# Clinical value of multi-parametric ultrasound and MRI/US fusion-guided biopsy for prostate cancer detection and visualization

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## Introduction

In Germany, most primary prostate biopsies are performed by urologists using transrectal ultrasound (TRUS) when elevated levels of prostate-specific antigen (PSA) were measured or after a suspicious digital rectal examination. The guidelines of the European Urological Association (EAU) for prostate cancer (PCa) recommend multiparametric magnetic resonance imaging (mpMRI) after initial negative prostate biopsy and indication for a re-biopsy as well as in active surveillance candidates (1). The most common mpMRI sequences are T2-weighted scans (T2w) followed by diffusion weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE) (2). Currently, the number of MR-guided biopsies appears to be decreasing due to costs while the number of MRI/USfusion-guided biopsies is increasing. However, MRI-guided biopsy techniques and MRI/ultrasound fusion biopsy have not yet been evaluated in direct comparison with regard to preparation and examination time, cost, and diagnostic accuracy (3).

## Pitfalls of traditional transrectal ultrasound-guided biopsy

According to the frequently cited prospective European Prostate Cancer Detection Study the initial cancer detection rate using TRUS-guided prostate biopsy was 22 % with even lower detection rates in repeat biopsies (4). While many clinically not relevant tumors are detected, reliable detection of clinically relevant tumors is not ensured. Gleason upgrading after prostatectomy and postoperatively identified high-risk PCa are potential risks due to the lack of information provided by TRUS-guided biopsy – risks that can be reduced by MRI/US fusion-guided biopsy (5, 6).

## MRI/US fusion-guided biopsy

The MRI/US fusion-guided biopsy set-up usually includes a magnetic field generator placed closely to the patient, a transrectal transducer with a fusion-position sensor attached to the US probe and a core biopsy instrument.

The mpMRI data are loaded to the US system (Aplio 500) via the DICOM network or a DVD and the live US image is linked with the MR image by Smart Fusion following a few simple steps. Re-registration if required can easily be performed. The image quality for both MRI and US in Smart Fusion mode has significantly improved through new technical developments. The most recent Aplio version offers enhanced features such as switching between different MRI sequences in just a few seconds which facilitates visualization of different MR information during MRI/US fusion, resulting in an optimized workflow and increased diagnostic accuracy.

We perform a contrast-enhanced ultrasound (CEUS) before biopsy to assess the size and vascular architecture of the targeted lesion which simplifies biopsy planning. After CEUS the US probe is re-registered, and anatomical markers are positioned including the target lesion. The biopsy needle can be visualized during real-time

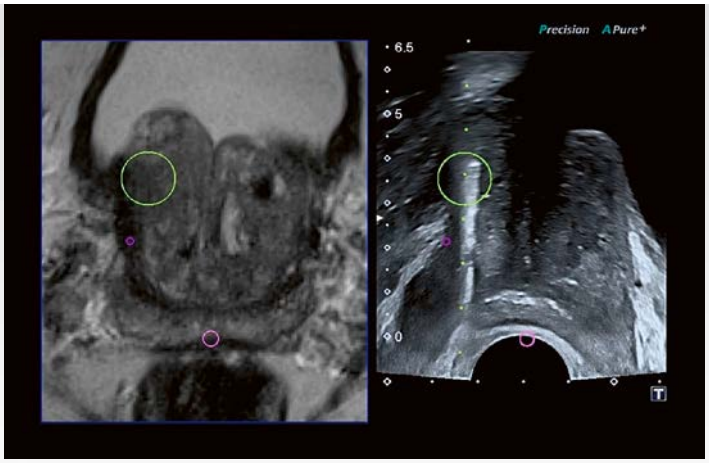


Fig. 1: MRI-US fusion guided biopsy. Left image: MRI, T2w axial. Right image: Realtime US image with biopsy.

fusion with an exellentmatch between MR and US image. Overall examination time for this procedure should be approximately 15 minutes.

In addition to the standard 12-core biopsy of the prostate, usually not more than two targeted biopsies are performed in order to minimize the total number of samples taken. Fig. 1 shows a tiny hypodense lesion on the T2w MR image and a small hypoechoic lesion on the US image that could be correlated during SmartFusion; a successful biopsy was performed.

The combination of MRI/US fusion-guided biopsy and multi-parametric ultrasound (mpUS), recently described by Maxeiner et al. (7), has been shown to be useful and highly effective for PCa detection. A novel mpUS-based scoring system for PCa prediction similar to the Prostate Imaging Reporting and Data System (PI-RADS) used for MRI findings to predict tumor aggressiveness was developed and evaluated.

A semiquantitative score, comparable to the PI-RAD system (8), was applied using an analog scale of 1 (clinically significant disease is highly unlikely to be present), 2 (clinically significant cancer is equivocal) and 3 (clinically significant cancer is highly likely to be present) for every single US modality. The mpUS performed on the ultrasound Aplio system included the following modalities: B-mode imaging, tissue Doppler imaging (TDI) for contour detection of the target or strain elastography for relative stiffness, power Doppler for tumor vascularity, and CEUS before and after the biopsy to quantify contrast inflow and peak enhancement (Fig. 2).

The study mentioned above was performed at Charité University Hospital in Berlin. In 71 (42 %) out of 169 patients with at least one negative previous biopsy PCa was detected. 46 of these 71 patients had a clinically significant PCa (Gleason score ≥ 7) and 31 of those were exclusively detected by MRI-US fusion (67.4 %). The highest sensitivity was observed in CEUS (85 %) and elastography (80 %).

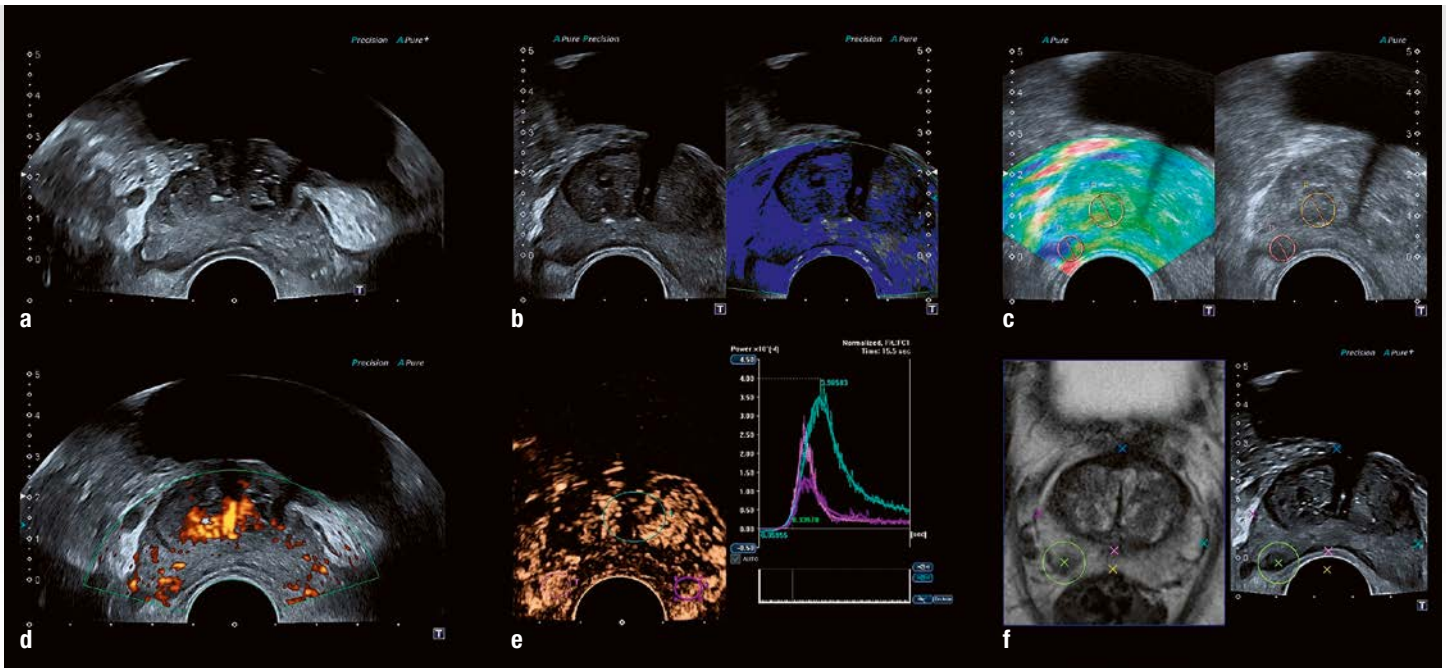


Fig. 2 (a–f): Example of the mpUS scoring system: 2 points in B-mode (a), 3 points in TDI or strain elastography (b & c) based on significant stiffness, 3 points in power Doppler (d) due to high vascularization and 2 points in CEUS (e) based on perfusion information. These results translated into a high mpUS score which indicated a clinically significant PCa. In this particular case MR/US fusion-guided biopsy into the marked region (f) yielded a high-grade Gleason of 4+4=8.

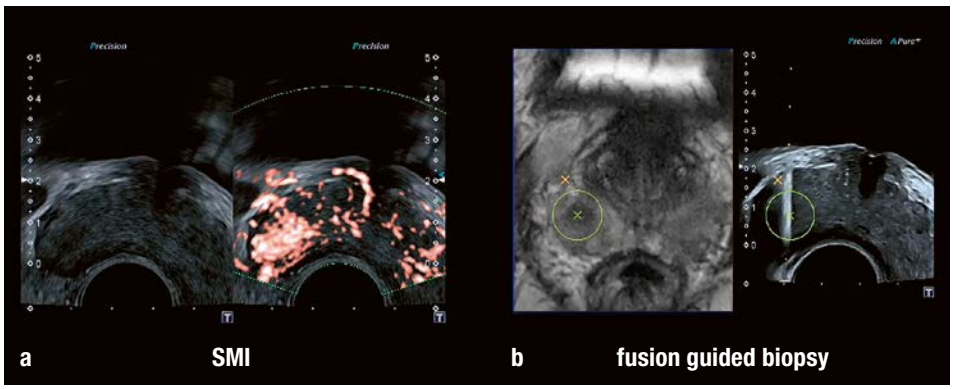


Fig. 3 (a–b): cSMI with contrast enhancement in dual-screen mode simultaneously with the corresponding B-mode image (a) and the MRI/US-fusion guided biopsy (b) of the lesion identified in (a).

## Update on Aplio 500 Platinum series for MRI/US fusion-guided biopsy

Superb Microvascular Imaging (SMI) technology was introduced on the Aplio Platinum Series to enable visualization of tiny low-flow vessels with high resolution and high frame rate. In a recent software upgrade SMI with a low mechanical index (MI) for the use with contrast agents was introduced (Fig. 3) which offers faster assessment of aggressive lesions and targeted mass size with perfusion information enhancing biopsy planning and guidance. In addition, shear wave elastography (SWE) with Propagation Mapping became available recently for prostate applications to quantitatively assess tissue elasticity in kPa or via shear wave propagation velocity in m/s (Fig. 4).

## Case 1

A 75-year-old patient who underwent trans-urethral resection of the prostate (TUR-P) was admitted for mpMRI of the prostate based on rising PSA from initially 2.4 ng/ml to 7 ng/ml. Digital rectal examination of a small gland was suspicious at the right lateral lobe. The MRI showed a suspicious area with a diameter of 10 mm and an overall PI-RADS Score 4, indicating a 70 % likelihood of prostate cancer (Fig. 5).

Before biopsy an mpUS (Fig. 6) and an US examination in fusion mode (Fig. 7) was performed.

During biopsy (Fig. 8) the defect of the TUR-P could be seen at the center of the gland. The final histopathological result reported a Gleason score of 4+4=8.

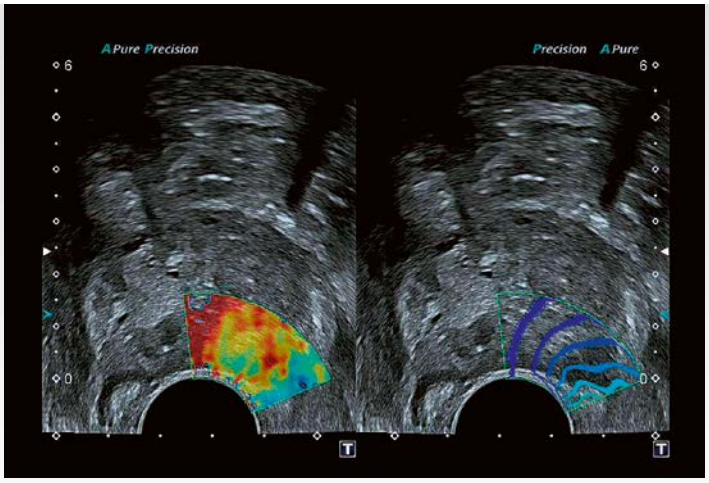


Fig. 4: Shear wave elastography of the prostate (left image) with a zone of elevated stiffness (red area) and the corresponding propagation map (right image) indicating the quality of the shear wave propagation related to the reliability of the measurement.

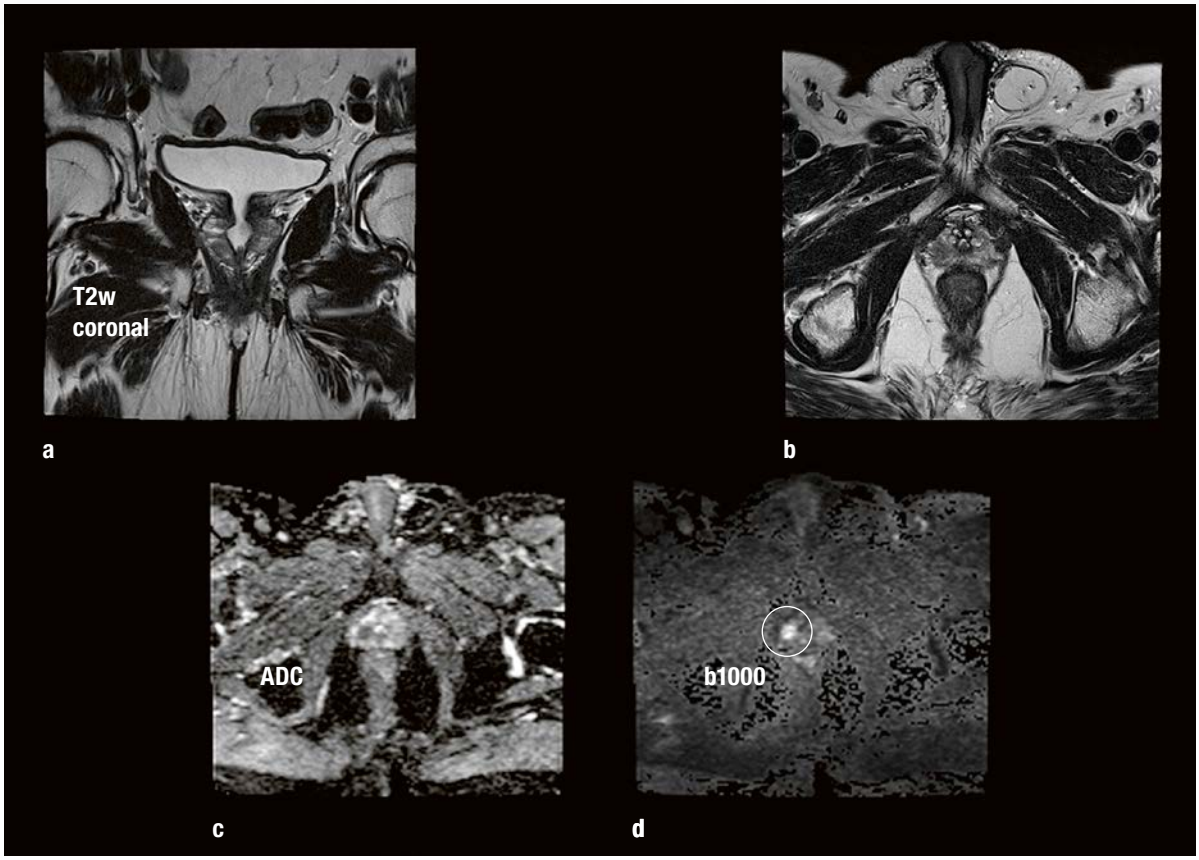


Fig. 5 (a–d): T2w MRI in coronal (a) and axial (b) orientation, and DWI (c) corresponding ADC mapping (d) both in axial orientation.

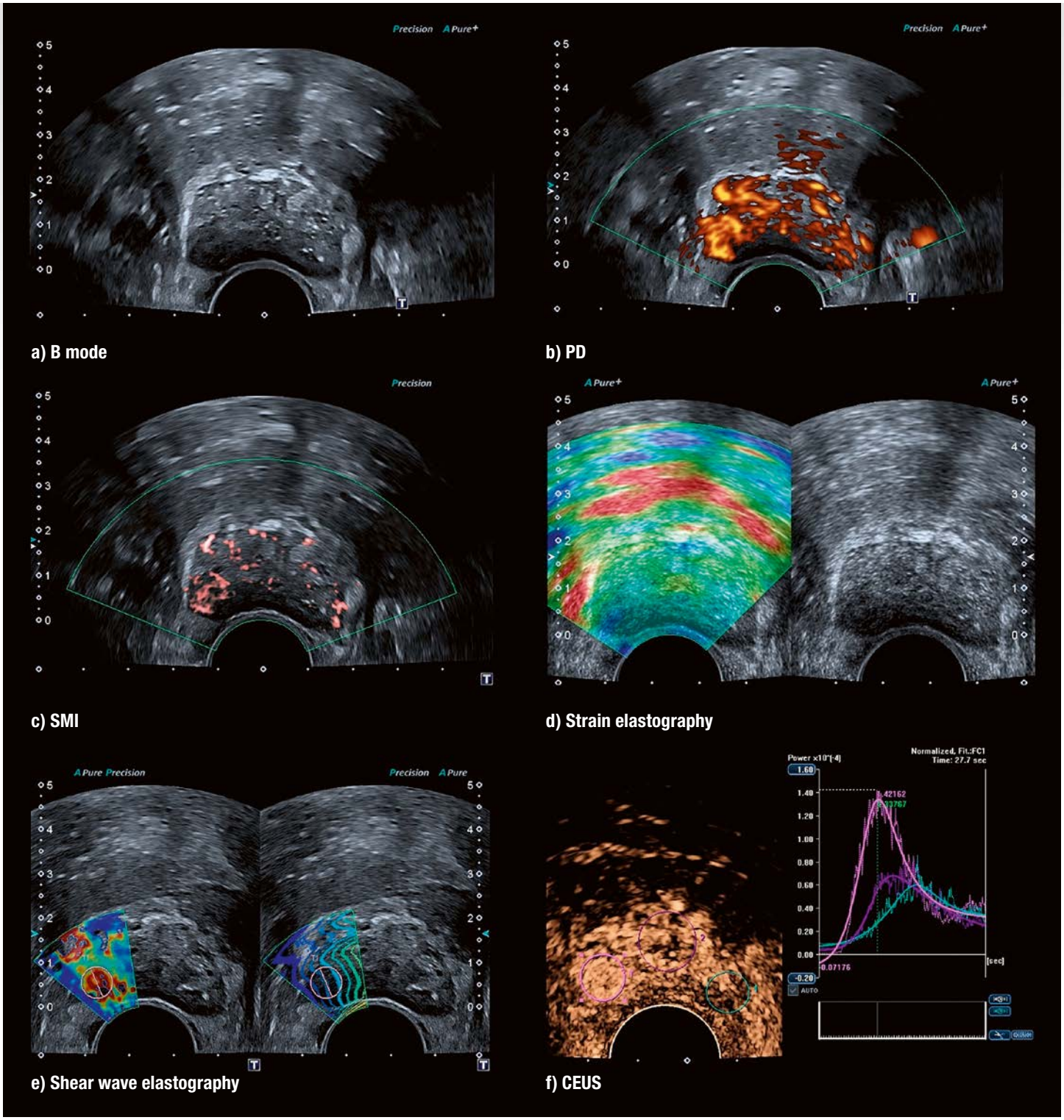


Fig. 6 (a–f): mpUS of the prostate.The tumor could hardly be visualized in B-mode (a), but PD (b) and even stronger SMI (c) showed increased vascularity, and especially smaller vessels could be easily visualized. Strain imaging (d) showed an increased relative stiffness (blue area), and shear wave elastography detected a “hard” lesion (red area) with an elasticity reading of 108 kPa. During CEUS (f) early wash-in could be observed with higher peak enhancement within the targeted region compared to the rest of the prostate tissue.

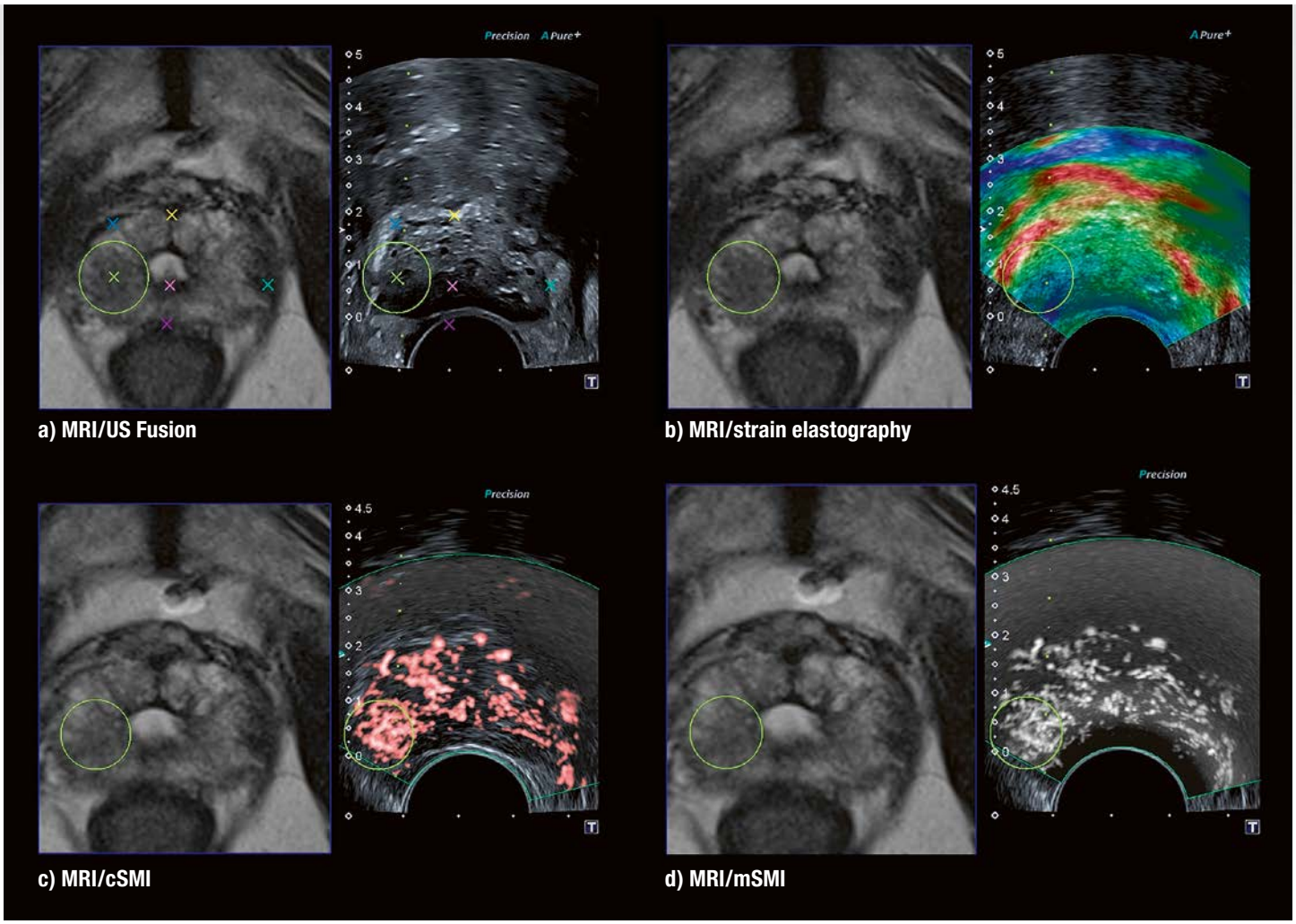


Fig. 7 (a–d): MRI/US fusion mode. The B-mode image (a) didn't show a specific change in echogenicity in the corresponding area, however, strain elastograhy showed a clear blue spot well correlated to the suspicious region in MRI, the fatty tissue of the capsule is displayed in red (soft area) (b). With contrast enhanced SMI postprocessed with an accumulation technique based on cSMI (c) and mSMI (d) the perfusion of the area is clearly demonstrated and the nature of vascular architecture and typical feeding vessels can be assessed indicating neoangenesis.

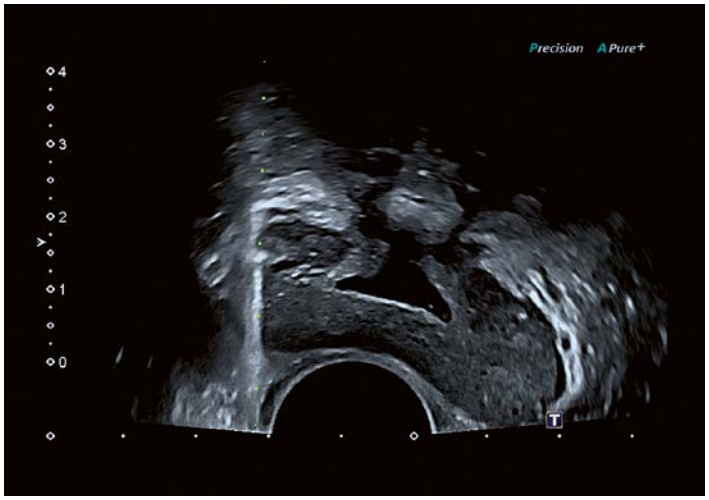

Fig. 8: Targeted biopsy of the prostate after mpUS.

## Case 2

A 70-year-old patient presented with one previous negative biopsy and an increased PSA from initially 5.0 ng/ml to 11.6 ng/ml. mpMRI detected a large lesion of 25 x 15 x 10 mm and an overall PIRADS Score 5. The digital rectal examination revealed an enlarged prostate with no significant indication for PCa. The prostate was assessed with US prior to biopsy (Fig. 9).

MRI/US fusion provided detailed information of the potential tumor (Fig. 10) and a targeted MRI/US fusion guided biopsy was performed (Fig. 11) followed by a random 12-core biopsy according to EAU guidelines for PCa.

## Conclusion

Our study confirmed that MRI/US fusion-guided biopsy detects more clinically significant PCa than conventional TRUS-guided biopsy. Using a novel mpUS scoring system, PI-RADS predefined tumor aggressiveness can be confirmed and localization and biopsy planning can be significantly improved. Recent SW upgrades of the Aplio system provide enhanced image quality of MR and US images in combination with multiple US modes such as CEUS, strain elastography, shear wave elastography, and SMI with or without contrast enhancement for a seamless workflow with high diagnostic confidence during MRI/US fusion-guided biopsy.

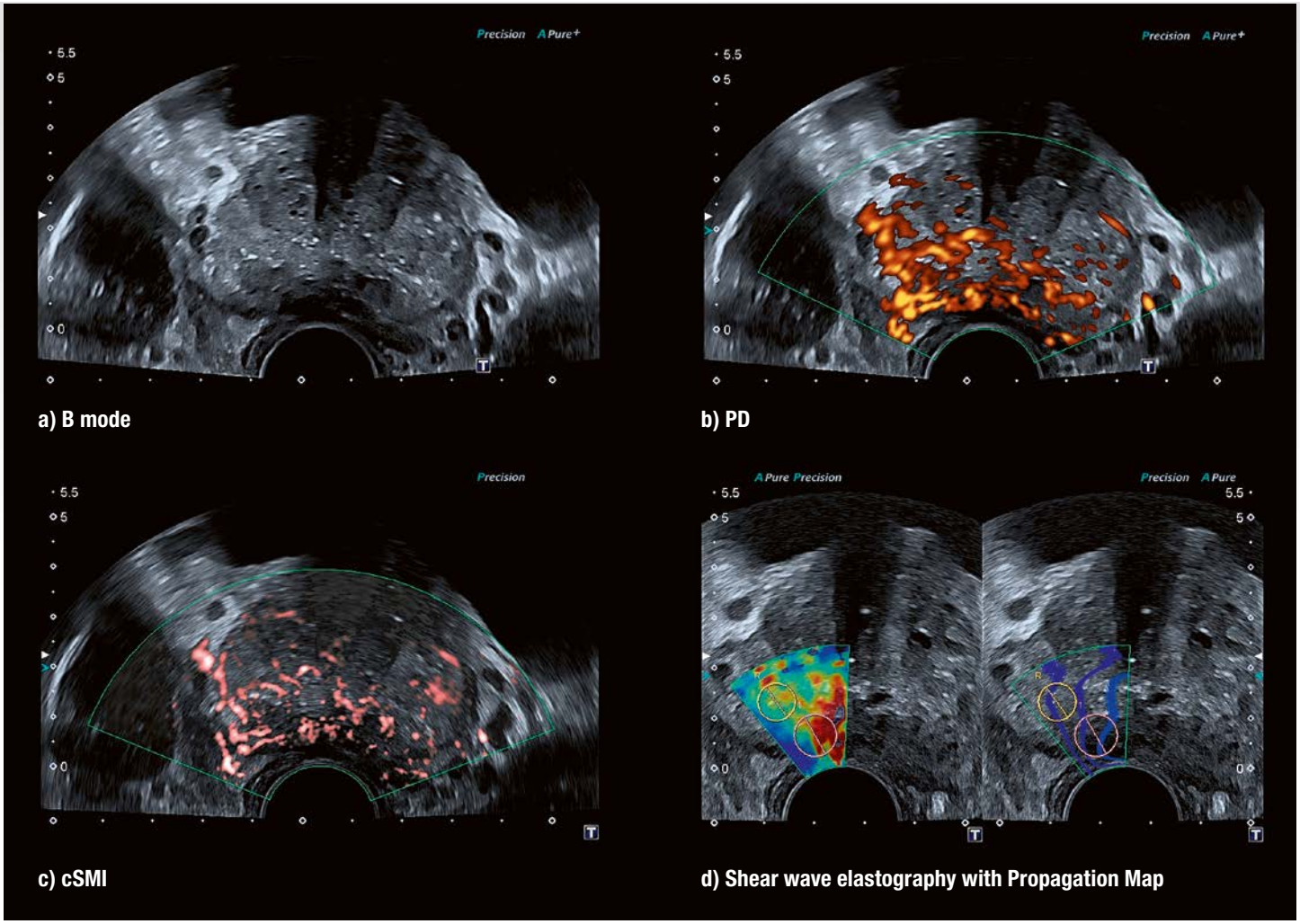


Fig. 9 (a–d): US assessment of the prostate: An area of lower echogenicity in B-mode (a) showed during Doppler evaluation with PD (a) and especially with SMI (b) a high peripheral vascularity. An elasticity value of 90 kPa within the area of interest was recorded by shear wave elastography (c).

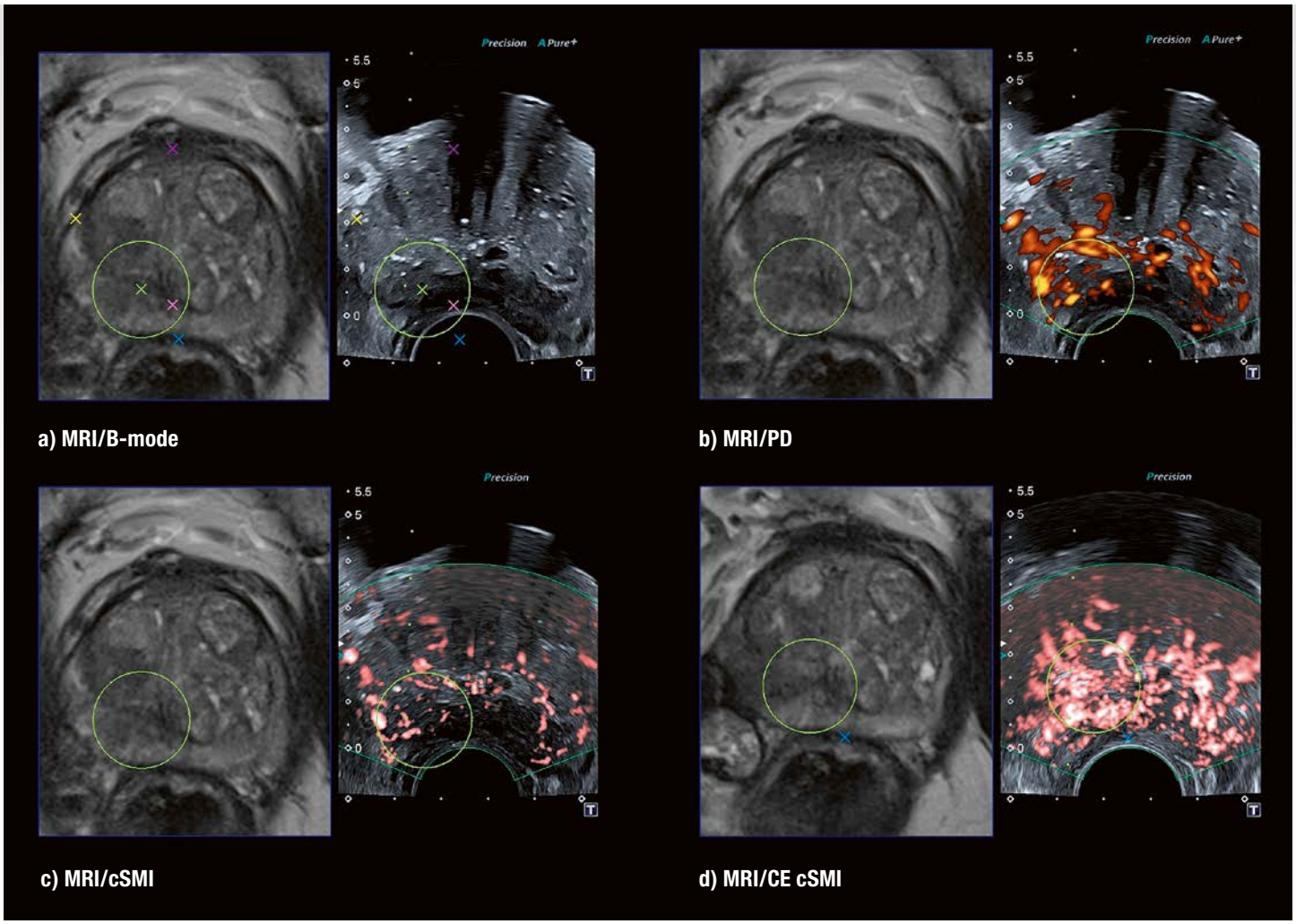


Fig. 10 (a–d): US assessment in MRI/US fusion mode: B-mode (a) and PD (b). During the combined performance of SMI (c) and contrast enhanced SMI (d) exact perfusion information with sharp outlines could be obtained.

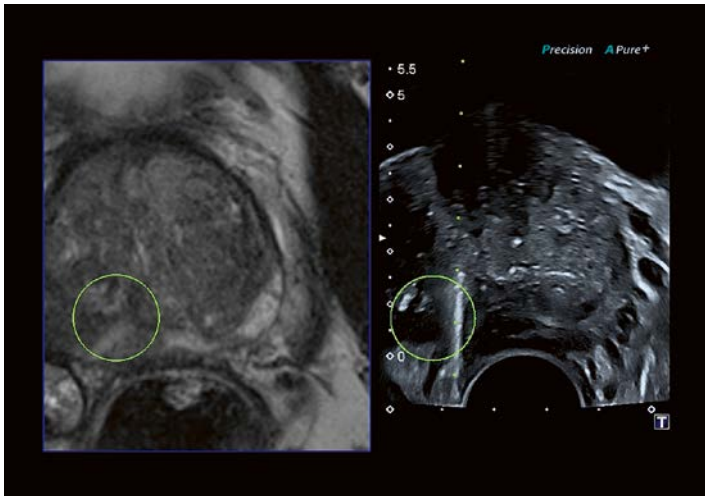

Fig. 11: Targeted MRI/US fusion-guided biopsy.

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