Accuracy of a New Echographic Method (RULES, Radiofrequency Ultrasonic Local Estimators) in Prostate Cancer Diagnosis

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Abstract. Background: This study evaluated the accuracy of a new echographic method named RULES (radiofrequency ultrasonic local estimators) in the diagnosis of prostate cancer. Patients and Methods: A double-blind prospective study was carried out on 105 patients mean age 66.6 years, prostate specific antigen (PSA) >4 ng/ml with clinical and/or biochemical suspicious of prostate cancer. Patients were submitted to transrectal prostate biopsy (8 to 12 cores) using a traditional echograph connected to a new hardware/software platform named FEMMINA (fast echographic multiparameter multi image novel apparatus) that processes the echo signal by a RULES (radiofrequency ultrasonic local estimators) algorithm. Histological findings were compared to B-mode and RULES modality. Results: Cancer was detected in 32/105 patients, of which 26/32 were determined as positive with the RULES method. RULES had better positive predictive value, negative predictive value, specificity and accuracy than B-mode. Conclusion: Results obtained with RULES are encouraging and, if further confirmed, could help to reduce the number of unnecessary prostatic biopsies.

Screening campaigns against prostate cancer using the prostate specific antigen (PSA) concentration have dramatically increased the number of patients diagnosed. Nowadays, prostate cancer is suspected for elevated PSA levels, for an abnormal digital rectal examination (DRE) and/or for the presence of hypoechoic areas at transrectal ultrasound (TRUS), and it is diagnosed through a needle biopsy. Unfortunately, traditional ultrasound has a low sensitivity and randomized biopsies, with at least 8 cores, are needed in order to find a neoplasia. Color Doppler (CDU) and power Doppler ultrasonography (PDU) have been used to gain sensitivity and specificity in standard diagnostic methods, but they were not able to increase the detection rate of the B-mode modality enough to justify their use in routine practice (1-3). In order to improve cancer detection over that using traditional ultrasound, we have developed a new ultrasound modality able to differentiate neoplastic from non-neoplastic areas within the prostate and to allow their identification by means of a chromatic image. This new technique processes the ultrasound signal by a mathematical algorithm called RULES (radiofrequency ultrasonic local estimators) that allows to extract, information on the amplitude and the phase of the radiofrequency ultrasound signal (radio-frequency signal - RF - is the ultrasonic signal collected by the receiving transducer) for each time instant (4-8). The innovation of this method consists in the analysis of the radiofrequency signal whose components are related to the architectural and mechanical structures of tissues. We have obtained our first results from an ex vivo study in which RULES accuracy was tested in 60 prostate specimens of patients undergoing radical retropubic prostatectomy for clinical localized prostate cancer (4). After those encouraging results on surgical specimens, we developed a primary study on 60 patients to verify the accuracy of RULES in detecting prostate cancer in vivo. Despite the small cohort of patients enrolled, data on sensitivity and specificity of RULES were found to be higher than those of the B-mode modality (sensitivity 77% vs. 61% and specificity 90% vs. 80%). The aim of the present study,
with a major number of patients enrolled (105) than the above cited research, was to report accurate data on the efficacy of RULES versus the standard B-mode modality.

Patients and Methods

This prospective double-blind study was developed over 2 years. One hundred and five men, aged 66.6 years on average, were enrolled on a clinical (positive digital rectal examination) and/or biochemical (PSA ≥10 ng/ml or PSA <10 ng/ml and F/T PSA ≤15%) basis of suspicious of prostate cancer. The study schedule included a transrectal ultrasound of the prostate (TRUS) performed with an ESAOTE Megus echograph connected to a 7.5 MHz probe and to a hardware-software echographic platform, named FEMMINA (fast echographic multiparameter multi image novel apparatus) employed for signal and image processing with respect to the RULES algorithm (Figure 1). The study of each patient was completed with a prostate biopsy. A urologist performed the TRUS and the biopsy, and engineers collected and subsequently processed the radiofrequency signal information as dictated by the RULES algorithm. The new echographic method allows suspect areas to be represented by means of a chromatic image superimposed on the conventional B-Mode image (5-10).

None of the engineers knew the B-mode findings during the phase of data acquisition, which consisted both of the acquisition of the RF ultrasound signals through the TRUS of the prostate and of performing a needle biopsy. In the same way, neither did the urologist know the RULES results. TRUS was performed moving
the probe axially from the base to the apex and laterally from right to left (Figure 2). The procedure was then repeated acquiring data with the echographic platform FEMMINA.

All patients subsequently underwent TRUS-guided biopsies of prostate and the biopitic scheme used was the sextant associated to bilateral cores of the peripheral gland and eventually of suspected hypoechoic areas (8 to 12 cores). Finally, histological findings of biopsies were compared with results of TRUS and RULES in order to assess sensitivity, specificity, and the positive and negative predictive value (PPV and NPV) of the two methods.

Results

Pathological areas were shown with the RULES method as chromatic zones (Figure 1). The cohort of patients studied (105) had a mean serum PSA of 7.75 ng/ml and mean total prostate volume of 57.7 cm³. Only 27 patients had a positive DRE (Table I). Thirty-two out of 105 patients had histological findings of prostate cancer, 26 of whom showed positive findings with the RULES method, 22 with the B-mode modality and 3 were negative in both. The PPV and NPV of the B-mode were 47% and 83% respectively, while RULES gave a PPV of 74% and NPV of 91%. Sensitivity and specificity of the B-mode resulted 68.8% and 91.4% respectively, while sensitivity and specificity of RULES were 81.2% and 91.4% respectively. B-mode diagnostic accuracy was 67.6% and RULES accuracy was 85.7% (Table II).

In the 6 patients in which the RULES method failed to recognize neoplastic tissue, we observed that these tumours were low grade (lower than 6) and low volume (only 1 positive core detected). Moreover, when we analyzed our cohort of patients according to PSA value (PSA less than 4 ng/ml, from 4 to 10 ng/ml and greater than 10 ng/ml), we noticed a decrease in sensitivity and in PPV (less than 40%) of the RULES method for patients with PSA ≤4 ng/ml (9 patients).

Discussion

This preliminary report of 105 patients represents the beginning of the future application of TRUS with the RULES method for acquiring prostate images. More patients are necessary in order to define the clinical application of this new echographic method even if RULES has demonstrated a superior test performance compared to the B-mode modality in detecting prostate cancer, in terms of sensitivity and PPV. The ability of RULES to better determine neoplastic areas than the traditional B-mode could be interesting for reducing the number of unnecessary biopsies largely in patients with suspicion of prostate cancer if chromatic areas allow a more accurate localization and the possibility to execute targeted biopsies. This is very important in order to reduce the number of biopsy cores, especially in re-biopsied patients, and in order to perform only targeted biopsies. The lack of sensitivity in detection of low-grade well-differentiated prostate carcinomas (the 10 patients with Gleason score lower than 6), which could appear to be a limit for the RULES modality, could be seen as an advantage for the discrimination between aggressive and non-aggressive neoplasms: the inability to detect such neoplasias could allow overdetection and subsequently overtreatment to be avoided. The results of this study are the basis for developing a study in which targeted biopsies on suspected areas are performed in real-time with the RULES method.

References


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