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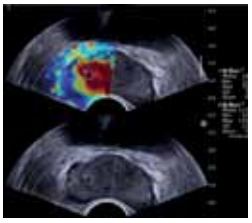
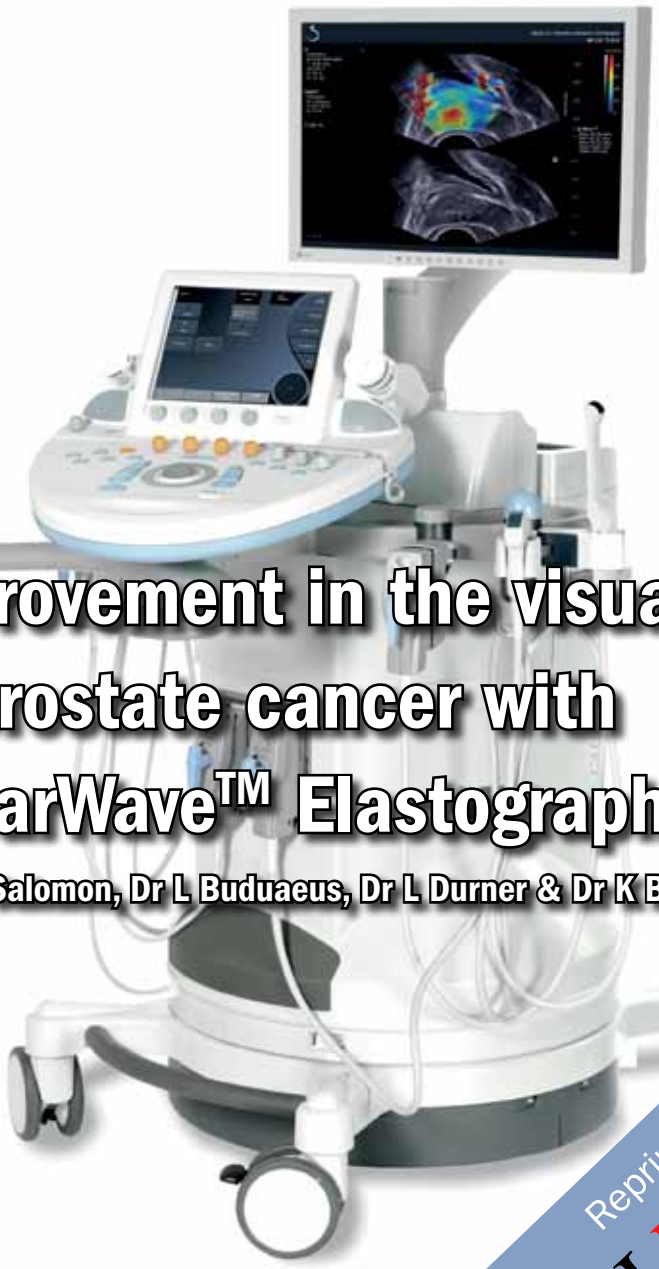


Elastography has been shown to improve visualization of prostate cancer. The innovative ShearWave™ Elastography technique is an automated, user-friendly and quantifiable method for the determination of prostatic tissue stiffness.



Improvement in the visualization of prostate cancer with ShearWave™ Elastography

by Dr G Salomon, Dr L Buduaeus, Dr L Durner & Dr K Boehm

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Improvement in the visualization of prostate cancer through the use of ShearWave™ Elastography

Prostate cancer is the most common cancer in males with more than 910,000 annual cases worldwide.

With early detection, excellent cure rates can be achieved. Today, prostate cancer is diagnosed by a randomized transrectal ultrasound guided biopsy. However, such randomized "blind" biopsies can miss cancer because of the inability of conventional TRUS to visualize small cancerous spots in most cases.

Elastography has been shown to improve visualization of prostate cancer. The innovative ShearWave Elastography technique is an automated, user-friendly and quantifiable method fore the determination of prostatic tissue stiffness.

The detection of prostate cancer (PCA) has become easier thanks to Prostate Specific Antigen (PSA) testing; the diagnosis of PCA has been shifted towards an earlier stage of the disease. Prostate cancer is, in more than 80 % of the cases, a heterogeneous and multifocal tumor. Conventional ultrasound has limitations to accurately define tumor foci within the prostate. This is due to the fact that most PCA foci are isoechogenic, so in these cases there is no differentiation of benign and malignant tissue. Because of this, a randomized biopsy is performed under ultrasound guidance with at least 10 to 12 biopsy cores, which should represent all areas of the prostate. Tumors, however, can be missed by this biopsy regimen since it is not a lesion-targeted biopsy. When PSA is rising — which usually occurs in most men — the originally negative biopsy has to be repeated.

The Authors :

Dr Georg Salomon[1], **Dr Lars Budaeus**[1], **Dr L Durner** [2] & **Dr K Boehm**[1]

1. Martini-Clinic – Prostate Cancer Center
University Hospital Hamburg Eppendorf
Martinistrasse 52
20253 Hamburg
Germany

2. Urologische Klinik Dr. Castringius München-Planegg
Germeringer Str. 32
82152 Planegg
Germany

Corresponding author: PD Dr. Georg Salomon
Associate Professor of Urology
Martini Clinic
Tel: 0049 40 7410 51300
gsalomon@uke.de

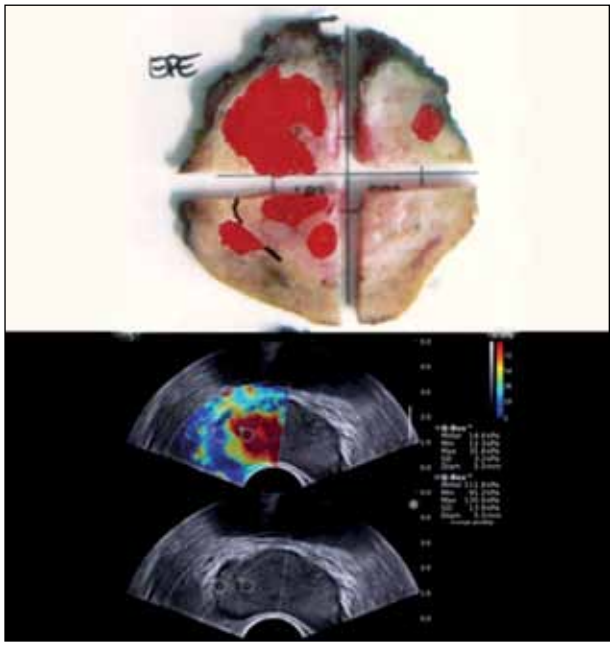

FIGURE 1. (Case #1): Huge area of hard tissue in the mid-right prostate, high suspicion of extracapsular penetration. Highly suspicious (kPascal value 111). Suspicious areas in SWE (red areas) correlate well with final histopathological whole mount of the prostate.
Patient data. Age 65 years. PSA: 45 ng/mL. DRE: suspicious on the left side. Final histopathological result: pT3a, N0, R0 (left anterior extracapsular extension).

What urologists expect from imaging and biopsy procedures is the detection of prostate cancer at an early stage and an accurate description of all foci within the prostate with different (Gleason) grades of differentiation for best treatment options.

In the past 10 years a couple of new innovative ultrasound techniques (computerized, contrast enhanced and real time elastography) have been introduced to the market and their impact on the detection of early prostate cancer has been evaluated.

The major benefit of elastography compared to the other techniques is its ability to provide visualization of suspicious areas and to guide the biopsy needle, in real time, to the suspicious and potentially malignant area.

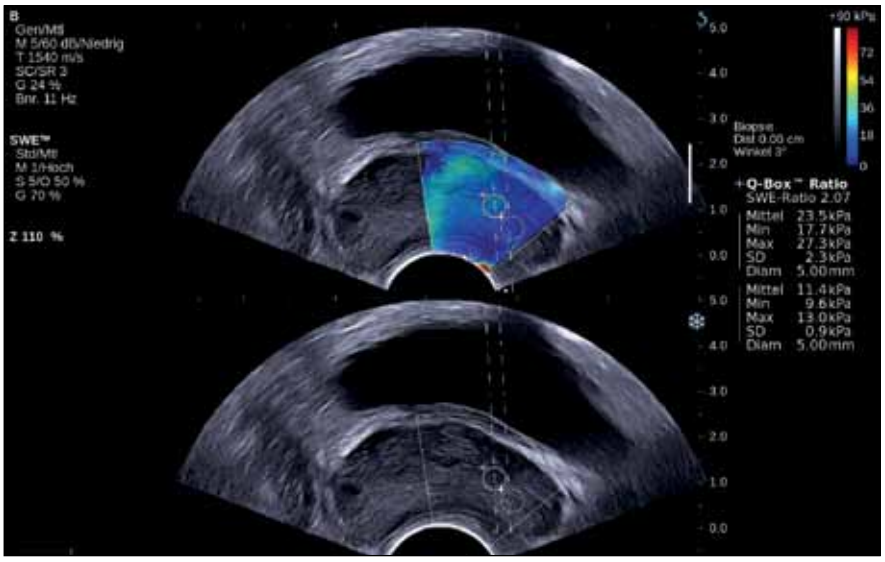

FIGURE 2. (Case #2): Mid-left side of the Prostate. ShearWave Elastography shows no hard tissue and no evidence of tumor.
Patient data. Age: 69 years. PSA: 4.8 ng/mL. DRE: not suspicious. Number of previous negative biopsies: 3. Biopsy result: no cancer.

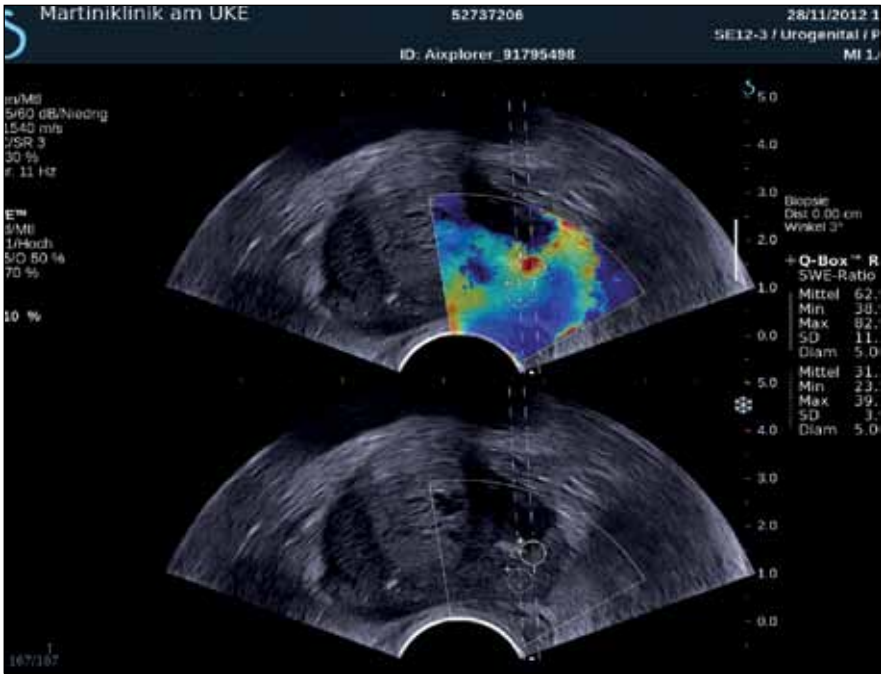

FIGURE 3. (Case #3): Mid-left side of the prostate: small hard suspicious tissue in the peripheral zone. (red, kPascal value: 62).
Patient data. Age: 67 years. PSA: 7.5 ng/mL. DRE: enlarged.
Number of previous negative biopsies: 2. Biopsy result: Gleason 3+4 in 10 out of 12 cores.
Radical prostatectomy: both sides nerve sparing (NeuroSafe).
Final histopathological result: pT2x Gleason 3+4, N0, R0.

Ultrasound-based elastography has been investigated over the years and has had a lot of success for increasing the detection rate of prostate cancer or reducing the number of biopsy samples required. [1-3]. Different companies have used different approaches to the ultrasound elastography technique (strain elastography vs. ShearWave Elastography). Medical centers have seen an evolution in better image quality with more stable and reproducible results from these techniques.

One drawback of real time strain elastography is that there is a significant learning curve to be climbed before reproducible elastograms can be generated. The technique has to be performed by compressing and then decompressing the ultrasound probe to derive a measurement of tissue displacement.

Today there are ultrasound scanners on the market, which have the ability to produce elastograms without this "manual" assistance: this technique is called ShearWave Elastography. While the ultrasound probe is being inserted transrectally, the "elastograms" are generated automatically by the calculation of shear wave velocity as the waves travel through the tissue being examined, thus providing measurements of tissue stiffness and not displacement measurements.

There are several different techniques for this type of elastography. The FibroScan system, which is not an ultrasound unit, uses shear waves (transient elastography) to evaluate the advancement of the stiffness of the liver. Another technique is Acoustic Radiation Force Impulse or ARFI technique, also used for the liver. These non real-time techniques only provide a shear wave velocity estimation for a single region of interest and are not currently used in prostate imaging.

A shear wave technology that provides specific quantification of tissue elasticity in real-time is ShearWave Elastography, developed by SuperSonic Imagine. This technique measures elasticity in kilopascals and can provide visual representation of tissue stiffness over the entire region of interest in a color-coded map on the ultrasound screen. On a split screen the investigator can see the

conventional ultrasound B-mode image and the color-coded elastogram at the same time. This enables an anatomical view of the prostate along with the elasticity image of the tissue to guide the biopsy needle.

In short, ShearWave Elastography (SWE™) is a different elastography technique that can be used for several applications. It automatically generates a real-time, reproducible, fully quantifiable color-coded image of tissue elasticity.

QUANTIFICATION OF TISSUE STIFFNESS

Such quantification can help to increase the chance that a targeted biopsy is positive for cancer.

It has been shown that elastography-targeted biopsies have an up to 4.7 times higher chance to be positive for cancer than a randomized biopsy [4]. ShearWave Elastography can not only visualize the tissue stiffness in color but also quantify (in kPa) the stiffness in real time, for several organs including the prostate. Correas *et al.* reported that with tissue stiffness higher than 45 to 50 kPa the chance of prostate cancer is very high in patients undergoing a prostate biopsy. The data from Gorreas *et al* showed a sensitivity of 80 % and a high negative predictive value of up to 90%. Another group (Barr *et al.*) achieved a negative predictive value of up to 99.6% with a sensitivity of 96.2% and specificity of 96.2%. With a cut-off of 40 kPa the positive biopsy rate for the ShearWave Elastography targeted biopsy was 50%, whereas for randomized biopsy it was 20.8 %. In total 53 men were enrolled in this study.

Our group used SWE prior to radical prostatectomy to determine if the ShearWave Elastography threshold had a high accuracy using a cutoff >55 kPa. (Fig 1)

We then compared the ShearWave results with the final histopathological results. [Figure 1]. Our results showed the accuracy was around 78 % for all tumor foci. We were also able to verify that ShearWave Elastography targeted biopsies were more likely to be positive compared to randomized biopsies. [Figures 2, 3]

CONCLUSION

SWE is a non-invasive method to visualize prostate cancer foci with high accuracy, in a user-friendly way.

As Steven Kaplan puts it in an editorial comment in the Journal of Urology 2013:

"Obviously, large-scale studies with multicenter corroboration need to be performed. Nevertheless, SWE is a potentially promising modality to increase our efficiency in evaluating prostate diseases."

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