

*Prostate histoscanning true targeting  
guided prostate biopsy: initial clinical  
experience*

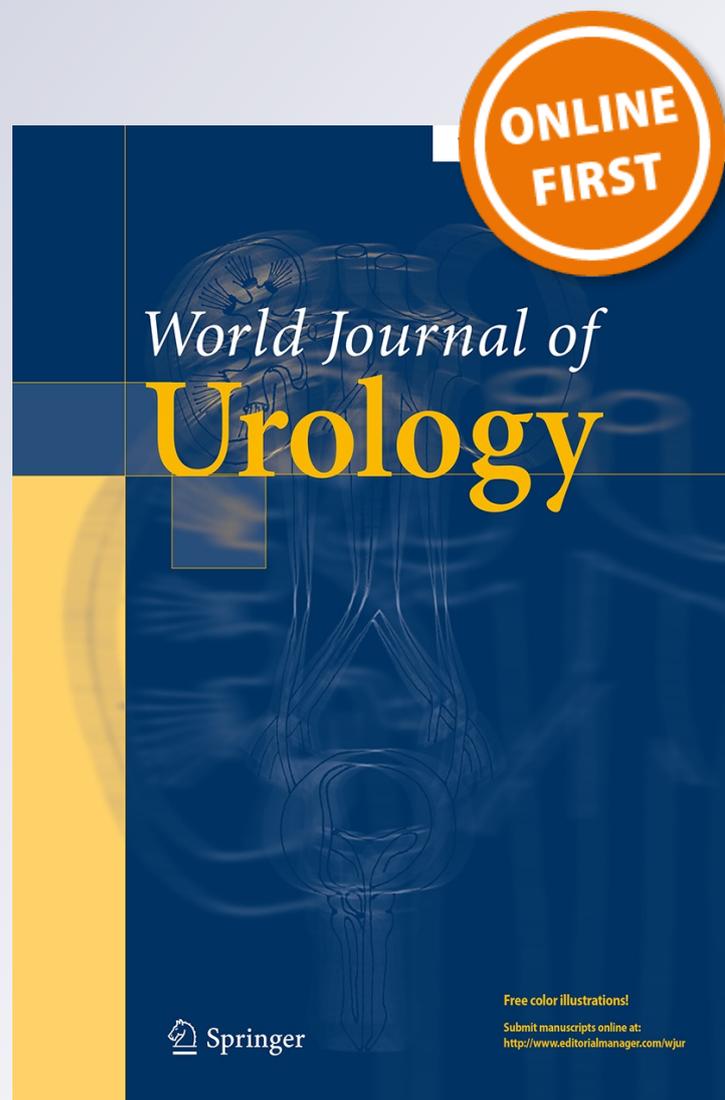
**Arjun Sivaraman, Rafael Sanchez-Salas,  
Eric Barret, Petr Macek, Pierre Validire,  
Marc Galiano, Francois Rozet & Xavier  
Cathelineau**

**World Journal of Urology**

ISSN 0724-4983

World J Urol

DOI 10.1007/s00345-014-1434-y



**Your article is protected by copyright and all rights are held exclusively by Springer-Verlag Berlin Heidelberg. This e-offprint is for personal use only and shall not be self-archived in electronic repositories. If you wish to self-archive your article, please use the accepted manuscript version for posting on your own website. You may further deposit the accepted manuscript version in any repository, provided it is only made publicly available 12 months after official publication or later and provided acknowledgement is given to the original source of publication and a link is inserted to the published article on Springer's website. The link must be accompanied by the following text: "The final publication is available at [link.springer.com](http://link.springer.com)".**

## Prostate histoscanning true targeting guided prostate biopsy: initial clinical experience

Arjun Sivaraman · Rafael Sanchez-Salas · Eric Barret ·  
Petr Macek · Pierre Validire · Marc Galiano ·  
Francois Rozet · Xavier Cathelineau

Received: 25 August 2014 / Accepted: 30 October 2014  
© Springer-Verlag Berlin Heidelberg 2014

### Abstract

**Objective** To evaluate the feasibility of prostate histoscanning true targeting (PHS-TT) guided transrectal ultrasound (TRUS) biopsy.

**Methods** This is a prospective, single center, pilot study performed during February 2013–September 2013. All consecutive patients planned for prostate biopsy were included in the study, and all the procedure was performed by a single surgeon aided by the specialized true targeting software. Initially, the patients underwent PHS to map the abnormal areas within the prostate that were  $\geq 0.2 \text{ cm}^3$ . TRUS guided biopsies were performed targeting the abnormal areas with a specialized software. Additionally, routine bisextant biopsies were also taken. The final histopathology of the target cores was compared with the bisextant cores.

**Results** A total of 43 patients underwent combined ‘targeted PHS guided’ and ‘standard 12 core systematic’ biopsies. The mean volume of abnormal area detected by PHS is  $4.3 \text{ cm}^3$ . The overall cancer detection rate was 46.5 % (20/43) with systemic cores and target cores detecting cancer in 44 % (19/43) and 26 % (11/43), respectively. The mean % cancer/core length of the PHS-TT cores were significantly higher than the systematic cores (55.4 vs. 37.5 %,  $p < 0.05$ ). In biopsy naïve patients, the cancer detection rate (43.7 % vs. 14.8 %,  $p = 0.06$ ) and the cancer positivity of

the cores (30.1 vs. 6.8 %,  $p < 0.01$ ) of target cores were higher than those patients with prior biopsies.

**Conclusion** PHS-TT is feasible and can be an effective tool for real-time guidance of prostate biopsies.

**Keywords** Prostate histoscanning · Prostate biopsy · Target biopsy · Prostate cancer · TRUS biopsy

### Introduction

Lack of an ideal imaging modality that accurately detects cancer within prostate is detrimental in prostate cancer (PCa) management. The conventional 2Dimension (D) gray scale—transrectal ultrasound (TRUS) guided biopsy used currently relies heavily on random biopsy process and hence suffers from the inaccuracies of non-targeted biopsies and systematic sampling errors [1]. Increasing the number of core resulted in relatively better cancer detection rate but was associated with increased complications [2]. Imaging adjuncts that can identify cancer suspicious areas in the conventional TRUS images can enhance the cancer detection rate with fewer targeted biopsy cores.

Prostate histoscanning (PHS) is a novel imaging modality that analyzes the data acquired from TRUS using computer aided application [3]. This software differentiates benign and malignant areas within prostate using various algorithms of discrimination [4]. In spite of overwhelming initial results [3–6], recent studies had shown that the sensitivity and specificity of PHS in detecting PCa lesion  $\geq 0.1 \text{ cm}^3$  was 60 and 66 %, respectively [7]. In the past, PHS generated images indicating the abnormal areas are used for performing targeted prostate biopsy but with the spatial memory of the surgeon. In the present study, we evaluated the feasibility of PHS guided target acquisition

A. Sivaraman · R. Sanchez-Salas (✉) · E. Barret · P. Macek ·  
M. Galiano · F. Rozet · X. Cathelineau  
Department of Urology, Institute Mutualiste Monsouris,  
42, Bd Jourdan, 75674 Paris Cedex 14, France  
e-mail: raersas@gmail.com

P. Validire  
Department of Pathology, Institute Mutualiste Monsouris,  
Paris, France

and TRUS biopsy using an additional specialized software that allows to perform the target biopsy with PHS in situ and provides real-time guidance.

## Methods

### Patient selection

The study was conducted prospectively as a feasibility project from February 2013 to September 2013. All consecutive patients requiring prostate biopsy under single surgeon were included in the study after informed consent. The study was approved by the institutional review board. All patients included in the study underwent combined PHS-TT (HistoScanning™, Advanced Medical Diagnostics, Waterloo, Belgium) and routine bisextant biopsy according to the standard institutional protocol for prostate biopsy.

### HistoScanning and true-targeted biopsy

Initial examination under anesthesia was performed in lateral position. Preliminary TRUS was performed with BK Pro Focus Ultraview ultrasound system with 8818 end-fire probe with ring adapter UA0512. The probe was magnetically attached to a UA0513 rotation mover. It rotates from left to right with a range of 179°, thus 895 sagittal frames (one frame per 0.2°) are acquired. The data were processed by HistoScanning™ workstation with software version 2.3. Scans with rectal artifacts were excluded. The volume of interest (VOI), i.e., prostate volume was defined by the operator through manual interaction with the embedded software. PHS was performed over the VOI by the software, and all abnormal areas (connections)  $\geq 0.2 \text{ cm}^3$  were highlighted within the VOI. The total volume of abnormal area within the VOI was noted. The computer generates a 3Dimension (D) image with spatial orientation of the abnormal areas with the VOI. Normally, the surgeons perform biopsy with cognitive guidance of the spatial orientation of abnormal areas within the prostate. But in this study, we used an additional specialized software that provides real-time guidance for target biopsy with the PHS probe in situ along with an image for directing the biopsy needle through TRUS (Fig. 1). This avoids the need for removing the PHS probe and replacing with TRUS probe. TRUS guided biopsies were taken from the target sites and the number of cores were subjectively decided by the operator depending on the volume of the abnormal areas. In general, two cores from connections  $>0.2\text{--}0.5 \text{ cm}^3$  and three cored from connections  $>0.5 \text{ cm}^3$  were taken. Targets were mainly focused in the more anterior regions of the prostate, which will be presumably missed in routine TRUS biopsies. Following the target biopsies, routine bisextant

biopsies were performed. All the cores were sent in separate labeled containers for histopathological examination (HPE). The final HPE of the target and systemic cores was evaluated and compared.

SPSS version 20 was used for the statistical analysis. *p* value  $<0.05$  was considered significant.

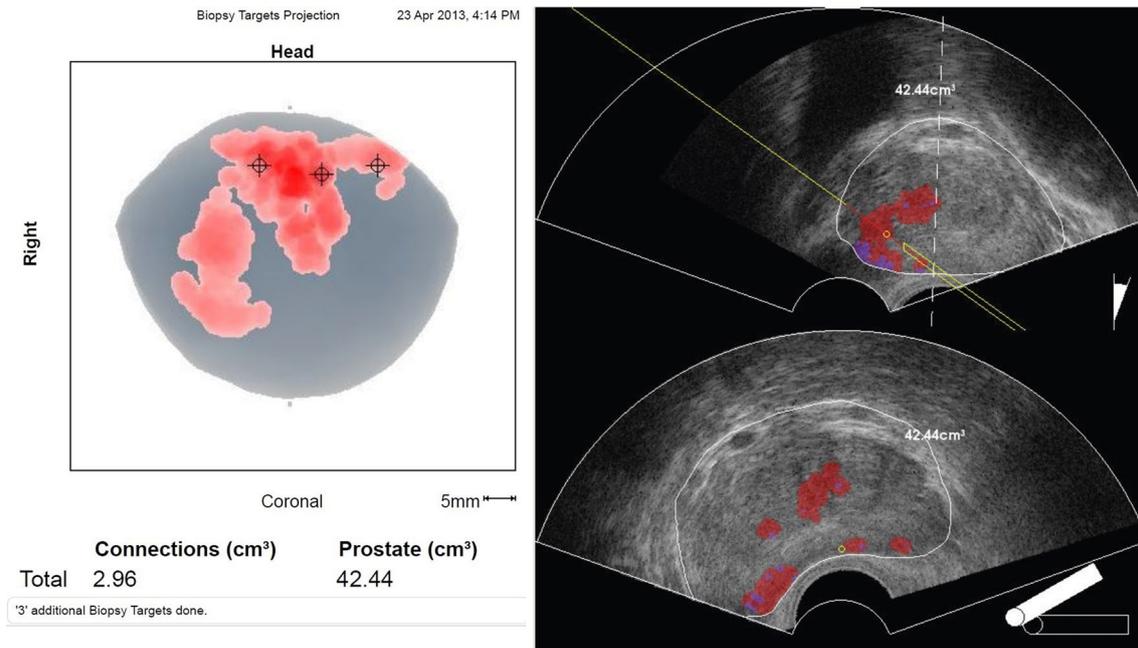
## Results

A total of 43 patients were included in the study and underwent combined 'true-targeted PHS guided' and 'standard 12 core systematic' biopsies. The clinical characteristics of the study population are shown in Table 1. All the patients had abnormal areas in the PHS with a mean volume of  $4.3 \text{ cm}^3$ . The overall cancer detection rate was 46.5 % (20/43). Individual cancer detection rates for systemic cores and target cores were 44 % (19/43) and 26 % (11/43), respectively. We found that 15.2 % (31/204) target cores and 17.4 % (90/516) systematic cores were positive for cancer, and one patient had cancer detected only in the target cores. The mean % cancer/core length of the PHS-TT cores was significantly higher than the systematic cores (55.4 vs. 37.5 %,  $p < 0.05$ ). The comparison of the overall performance of the systematic and PHS-TT cores is shown in Table 2. Among the biopsy naïve patients, the cancer detection rate (43.7 vs. 14.8 %,  $p = 0.06$ ) and the cancer positivity of the cores (30.1 vs. 6.8 %,  $p < 0.01$ ) of target cores were higher than those patients with prior biopsies. This difference was not noted in the systematic cores. The grade of the cancer in target cores was similar to systematic cores in all patients (Table 2).

Using the Clavien-Dindo classification, we observed grade 2 complication in five patients (11.6 %) developing acute retention of urine requiring short term urethral catheterization and alpha blockers. Three of these patients also had mild prostatitis, which was treated with antibiotics. No major complication was noted.

## Discussion

In the present era of advanced imaging techniques, invasive biopsies of solid organ cancers are guided by cross-sectional imaging to accurately target the cancer tissue. Prostate cancer is still outdated in its biopsy technique and relies on chance to pick up cancer in the standard 10- or 12-core biopsy. Increasing the number cores resulted in higher probability of detecting cancer but was also associated with increased complication rates. Several imaging adjuncts to conventional TRUS—color doppler, power doppler, contrast enhanced US, real-time elastography, shear wave elastography and MRI have been used to accurately



**Fig. 1** Sample PHS-TT report with real time guidance

map the cancer suspicious areas within prostate and target the biopsy cores [1, 8–11]. The targeted biopsy techniques were aimed at precise detection and localization of clinically significant prostate cancer with fewer biopsy cores and hence fewer complications. The techniques of these imaging modalities are still evolving, and results are being evaluated. The possibility of using these imaging adjuncts as a triage tool to select patients who are likely to be benefited from the diagnosis is also being investigated [12].

Prostate Histoscanning is another novel ultrasound-based imaging modality currently available and being evaluated for prostate cancer detection. Initial

studies by Braeckman et al. [3, 4] and Simmons et al. [5] in small group of patients had shown superior sensitivity (90–100 %) and concordance (100 %) of PHS detected tumor with radical prostatectomy specimens. Macek et al. [7] had mapped the PHS detected lesions into sectors and compared with corresponding post-prostatectomy specimens and found that for prostate lesions of 0.1 cm<sup>3</sup>, PHS achieved overall sensitivity 73.4 % and specificity 65.7 %. This drop in sensitivity was noted in sector model of other imaging modalities like MRI also [13, 14].

Experience with PHS guided target biopsy is very minimal. Coninck et al. [15] performed combined PHS-targeted and systemic biopsies in 41 patients with suspected prostate cancer and found that PHS-targeted biopsies had a cancer detection rate of 58 % compared to 13 % for random biopsies. Hamann et al. [16] evaluated combined systemic, transrectal PHS-targeted and transperineal PHS-targeted biopsies in 80 patients and had shown that the cancer detection rates were 78.6, 53.6 and 82.1 %, respectively. Javed et al. [17] had compared PHS-targeted biopsies in three small sets of patients against systemic TRUS, transperineal biopsies and radical prostatectomy specimens and showed PHS had 100 % sensitivity with very poor specificity in localizing prostate cancer. The cancer detection rate of PHS was 38.1 %. The present study is the first published experience with PHS guided true targeting software, and the cancer detection rate of PHS-targeted biopsies was 26 % against 44 % for systemic cores. This study was performed as a pilot project to check the feasibility of the PHS embedded with true

**Table 1** Patient characteristics

Number of patients-43	
Mean age	63.7 years
Mean PSA	16.06 ng/mL
Indication	
High PSA (Group 1)	28
Active surveillance (Group 2)	10
Prostate nodule on examination (Group 3)	5
Prior biopsy/TURP	27
Mean prostate volume (TRUS)	57.4 g
Mean prostate volume (PHS)	56.5 g
Mean volume of suspicious area in PHS	4.35 g
Total number of targets-204	
No. of cores in biopsy naïve patients	72
No. of core in patients with Prior biopsy/TURP	132

**Table 2** Overall performance of systematic cores and PHS-TT cores

	Group 1	Group 2	Group 3
<i>Systematic cores</i>			
Cancer detection rate (%)	28.6	50	100
Gleason score			
6 (3 + 3)	6	5	
7 (3 + 4)	2		3
7 (4 + 3)			2
Mean % cancer/core length	43.6	22.4	46.6
<i>PHS-TT cores</i>			
Cancer detection rate (%)	14.3	20	100
Gleason score			
6 (3 + 3)	3	2	
7 (3 + 4)	1		3
7 (4 + 3)			2
Mean % cancer/core length	60.5	45.8	59.9

targeting software. The targets were selected in the more anterior regions of the prostate where the performance of PHS is known to be poor [7], and this resulted in lower cancer detection rate of the PHS-TT cores as compared to systematic cores. However, the mean % cancer/core length of the PHS-TT cores was significantly higher than the systematic cores inspite of this disadvantage. We also observed that the cancer detection rate (43.7 vs. 14.8 %,  $p = 0.06$ ) and the cancer positivity of the cores (30.1 vs. 6.8 %,  $p < 0.01$ ) of PHS targets were higher in patients without prior biopsies/TURP.

With our experience and the available literature, we can propose that PHS has excellent sensitivity in locating abnormal areas within the prostate but not all the abnormal areas detected by PHS are cancers. Many factors may be responsible for this discrepancy. The PHS system is not accurate in prostate volumes greater than 50 g. Macek et al. [7] showed that the overall performance of PHS was affected by rectal distance, bladder fullness, index cancer volume, total cancer volume and the sector location. In our study, we observed that PHS performance was affected by prior TURP/biopsy. We can hypothesize that PHS detects any altered echo texture within the prostate. The micro-architectural disturbances can be produced by prostatitis, prostate biopsy, prior prostate surgery and prostate cancer. Attempts should be made to improve the ability of PHS to effectively differentiate cancer from other textural alterations.

The complications following PHS and targeted biopsies are not specifically reported in literature. Logically, the complications should be proportional to the number biopsy cores taken. Most of the complications in our experience were Dindo-Clavien grade 1 and 2 and no major complications noted.

The level and degree of evidence available before recommending these new interventions and technologies to wider clinical use are inferior, and it will be very challenging to obtain level 1 evidence before implementation [18]. Valerio et al. [19] have proposed alternative models to achieve acceptable evidence. Paired validating cohort design used is Prostate MRI Imaging Study (PROMIS) and is an attractive model that can be used to validate PHS system also [20]. The Standards for Reporting of Diagnostic Studies (STARD) statement have provided researchers with minimum requirements for reporting studies that evaluate diagnostic tests [21]. Future research will decide the clinical use of PHS system in prostate cancer management.

The present study has potential limitations. This was performed on a small group of unselected patients. Single institution and single operator involved in the study may mask the degree of inter operator variability inherent to most of the US-based imaging.

## Conclusion

In this study, we evaluated the feasibility of true-targeted PHS guided prostate biopsy in an unselected patient population and initial clinical experience showed encouraging results. The results of target biopsies were comparable to systematic biopsies and were better in certain variables. Prior biopsy/TURP appears to produce false positive signals in PHS and hence reduce the accuracy of target biopsies. Further studies are needed to evaluate the appropriate technique, clinical efficacy and the limitations of true-targeted PHS guided biopsies in clinical practice. This can potentially be an effective tool for identifying prostate cancer in biopsy naïve patients with better detection rate in fewer biopsy cores and hence less complications.

**Conflict of interest** None.

**Ethical standard** We declare that prior to the start of the study, Independent Ethical Committee (IEC) was obtained. All the patients (or the legal representative) enrolled in the study completed and signed the written informed consent form. The study was conducted in accordance with the Declaration of Helsinki and the EU clinical directive on GPC (2001/20/EC).

## References

1. Smeenge M, de la Rosette JJ, Wijkstra H (2012) Current status of transrectal ultrasound techniques in prostate cancer. *Curr Opin Urol* 22(4):297–302
2. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M et al (2013) Systematic review of complications of prostate biopsy. *Eur Urol* 64(6):876–892
3. Braeckman J, Autier P, Garbar C, Marichal MP, Soviany C, Nir R et al (2008) Computer-aided ultrasonography (HistoScanning): a

- novel technology for locating and characterizing prostate cancer. *BJU Int* 101(3):293–298
4. Braeckman J, Autier P, Soviany C, Nir R, Nir D, Michielsen D et al (2008) The accuracy of transrectal ultrasonography supplemented with computer-aided ultrasonography for detecting small prostate cancers. *BJU Int* 102(11):1560–1565
  5. Simmons LA, Autier P, Zatura F, Braeckman J, Peltier A, Romic I et al (2012) Detection, localisation and characterisation of prostate cancer by Prostate HistoScanning™. *BJU Int* 110(1):28–35
  6. Salomon G, Spethmann J, Beckmann A, Autier P, Moore C, Durner L et al (2012) Accuracy of HistoScanning for the prediction of a negative surgical margin in patients undergoing radical prostatectomy. *BJU Int* 111(1):60–66
  7. Macek P, Barret E, Sanchez-Salas R, Galiano M, Rozet F, Ahalal Y et al (2014) Prostate histoscanning in clinically localized biopsy proven prostate cancer—an accuracy study. *J Endourol* 28(3):371–376
  8. Remiz M, Dobrovits M, Reissigl A, Ravery V, Waldert M, Wiunig C et al (2004) Can power Doppler enhanced transrectal ultrasound guided biopsy improve prostate cancer detection on first and repeat prostate biopsy? *Eur Urol* 46(4):451–456
  9. Li Y, Tang J, Fei X, Gao Y (2012) Diagnostic performance of contrast enhanced ultrasound in patients with prostate cancer: a meta-analysis. *Acad Radiol* 20(2):156–164
  10. Salomon G, Kollerman J, Thederan I, Chun FK, Budaus L, Schlomm T et al (2008) Evaluation of prostate cancer detection with ultrasound real-time elastography: a comparison with step section pathological analysis after radical prostatectomy. *Eur Urol* 54(6):1354–1362
  11. Barr RG, Memo R, Schaub CR (2012) Shear wave ultrasound elastography of the prostate: initial results. *Ultrasound Q* 28(1):13–20
  12. Bossuyt PM, Irwig L, Craig J, Glasziou P (2006) Comparative accuracy: assessing new tests against existing diagnostic pathways. *BMJ* 332(7549):1089–1092
  13. Rosenkrantz AB, Deng FM, Kim S, Lim RP, Hindman N, Mussi TC et al (2012) Prostate cancer: multiparametric MRI for index lesion localization—a multiple-reader study. *Am J Roentgenol* 199(4):830–837
  14. Isebaert S, Van den Bergh L, Haustermans K, Joniau S, Lerut E, De Wever L et al (2012) Multiparametric MRI for prostate cancer localization in correlation to whole-mount histopathology. *J Magn Reson Imaging: JMRI*. doi:10.1002/jmri.23938. Epub 2012/11/23
  15. De Coninck V, Braeckman J, Michielsen D (2013) Prostate histoscanning: a screening tool for prostate cancer? *Int J Urol* 20(12):1184–1190
  16. Moritz FH, Claudius H, Eckhard S, Al-N Amr, Naumann CM, Jeunemann KP (2013) Computer-aided (HistoScanning) biopsies versus conventional transrectal ultrasound-guided prostate biopsies: do targeted biopsy schemes improve the cancer detection rate? *Urology* 81(2):370–375
  17. Javed S, Chadwick E, Edwards AA, Beveridge S, Laing R, Bott S et al (2013) Does prostate HistoScanning™ play a role in detecting prostate cancer in routine clinical practice? Results from three independent studies. *BJU Int* doi:10.1111/bju.12568. [Epub ahead of print]
  18. Cook JA (2009) The challenges faced in the design, conduct and analysis of surgical randomized controlled trials. *Trials* 10:9
  19. Valerio M, El-Shater Bosaily A, Emberton M, Ahmed HU. (2013) Defining the level of evidence for technology adoption in the localized prostate cancer pathway. *Urol Oncol*. pii: S1078-1439(13)00448-1. doi:10.1016/j.urolonc.2013.10.008. [Epub ahead of print]
  20. Lijmer JG, Mol BW, Heisterkamp S, Bossel GJ, Prins MH, van der Meulen JH, Bossuyt PM (1999) Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 282(11):1061–1066
  21. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, Moher D, Rennie D, de Vet HC, Lijmer JG (2003) The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. The Standards for Reporting of Diagnostic Accuracy Group. *Croat Med J* 44(5):639–650