Review Article

What's new in urologic ultrasound?

Anupam Lal, Priyanka Naranje, Santhosh Kumar Pavunesan

Department of Radiodiagnosis, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Ultrasound is an imaging technology that has evolved swiftly and has come a long way since its beginnings. It is a commonly used initial diagnostic imaging modality as it is rapid, effective, portable, relatively inexpensive, and causes no harm to human health. In the last few decades, there have been significant technological improvements in the equipment as well as the development of contrast agents that allowed ultrasound to be even more widely adopted for urologic imaging. Ultrasound is an excellent guidance tool for an array of urologic interventional procedures and also has therapeutic application in the form of high-intensity focused ultrasound (HIFU) for tumor ablation. This article focuses on the recent advances in ultrasound technology and its emerging clinical applications in urology.

Key words: Advances, cancer, kidney, prostate, ultrasonography, urology

INTRODUCTION

A significant landmark in the evolution of ultrasound technology has been a transition from the cumbersome static B-mode imaging into real-time imaging systems with improved resolution. Innovations in hardware with a short learning curve addressing shortcomings of this modality have revolutionized the use of ultrasound with emergence of a variety of new clinical applications. The advancements that have had significant clinical implications include tissue harmonic imaging (THI), spatial compound imaging, three-dimensional (3D) and four-dimensional ultrasound, contrast-enhanced ultrasound (CEUS), elastography, endoscopic ultrasound, and fusion imaging.

THI

In conventional grayscale sonography, a spectrum of sound frequency (bandwidth) is transmitted into the body of the patient and is subsequently received to produce the ultrasound image. In contrast, THI depends on the generation of higher harmonic frequencies by the propagation of the ultrasound beam through tissues to produce the image. Harmonics are integral multiples of the transmitted frequency generated by the nonlinear propagation of ultrasound waves in the tissue. Harmonics cause decreased body wall artifact as they are generated in tissues deep to body wall and they pass through the body wall only once.[1] Better images are provided by THI than conventional sonography, by using information from harmonics with improved axial and lateral resolution, signal-to-noise ratio, reduced reverberation, and side-lobe artifacts.[2] Harmonic imaging is especially useful in obese patients because a higher amount of fat has higher nonlinearity coefficients, which increases the intensity of harmonic waves and reduces the confounding artifacts produced by the body wall, thus improving lesion visibility.[3] Because of reduction of side-lobe artifacts, the cavities appear darker and tissues appear brighter. THI provides a good demonstration of both cystic and solid lesions [Figure 1].[2] Other advantages include improved near-field resolution (closer to the transducer) and improved contrast resolution, i.e., the ability to perceive subtle changes between adjacent tissues.

One of the most useful applications of THI is characterization of cysts. Simple renal cysts are commonly seen in about half of patients over 50 years of age, and account for a large percentage of masses detected incidentally on imaging. Simple cysts must have sharply defined margins of imperceptible thickness and show complete sound transmission. Despite the familiarity of these findings,

For correspondence: Dr. Anupam Lal, Department of Radiodiagnosis and Imaging, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, Haryana and Punjab, India. E-mail: dralal@rediffmail.com

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/0970-1591.159604

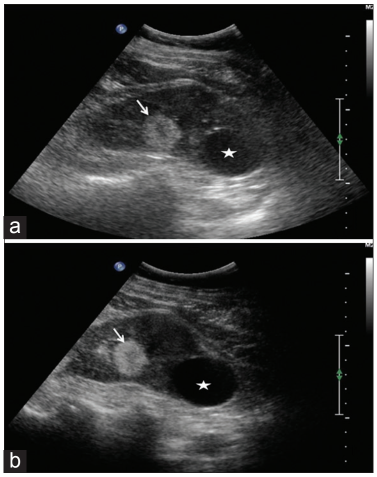

Figure 1: Conventional B-mode image (a) and THI (b) showing better visualization of renal angiomyolipoma (arrow) and renal cyst (star) in harmonic image

difficulty arises in concluding whether a cystic renal lesion is simple or complex in the setting of a noisy image. Bosniak staging of cystic renal lesions depends on the internal architecture that determines its likelihood of malignancy. Diagnosing a lesion as a simple cyst depends on establishing the complete absence of any septations, internal echoes, or mural nodules. As THI better delineates these features, it is more useful than conventional imaging in evaluating the Bosniak stage and the nature of cystic lesions.[1]

Posterior acoustic shadowing from the calculi is more prominent in harmonic mode, allowing a more confident diagnosis of renal or ureteric calculi. In a study by Mitterberger *et al*., comparing a combination of plain radiograph of the kidneys, ureters, and bladder (KUB) and transabdominal native THI (NTHI) versus unenhanced computed tomography (CT), the former detected 72 of the 75 urinary calculi (sensitivity 96%, specificity 91%, and accuracy 95%), while unenhanced CT detected all 75 calculi.[4] They concluded that even though CT is the most accurate technique for detecting urolithiasis, plain film KUB with ultrasound using transabdominal NTHI can give results comparable to CT. Mohammed *et al.* evaluated 30 patients with cystic renal lesions on conventional grayscale ultrasound and THI.[5] Abdominal CT was carried out within 1 week of the ultrasound examinations. The images obtained by conventional ultrasound, THI, and contrast-enhanced CT (CECT) were evaluated for image quality, lesion conspicuity, and solid-cystic differentiation. THI showed better image quality in 27 of 34 lesions, improvement in lesion conspicuity in 27 of 34 cystic lesions, and an improved solid-cystic differentiation in 30 of 34 lesions, when compared to conventional ultrasound. Additional information was provided in 8 patients by THI compared to conventional ultrasound. The CT grading was significantly higher for overall image quality (P = 0.007) and lesion conspicuity (P = 0.004), but not for solid-cystic differentiation (P = 0.23). Thus, THI provides better quality image and details of lesions compared to conventional grayscale ultrasound.

THI is particularly sensitive in recognition of pyonephrosis, increasing the conspicuity of fine internal echoes within the obstructed collecting system. In addition, improved lesion-to-background contrast in the harmonic mode facilitates the detection of subtle hypoechoic lesions.[6]

SPATIAL COMPOUND IMAGING

Spatial compound sonography uses the electronic steering of ultrasound beams from a transducer array to obtain overlapping scans of a target tissue from different angles. The given tissue is imaged multiple times from different directions using parallel beams. The resulting echoes from these multiple acquisitions are then frameaveraged to produce a single compound image of improved quality due to a reduction in image speckle.[7] It achieves an improved visualization of details compared to what is available with the conventional B-mode image.[8] Spatial compound imaging demonstrates a low level of noise, refraction, reduced shadowing, speckle and enhancement artifacts, and improved contrast and margin definition, thus improving visualization of tissue details, including lesion margins [Figure 2].

Compound imaging allows an excellent definition of kidney profiles, detection of renal calculi, and more accurate evaluation of parenchymal echotexture and calcifications.[9] It is subjectively superior to conventional ultrasound in evaluating patients with Peyronie's disease, as microcalcifications are better detected.[10]

Oktar *et al*. evaluated 150 lesions in 122 randomly selected patients with various abdominal and pelvic pathologies.[11] For each lesion, sonograms were obtained with four techniques: Conventional sonography, real-time spatial compound sonography, tissue harmonic sonography, and tissue harmonic compound sonography. All images were reviewed and graded independently by two observers for overall image quality, lesion conspicuity, and elimination of artifacts. Tissue harmonic compound sonography was found to be significantly superior to all of the other techniques; real-time spatial compound sonography performed better than tissue harmonic sonography; and conventional sonography was the least valuable of all (P < 0.001).

THREE-DIMENSIONAL (3D) AND FOUR-DIMENSIONAL (4D) ULTRASONOGRAPHY

3D ultrasonography or volume sonography involves acquisition of several datasets of 2D images from the patient. After acquisition, this volumetric data is qualitatively and quantitatively postprocessed with the use of many analysis tools, such as surface and volume rendering, multiplanar

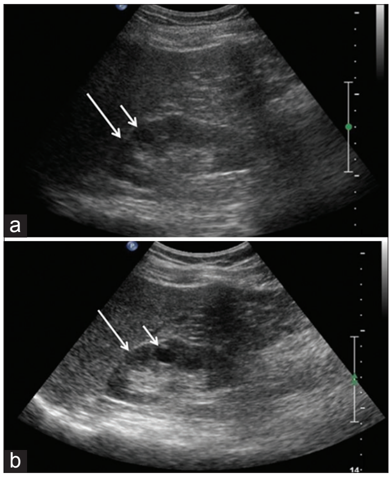

Figure 2: Images of conventional ultrasound (a) and compound image (b) showing improved visualization of renal cyst (short arrow) and clear demarcation of renal outline (long arrow) in compound image

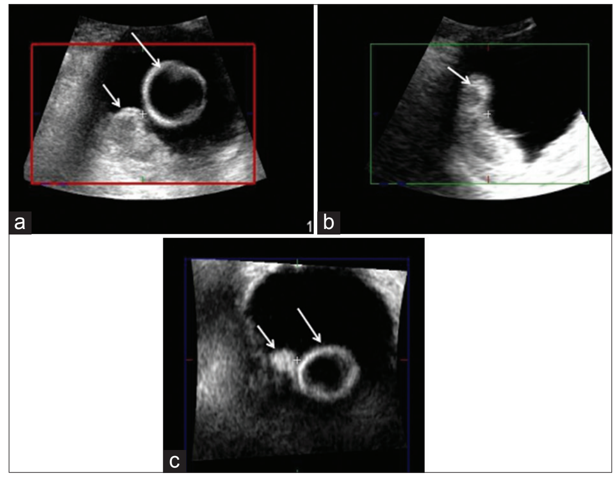

Figure 3: 3D-ultrasound image (a- axial, b- coronal and c- sagittal) of a patient with hematuria showing bladder growth (short arrows) in all the three axes in an image acquired in a single acquisition. Foley's catheter bulb is seen *in situ* (long arrows)

imaging, and volume calculation techniques. Features in the individual 2D image datasets are registered in various image planes with respect to one another to form a 3D-rendered display of tissue structures[12] [Figure 3]. When real-time 3D ultrasound allows image display over time, the technique is referred to as 4D ultrasound.

Currently, there are two commonly used techniques to acquire 3D volumetric data: Freehand technique and automated technique. The commercially available sophisticated equipment uses a freehand approach to 3D ultrasonography, allowing the operator to image a volume of tissue by slowly and manually scanning through the imaging plane. In the automated technique, the dedicated 3D probe is used. Here the probe is held stationary, and on activation the transducer elements within the probe automatically sweep through the volume box selected by the operator. The resultant images are digitally stored and can be processed later in various display modes for analysis.

3D ultrasound has several benefits, related to an improved spatial orientation and demonstration of multiplanar views. Three-dimensional prostate ultrasonography is more accurate for repetitive measurements, compared to 2D imaging. This makes it a valuable tool for the accurate volume assessments required for radiation dosimetry during radiotherapy planning for prostate cancer or for estimation of prostate specific antigen (PSA) density.[12]

Mitterberger *et al.* compared 3D-ultrasound versus 2D-ultrasound of the urinary bladder for the evaluation of hematuria.[13] They found that 3D-ultrasound yielded an overall correct diagnosis in 86% of the cases, providing better diagnostic features than 2D-ultrasound, with 100% sensitivity for malignant bladder lesions, and 71% sensitivity for benign bladder changes. In a similar study, Kocakoc *et al.*[14] evaluated the potential value of 3D-ultrasound and sonographic cystoscopy in the detection of bladder tumors. They found that 3D virtual sonography had a sensitivity of 96.2%, specificity of 70.6%, positive predictive value of 93.9%, and negative predictive value of 80% for tumor detection. The combination of grayscale sonography, multiplanar reconstruction, and 3D virtual sonography improved the diagnostic accuracy by increasing the sensitivity to 96.4%, specificity to 88.8%, positive predictive value to 97.6%, and negative predictive value to 84.2%. So, 3D sonography is considered as a promising alternative noninvasive technique for detection, localization, and assessment of the perivesical spread of bladder tumors. The findings of tumors shown on 3D sonography agreed well with conventional cystoscopy in terms of the location, size, and morphologic features. Thus, 3D-ultrasound outperforms 2D-ultrasound in both diagnosis and therapeutic planning for urinary bladder carcinoma.

CEUS

Two basic elements of CEUS are the ultrasound contrast agent (UCA) and the contrast-specific imaging mode.

The first generation of UCAs, such as agitated saline, hydrogen peroxide, air, and carbon dioxide achieved only right heart (cardiac) imaging as they could not pass through the pulmonary circulation. The second generations of UCAs are microbubbles of insoluble gas, which are stabilized with phospholipid, albumin, or polymer surface shell. The gas gets exhaled, while the shell gets metabolized in the liver.[15] The smaller size of the second-generation UCAs with a mean diameter less than 8 μm can easily pass through the pulmonary circulation to various organs. They possess a strong harmonic response and an extended half-life in circulation due to their lower solubility in water.

The first step in the CEUS procedure is an injection of UCA through the peripheral veins, following which the region of interest (ROI) is exposed to the ultrasound beam. As soon as the UCA microbubbles reach the ROI, interaction takes place between the ultrasound beam and the UCA in the micro- and macro-circulation, resulting in the generation of the nonlinear signals, whereas no or few nonlinear signals are generated from the tissues. This improved signal-to-noise ratio makes UCA a tracer to depict the micro- and macro-circulation.[16,17]

In CEUS, a low mechanical index (MI) mode is selected by the user from the operator console. This ensures that the incident ultrasound beam is of low energy, preventing the destruction of microbubbles in circulation and thereby prolonging the effective scanning time.

Currently, the UCAs commercially available in India are SonoVue® (Sulfur hexafluoride) (Bracco International, Milan, Italy), Definity® (perflutren lipid microspheres, Lantheus Medical Imaging, London, UK), and Luminity (perflutren lipid-coated microspheres, Lantheus Medical Imaging, London, UK).

CEUS is also used for quantitative assessment of the perfusion of the tumors. Dedicated software is used for generating perfusion maps of the tumor vascularity, using the acquired data of tumoral enhancement obtained by continuous recording after contrast injection. The time to peak, estimated perfusion, peak intensity, and area under the time-intensity curve can be generated, providing quantitative information on tumor vascularity.[18,19]

Renal applications of CEUS include characterization of complex renal cysts, distinguishing pseudotumors from true masses, evaluation of renal trauma, ischemia and perfusion. It is also an important tool to aid interventional procedures like biopsy and ablation of lesions. It has the potential to distinguish postoperative changes from recurrence in patients undergoing minimally invasive treatment of renal tumors (i.e., laparoscopic/robotic-assisted nephron-sparing surgery, cryoablation, and radiofrequency ablation).

CEUS is useful for characterizing focal renal lesions[20-22] [Figures 4 and 5]. Renal cell carcinomas (RCCs) are the most common malignant renal neoplasm. On CEUS, RCCs typically show heterogeneous hypervascularity, with an early washout on the delayed phase. A pseudocapsule may be present.[23] Oncocytoma is the most common benign solid renal tumor; however, it shares many imaging features of RCC. On conventional ultrasound, angiomyolipomas (AMLs) are hyperechoic. On CEUS, these lesions tend to enhance peripherally and show less enhancement than the normal cortical renal parenchyma in its central part.[23] Emilio Quaia *et al.* found that the overall diagnostic accuracy of CEUS was significantly better than unenhanced sonography or CT in the diagnosis of malignancy in complex cystic renal masses.[24]

Oh *et al.*[25] retrospectively evaluated the CEUS findings of 38 small RCC cases and 11 AML cases among 85 patients. Diagnostic efficacy in differentiating the two diseases was compared in terms of tumor echogenicity, pattern, and degree of enhancement. There were significant differences between AML and RCC in diffuse heterogeneous enhancement (observed in 78.9% of RCCs and 27.3% of AMLs, $P = 0.003$), washout in late phase (73.7% of RCCs and 18.2% of AMLs, $P = 0.001$), and perilesional, rimlike enhancement (57.9% of RCCs and 9.1% of AMLs, $P = 0.006$) with sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 86.8%, 63.6%, 89.2%, 58.3%, and 81.6% respectively. Thus, CEUS was shown to possess higher diagnostic utility than conventional ultrasound in the evaluation of small renal masses and differentiating RCCs from AMLs.

Nicolau *et al.*[26] evaluated 72 patients with 83 indeterminate renal nodules detected on CT using baseline ultrasound and CEUS and found that the addition of CEUS allowed a correct diagnosis of 48/50 (96%) benign cysts and of 31/33 (93.9%) nodules as potentially malignant, with a sensitivity of 96%, specificity of 93.9%, and overall accuracy of 95.2%.Thus, CEUS can differentiate benign complex cysts from other lesions that are inconclusive on CT and require further investigation. CEUS improves the accuracy of baseline ultrasound from 42.2% to 95.2%.

Kidneys are highly perfused organs, and a typical microbubble contrast-enhancement pattern is observed. After administration of UCAs, the vascular pedicle of kidneys enhance first, followed by the cortex and finally the medulla. The tip of the renal medullary pyramid is the last to enhance. UCAs do not show excretion into the pelvicalyceal system. CEUS is a reproducible tool to detect acute renal infarcts with a diagnostic performance approaching that of CECT.[27]

Renal infarcts appear as wedge-shaped areas of non-perfusion on CEUS. Further it can detect a nonperfused or hypoperfused renal grafts. Normal organs usually show homogeneous increased echogenicity in the parenchymal phase of the examination. A contusion is seen as a hypoechoic area within the enhancing parenchyma with ill-defined borders; a laceration is seen as a well-defined linear nonenhancing area. In hypovolemic shock, abdominal solid organs show reduced enhancement. As UCAs are not excreted in the urine, they cannot be used to detect any renal collecting system injury.

CEUS can assist in differentiating focal pyelonephritis from mass lesions and aids in delineating abscesses, either parenchymal or perinephric, and also in the evaluation of

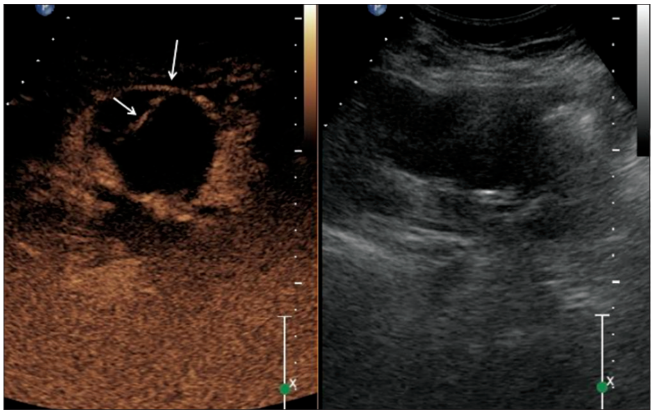

Figure 4: Paired CEUS and corresponding conventional image showing better visualization of complicated renal cyst (long arrow) with enhancing septation (short arrow). It was found to be papillary RCC at histopathology

vascular malformations of the kidney. It can also be used in to monitor the development of renal abscesses in known cases of urinary tract infection. Multiple studies have shown encouraging results in assessing vesicoureteral reflux with voiding urosonography (VUS) on comparison with voiding cystourethrography (VCUG).

Papadopoulou *et al.*[28] evaluated 228 children with 463 kidney-ureter units (KUUs). Two cycles of VUS and VCUG were done at the same session. VUR was demonstrated in 161/463 (34.7%) KUUs, 57 by both methods, 90 only by VUS, and 14 only by VCUG. Concordance in findings was found in 359/463 (77.5%) KUUs with significant difference in the detection rate of reflux between the two methods ($P < 0.01$). More importantly, reflux missed by VCUG was of higher grade than that missed by VUS. Thus, VUS harmonic imaging with a second-generation UCA improved the identification of reflux in children and showed higher sensitivity compared to VCUG. Kis *et al.*[29] evaluated 183 children with 366 KUUs using VUS and VCUG in the same session with the same catheterization. VUR was detected in 140 out of 366 cases (38%); in 89 (24.3%) by both methods; in 37 (10.1%) by VUS only; and in 14 (3.8%) by VCUG only. Significant difference in the detection rate of reflux was found between two methods ($P < 0.00001$) even with considerable agreement in the diagnosis of VUR by both methods. With moderate agreement between the grades of VUR detected with both methods, VUS is superior to VCUG in the detection and grading of VUR, and it should be the method of choice for this clinical indication.

A recent large prospective study[30] has shown no serious adverse events related to CEUS. Only a few minor events were reported, most likely due to the catheterization process. Thus, contrast-enhanced VUS with intravesical administration of the second-generation UCA for vesicoureteral reflux detection or exclusion has a favorable safety profile, and contrast-enhanced voiding urosonography

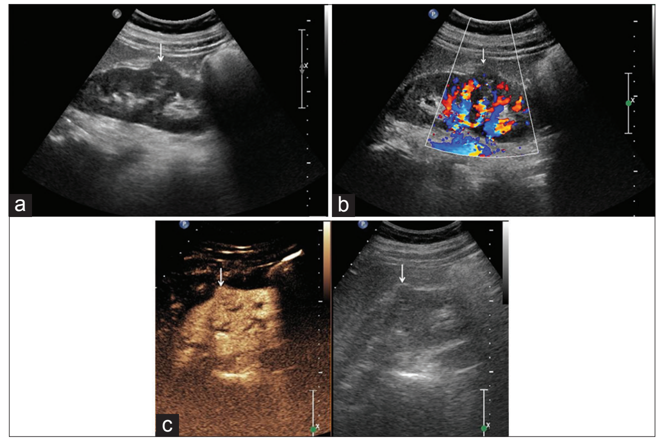

Figure 5: Conventional ultrasound (a) color Doppler (b) and paired CEUS with corresponding conventional image (c) show partially exophytic solid renal lesion (arrows) with focal color flow and homogeneous enhancement in postcontrast images (c). It was found to be clear-cell RCC at histopathology

is a viable alternative tool in the diagnosis of vesicoureteral reflux. For this application, it has the potential to replace other radiological methods and save radiation exposure.[31]

In bladder carcinomas, CEUS reliably differentiates low- and high-grade tumors by providing typical enhancement patterns and specific contrast-sonographic perfusion curves. Although both high- and low-grade bladder carcinoma can be hypervascular, specific perfusion parameters on CEUS such as time intensity curves calculated based on ROI drawn in the lesion and the closest normal bladder wall show characteristic shapes for high-grade carcinoma, low-grade carcinoma, and normal bladder wall.[32]

The neovascularity associated with prostatic adenocarcinoma is beyond the resolution of Doppler ultrasound. The use of UCAs in combination with color and power Doppler imaging increases the signal from foci of increased vascularity. Prostatic adenocarcinoma tends to show early enhancement after administration of UCAs. Several studies have compared the efficacy of CEUS-guided targeted biopsy with systematic biopsy. It has been demonstrated that CEUS increased the detection rate of malignancy in the peripheral zone but was not helpful in the central zone.[33] A few recent studies have demonstrated a significantly increased detection rate of prostate cancer using CEUS-guided targeted biopsy compared to the standard random systematic biopsy.[34,35]

CEUS can be used to increase tumor visibility before the ablation of renal masses. Following the ablation procedure, it has been used to distinguish the enhancing residual tumor from the non-enhancing ablated tissue. However, this distinction is only possible ten minutes after the procedure as by this time the artifacts arising from the gas produced as a result of ablation procedure tends to disappear. Studies have demonstrated CEUS to be as accurate as CT and magnetic resonance imagining (MRI) in assessing adequacy of ablation treatment.[36,37] Thus, CEUS can provide an accurate diagnosis comparable to CECT and MRI without any risk of radiation or nephrotoxicity.

Ultrasound elastography

It is a noninvasive technique of imaging the stiffness or elasticity of the tissue by measuring the deformation of the tissue to the small applied pressure. It exploits the fact that a pathological process alters the elastic properties of the involved tissue. This change in elasticity is detected and imaged using elastography. It is a method of "virtual palpation" of the tissue or lesions.

Elastography aims to quantitatively image the Young's modulus (E), the physical parameter corresponding to the stiffness. Young's modulus (also known as tensile modulus or elastic modulus) quantitatively measures stiffness of an elastic material (in kPa) and helps in characterizing the materials. It is represented as the ratio of the stress (force per unit area) along an axis to the strain (amount of deformation) in accordance with Hooke's law, which states that stress is proportional to strain within an object's elastic limit.

To assess the Young's modulus of the tissue, all elastography techniques rely on this principle. The external force could be applied by static (or quasistatic) or dynamic methods. The elastography technique based on the static method is strain or compression elastography and the dynamic methods (based on shear wave) are vibroacoustography, acoustic radiation force impulse imaging (ARFI), one- or two-dimensional (1D or 2D) transient elastography, and ultrafast imaging, such as supersonic shear imaging.

In the case of quasistatic elastography, a constant stress is applied to the tissue. The displacement and the generated strain are then estimated using 2D correlation of ultrasound images. In practice, because the applied stress is unknown, only the strain is displayed and this strain map is called the Elastogram. This technique has the advantage of being easy to implement, but the unknown stress distribution prevents any quantitative estimation of the local Young modulus.

In dynamic methods, a time-varying force is applied to the tissue. It can be either a short transient mechanical force or an oscillatory force with a fixed frequency. A time-varying mechanical perturbation will propagate as mechanical waves, which in solid tissue can be compressional waves or shear waves.

Renal transplant assessment

Due to the more superficial location of the transplant kidney, chronic allograft injury can be potentially diagnosed using dynamic elastography techniques. It can be used to monitor allograft stiffness so that specifically patients with serial increase can be subjected to a biopsy before renal function deteriorates, instead of all patients undergoing routine protocol biopsies. It can also be used to monitor the effect of the treatment. However, subclinical rejection, infection, or recurrence of the underlying disease cannot be detected.[38]

Prostate elastography

Endorectal real-time elastography enables the diagnosis of prostate cancer with a reported accuracy of 76%.[39] Both quasistatic techniques and shear wave elastography have been used. Based on static qualitative elastographic findings, a prostate elastography scoring system has been proposed by Kamoi *et al*.[40] Scores 1 to 5 has been devised based on strain pattern and corresponding color map, score 1 indicating normal and score 5 definite carcinoma. Score 2 is "probably normal," score 3 is "indeterminate," and score 4 is "probably carcinoma."

Shear wave elastography generates both qualitative color-coded elastograms and quantitative maps [elasticity (kPa) or shear wave velocity (cm s^{-1})]. This method is more objective than strain elastography, and values of >37 kPa were found to represent prostate cancer. This cutoff produced a sensitivity of 96.0%, specificity of 96.0%, positive predictive value of 69.0%, and negative predictive value of 99.6%[41] [Figure 6].

Transrectal ultrasound elastography has multiple applications in the prostatic cancer, such as screening of prostate cancer, cancer detection and nodule characterization, biopsy guidance on the suspicious nodule at TRUS elastography, grading and staging of prostate cancer, therapy guidance, and monitoring therapeutic response by using serial elastographic measurements to detect interval change.[42]

Sonoelastography for the detection of the prostate carcinoma has been subject to inaccuracies. False positive results may be seen in a variety of conditions, such as prostatitis, calcification, hard nodule in benign prostate hypertrophy, periurethral central zone, and attenuation, and false negative results can be seen in small tumor, soft carcinoma, very large diffuse tumor, etc.[43]

A small single-center prospective study of 53 patients using shear wave elastography found excellent detection rates for cancer in the peripheral zone of prostate gland.[41] The elasticity for cancers ranged 30-110 kPa, with a mean value of 58.0 ± 20.7 kPa, whereas benign lesions had values ranging from 9-107 kPa, with a mean value of 21.5 ± 11.5 kPa.

The strain elastography is not considered for assessment of stiffness of renal tissue for two main reasons. First, the kidneys are usually located deeply in the body, making effective external compression difficult. Second, the abnormal tissue in the kidney cannot be compared to a

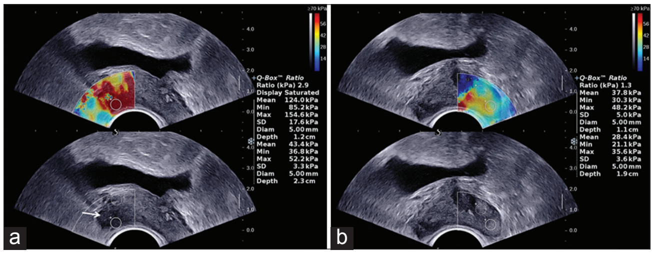

Figure 6: Paired TRUS elastography images (a- shear wave elastogram, top and b- B-mode image, bottom) showing hypoechoic lesion in the right posterolateral aspect of the prostate (arrow) (a) and a corresponding elastogram color map showing high stiffness (124 kPa) and was found to be prostate cancer on biopsy. Note the normal tissue on the left side (b) with uniform low stiffness (28-37 kPa)

normal tissue standard. An assessment of absolute stiffness of the tissue is required and quasistatic elastography does not provide quantitative data. The dynamic techniques like ARFI and supersonic shear imaging are more appropriate for renal evaluation because it is possible to selectively assess the cortex or the medulla, avoiding perirenal or sinus fat. Thus, ultrasound elastography is a rapidly evolving technique, with diverse potential clinical applications in clinical urology.

FUSION IMAGING

Fusion or hybrid imaging means combining images from different imaging modalities. It is now being used as a real-time, 3D visualization and navigation tool. The previously recorded CT, MRI, or positron emission tomography (PET)/CT dataset is transferred to the ultrasound system and a coregistration from external or internal markers is performed either static or real time. It improves diagnostic accuracy and guidance in prostatic biopsy procedures.[44] Here, the real-time capability of ultrasonography is retained while biopsying the targets that are better seen on MRI [Figure 7]. Valerio M *et al.*[45] have done a systematic review of 14 papers reporting the outcomes of 15 studies comparing the detection rate of clinically significant prostate cancer with software-based MRI-ultrasound fusion targeted biopsy against standard biopsy. Detection of all cancers, sampling utility, efficiency, and rate of serious adverse events were compared. MRI-US (ultrasound) fusion targeted biopsies detected more clinically significant cancers (median: 33.3% vs 23.6%; range: 13.2-50% vs 4.8-52%) using fewer cores (median: 9.2 vs 37.1) compared with standard biopsy techniques respectively. Some clinically significant cancers that would have been missed by using only standard biopsy were detected by targeted biopsy (median: 9.1%; range: 5-16.2%). Siddiqui *et al.*[46] compared standard 12-core biopsy and targeted MRI/US-fusion biopsy of the prostate showed that addition of targeted biopsy upgraded Gleason score in 32% of cases, compared to standard extended 12-core biopsy alone. In addition, targeted biopsy preferentially detected higher-grade prostate cancer while missing low-grade tumors. Thus, targeted biopsies using fusion imaging are

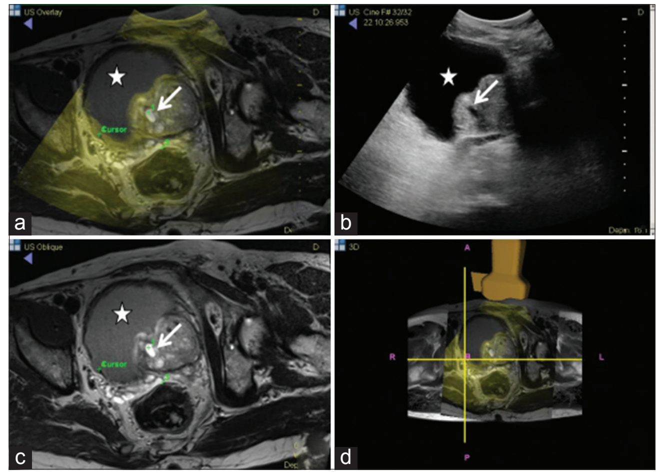

Figure 7: Fusion imaging of prostate: T2-weighted axial MRI image (a) and the corresponding ultrasound image (b) showing a focal cystic area in enlarged prostate (arrow) projecting into base of the urinary bladder (star) and the corresponding overlay image (c) and 3D display (d)

more accurate than systematic biopsies using ultrasound alone in diagnosing prostate cancer.

FORTHCOMING ADVANCES

Many forthcoming advances in ultrasound imaging under evaluation are likely to be available for clinical applications in the near future. Noteworthy among them are the following:

Capacitative micromachined ultrasonic transducers

These are transducers constructed of new materials such as silicon wafers rather than piezoelectric crystals.[47] It is anticipated that this technology will allow one single transducer head to generate multiple frequencies and wavelengths, eliminating the need to use several transducers during an examination.

HistoScanning

It is an ultrasound-based software program for tissue characterization. This 3D ultrasound imaging technology utilizes the raw data usually obtained by the use of backscattered ultrasound, to detect and visualize prostate cancer. HistoScanning has shown encouraging results in the detection of clinically significant prostate cancer.[48]

CONCLUSION

Ultrasonography is an integral part of the diagnostic armamentarium in the practice of modern urology. Ultrasound technology and its applications for urologic disease continue to evolve. These advances continue to play an important role in the characterization of cystic lesions, detecting contrast enhancement, vascularity of focal lesions, and real-time guidance of biopsies. The multidimensional imaging techniques of ultrasound have now made it possible to achieve improved understanding of detailed spatial relationships, which was previously possible only with CT and MRI.

REFERENCES

1. Desser TS, Jeffrey RB. Tissue harmonic imaging techniques: Physical principles and clinical applications. Semin Ultrasound CT MR 2001;22:1-10.
2. Sodhi KS, Sidhu R, Gulati M, Saxena A, Suri S, Chawla Y. Role of tissue harmonic imaging in focal hepatic lesions: Comparison with conventional sonography. J Gastroenterol Hepatol 2005;20:1488-93.
3. Choudhry S, Gorman B, Charboneau JW, Tradup DJ, Beck RJ, Kofler JM, *et al*. Comparison of tissue harmonic imaging with conventional US in abdominal disease. Radiographics 2000;20:1127-35.
4. Mitterberger M, Pinggera GM, Pallwein L, Gradl J, Feuchtner G, Plattner R, *et al*. Plain abdominal radiography with transabdominal native tissue harmonic imaging ultrasonogarphy vs unenhanced computed tomography in renal colic. BJU Int 2007;100:887-90.
5. Mohammed A, Sandhu MS, Lal A, Sodhi KS, Sud K, Kohli HS. Role of tissue harmonic imaging in characterization of cystic renal lesions. Saudi Med J 2008;29:1769-74.
6. Schmidt T, Hohl C, Haage P, Blaum M, Honnef D, Weibeta C, *et al*. Diagnostic accuracy of phase-inversion tissue harmonic imaging versus fundamental B-mode sonography in the evaluation of focal lesions of the kidney. AJR Am J Roentgenol 2003;180:1639-47.
7. Harvey CJ, Pilcher JM, Eckersley RJ, Blomley MJ, Cosgrove DO. Advances in ultrasound. Clin Radiol 2002;57:157-77.
8. Heynemann H, Jenderka KV, Zacharias M, Fornara P. New techniques in uro-sonography. Urologe A 2004;43:1362-70.
9. Quaia E. Radiological Imaging of the Kidney: Ultrasound of the Kidney. Berlin, Heidelberg: Springer-Verlag; 2011.
10. Bertolotto M, Perrone R, Bucci S, Zappetti R, Coss M. Comparison of conventional ultrasound and real-time spatial compound imaging in evaluation of patients with severe Peyronie's disease. Acta Radiol 2008;49:596-601.
11. Oktar SO, Yücel C, Ozdemir H, Ulutürk A, Işik S. Comparison of conventional sonography, real-time compound sonography, tissue harmonic sonography, and tissue harmonic compound sonography of abdominal and pelvic lesions. AJR Am J Roentgenol 2003;181:1341-7.
12. Downey DB, Fenster A, Williams JC. Clinical utility of three-dimensional US. Radiographics 2000;20:559-71.
13. Mitterberger M, Pinggera GM, Neuwirt H, Maier E, Akkad T, Strasser H, *et al*. Three-dimensional ultrasonography of the urinary bladder: Preliminary experience of assessment in patients with haematuria. BJU Int 2007;99:111-6.
14. Kocakoc E, Kiris A, Orhan I, Poyraz AK, Artas H, Firdolas F. Detectoin of bladder tumors with 3-dimensional sonography and virtual sonographic cystoscopy. J Ultrasound Med 2008;27:45-53.
15. Brannigan M, Burns PN, Wilson SR. Blood flow patterns in focal liver lesions at microbubble-enhanced US. Radiographics 2004;24:921-35.
16. Correas JM, Bridal L, Lesavre A, Méjean A, Claudon M, Hélénon O. Ultrasound contrast agents: Properties, principles of action, tolerance, and artifacts. Eur Radiol 2001;11:1316-28.
17. Leen E. The role of contrast-enhanced ultrasound in the characterisation of focal liver lesions. Eur Radiol 2001;11(Suppl 3):E27-34.
18. Gerst S, Hann LE, Li D, Gonen M, Tickoo S, Sohn MJ, *et al*. Evaluation of renal masses with contrast-enhanced ultrasound: Initial experience. AJR Am J Roentgenol 2011;197:897-906.
19. Lu Q, Huang BJ, Wang WP, Li CX, Xue LY. Qualitative and quantitative analysis with contrast-enhanced ultrasonography: Diagnosis value in hypoechoic renal angiomyolipoma. Korean J Radiol 2015;16:334-41.
20. Clevert DA, Minaifar N, Weckbach S, Jung EM, Stock K, Reiser M, *et al*. Multislice computed tomography versus contrast-enhanced ultrasound in evaluation of complex cystic renal masses using the Bosniak classification system. Clin Hemorheol Microcirc 2008;39:171-8.
21. Park BK, Kim B, Kim SH, Ko K, Lee HM, Choi HY. Assessment of cystic renal masses based on Bosniak classification: Comparison of CT and contrast-enhanced US. Eur J Radiol 2007;61:310-4.
22. Ascenti G, Mazziotti S, Zimbaro G, Settineri N, Magno C, Melloni D, *et al*. Complex cystic renal masses: Characterization with contrast-enhanced US. Radiology 2007;243:158-65.
23. Malhi H, Grant EG, Duddalwar V. Contrast-enhanced ultrasound of the liver and kidney. Radiol Clin North Am 2014;52:1177-90.
24. Quaia E, Bertolotto M, Cioffi V, Rossi A, Baratella E, Pizzolato R, *et al*. Comparison of contrast-enhanced sonography with unenhanced sonography and contrast-enhanced CT in the diagnosis of malignancy in complex cystic renal masses. AJR Am J Roentgenol 2008;191:1239-49.
25. Oh TH, Lee YH, Seo IY. Diagnostic efficacy of contrast-enhanced ultrasound for small renal masses. Korean J Urol 2014;55:587-92.
26. Nicolau C, Buñesch L, Paño B, Salvador R, Ribal MJ, Mallofré C, *et al*. Prospective evaluation of CT indeterminate renal masses using US and contrast-enhanced ultrasound. Abdom Imaging 2015;40:542-51.
27. Bertolotto M, Martegani A, Aiani L, Zappetti R, Cernic S, Cova MA. Value of contrast-enhanced ultrasonography for detecting renal infarcts proven by contrast enhanced CT. A feasibility study. Eur Radiol 2008;18:376-83.
28. Papadopoulou F, Anthopoulou A, Siomou E, Efremidis S, Tsamboulas C, Darge K. Harmonic voiding urosonogarphy with a second-generation contrast agent for the diagnosis of vesicoureteral reflux. Pediatr Radiol 2009;39:239-44.
29. Kis E, Nyitrai A, Várkonyi I, Máttyus I, Cseprekál O, Reusz G, *et al*. Voiding urosonography with second-generation contrast agent versus voiding cystourethrography. Pediatr Nephrol 2010;25:2289-93.
30. Papadopoulou F, Ntoulia A, Siomou E, Darge K. Contrast-enhanced voiding urosonography with intravesical administration of a second-generation ultrasound contrast agent for diagnosis of vesicoureteral reflux: Prospective evaluation of contrast safety in 1,010 children. Pediatr Radiol 2014;44:719-28.
31. Darge K, Heidemeier A. Modern ultrasound technologies and their application in pediatric urinary tract imaging. Radiologe 2005;45:1101-11.
32. Drudi FM, Di Leo N, Malpassini F, Antonini F, Corongiu E, Iori F. CEUS in the differentiation between low and high-grade bladder carcinoma. J Ultrasound 2012;15:247-51.
33. Halpern EJ, McCue PA, Aksnes AK, Hagen EK, Frauscher F, Gomella LG. Contrast-enhanced US of the prostate with Sonazoid: Comparison with whole-mount prostatectomy specimens in 12 patients. Radiology 2002;222:361-6.
34. Pelzer A, Bektic J, Berger AP, Pallwein L, Halpern EJ, Horninger W, *et al*. Prostate cancer detection in men with prostate specific antigen 4 to 10 ng/ml using a combined approach of contrast enhanced color Doppler targeted and systematic biopsy. J Urol 2005;173:1926-9.
35. Halpern EJ, Ramey JR, Strup SE, Frauscher F, McCue P, Gomella LG. Detection of prostate carcinoma with contrast-enhanced sonography using intermittent harmonic imaging. Cancer 2005;104:2373-83.
36. Hoeffel C, Pousset M, Timsit MO, Elie C, Méjean A, Merran S, *et al*. Radiofrequency ablation of renal tumours: Diagnostic accuracy of contrast-enhanced ultrasound for early detection of residual tumour. Eur Radiol 2010;20:1812-21.
37. Meloni MF, Bertolotto M, Alberzoni C, Lazzaroni S, Filice C, Livraghi T, *et al*. Follow-up after percutaneous radiofrequency ablation of renal cell carcinoma: Contrast-enhanced sonography versus contrast-enhanced CT or MRI. AJR Am J Roentgenol 2008;191:1233-8.
38. Arndt R, Schmidt S, Loddenkemper C, Grünbaum M, Zidek W, van der Giet M, *et al*. Noninvasive evaluation of renal allograft fibrosis by transient elastography--a pilot study. Transpl Int 2010;23:871-7.
39. Ginat DT, Destounis SV, Barr RG, Castaneda B, Strang JG,

Rubens DJ. US elastography of breast and prostate lesions. Radiographics 2009;29:2007-16.
40. Kamoi K, Okihara K, Ochiai A, Ukimura O, Mizutani Y, Kawauchi A, *et al*. The utility of transrectal real-time elastography in the diagnosis of prostate cancer. Ultrasound Med Biol 2008;34:1025-32.
41. Barr RG, Memo R, Schaub CR. Shear wave ultrasound elastography of the prostate: Initial results. Ultrasound Q 2012;28:13-20.
42. Correas JM, Tissier AM, Khairoune A, Khoury G, Eiss D, Hélénon O. Ultrasound elastography of the prostate: State of the art. Diagn Interv Imaging 2013;94:551-60.
43. Dudea SM, Giurgiu CR, Dumitriu D, Chiorean A, Ciurea A, Botar-Jid C, *et al*. Value of ultrasound elastography in the diagnosis and management of prostate carcinoma. Med Ultrason 2011;13:45-53.
44. Ewertsen C, Săftoiu A, Gruionu LG, Karstrup S, Nielsen MB. Real-time image fusion involving diagnostic ultrasound. AJR Am J Roentgenol 2013;200:W249-55.
45. Valerio M, Donaldson I, Emberton M, Ehdaie B, Hadaschik BA, Marks LS, *et al*. Detection of clinically significant cancer using magnetic resonance imaging-ultrasound fusion targeted biopsy: A systematic review. Eur Urol 2014. [Epub ahead of print].
46. Siddiqui MM, Rais-Bahrami S, Truong H, Stamatakis L, Vourganti S, Nix J, *et al*. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer versus systematic 12-core transrectal ultrasound biopsy. Eur Urol 2013;64:713-9.
47. Ergun AS, Huang Y, Zhuang X, Oralkan O, Yaralioglu GG, Khuri-Yakub BT. Capacitive micromachined ultrasonic transducers: Fabrication technology. IEEE Trans Ultrason Ferroelectr Freq Control 2005;52:2242-58.
48. Simmons LA, Autier P, Zát'ura F, Braeckman J, Peltier A, Romic I, *et al*. Detection, localisation and characterisation of prostate cancer by prostate HistoScanning(™). BJU Int 2012;110:28-35.

How to cite this article: Lal A, Naranje P, Pavunesan SK. What's new in urologic ultrasound?. Indian J Urol 2015;31:176-84.

Source of Support: Nil, **Conflict of Interest:** None declared.