Med Ultrason 2016, Vol. 18, no. 3, 362-369
DOI:

Value of ultrasound elastography in the diagnosis of native kidney fibrosis

Ileana Peride[1], Daniela Rădulescu[1], Andrei Niculae[1], Vladimir Ene[2], Ovidiu Gabriel Bratu[3], Ionel Alexandru Checheriță[1]

[1]Department of Nephrology and Dialysis, "St. John" Emergency Clinical Hospital, "Carol Davila" University of Medicine and Pharmacy, [2]Department of Radiology, "St. John" Emergency Clinical Hospital, "Carol Davila" University of Medicine and Pharmacy, [3]Department of Urology, "Dr. Carol Davila" Central Military Emergency University Hospital, "Carol Davila" University of Medicine and Pharmacy

Abstract

In the last decade ultrasound elastography, an already widely used technique in the diagnosis of hepatic fibrosis, has raised the attention of nephrologists as a potential valuable noninvasive tool for the diagnosis of renal fibrosis. Due to renal deep location and anatomic complexity, the shear wave techniques are the most appropriate elastography methods for exploring native kidneys. Recent research offers promising results, but further larger studies are required for a better standardization of this method and also for establishing reference values of normal kidney elasticity. This article reviews the studies conducted for exploring the native kidney, highlighting the advantages and limitations of ultrasound elastography for assessing fibrosis development in chronic kidney diseases.

Keywords: renal elasticity, ultrasound elastography, kidney fibrosis, chronic kidney disease.

Introduction

For many years, ultrasonography has become the most valuable imagistic investigation in renal diseases. It can be used regardless of serum creatinine, it is noninvasive and it is also applicable in pregnancy. Renal biopsies under ultrasonography guidance are already performed as routine in clinical practice. Thus, since the incidence of chronic kidney disease (CKD) is constantly increasing [1], new methods are required for a non-invasive early detection of renal fibrosis and for assessing the degree of fibrosis in different stages of CKD. In the last decades, promising results in this respect have emerged not just from various biological markers [2], but also from a new field of ultrasound examination, i.e. elastography. Elastography – a method which provides information about tissue stiffness [3] – has already proved valuable for the diagnosis and assessment of the severity of liver fibrosis. However, regarding renal diseases, ultrasound (US) elastography is still in the pioneering stage due to anatomical characteristics of the kidney and the complexity of the pathological processes incriminated by renal dysfunction.

The present article reviews the existing ultrasound elastography techniques and their applicability in renal pathology, focusing on renal fibrosis and CKD.

Ultrasound elastography techniques

Elastography uses ultrasound to asses and quantify the stiffness or the elasticity of a tissue. The method permits an accurate quantitative diagnosis of the differences in tissues stiffness in contrast with the classic palpation which is subjective. Additionally, it is superior to conven-

Received 01.04.2016 Accepted 28.04.2016
Med Ultrason
2016, Vol. 18, No 3, 362-369
Corresponding author: Andrei Niculae, MD, PhD;
Department of Nephrology and Dialysis,
"Carol Davila" University of Medicine
and Pharmacy
37 Dionisie Lupu Street
020021, Sector 2, Bucharest, Romania
Phone: +40.021.318.07.19
E-mail: niculaeandrei@yahoo.com

tional ultrasonography which does not provide accurate information on elastic properties of an organ, because the propagation of ultrasound is relative homogeneous in different biological tissues [4].

The basic principle of elastography is to generate a stress in a tissue and then to measure the strain induced by this stress [5]. The tissue stiffness is quantified with Young modulus, defined by the ratio between the applied stress and the induced strain and expressed in pressure units – Pascals or kilo Pascals [6,7]. Depending on the external force applied on a tissue, several types of elastography can be performed.

In *static or quasi-static US elastography*, an external compression is applied on the interest organ and a qualitative map with the tissue strains before and after compression is provided. Young module cannot be calculated in this method, because the magnitude of the stress applied is unknown; an image with the strain, frequently called elastogram, is displayed and compared with healthy tissue [7,8].

Transient elastography provides a one-dimensional quantitative image of examined tissue stiffness. The underlying principle is to produce a transient skin vibration with a device and then to record, with a 1D transducer, the shear waves that propagates within the examined tissue. A quantitative line of tissue stiffness is obtained [7]. This method, also developed in 2D with the result of obtaining a map of Young's modulus in the examined tissue [7], is already approved in clinical guidelines for the quantification of hepatic fibrosis [9].

Acoustic Radiation Force Impulse Imaging (ARFI) or *Acoustic Radiation Force Imaging* is another elastography method which allows construction of a qualitative stiffness map of the examined tissue. It uses a focused beam of ultrasound to apply a localized radiation force in small volumes of the tissue to be tested and for short durations [10]; this force induces variable tissue displacement varying upon the stiffness of the tissue at the focal spot [7,10]. Making measurements in different places, finally it can be obtained a 2D map stiffness [7].

Shear Wave Elasticity Imaging (SWEI) is a method similar to ARFI – a radiation force is sent into the tissue, but, in contrast with ARFI, the shear waves created by this push and propagated laterally from the beam axis are measured [11]. A limitation of US generated shear waves is the weakness of these waves, with little displacement of the tissue and rapid dissipation of the propagation; therefore, for larger displacements, increased power of the focused beam is required with the risk of overheating [10,12].

The shear wave velocity measurement is also the principle of the most advanced type of US elastography – *Supersonic Shear Imaging* (SSI) [13,14]. In SSI technology, a supersonic shear wave source is generated within the tissue, the amplitude of shear waves being increased while limiting the acoustic power; multiple radiation beam pushes can be successively focused at different points in the examined tissue and they generate a shear wave with a supersonic speed [13,15]. The pushes are sent from the source at different depths at a higher speed than the speed of the generated shear waves; in the end, all shear waves concentrate in a small area, a "Mach cone" shape, which increases their amplitude and the distance of their propagation [13]. The generated shear waves are then mapped quantitatively by using ultrafast imaging technique [13].

Ultrasound elastography in renal diseases

Static elastography methods, with extensive usage in the pathology of superficial organs [16] such as thyroid or breast, have no utility in renal exploration because of the deeply profound location of the native kidney, a situation in which a compression directly on the organ cannot be applied [17]; furthermore, because of the non-uniform pattern of fibrosis in CKD or other diffuse pathologies (such as glomerulonephritis or renal allograft fibrosis), there is no healthy tissue to compare with the elastography results [18].

In addition, in renal diseases, 1D transient elastography has an applicability only in the transplanted kidney [19,20], because this is positioned superficially, under the skin. In transient elastography, the sample volume is placed 4 cm long in a window with little variations below the skin surface (25-65 mm) and there is no ultrasound guidance to position the sample on the native kidney which is located at variable depths [18]. Therefore, errors of interpretations of the results may arise when exploring native kidneys. Additionally, the sample must be positioned behind a solid structure, which may further complicate the kidney exploration because several organs are present in the way to the kidney [18].

Shear wave-based techniques seem to be more appropriate for native kidney stiffness assessment because they allow exploring selectively the different compartments in the kidney; several animal or human studies have been performed with varying results (Tables I). The results are encouraging but, at the same time, numerous uncertainties arise from this research as a result of the modalities to perform the technique, the complexity of the kidney architecture or the heterogeneous and dynamic processes possible at this site without a pathognomonic marker to compare with.

Table I. Shear wave-based US elastography studies performed in the native kidney

Study number of patients or animal models	Technique	Type of research	Conclusions with statistic relevance	Mean value of YM (kPa) or SWV (m/s)
Arda et al (2011) 127 patients [21]	SWEI	healthy kidneys		cortex: 5.2±2.9 kPa (men); 4.9±2.9 kPa (women) renal pelvis: 24.7±4.9 kPa (men); 23.1±5.5 kPa (women)
Gennisson et al (2012) 3 pigs [22]	SSI	healthy kidneys (pig kidney)	– elasticity varies with tissue anisotropy and, with vascular and urinary pressure levels; – inner cortex higher elasticity values than outer cortex, attributable to perfusion differences	inner cortex: 8.1±1.9 kPa outer cortex: 6.9±1.4 kPa
Grenier et al (2013) [18]	SSI	healthy kidney	cortical elasticity values were higher than medullary values	medullary stiffness: 10.8±2.7 kPa cortical stiffness: 15.4±2.5 kPa
Guo et al (2013) 327 healthy patients, 64 CKD [23]	ARFI	healthy versus CKD	– comparing with each CKD stage, SWV was clearly increased in healthy individuals – ARFI predicts only CKD stage 5 – SWV linked only to e-GFR, urea nitrogen, and creatinine	healthy controls: 2.15±0.51 m/s CKD stage 1, 2, 3, 4 and 5: 1.81±0.43 m/s, 1.79±0.29 m/s, 1.81±0.44 m/s, 1.64±0.55 m/s, respectively 1.36±0.17 m/s *Cut-off value for predicting CKD* = 1.88 m/s
Bruno et al (2013) 28 with VUR, 16 healthy pts [24]	ARFI	healthy versus primary or secondary VUR	– SWVs in the “affected” kidneys significantly higher than SWVs in both “contralateral” and “healthy” kidneys – significant difference between SWVs in the “contralateral” and “healthy” kidneys – significant higher SWV in secondary VUR comparing with primary VUR	SWV in the “affected” kidneys: 5.70±1.71 m/s; in contralateral: 4.09±0.97 m/s; in healthy kidneys: 3.13±0.09 m/s. SWV in secondary VUR: 6.59±1.45 m/s; in primary VUR: 5.35±1.72 m/s
Cui et al (2014) 76 patients [25]	ARFI	healthy versus CKD – renal biopsy outer cortex	– SWV values were significantly increased in the mild and moderate fibrosis groups when comparing with non-fibrosis – no significant difference between the mild and moderate fibrosis groups	non-fibrosis: 1.59±0.14 mild fibrosis: 2.15±0.38 moderate fibrosis: 2.29±0.53 severe fibrosis: 2.24 m/s *Cut off for predicting renal fibrosis* > 1.67 m/s
Sohn et al (2014) 19 healthy subjects, 30 hydronephrosis patients [26]	ARFI	healthy versus hydronephrosis	median SWV in kidneys with high-grade hydronephrosis were higher than those in normal kidneys but were not different between hydronephrotic kidneys with and without uretero-pelvic junction obstruction	high-grade hydronephrosis: 2.02 m/s normal kidneys: 1.75 m/s
Bob et al (2014) 68 healthy subjects, 20 kidney pathology [27]	ARFI	healthy versus different kidney diseases	– mean kidney SWVs were higher, but not statistically significant, in subjects without known kidney pathology as compared with those with kidney diseases	without kidney pathology: 2.42±0.70 m/s (operator 1); 2.54±0.83 m/s (operator 2) with kidney diseases: 2.11±0.79 m/s (operator 1); 2.14±0.84 m/s (operator 2)

Asano et al (2014) 14 healthy subjects, 319 CKD [28]	ARFI	healthy versus CKD	– SWV is more influenced by the decrease of renal blood flow than the progression of tissue fibrosis – significant positive correlation between the SWV and eGFR in both cortex and medulla	SWV in healthy: 2.20 m/s in the cortex and 2.75 m/s in the medulla
Hu et al (2014) 163 CKD, 32 healthy subjects [29]	ARFI	healthy versus CKD	– mean SWV in kidneys severely impaired was significant lower than that mildly impaired, moderately impaired, and control groups – in CKD patients, SWV correlated significantly with pathological parameters, serum creatinine, and eGFR	*Cut-off values: 2.65 m/s* for mildly impaired kidneys; 2.50 m/s for moderately impaired kidneys; 2.33 m/s for severely impaired kidneys
Yu et al (2014) 120 diabetes type 2 patients, 30 healthy subjects [30]	ARFI	diabetes mellitus versus healthy	– no significant difference between the normoalbuminuria and control significant difference between the microalbuminuria and macroalbuminuria and control – significant difference between each pair of type 2 diabetes groups	control: 2.22±0.47 m/s normo-albuminuria: 2.29±0.20 m/s microalbuminuria: 2.53±0.16 m/s macroalbuminuria: 2.98±0.32 m/s *Cut-off value for predicting* DN = 2.43 m/s
Tian et al (2014) 259 gouty kidney, 200 healthy subjects [31]	ARFI	gouty kidney versus healthy	– parenchymal and sinus SWV significant higher in gouty kidney than in control – urinary β2-microglobulin positively correlated with the SWV of renal parenchyma in gouty kidney	
Samir et al (2015) 20 healthy subjects, 25 CKD [32]	SWEI	healthy versus CKD	CKD was associated with increased median YM and higher median intra-subject inter-measurement estimated YM's variability	healthy controls: 4.40 kPa (3.68, 5.70) CKD: 9.40 kPa (5.55 – 22.35) *Cut-off value for predicting* CKD = 5.3 kPa
Goya et al (2015) 281 healthy subjects, 114 DN [33]	ARFI	healthy versus DN	– in healthy volunteers, there was a statistically significant correlation between SWV and age and sex – ARFI was able to distinguish between the different DN, except for stage 5	healthy controls: 2.35 m/s DN stage 1, 2, 3, 4 and 5: 2.87; 3.14; 2.95; 2.68; 2.55 m/s *Cut-off value for predicting* DN = 2.43 m/s
Bota et al (2015) 91 patients [34]	ARFI	healthy kidneys	SWVs are influenced mainly by age and gender and less by measurement depth	Right kidney – 2.49±0.81 m/s Left kidney – 2.36±0.75 m/s
Göya et al (2015) 88 with VUR, 20 healthy subjects [35]	ARFI	healthy versus VUR	– significantly higher SWV in non-damaged kidneys – SWV decreases with increasing grades of VUR, increasing DMSA-assessed renal damage and decreasing DMSA-assessed differential function	

*SWEI = Shear Wave Elasticity Imaging; SSI = Supersonic Shear Imaging; ARFI = Acoustic Radiation Force Impulse Imaging or Acoustic Radiation Force Imaging; CKD = chronic kidney disease; DN = diabetic nephropathy; VUR = vesicoureteral reflux; SWV = shear wave velocity; DMSA = dimercaptosuccinic acid

The most important problem is the lack of defining the normal limits of stiffness in the native, healthy kidney, as it is already defined for other organs as liver [36-38], breast [39], or thyroid [40]. Measurements taken so far have significant variations between studies, highlighting the necessity for extensive trials on healthy kidneys. For example, the elasticity values of renal cortex varies, upon different assessments, between 15.4±2.5 kPa [18] to 5.0±2.9 kPa [21] or even 4.40 (3.68, 5.70) kPa [32] for Young's modulus in SSI or SWEI, and between 1.75 m/s [25] to 2.54±0.83 m/s [27] for shear wave velocity in ARFI. The kidney region examined is important, as significant differences in elasticity have been reported between the outer and inner cortex [22], between the medullary and cortical portion of the kidney [18], and between the cortex and renal pelvis [21]. Several factors may influence the variability of the results.

In ARFI, the power of the force applied on the transducer by the operator [18,41,42], the distance from source to target [21,27,34,42] – in current imaging methods is important as is the maximal depth is 8 cm [8], and also the frequency of the probe [42,43], all of these being potential modifiers of measured shear wave velocity. Furthermore, placement of the probe on the cortex may be difficult in advanced CKD because of a small cortical parenchyma thickness.

Anisotropy is present in all renal compartments, especially in the medullary region [22,44,45], and this is important when interpreting the results; sending the ultrasound beam in a perpendicular axis on these structures will lead to higher elasticity values because the shear waves propagate more rapid; when the ultrasound beam is sent parallel to a highly anisotropic structure, the elasticity values will be lower because the shear waves will propagate slower and will dissipate as a result of multiple interfaces created by the blood vessels, renal tubuli and stromal compartments [18,22]. Therefore, measurements of the stiffness in the same part of the kidney (subcapsular, cortex and medulla) are advisable to obtain valid and uniform results [20,27] and also establish universal technique standards in the future for reliable and comparable results.

Vascularization is another factor influencing the measured elasticity values of the kidney. Reduced kidney elasticity after ligation renal artery and, conversely increased elasticity after ligation in the renal vein were reported in an animal study by Genisson et al [22]. Moreover, Asano et al raised the possibility that, in CKD, increased stiffness kidney measured in ARFI may be induced more by vascular abnormalities in this disease than by renal parenchymal fibrosis [28].

Urinary obstruction must be ruled out before performing US elastography, as several studies have reported the linear increase of renal tissue elasticity associated with elevated urinary pressure [22,26].

Gender [21,34], race [27], weight or body mass index (BMI) [20], and also age [23,34,46] can modify the results in US elastography and several studies have found significant variations of renal parenchymal elasticity in these parameters [20,21,23,27,34,46].

The examinations must be performed while the subjects hold their breath, which can be difficult especially in pediatric patients [26].

Inter-observer agreement is reported in various studies at different ICC (intra-class coefficients correlation), from 0.71 [27] to 0.47 [47] or even 0.31 [48], being smaller than those for the assessment of liver fibrosis [49,50]. These variations are explained by the deeper location of the native kidney compared to the liver, by the different experience of the operators in the field of renal US elastography, or may be due to the type of kidney examined, native or transplanted [27]. Intra-observer variation coefficients are also reported between 20% [51] and 24% [48].

Evaluating fibrosis in native kidney with US elastography

CKD is characterized by progressive scarring of the renal parenchyma with loss of intrinsic renal cells and increased production of extracellular matrix, ultimately leading to fibrosis that affects all components of the kidney – glomeruli, tubules, interstitium and vessels, irrespective of the primary renal insult [52]. Several mediators that induce fibrosis in the common pathway of CKD progression have been identified (transforming growth factor β1 (TGF-β1), connective tissue growth factor (CTGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF) etc) [52] and experimental studies performed until the present offer hope for reversal or stopping the fibrogenic process in CKD using various interventions (anti-TGF-β1 or anti-EGF antibodies, inhibitors of TGF-β1 or EGF receptors, administration of hepatocyte growth factor or bone morphogenic protein 7 (BMP-7), synthetic inhibitors of tissue transglutaminase etc) [52]. Unfortunately, ideal markers for assessing the degree of fibrosis are lacking, except for the kidney biopsy which is not only an invasive procedure, but has several limitations and contraindications [53]. Therefore, kidney US elastography opens new perspectives as it would permit the decrease of biopsy and also can be used to track fibrosis progression in repeatable examinations.

Several US elastography studies have been performed until the present for assessing fibrosis in the native kidney. In an experimental study performed by Derieppe et al [54], glomerulosclerosis and increased urinary protein / creatinine ratio were associated with an increased elasticity of renal parenchyma. In the native kidney, human studies have reported various markers associated with increased kidney stiffness: estimated glomerular filtrate rate (eGFR) [23,28,29], urinary albumin / creatinine or protein / creatinine ratio [30,33], serum creatinine [23,29], urea nitrogen [23], elasticity values in healthy native kidneys [23-33,35], kidney biopsies [25], other imaging tests etc [24,26,35]. Thus, there are studies finding no significant correlation between markers of chronic kidney injury and elasticity of renal parenchyma in native [27] or transplanted kidney [48,51], and also studies which could not prove a significant difference of elasticity between different stages of CKD [23,25]; in addition, it has been reported an increased intra-subject variability of results in CKD versus healthy controls [33] or a higher influence of arteriosclerosis markers, such as pulsatility index or resistivity index, on kidney stiffness than eGFR [28]. Such discrepancies may be explained not only by the heterogeneity of the markers utilized for the presence of fibrosis, by anatomic features of the kidney or by several confounders (age, BMI, technique variations etc), but also by the heterogeneity of primary kidney diseases which may be accompanied, in different stages of evolution, by inflammation, as it happens in the early phase of graft rejection or in vesicoureteral reflux.

Despite these limitations, ultrasound elastography shows the potential for becoming a valuable tool in non-invasive assessment of kidney fibrosis.

Conclusions

Recent studies based on shear wave techniques which have explored different compartments of the native kidney are encouraging, but many gaps have to be filled and questions to be answered, mainly due to the complexity of the kidney architecture or the heterogeneous and dynamic processes possible at this site without a pathognomonic marker to compare with.

The most important problem is the lack of defining the normal limits of stiffness in the native, healthy kidney, as it is already defined for other organs (e.g. liver, breast, thyroid). Up to this moment, there is no consensus between trials regarding the reference values for the normal stiffness / elasticity of the native kidney, high variations being noticed in intra- and inter-operator measurement. Several factors may influence the variability of the results and therefore there are significant differences in elasticity between various renal regions in healthy kidneys: outer and inner cortex, medullary and cortical portion of the kidney, cortex and renal pelvis. Furthermore, the impact of various pathological processes (e.g. diabetic nephropathy, hydronephrosis, glomerulopathies etc) on the stiffness of the kidney presents large variations in different studies.

In conclusion, elastography is a promising tool for assessing kidney fibrosis; further studies are required in order to establish a standardized technique method and also normal and pathological reference values.

Conflict of interests: none

References

1. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systemic review. BMC Public Health 2008; 8: 117.
2. Fassett RG, Venuthurupalli SK, Gobe GC, Coombes JS, Cooper MA, Hoy WE. Biomarkers in chronic kidney disease: a review. Kidney Int 2011; 80: 806-821.
3. Ophir J, Céspedes I, Ponnekanti H, Yazdi Y, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging 1991; 13: 111-134.
4. Sarvazyan AP, Skovoroda AR, Emelianov SY, et al. Biophysical bases of elasticity imaging. In: Jones JP (ed). Acoustical Imaging. New York, USA: Springer Science + Business Media, LLC, 1995: 223-241.
5. Dewall RJ. Ultrasound elastography: principles, techniques, and clinical applications. Crit Rev Biomed Eng 2013; 41: 1-19.
6. http://www.slideshare.net/cpmrocksatgmc/elastography?next_slideshow. Accessed March 2016.
7. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. Diagn Interv Imaging 2013; 94: 487-495.
8. Bamber J, Cosgrove D, Dietrich CF, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall Med 2013; 34: 169-184.
9. European Association for Study of Liver. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol 2014; 60: 392-420.
10. Nightingale K, Soo MS, Nightingale R, Trahey G. Acoustic radiation force impulse imaging: in vivo demonstration of clinical feasibility. Ultrasound Med Biol 2002; 28: 227-235.
11. Sarvazyan AP, Rudenko OV, Swanson SD, Fowlkes JB, Emelianov SY. Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics. Ultrasound Med Biol 1998; 24: 1419-1435.
12. Palmeri ML, Nightingale KR. On the thermal effects associated with radiation force imaging of soft tissue. IEEE Trans Ultrason Ferroelectr Freq Control 2004; 51: 551-565.
13. Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. IEEE Trans Ultrason Ferroelectr Freq Control 2004; 51: 396-409.
14. Gennisson JL, Rénier M, Catheline S, et al. Acoustoelasticity in soft solids: assessment of the nonlinear shear modulus

with the acoustic radiation force. J Acoust Soc Am 2007; 122: 3211-3219.
15. Nightingale K, McAleavey S, Trahey G. Shear-wave generation using acoustic radiation force: in vivo and ex vivo results. Ultrasound Med Biol 2003; 29: 1715-1723.
16. Cosgrove D, Piscaglia F, Bamber J, et al; EFSUMB. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: Clinical applications. Ultraschall Med 2013; 34: 238-253.
17. Parker KJ, Doyley MM, Rubens DJ. Imaging the elastic properties of tissue: the 20 year perspective. Phys Med Biol 2011; 56: R1-R29.
18. Grenier N, Gennisson JL, Cornelis F, Le Bras Y, Couzi L. Renal ultrasound elastography. Diagn Interv Imaging 2013; 94: 545-550.
19. Lukenda V, Mikolasevic I, Racki S, Jelic I, Stimac D, Orlic L. Transient elastography: a new noninvasive diagnostic tool for assessment of chronic allograft nephropathy. Int Urol Nephrol 2014; 46: 1435-1440.
20. Sommerer C, Scharf M, Seitz C, et al. Assessment of renal allograft fibrosis by transient elastography. Transpl Int 2013; 26: 545-551.
21. Arda K, Ciledag N, Aktas E, Aribas BK, Köse K. Quantitative assessment of normal soft-tissue elasticity using shear-wave ultrasound elastography. AJR Am J Roentgenol 2011; 197: 532-536.
22. Gennisson JL, Grenier N, Combe C, Tanter M. Supersonic shear wave elastography of in vivo pig kidney: influence of blood pressure, urinary pressure and tissue anisotropy. Ultrasound Med Biol 2012; 38: 1559-1567.
23. Guo LH, Xu HX, Fu HJ, Peng A, Zhang YF, Liu LN. Acoustic radiation force impulse imaging for noninvasive evaluation of renal parenchyma elasticity: preliminary findings. PLoS One 2013; 8: e68925.
24. Bruno C, Caliari G, Zaffanello M, et al. Acoustic radiation force impulse (ARFI) in the evaluation of the renal parenchymal stiffness in paediatric patients with vesicoureteral reflux: preliminary results. Eur Radiol 2013; 23: 3477-3484.
25. Cui G, Yang Z, Zhang W, et al. Evaluation of acoustic radiation force impulse imaging for the clinicopathological typing of renal fibrosis. Exp Ther Med 2014; 7: 233-235.
26. Sohn B, Kim MJ, Han SW, Im YJ, Lee MJ. Shear wave velocity measurements using acoustic radiation force impulse in young children with normal kidneys versus hydronephrotic kidneys. Ultrasonography 2014; 33: 116-121.
27. Bob F, Bota S, Sporea I, Sirli R, Petrica L, Schiller A. Kidney shear wave speed values in subjects with and without renal pathology and inter-operator reproducibility of acoustic radiation force impulse elastography (ARFI) – preliminary results. PLoS One 2014; 9: e113761.
28. Asano K, Ogata A, Tanaka K, et al. Acoustic radiation force impulse elastography of the kidneys: is shear wave velocity affected by tissue fibrosis or renal blood flow? J Ultrasound Med 2014; 33: 793-801.
29. Hu Q, Wang XY, He HG, Wei HM, Kang LK, Qin GC. Acoustic radiation force impulse imaging for non-invasive assessment of renal histopathology in chronic kidney disease. PLoS One 2014; 9: e115051.
30. Yu N, Zhang Y, Xu Y. Value of virtual touch tissue quantification in stages of diabetic kidney disease. J Ultrasound Med 2014; 33: 787-792.
31. Tian F, Wang ZB, Meng DM, et al. Preliminary study on the role of virtual touch tissue quantification combined with a urinary β2-microglobulin test on the early diagnosis of gouty kidney damage. Ultrasound Med Biol 2014; 40: 1394-1399.
32. Samir AE, Allegretti AS, Zhu Q, et al. Shear wave elastography in chronic kidney disease: a pilot experience in native kidneys. BMC Nephrol 2015; 16: 119.
33. Goya C, Kilinc F, Hamidi C, et al. Acoustic radiation force impulse imaging for evaluation of renal parenchyma elasticity in diabetic nephropathy. AJR Am J Roentgenol 2015; 204: 324-329.
34. Bota S, Bob F, Sporea I, Şirli R, Popescu A. Factors that influence kidney shear wave speed assessed by acoustic radiation force impulse elastography in patients without kidney pathology. Ultrasound Med Biol 2015; 41: 1-6.
35. Göya C, Hamidi C, Ece A, et al. Acoustic radiation force impulse (ARFI) elastography for detection of renal damage in children. Pediatr Radiol 2015; 45: 55-61.
36. Fung J, Lai CL, Chan SC, et al. Correlation of liver stiffness and histological features in healthy persons and in patients with occult hepatitis B, chronic active hepatitis B, or hepatitis B cirrhosis. Am J Gastroenterol 2010; 105: 1116-1122.
37. Popescu A, Sporea I, Şirli R, et al. The mean values of liver stiffness assessed by Acoustic Radiation Force Impulse elastography in normal subjects. Med Ultrason 2011; 13: 33-37.
38. Fung J, Lee CK, Chan M, et al. Defining normal liver stiffness range in a normal healthy Chinese population without liver disease. PLoS One 2013; 8: e85067.
39. Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006; 239: 341-350.
40. Monpeyssen H, Tramalloni J, Poirée S, Hélénon O, Correas JM. Elastography of the thyroid. Diagn Interv Imaging 2013; 94: 535-544.
41. Syversveen T, Midtvedt K, Berstad AE, Brabrand K, Strøm EH, Abildgaard A. Tissue elasticity estimated by acoustic radiation force impulse quantification depends on the applied transducer force: an experimental study in kidney transplant patients. Eur Radiol 2012; 22: 2130-2137.
42. Zaffanello M, Bruno C. Clinical perspective on renal elasticity quantification by acoustic radiation force impulse: Where we are and where we are going. World J Clin Urol 2015; 4: 100-104.
43. Chang S, Kim MJ, Kim J, Lee MJ. Variability of shear wave velocity using different frequencies in acoustic radiation force impulse (ARFI) elastography: a phantom and normal liver study. Ultraschall Med 2013; 34: 260-265.
44. Ries M, Jones RA, Basseau F, Moonen CT, Grenier N. Diffusion tensor MRI of the human kidney. J Magn Reson Imaging 2001; 14: 42-49.

45. Goertz RS, Amann K, Heide R, Bernatik T, Neurath MF, Strobel D. An abdominal and thyroid status with Acoustic Radiation Force Impulse Elastometry - a feasibility study: Acoustic Radiation Force Impulse Elastometry of human organs. Eur J Radiol 2011; 80: e226-e230.
46. Lee MJ, Kim MJ, Han KH, Yoon CS. Age-related changes in liver, kidney, and spleen stiffness in healthy children measured with acoustic radiation force impulse imaging. Eur J Radiol 2013; 82: e290-e294.
47. Ozkan F, Yavuz YC, Inci MF, et al. Interobserver variability of ultrasound elastography in transplant kidneys: correlations with clinical-Doppler parameters. Ultrasound Med Biol 2013; 39: 4-9.
48. Syversveen T, Brabrand K, Midtvedt K, et al. Assessment of renal allograft fibrosis by acoustic radiation force impulse quantification – a pilot study. Transpl Int 2011; 24: 100-105.
49. Bota S, Sporea I, Sirli R, Popescu A, Danila M, Costachescu. Intra- and interoperator reproducibility of acoustic radiation force impulse (ARFI) elastography – preliminary results. Ultrasound Med Biol 2012; 38: 1103-1108.
50. Guzmán-Aroca F, Reus M, Berná-Serna JD, et al. Reproducibility of shear wave velocity measurements by acoustic radiation force impulse imaging of the liver: a study in healthy volunteers. J Ultrasound Med 2011; 30: 975-979.
51. Grenier N, Poulain S, Lepreux S, et al L. Quantitative elastography of renal transplants using supersonic shear imaging: a pilot study. Eur Radiol 2012; 22: 2138-2146.
52. Bello A, Kawar B, El Kossi M, El Nahas M. Epidemiology and pathophysiology of chronic kidney disease. In: Floege J, Johnson RJ, Feehally J (eds). Comprehensive Clinical Nehrology. 4th Ed. St. Louise, Missouri, USA: Saunders Elsevier, 2010: 907-918.
53. Topham PS, Chen Y. Renal biopsy. In: Floege J, Johnson RJ, Feehally J (editors). Comprehensive Clinical Nehrology. 4th Ed. St. Louise, Missouri, USA: Saunders Elsevier, 2010: 75-82.
54. Derieppe M, Delmas Y, Gennisson JL, et al. Detection of intrarenal microstructural changes with supersonic shear wave elastography in rats. Eur Radiol 2012; 22: 243-250.