

## ARTICLE

## Improving Diagnostic Accuracy of Prostate Carcinoma by Systematic Random Map-biopsy

János SZABÓ,<sup>1</sup> György HEGEDŰS,<sup>1</sup> Katalin BARTÓK,<sup>2</sup> Tibor KERÉNYI,<sup>3</sup> Attila VÉGH,<sup>1</sup> Imre ROMICS,<sup>4</sup>  
Béla SZENDE<sup>5</sup>

<sup>1</sup>Department of Urology, <sup>2</sup>Department of Pathology Central Military Hospital, <sup>3</sup>2<sup>nd</sup> Institute of Pathology,  
<sup>4</sup>Department of Urology, <sup>5</sup>1<sup>st</sup> Institute of Pathology and Experimental Cancer Research, Semmelweis University,  
Budapest, Hungary

**Systematic random rectal ultrasound directed map-biopsy of the prostate was performed in 77 RDE (rectal digital examination) positive and 25 RDE negative cases, if applicable. Hypoechoic areas were found in 30% of RDE positive and in 16% of RDE negative cases. The score for carcinoma in the hypoechoic areas was 6.5% in RDE positive and 0% in RDE negative cases, whereas systematic "map"**

**biopsy detected 62% carcinomas in RDE positive, and 16% carcinomas in RDE negative patients. The probability of positive diagnosis of prostate carcinoma increased in parallel with the number of biopsy samples/case. The importance of systematic map biopsy is emphasized.** (Pathology Oncology Research Vol 6, No 2, 111–113, 2000)

**Keywords:** map-biopsy, prostate, carcinoma, RDE

### Introduction

The ultrasound-directed systematic prostate biopsy, which creates a real "map" of the prostate, was introduced more than 10 years ago and is now considered the most effective diagnostic tool to detect prostate carcinoma.<sup>1,2,3</sup> This method facilitates the preoperative estimation of extracapsular invasion and decreases the rate of preoperative down-staging. Furthermore, systematic map-biopsy of the prostate promotes the distinction between clinically significant and so-called "infraclinical" prostate carcinomas indicating therapeutical consequences.<sup>4,5</sup> Ultrasonically guided prostatic biopsies enabled the histological investigation of prostatic hypoechoic areas.<sup>6</sup> The diagnostic value of this method versus random systematic biopsies has been studied and questioned.<sup>7,8,9</sup>

The aim of our study was to compare the diagnostic efficacy of directed ultrasound guided transrectal core biopsies and random systematic "map" biopsies of the prostate in both suspicious and non suspicious cases according to rectal digital examination.

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*Correspondence:* Prof. Dr. Béla SZENDE, 1<sup>st</sup> Institute of Pathology and Experimental Cancer Research, Semmelweis University, Üllői út 26, 1085 Budapest; Tel.: 36-1-266-0451; Fax: 36-1-317-1074; E-mail: bszende@korb1.sote.hu

### Materials and Methods

Altogether 102 patients were map-biopsied, 77 of them were positive by rectal digital examination (RDE) and 25 were negative. The age of RDE positive patients was 71.66 in average ( $\pm 8.84$ , median: 71, range 55–88) and of RDE negative patients 67.11 in average ( $\pm 7.65$ , median: 68, range 52–83). The serum PSA level was  $59.47 \pm 270.83$  ng/ml in average (median: 63.08 ng/ml, range: 0–2210 ng/ml) in the RDE positive patients and  $8.55 \pm 8.18$  ng/ml in average (median: 8.70 ng/ml, range 0–418 ng/ml) in the RDE negative patients. PSA was determined using the AXSYM PSA Monoclonal test Kit (Abbott, USA). The normal values of PSA by this method are 0.0–4.0 ng/ml. The indication of prostate biopsy in RDE negative cases was serum PSA level above 4.0 ng/ml.

Map-biopsy was performed under antibiotic prophylactic treatment (Fluorokinolon and Metronidasol) by means of a PRO-MAG Biopsy-gun (Manan, Medical, USA) with 18 gauge needle.

Hypoechoic zones were detected using a 7.0 MHz 2001 Leogard multiplane transrectal transducer ultrasound head (Brüel Kjaer, Denmark).

Nine needle biopsies were taken regularly, first in transversal, then in longitudinal section from both lobes, according to the method described by Resnick<sup>1</sup> and Gasman.<sup>10</sup> If necessary, supplementary biopsies were taken

from the hypoechoic zones, from the seminal vesicle and from the palpable nodules. Formalin-fixed, paraffin embedded blocks were made and 8 µm sections were stained with haematoxylin and eosin (HE). The following histopathological categories were registered: carcinoma (CA), benign prostate hyperplasia (BPH), chronic prostatitis (CP) and prostatic intraepithelial neoplasia (PIN).

### Results

Hypoechoic zones were observed in 23 of the 77 RDE positive cases (30%). Only 5 samples taken from the 23 hypoechoic zones proved to be CA (6.5%) in the RDE positive cases and 21.7% of the hypoechoic zones. However, systematic map-biopsy detected 48 CAs in the 77 RDE positive cases (62%). Out of these, in 43 cases the CA was diagnosed from biopsies taken from other parts of the prostate than the hypoechoic zones and in 5 cases both the hypoechoic zones and other parts of the prostate contained CA. Altogether 29 RDE positive cases proved to be

**Table 1. Hypoechoic zones (HZ) and CA in the 77 RDE positive cases**

Case number	HZ	CA in HZ	CA in non HZ	CA total
77	23 (30%)	5 (6.5 %)	43	48 (62%)

**Table 2. Hypoechoic zones (HZ) and CA in the 25 RDE negative cases**

Case number	HZ	CA in HZ	CA in non HZ	CA total
25	4 (16%)	-	4 (16%)	4 (16%)

**Table 3. Number of CA positive biopsy samples in the CA positive cases**

Number of CA+ cases	CA + in sample										
	1	2	3	4	5	6	7	8	9	More	
RDE +	48	7	5	1	6	4	3	4	4	11	3
RDE -	4	3	1								

**Table 4. Histological changes in the 77 RDE positive and 25 RDE negative prostates**

Cases	CA	CA + BPH	CA + CP	BPH	CP	CP + BPH	BPH + PIN	Normal
RDE + 77	31 (40.2%)	13 (16.9%)	4 (5.2%)	6 (7.8%)	5 (6.5%)	6 (7.8%)	5 (6.5%)	7 (9.1%)
RDE - 25	1 (4%)	3 (12%)	-	11 (44%)	1 (4%)	2 (8%)	2 (8%)	5 (20%)

CA negative after systematic map-biopsy (false positive cases, 38%) (see *Table 1*).

Only 4 of the 25 RDE negative prostates showed hypoechoic zones (16%). None of these zones contained CA, according to the result of biopsy. However, 4 CAs were detected (16%) by systematic map-biopsy among the 25 RDE negative cases. These 4 cases can be considered as false negative, regarding RDE (see *Table 2*).

*Table 3* shows the number of samples of systematic biopsies in which CA could be detected. It is noteworthy, that in 10 cases only 1 sample was CA positive.

Histological changes, including CA, BHP, CP and PIN, detected in the 102 cases by systematic map-biopsy are shown in details in *table 4*.

After establishing the diagnosis of prostate carcinoma, total prostatectomy was performed in 22 cases and hormonal therapy was induced in 30 cases.

### Discussion

The classical method for detection of prostate carcinoma, rectal digital examination is still the most important diagnostic tool,<sup>11</sup> which helps to apply more sophisticated techniques, such as ultrasound and ultrasound directed core biopsy.<sup>12</sup> In the earlier era of rectal ultrasound examination the hypoechoic area biopsy was considered as most specific diagnostic method.<sup>13</sup> According to the summarised data of Devonec et al,<sup>6</sup> Cooner et al,<sup>14</sup> and Hodge et al,<sup>7</sup> out of 880 RDE positive patients 761 showed hypoechoic areas and 394 carcinomas were found by biopsy in these areas (52%). The relatively low diagnostic score led to the development of ultrasound directed systematic "map" biopsy of the prostate.<sup>15,16</sup> Hammerer et al<sup>8</sup> reported 55.8% and Hodge et al<sup>7</sup> 62% tumor positivity applying this method.

In our study, the proportion of carcinoma positive cases among the cases with hypoechoic areas was lower (approximately 22%) than that described in the literature (approximately 52%) which may be explained by the fact, that we have taken the samples randomly, from unselected cases. When the hypoechoic area biopsy was supplemented with systematic biopsies, the score reached 62% in our material, which equals the best results reported.<sup>7</sup> We have also shown that in systematic biopsies, the probability of correct diagnosis of carcinoma increases in parallel with the number of biopsies. From the opposite point of view,

an increasing number of carcinomas would have been missed, if the number of biopsies/case had been kept lower. We may also confirm the data previously reported<sup>7,8,15,16</sup> that hypoechoic area biopsy alone is insufficient for diagnosis of prostate carcinoma. In accordance with the literature<sup>6,9,14,16</sup> the proportion of cases with hypoechoic areas was lower among RDE negative than in RDE positive patients. None of these areas contained carcinoma in our material, however with systematic biopsy four carcinomas could be detected in our RDE negative patients, which confirms the importance of elevated serum PSA levels even in RDE negative cases.<sup>17,18</sup>

Our results provided further data on the diagnostic value of systematic prostate map biopsy and may facilitate the selection of patients for total prostatectomy.

### References

- 1.<sup>2</sup>Resnick MF: Transrectal ultrasound guided versus digitally directed prostatic biopsy: A comparative study. *J Urol* 139:754-757, 1988.
- 2.<sup>2</sup>Hodge KK, McNeal JE, Stamey TA: Ultrasound guided transrectal core biopsies of the palpably abnormal prostate. *J Urol* 142:66-70, 1989.
- 3.<sup>2</sup>Lippman HR, Ghiatas AA, Sarosdy MF: Systematic transrectal ultrasound guided prostate biopsy after negativ digitally directed prostate biopsy. *J Urol* 147:827-829, 1992.
- 4.<sup>2</sup>Terris MK, McNeal JE, Stamey TA: Detection of clinically significant prostate cancer by transrectal ultrasound guided systematic biopsies. *J Urol* 148:829-832, 1992.
- 5.<sup>2</sup>Irwin MB, Trapasso JG, Stamey TA: Identification of insignificant prostate cancers. Analysis of preoperative parameters. *Urology* 44:862-868, 1994.
- 6.<sup>2</sup>Devonec M, Fendler JP, Monsallier M, et al: The significance of the prostatic hypoechoic area: results in 226 ultrasonically guided prostatic biopsies. *J Urol* 143:316-319, 1990.
- 7.<sup>2</sup>Hodge KK, McNeal JE, Terris MK, et al: Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol* 142:71-75, 1989.
- 8.<sup>2</sup>Hammerer P, Huland H, Cooner WH: Systematic sextant biopsies in 651 patients referred for prostate evaluation. *J Urol* 151:99-104, 1994.
- 9.<sup>2</sup>Vallancien G, Prapotnich D, Veillon B, et al: Systematic prostatic biopsies in 100 men with no suspicion of cancer on digital rectal examination. *J Urol* 146:1308-1312, 1991.
- 10.<sup>2</sup>Gasman D, Abbou CC: Biopsies prostatiques: technique, intérêts et complitatus. *Entretiens de Bichat Urologie*. Abstract. 1995.
- 11.<sup>2</sup>Jewett HJ: Significance of the palpable prostatic nodule. *JAMA* 160:838-839, 1956.
- 12.<sup>2</sup>Lee F, Trop-Pedersen S, Littrup PJ, et al: Hypoechoic lesions of the prostate: clinical relevance of tumor size, digital rectal examination, and prostate specific antigen. *Radiology* 170:29-32, 1989.
- 13.<sup>2</sup>Holm HH, Gammelgaard J: Ultrasound guided precise needle placement in the prostate and seminal vesicles. *J Urol* 125:385-387, 1981.
- 14.<sup>2</sup>Cooner WH, Mosley BR, Rutherford Jr CL, et al: Prostate cancer detection in a clinical urological practice by ultrasonography, digital rectal examination and prostate specific antigen. *J Urol* 143:1146-1154, 1990.
- 15.<sup>2</sup>Topr-Pedersen S, Lee F, Littrup PJ, et al: Transrectal biopsy of the prostate guided with transrectal US: Longitudinal and multiplanar scanning. *Radiology* 170:23-27, 1989.
- 16.<sup>2</sup>Coplen DE, Andriole GL, Yuan JJJ, et al: The ability of systematic transrectal ultrasound guided biopsy to detect prostate cancer in men with the clinical diagnosis of benign prostatic hyperplasia. *J Urol* 146:75-77, 1991.
- 17.<sup>2</sup>Vashi AR, Wójno KJ, Henricks W, et al: Determination of the reflex range and appropriate cutpoints for percent free PSA prostate specific antigen in 413 men referred for prostatic evaluation using the AxSYM system. *Urology* 49:19-27, 1997.
- 18.<sup>2</sup>William J, Catalona, et al: Evaluation of percentage of free serum prostatic specific antigen to improve specificity of prostate cancer screening. *JAMA* 274:1214-1220, 1995.