The utility of transrectal sonoelastography in preoperative prostate cancer assessment

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Abstract

Aim: To determine the diagnostic quality of transrectal sonoelastography (SE) in the prediction and localisation of prostate cancer, we prospectively examined patients treated with radical prostatectomy in our urology department. **Methods:** From April 2010 to January 2011, 61 patients with biopsy-proven prostate cancer underwent preoperative transrectal gray-scale (b-mode) ultrasound and SE of the prostate. Cancer-suspicious areas were documented for b-mode and SE, dividing the prostate into six topographic sectors. Suspicious areas in both modalities were compared to tumour localisation in the prostatectomy specimen. Sensitivity, specificity, positive- and negative predictive values were calculated for both investigation techniques. **Results:** Prostate cancer was present in 232 of 366 pathological sectors (62 %). B-mode ultrasound showed 113 suspicious sectors, while SE indicated prostate cancer in 157 areas. The precise localisation of at least one pathologically confirmed cancerous lesion was possible in 42/61 (69 %) patients by b-mode ultrasound and 56/61 (92 %) patients by SE ($P < 0.005$). The sensitivity for b-mode ultrasound was 33 % and specificity 74 %. For SE sensitivity was 53 %, while specificity was 74 %. **Conclusions:** SE offers a more precise localisation of prostate carcinoma than conventional ultrasound. To investigate the possible advantages of SE in during prostate biopsy and its value in the prediction of extracapsular cancer further studies are required.

Keywords: prostate cancer, elastography, ultrasound, prostatectomy

Introduction

As continuous efforts are undertaken to improve prostate cancer diagnosis, imaging represents a diagnostic sector with a high potential to offer relevant information on cancer staging and therapy planning. Within the setting of prostate biopsy, improved imaging modalities could assist investigators in identifying and localising cancer suspicious areas for targeted samples. So far, no imaging modality has established itself as practical in a broad clinical routine to close these diagnostic gaps, and

meanwhile clinical studies are being conducted to evaluate various diagnostic procedures. To date, 10-12 core randomised prostate biopsy remains the gold standard for cancer diagnosis [1-3], with acceptance of its known limitations.

Sonoelastography (SE) has recently been described as an emerging imaging modality for prostate carcinoma [4-9]. As available data on SE are merely based on *Hitachi* technology and heterogeneous towards patient numbers and sensitivities, we prospectively evaluated our experience using an ultrasound device from an alternative manufacturer (*Siemens*).

Methods

From April 2010 to January 2011, 61 patients with biopsy-proven prostate carcinoma designated to undergo radical prostatectomy at our Department of Urology were preoperatively examined by transrectal gray-scale (b-mode) ultrasound and transrectal SE. A *Siemens*

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Acuson S2000 ultrasound device with an EC9-4 transrectal transducer and eSie Touch™ elasticity imaging was used to conduct the studies. Written informed consent was obtained by all participating patients. All patients were investigated by the same examiner who was blinded to all preoperatively available data, such as level of prostate specific antigen (PSA), digital rectal examination, and the pathological reports of prior prostate biopsies. Patients were examined in the left lateral position. In order to validate the potential of localising prostate carcinoma in both imaging modalities, suspicious areas were documented in six topographic sectors, left and right prostate apex, mid gland and base. Areas were classified as suspicious, when a demarked, hypo-echogenic pattern was present in gray-scale imaging. Elastographic images were generated by soft and rhythmic compression of the prostate using the ultrasound transducer.

Tumour suspicion was defined as a demarked section of increased tissue stiffness, suggested by colour scaling and a particular quality factor of the elastography software (>70), indicating quality of compression and reproducibility of images.

In both imaging modalities, the investigation focused on the peripheral zone of the prostate. Furthermore, prostate size and morphological suspect of capsular excess or seminal vesicle invasion were recorded. The included patients all underwent open radical retro-pubic prostatectomy with bilateral iliac lymph node dissection. The histological analysis was performed by two pathologists. Prostatectomy specimens were step sectioned and processed according to a standard protocol. Postoperatively the localisation of suspicious areas in prostate imaging was compared to the pathology results. Sensitivity, specificity, positive- (PPV) and negative predictive values (NPV) for conventional ultrasound and SE were calculated. To evaluate the influence of prostate size on diagnostic quality, we analysed sensitivity in dependence of prostate volume. A chi-square test was used to determine statistical significance.

Results

We prospectively examined 61 patients with prostate carcinoma prior to open radical retro-pubic prostatectomy. Median preoperative PSA was 6.40ng/ml. The mean age at surgery was 63.8 years. Median prostate size measured 37 cm³, with a range of 16 cm³ to 78 cm³. In conventional gray-scale ultrasound a total of 113 sectors were classified as suspicious for prostate cancer, SE indicated prostate cancer in 157 areas. Pathological analysis detected prostate cancer in 232 of 366 sectors

(62%). Histological tumour detection was most prominent in the mid gland area (44%), apical carcinoma was detected in 38%, while basal tumours occurred in 18% of all cases. There was no difference regarding the side of tumour incidence. Figure 1 shows an exemplary examination picture and the corresponding post-operative histological analysis. Patient characteristics and postoperative stage distribution are shown in table I. The correct detection of at least one pathologically confirmed tumour lesion (index tumour) was possible for 56 patients (92%) by SE, whereas conventional ultrasound predicted cancer localisation correctly in 42 (69%) patients ($P<0.005$). Overall, the sensitivity for the correct localisation of prostate cancer was 33% using gray-scale ultrasound. The specificity accounted for 74%, the respective positive predictive value and negative predictive values were 70% and 38%. SE allowed

Fig 1. Examination pictures and histopathological analysis – A: elastographic image without pathological findings at the prostate apex/urethral intersection (QF:75=quality factor) – B: suspicious area in the right mid-gland section, the marked sector (box) is shown in C (QF:75)– C: histological slide with confirmation of prostate cancer according to B.

Table I. Patient characteristics.

Age at surgery, mean (IQR)		63.8 y (59.02-69.81y)
PSA, median (IQR)		6.4 ng/ml (4.97–8.75ng/ml)
Prostate volume, median (range)		37 cc (16 – 79cc)
Clinical staging	T1	39 (64%)
	T2	20 (33%)
	T3	2 (3%)
Pathological staging	pT2	40 (66%)
	pT3a	15 (25%)
	pT3b	6 (10%)
	pT4	-
Pathological Gleason Score	≤ 6	37 (61%)
	7a	8 (13%)
	7b	8 (13%)
	≥ 8	8 (13%)
Nodal status	N0	57 (93%)
	N+	4 (7%)

IQR=inter-quartile range

Table II. Sensitivity, specificity, positive and negative predictive values for correct localisation of prostate cancer using conventional ultrasound and sonoelastography.

Suspicious area, B-mode	113/366			
Suspicious area, SE	157/366			
Tumour foci, histology	232/366			
	Sensitivity	Specificity	PPV	NPV
B-mode (95% CI)	33% (27-40)	74% (65-81)	70% (61-78)	38% (32-44)
SE (95% CI)	52% (45-58)	73% (65-81)	78% (70-84)	46% (39-53)
Size ≤ 40cc, n=38	59% (50-56)	71% (61-80)		
Size > 40cc, n=23	42% (32-52)	73% (65-81)		
Detection index tumour, b-mode	42/61 (62%)			
Detection index tumour, SE	56/61 (92%)			
Chi-square-test	P<0.005			

SE=sonoelastography, CI= confidence interval, PPV=positive predictive value, NPV=negative predictive value

a more precise detection of tumour infiltration with a sensitivity of 52% and a specificity of 74%. Positive- and negative predictive values are shown in table II. In comparison to small prostate volumes, the sensitivity for glands larger than 40 cm³ was reduced.

Due to the low number of patients with extracapsular prostate cancer growth in our collective no clear conclusion can be drawn for the worthiness of SE in terms of predicting extracapsular extension or seminal vesicle infiltration.

Discussion

In accordance to previous single centre reports, our data underline the potential capacity of prostate SE for prostate cancer assessment. A closer view at the currently available clinical reports on SE shows that the results are either based on the comparison of preoperative prostate imaging and postoperative histological cancer localisation or on clinical trials with patients undergoing elastography-guided biopsies according to specific pro-

Table III. Published data regarding the sensitivity and specificity of sonoelastography for prostate cancer detection [4,7,8,9,12].

Author	Journal	n	Design	Sensitivity /specificity	Device
Salomon et al.	Eur Urol (2008)	109	comparison SE/ histology	75.4%/76.6%	Hitachi
Eggert et al.	Urologe (2008)	351	biopsy	44,5% / 89%	Voluson, GE medical
Pallwein et al.	Eur J Radiol (2008)	492	biopsy	87% / 72%	Hitachi
Tsutsumi et al.	Int J Clin Oncol (2007)	51	comparison SE/ histology	Sensitivity 57-94%	Hitachi
Sumura et al.	Int J Urol (2007)	17	comparison SE/ histology	Sensitivity 74,1%	Hitachi

n= patients' number

TOCOLS. [4-9]. Relating to the used ultrasound devices, it is conspicuous that the majority of studies are based on *Hitachi* systems; only few available data rest upon other ultrasound systems and techniques. Table III illustrates the heterogeneity of published data regarding the sensitivity of SE.

With regard to technical variability, different systems of imaging and scaling represent a relevant difference. To obtain reproducible images during *Siemens*-SE the system implements a quality factor indicating the measure of (passive) pressure and examination quality. In our study, we observed a sensitivity of 53% and a positive predictive value of 78% for *Siemens*-SE. Especially the low sensitivity represents an unsatisfying result in relation to the requirements for local prostate cancer imaging and in comparison to previous studies and varying ultrasound devices.

In our opinion it is speculative whether these differences are based on a minor diagnostic power of the used SE device or potentially a lower examiner experience.

Previous publications agree with the statement that SE is an examiner dependant diagnostic tool [4,9].

Despite a lack of available data regarding the practical use of the *Siemens* device, we were able to obtain a significant improvement of prostate cancer detection with SE compared to conventional transrectal ultrasound. Sedelaar et al. systematically reviewed the literature on prostate ultrasound revealing that the biopsy of a suspicious hypo-echogenic area detects prostate cancer in only 17-57% [10]. The results are in line with our own observations. The sensitivity for gray-scale ultrasound was low, accounting for only 33%. As in the majority of conducted studies on prostate SE, cancer assessment was performed on an indirect basis, comparing preoperatively stored ultrasound pictures to postoperative pathological analysis. In order to increase the accuracy of analysing a suspicious electrographic region and to compare the practicability of SE-guided biopsies in contrast to diagnostic standard 10-12 core biopsies, further clinical trials should follow.

Artefacts during SE are a common finding and represent a problem concerning the interpretation of examination results. In accordance to our own experience with *Siemens*-SE, sensitivity of elastography decreases with increasing prostate size and the presence of benign prostate hyperplasia (BPH) [5]. In our series, the observed sensitivity of 42% for glands larger than 40 cm³ was noticeably low in contrast to 59% sensitivity for prostates smaller than 40 cm³. Some reports quote that routinely appearing examination artefacts, like the "soft-rim-artefact", a soft layer surrounding the prostate tissue as an indication of the adventitial connective tissue, could predict capsular infiltration or extracapsular growth [9,11]. Since our own observations and the majority of available studies are based on the examination results of patients with merely organ confined disease, larger series are required to further validate these observations. The impact of prostate carcinoma differentiation on SE results is controversial. As Miyagawa and co-workers report from equality of diagnostic sensitivities of SE in relation to the Gleason score, a publication by Sumura et al. and the analysis of Salomon et al. showed an increased sensitivity for higher graded carcinoma [5,9,12]. In contrast, another Japanese single centre trial obtained best detection rates for low grade prostate cancer [8].

As most modern ultrasound devices offer a variety of examination techniques, combinations of e.g. SE, conventional gray-scale ultrasound, colour-Doppler or contrast enhanced ultrasound are generally feasible in order to raise detection rates. Miyagawa et al. observed an improved detection of prostate cancer combining SE and conventional gray-scale transrectal ultrasound [5].

Magnetic resonance imaging (MRI) has been described as a valid instrument referring to local prostate cancer staging and MRI guided biopsy has demonstrated its potential value in clinical trials. Turkbey et al observed a sensitivity of 60.7% and a specificity of 72.7% for the prediction of prostate cancer applying multi-parametric MRI [13]. Recently, an expert panel established stand-

ardized conduct and interpretation for the use of MRI in the diagnosis and staging of prostate cancer. Nevertheless, a general recommendation for the routine use of multi-parametric MRI should follow further validation in prospective studies [14-15].

With regard to costs, eligibility and the duration of the examination, SE is a promising alternative diagnostic tool with good feasibility in an ambulatory setting, which warrants further efforts in technical development and clinical investigation.

The investigator dependency of SE and the indirect approach of comparing preoperatively stored images to postoperative histological slides represent major limitations of our study.

Conclusions

Transrectal sonoelastography allows a more precise prostate cancer localisation than conventional ultrasound. SE may close diagnostic gaps in local staging and in the setting of prostate biopsy, especially in absence of extensive BPH. As the method is closely related to the experience of the examiner and the specifics of the used device and technique, studies are needed to evaluate these influences. Furthermore, it is worthwhile to determine the potential of SE in optimizing cancer detection during prostate biopsy.

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