

The TRUS guided prostate extended biopsy in the detection of prostate cancer

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ABSTRACT

Introduction: the prostate cancer (PC) represents an important health problem, because of its high incidence and the increase number of deaths. The new strategies consider that the sextant biopsy (PS), first used by Hodge and al, isn't very accurate, the detection rate of PC decreasing with the increase of prostate volume. It was demonstrated using mathematics models, that a bigger number of biopsies can increase the detection of PC.

Objectives: We tried to evaluate, retrospectively, the extended prostate biopsy (PPE) results in the detection of PC. The evaluation makes a competent analysis between classic SB and the 10 cores extended prostate biopsy.

Materials and method: During March 2003 – April 2006, 180 patients with suspicions of prostate cancer were investigated using TRUS extended prostate biopsy. The average age of the patients was 61, 5 years (45-76 years). In all the cases, we performed 10 prostate punctions. The 4 supplementary cores, practiced beside the sextant puncture were bilaterally made.

Results: The general detection rate of PC using the multiple puncture (10 cores) was 32.7 % (59 of 180 cases). The detection rate using the sextant biopsy was 19.44% (35 of 180 cases). The multiple 10 cores puncture increased the detection rate with 40.67% (24 of 59 cases), compared to the classic technique. The results were better both for the patients with prostate volume smaller than 60 cc (38.75% vs 26.25 %) and for those with bigger prostates (>60 cc) (28% vs 14%).

Conclusions: The general detection rate of PC decreases with the increase of prostate volume. The PPE has a PC detection rate higher with 40.67 % than PS.

We consider that the PSA level is very important in establishing the PPE indication and the normal value of PSA level should be decreased.

Key words: prostate cancer, sextant puncture, extended puncture

Abbreviations

PC	= Prostate cancer	PPE	= Extended prostate biopsy
TRUS	= Transrectal ultrasound examination	BPH	= Benign prostatic hyperplasia
PSA	= Prostate specific antigen	DRE	= Digital rectal examination
PS	= Sextant puncture, sextant biopsy	PIN	= Prostate intraepithelial neoplasia
		PNL	= Percutaneous nephrolithotomy

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INTRODUCTION

The prostate cancer represents an important health problem, because of its high incidence and the increase number of deaths. In 2006 was recorded a sudden but evident decrease of mortality (6). This decrease of deaths number was determined by the PSA screening and especially by using, the TRUS guided prostate extended biopsy at patients with risk of PC (1). The prostate biopsy, recommended by increased PSA values, registered significant progress.

The TRUS guided prostate extended biopsy represents already a classic procedure in PC diagnosis. The TRUS prostate puncture is more precise, faster and less traumatic than the direct puncture, digitally guided; the ultrasound guidance allows a more precise needle positioning, permitting the separate puncture of the base, mid and apex of each prostate lobes. Since its introduction in medical practice, beside the technical improvements (biplane transducer, real time image, Doppler and harmonic system, automatic systems – biopsy – gun, etc) were adopted changes in the protocol regarding the number of punctures (multiple, sextant, extended, saturation) and the punctures localizations (apex, mid lobe, base etc). The number of punctures and the puncture zones still represent a controversial discussion subject. The new strategies consider that the sextant biopsy (PS), first used by Hodge and al (4) is not very accurate, the detection rate of PC decreasing with the increase of prostate volume. The PC general detection rate using sextant biopsy is 22.6%, decreasing with the increase of prostate volume (3): for a prostate volume of 25 g, the detection rate is 49%, for a volume of 50 g is 38% and for a volume of 100 g, the detection rate is 14%. Recent studies demonstrated that is more difficult to diagnose PC, when the prostate volume increases (7).

It was demonstrated using mathematics models, that a bigger number of biopsies can increase the detection of PC (9).

For this reason, in the last years, the number of punctures increases, in correlation with the prostate volume, PSA value and/or the patients' ages. According with the algorithm, if the prostate volume is 3-4 times larger than the normal volume, there are necessary 8 to 15

punctures. The PC detection rate increases in these conditions with 42%. □

MATERIALS AND METHOD

During March 2003 – April 2006, 180 patients with suspicions of prostate cancer were investigated using TRUS extended prostate biopsy. The average age of the patients was 61.5 years (45-76 years).

The new protocols of prostate biopsy promote the extended TRUS guided prostate biopsy (8-12 cores). The clinical studies showed that these techniques do not significantly increase the morbidity and/or the number of PC with no clinical significance detected (tumoral volume <0.5, Gleason score < 4).

In the "Prof. Dr. Th. Burghel" Clinical Hospital, we have been using since 2003, for most of the patients, beside the sextant biopsy, the extended prostate biopsy (PPE). Therefore, we tried to evaluate retrospectively the PPE results in the detection of PC. The evaluation makes a competent analysis between classic sextant biopsy and the 10 cores extended prostate biopsy.

During March 2003 – April 2006, 180 patients with suspicions of prostate cancer were investigated using TRUS extended prostate biopsy. The average age of the patients was 61.5 years (45-76 years) (TABLE 1)

Characteristics	Values
Number of patients	180
PC number	59
Average age	61.5 years
PSA	3-35.3 ng/ml
Prostate volume	34-89 cc
Number of punctures	10

TABLE 1. The characteristics of the study group

In all the cases, we performed 10 prostate punctures. The 4 supplementary cores, practiced beside the sextant puncture were bilaterally made (2 for each lobe) as lateral as possible, in the peripheral area (FIGURE 1).

If "suspect" zones were detected at TRUS examination (hypoechoic or modified zones), two more punctures were performed in those areas. We did not include in our study the patients who needed to be repunctured, after a period, because of the persistence of high levels of PSA (despite the initial diagnosis of BPH)

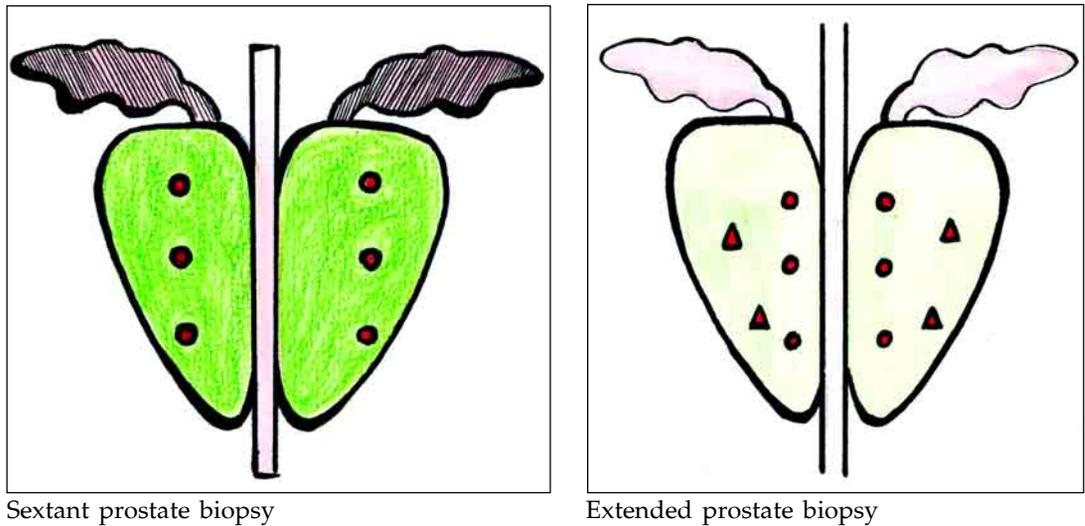


FIGURE 1. Sextant biopsy (PS) compared with extended prostate biopsy (PPE)

or the presence of high-grade intraepithelial neoplasia (PIN) at anterior biopsy.

The punction indication was established on abnormal DRE and/or PSA levels higher than 3 ng/ml. We considered pathologic this PSA value, because the percent of PC with PSA levels between 3-4 ng/ml is, according the statistics, of 26,9%, most of PC being clinically significant (8). In that way, we tried to determine if this PSA level brings a benefit in PC diagnosis. To determine the PSA levels, we used the ELISA method, and for the TRUS guided biopsies an Aloka Sonoline device, with a 7.5 Mhz transducer, "end-firing" type and punction needles 18G, with an automatic punction system "biopty-gun". The length of the prostatic fragment obtained by punction was 17 mm.

The biopsies were performed in ambulatory, based on the written consignment after complete oral and written information.

The patients received antibiotics, therapy which started 24 h before the punction (ex., Ciprofloxacin 500 mg x 3/day). For patients with valvular cardiac diseases, we considered also iv associated therapy (ex., Gentamicin 80 mg x 3/day). The antibiotic treatment was continued 3 days after punction.

For the patients with urinary symptoms, mainly obstructive, an alfa blocker treatment was recommended once or two weeks before the punction.

All patients received an enema the evening before the punction or 2 hours before. In 30 cases, at the patients' will, we recommended Fortrans (to evacuate the colon).

A DRE was performed at all patients before the punction.

For all the patients who needed more than 6 punctions we performed local anaesthesia. We realized that the discomfort produced by the multiple punctions, conducted to less accurate punctions, caused by patients movements during the procedure and the decrease number of punctions. We considered the pain control essential for the success of the punctions. The local anaesthesia consisted in periprostatic nervous infiltration with 5 ml lidocaine 1%. The infiltrations were made at 105 patients at the apex and the base of the prostate, postero-lateral, bilaterally, using long PNL needles (FIGURE 2).

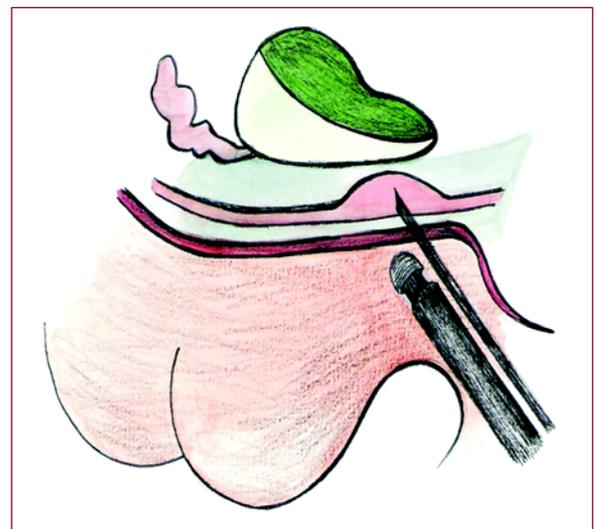


FIGURE 2. The needle position for local anesthesia (between rectum and the prostate)

In 80% of the patients, we used the colour Doppler ultrasound on transversal images at the base of the prostate, in order to identify the neurovascular bundles. We tried to infiltrate with anaesthetic laterally from each bundle.

The use of the colour Doppler ultrasound did not significantly increase the detection zones suspect of PC.

The patients were positioned in lateral decubitus, for biopsy, as seen in PICTURE 1.

This position is favourable to the right-handed doctors.

We need to monitor the patient's status during the procedure, because of the reactions determined by the introduction of the transducer

into the rectum and the punctions themselves. In two patients, we noticed vagal reactions (pale face, bradycardia, dizziness, hypotension), which disappeared in a few minutes after oxygen administration and positioning the patients in declive position. In these situations, we decided to postpone the procedure and we better psychically prepared the patients.

In these cases, we started the procedure with a transrectal ultrasound examination in which we examined the prostate, the rectum wall, the seminal vesicles and the bladder trigonum in longitudinal and transversal incidents. We determined the prostate volumes at all patients, using the method of the ellipse. For most of the patients, we used the colour Doppler ultrasound.

We used a needle for each prostate lobe. Each biopsy was separately preserved in boxes containing formol, each box being labelled. If the length of the fragment biopsy was shorter than the space of the biopsy needle, we repeated the puncture.

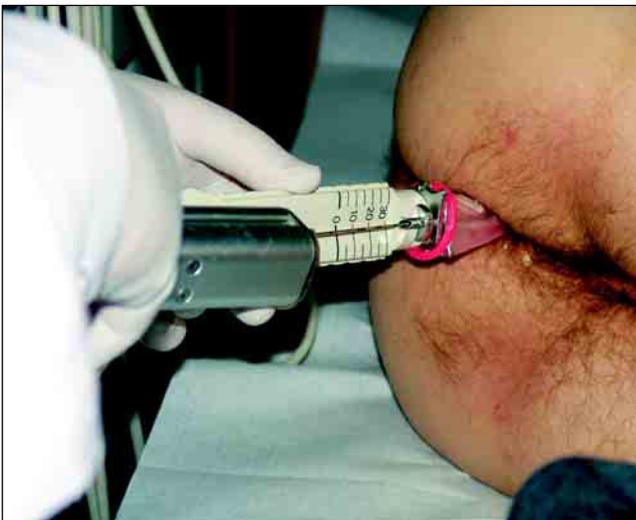
We positioned the needle, near the prostate, in a way in which it would not depress the prostate capsule over the prostate tissue. The punctures were performed at 10-15 mm distance, in an antero-posterior plan. We used as a mark, the hyperechoic trace of the precedent puncture.

When we detected a suspect zone, near the base of the prostate, we also punctured, in most cases, the seminal vesicle from that side. The punctures were made directly, but the material obtained was in most cases non-interpretable or did not help to establish the diagnostic.

The punctions direction was as laterally as possible, parasagittal, in order to pass as much as possible from the peripheral zone of the gland (FIGURE 3).

The direction of the needle, in order to obtain more tissue, must be very close to the posterior rectal wall (in transversal incidence the angle between the rectal wall and the puncture needle must be as low as possible). The exception for us was represented by the apex punctures, where the needle must have a vertical direction.

The TRUS guided biopsy is more precise, faster and less traumatic than the direct puncture, digitally guided; the ultrasound guidance gives more accuracy to the position of the needle puncture and allows a separate puncture of the prostate; this way the base, mid and prostate apex can be punctured. □



PICTURE 1. The patient's position and the using of the transducer and the automatic puncture system

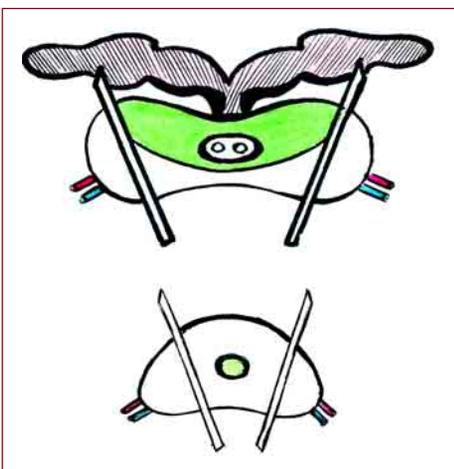


FIGURE 3. The direction of the needle (as lateral as possible): A – at the base level; B – at the apex level

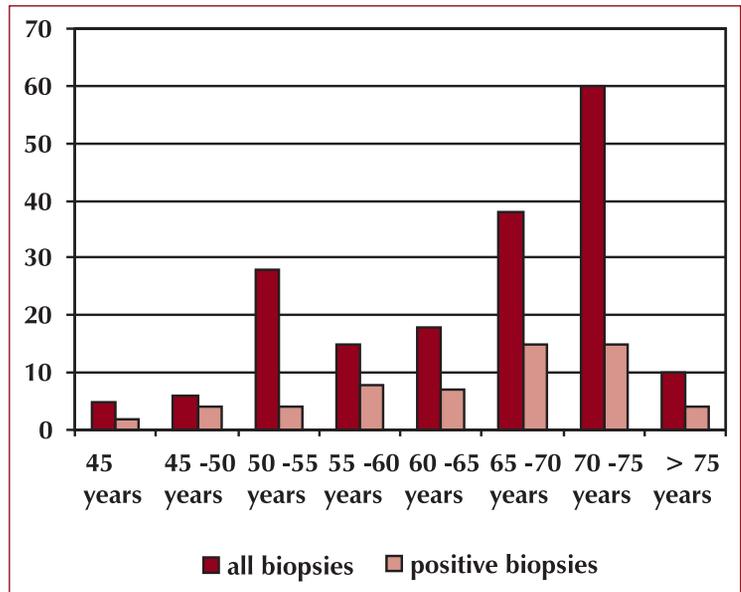


FIGURE 4. The correlation between the number of cases and the patients' ages

Prostate volume	Sextant	10 biopsies	The amelioration of the PC detection rate while using the 10 cores biopsies (vs sextant biopsies)
≥ 60 cc	21/80 (26.25%)	31/80 (38.75%)	10/31 (32.25%)
>60 cc	14 /100 (14%)	28/100 (28 %)	14/28 (50%)

TABLE 2. The PC detection rate corelated with the prostate volume

RESULTS

Over half of the 180 patients were over 65 years old (FIGURE 4).

Most of the 59 cases detected with PC, were between 65-75 years old. One of four patients over 75 detected with PC, had the conditions to perform a radical treatment.

The PC general detection rate was 32.77% (59 cases from 180) (TABLE 2).

The sextant biopsy detection rate was 19, 44% (35 cases over 180). The extended biopsy increased the detection rate, comparative with the sextant biopsy with 40.67% (24 cases of 59 cases). The sextant biopsy is more efficient at patients with prostate volume lower than 60 cc, with a detection rate of 26.25%, compared with 14% for prostate volumes higher than 60 cc.

As expected, the extended biopsy registered a PC detection rate higher than PS, no matter the prostate volume (38.75% vs 26.25% for volumes lower than 60 cc and 28% vs 14% for over 60 cc).

An acceptable detection rate for PS (32%) was registered only at patients with PSA levels higher than 10 ng/ml and with „suspect” DRE.

In 42 cases (71.18 %) of 59 patients detected with PC, the PSA levels were higher than 10 ng/ml, and in 17 (28, 81 %) under 10 ng/ml.

We registered 10 patients with PSA between 3-4 ng/ml, with normal DRE. 2 patients (20%) were detected with PC. If we would not consider a lower limit of PSA, these patients would not have been diagnosed. At these 2 patients, the PS did not detect PC, only PPE. All these patients had prostate volume lower 60 cc and the Gleason score was 6 and respectively 7.

We established the clinical stage of PC using DRE, PSA and the extended punction for all 59 patients diagnosed with PC:

The Gleason score = 4 was present at 15 patients (25.42 %), between 4-8 at 37 patients (62.71 %) and >8 at 7 patients (11.86 %) (FIGURE 5).

Clinical stage	59 patients with PC
cT1c	25 (42.37 %)
cT2a	14 (23.72 %)
cT2b	17 (28.81 %)
≥ cT 3	3 (5.08 %)

TABLE 3. Clinical stages of the 59 patients detected with PC

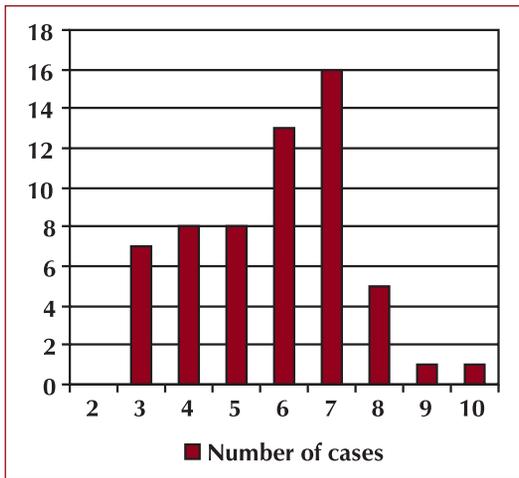


FIGURE 5. The repartition of the 59 PC cases after the Gleason score

Histological aspect 121 cases	Number of cases
High grade PIN	10 (8.26 %)
Atypical proliferation	4 (3.30 %)
Prostate inflammation	39 (32.23 %)
Normal prostate	68 (56.19 %)

TABLE 4. Histological aspect at patients not detected with PC

PROSTATE ZONE	DETECTION RATE %
LEFT BASE	6 (10.16 %)
LEFT MID	6 (10.16 %)
LEFT APEX	8 (13.55 %)
LEFT LATERAL MID	12 (20.32 %)
LEFT LATERAL APEX	5 (8.47 %)
RIGHT BASE	4 (6.77 %)
RIGHT MID	2 (3.38 %)
RIGHT APEX	7 (11.86 %)
RIGHT LATERAL MID	8 (13.55 %)
RIGHT LATERAL APEX	1 (1.69 %)

TABLE 5. The PC detection rate correlated with the puncture site

The histological aspect of the 121 patients not detected with PC showed normal prostatic tissue in most cases (56.1%). We registered in these cases 680 negative punctures. The prostate inflammation was present in a significant number of patients (32%), being partially justified by higher PSA levels, noticed in these cases (TABLE 4).

The correlation between PC detection rate and localization is shown in TABLE 5.

From the 59 patients diagnosed with PC, in 14 cases (23.7%) we practiced the direct puncture of the „suspect” zones. In all these cases, the PC was confirmed by the extended punctures and by the sextant biopsy in only one case (1.69 %).

We did not register severe complications. From all the patients, the transitory hematuria was present in 78% of the cases. In 43 of the 59 positive cases (72,88%), we noticed macroscopic hematuria and in 6 cases urethroragia, during or immediately after the procedure. All these cases solved spontaneously in 7 days maximum. The urethroragia appeared when the sagittal plan was not respected during the procedure and the punctures were made near the median line – at patients with small prostates.

In 14 cases, we recorded hematokesis and at 22 patients, hemospermya.

Only one patient needed admission in hospital for hematuria, which solved spontaneously. In that case, haemoglobin decreased from 15 g/dl to 13 g/dl. We recorded a case with a septic complication, which was solved with antibiotherapy (ciprofloxacin+ amikacin+ metronidazol) after 7-10 days of treatment. □

DISCUSSIONS

If 15-20 years ago, the prostatic puncture, which was in the most cases unique, was indicated when there was a DRE suspicion of PC, after the introduction of PSA in 1981, in the US, things changed. The sextant biopsy started to be more and more used and was indicated if at cases with normal DRE and/or when PSA levels were higher than 4 ng/ml. These days, more of 90% PC detected at patients with normal DRE are diagnosed using PS.

Studies revealed that the increasing number of biopsies from 6 to 12, ameliorates the PC detection rate with 29% (3). In US, over 1 million biopsies with 10 cores on average are performed every year.

After having gotten a considerable experience using this type of biopsy, we noticed that there were many cases of undiagnosed PC.

From our experience the main indications of extended biopsy are:

- PSA levels higher than the normal limit (we decreased this limit from 4 to 3 ng/ml and we discovered 2 more PC patients)
- Suspicion of PC at DRE
- PSA level that significantly increase in time (PSA velocity > 0.76 ng/ml/year)

We consider that PPE is correctly indicated at patients for which the diagnosis permits a treatment that will ameliorate the patient’s quality of life.

The PC general detection rate using PS decreases with the increasing of the prostate volume.

A solution is the increasing the number of the prostatic punctions, which can ameliorate the detection rate, fact confirmed by authors (2).

The problems that raise discussions are the optimal number of punctions and their positions, in order „to scan“ the prostate.

Regarding the optimal number of punctions, it was proposed to be linked to the prostate volume – a puncture for 10 grams. According to this theory, the sextant puncture represents a very good alternative for a prostate with a volume under 60 gr. At this volume, the extended puncture, demonstrated its superiority, with an improved detection rate with 32.2% (10 cases). When the prostate volume is bigger than 60 cc, the extended puncture represents the main choice.

In our statistics, the extended puncture increased the PC detection rate with 40.67 %.

We consider that our detection rate (32.77%) is comparable with that obtained by Remzi, Marberger and Djavan (8) (36.7%). The increased number of biopsies (recommended

by Vienna Nomogram) is dependent in our experience with the patient disponibility. The patients are usually reluctant to the proposal of increasing the number of biopsy cores.

We consider that PSA levels and the prostate volume remain the main indications for extended punctions, with the mention that it should be considered a lower limit for PSA.

From our experience, the supplementary puncture of „suspect“ zones did not improve the detection rate for PC (1 case – 3%).

The prostate puncture represents a painful investigation for the patient. The discomfort of this procedure can be eliminated using a local anaesthesia. The local anaesthesia is safe, easy to perform and efficient, it permits to obtain supplementary biopsies without pain and without significantly increasing the morbidity. This method allows the urologist to perform the extended biopsies in ambulatory, in comfortable conditions for the patient.

In conclusion, from our day to day experience, we consider that 10 cores biopsy can be used for all the patients with an acceptable detection rate.

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