transpubic method) in a 70-year-old man with nonspecific granulomatous prostatitis. It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images at frequencies of 60 and 90 Hz. DWI, diffusion-weighted imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.

FIGURE 4.

MRE of the prostate performed using a pelvic wall actuator (or the so-called transpubic method) in a 75-year-old man with prostatitis. It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images at frequencies of 60- and 90 Hz. DWI, diffusion-weighted imaging, T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.

FIGURE 5.

MRE of the prostate performed in a 55-year-old man with PCa (Gleason score $5 + 4 = 9$). It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images using modified transurethral actuator (T) at frequencies of 60 to 150 Hz and using pelvic wall actuator (P) at frequencies of 60 and 90 Hz. T2WI, T2-weighted imaging.

FIGURE 6.

MRE of the prostate performed in a 78-year-old man with BPH. It shows T2WI, T1WI, DWI, dynamic contrast-enhanced images, and MRE images using pelvic wall actuator (P) at frequencies of 60 and 90 Hz and using modified transurethral actuator (T) at frequencies of 60 to 150 Hz. BPH, benign prostate hyperplasia; DWI, diffusion-weighted imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.

FIGURE 7.

MRE of a T2 bright fibroid. Mean fibroid stiffness was 3.8 kPa. A, The T2 signal brightness compared to the myometrium. B, The MR elastogram showing relatively low stiffness. C, The T1 precontrast imaging. D, T1 postcontrast imaging with fibroid enhancement.

FIGURE 8.

MRE of a T2 dark fibroid. Mean fibroid stiffness was 5.2 kPa. A, The T2 signal darkness compared to the myometrium. B, The MR elastogram showing relatively higher stiffness. C, The T1 precontrast imaging. D, T1 postcontrast imaging with fibroid enhancement.

FIGURE 9.

MRE stiffness maps obtained at 40 Hz (upper row) and 60 Hz (lower row) in a healthy control subject with body mass index 29.3 kg/m^2 . The first column shows the magnitude images, the second column the elastograms, and the third, fourth, and fifth columns the wave images of the 3 components of the vector displacement field. Pancreatic stiffness is $1.3 \pm 0.33 \text{ kPa}$ at 40 Hz and $2.01 \pm 0.45 \text{ kPa}$ at 60 Hz. The range of the color bar is 0 to 4 kPa at 40 Hz, and 0 to 8 kPa at 60 Hz. MEG, motion encoding gradient.

FIGURE 10.

MRE of the pancreas in a patient with PDAC presenting as a solid mass in the head of the pancreas (upper row) and the tail of the pancreas (lower row). The mass in the pancreatic head has a stiffness of 3.97 ± 1.28 kPa and the mass in the tail has a stiffness of 4.32 ± 0.33 kPa. The range of the color bar is 0 to 4 kPa at 40 Hz.

FIGURE 11.

MRE of chronic pancreatitis in a 42-year-old man (upper row) and a 54-year-old woman (lower row). The patient has pathologically proven stage F2 fibrosis and MRE stiffness of 1.56 ± 0.23 kPa. The patient in the lower row has stage F3 fibrosis with MRE stiffness of 1.88 ± 0.36 kPa. The range of the color bar is 0 to 4 kPa at 40 Hz.

FIGURE 12.

MRE of acute necrotic pancreatitis in a 36-year-old man. The area outlined in red in the upper row is an area of inflammation with a stiffness of 2.37 ± 0.93 kPa. At the lower row, the area outlined in red is necrotic and the stiffness value is lower (1.91 ± 0.83 kPa) than the inflammatory area. The range of the color bar is 0 to 4 kPa at 40 Hz.

FIGURE 13.

MRE of the pancreatic stump in a 45-year-old man with cancer at the pancreatic head. The stiffness at the site of the pancreaticojejunal anastomosis is 1.87 ± 0.38 kPa. Postoperative computed tomography (third column) and further clinical monitoring confirmed that there was no postoperative pancreatic fistula. The range of the color bar is 0 to 4 kPa at 40 Hz.

FIGURE 14.

MRE of the pancreas in a 65-year-old woman with autoimmune pancreatitis. The involved area in the pancreatic body and tail is longitudinal in shape with a high stiffness value of 4.72 ± 1.38 kPa.

FIGURE 15.

MRE of spleen in 2 patients with chronic liver disease. Top row: contrast enhanced T1-W image (A) and MRE stiffness map (B) in a 39-year-old man with nonalcoholic fatty liver disease and no portal hypertension. Mean spleen stiffness in 3.6 kPa. Bottom row: contrast-enhanced T1-W image (C) and MRE stiffness map (D) in a 41-year-old man with chronic hepatitis C presenting with acute gastrointestinal bleeding and normal liver function tests. Mean spleen stiffness is 16 kPa. Note splenomegaly. Endoscopy showed esophageal varices and portal gastropathy.

FIGURE 16.

MRE of the native kidneys in normal healthy volunteers. Top row: MRE obtained with a single large driver and 2D-GRE MRE at 60 Hz frequency. Coronal T2-weighted image (A) at the same level of 10 mm thick slice MRE showing both kidneys. The wave image (B) demonstrates excellent propagation of waves in both kidneys (B) and stiffness map (C) showing slight heterogeneity of stiffness in both kidneys Bottom row: 3D MRE of native kidneys performed in a different normal healthy adult using 2 soft kidney drivers and with 3D-echoplanar imaging MRE at 90 Hz. Magnitude image (D) and corresponding stiffness map (E) show nice demarcation of kidneys on the stiffness maps.

FIGURE 17.

3DMRE of the kidneys in a 36-year old patient with primary hyperoxaluria type-1 with elevated plasma and urinary oxalates and eGFR >60 and serum creatinine of 0.8 mg/dL. Coronal T2 image (A) shows small and atrophic right kidney with compensatory hypertrophy of the left kidney. Magnitude image (B) and stiffness maps obtained during the MRE show reduced tissue stiffness in the right kidney due to atrophy as compared to hypertrophied left kidney.