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Multiparametric MRI for prostate cancer detection: Preliminary results on quantitative analysis of dynamic contrast enhanced imaging, diffusion-weighted imaging and spectroscopy imaging

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ABSTRACT

Introduction: Early promising data suggest that combined use of both morphological and functional MRI (multi-parametric MR, mpMRI) including MRSI, DWI and DCE may be of additional value for prostate cancer localization and its local staging. The objective of this paper is to evaluate the diagnostic performance of mpMRI in the detection of prostate cancer.

Methods: Thirty-one consecutive male patients were screened to be enrolled in a single center prospective observational study. All eligible patients underwent multi-parametric MRI and TRUS (Trans Rectal Ultra Sound) guided prostate biopsies. A register, approved by the Institutional Ethics Committee, included patients enrolled in this study. All patients who decided to undergo the MRI examination signed an explicit informed consensus. MRI data were aligned on a common spatial grid and several functional parameters (perfusion, diffusion and metabolic parameters) were computed. Statistical analysis was conducted in order to compare mpMRI with biopsy-based analysis.

Results: Statistically significant differences between median values in high Gleason score (≥5) and low Gleason score (<5) to Wilcox on rank sum test were obtained for MRSI parameters and for plasma fraction (Tofts model) of DCE-MRI. The area under curve obtained with ROC analysis showed that the best-performing single-parameter was v_p (plasma fraction of Tofts model), while the best parameters combination to discriminate the area with high Gleason score were (Cho + Cr)/Cit and Cho + Cr. Linear Discrimination Analysis showed that the best results were obtained considering the linear combination of all MRSI parameters and the linear combination of all features (perfusion, diffusion and metabolic parameters).

Conclusions: In conclusion, our findings showed that by combining morphological MRI, DWI, DCE-MRI and MRSI, an increase in sensitivity and specificity correlated to biopsy Gleason grade could be obtained. Furthermore, morphological and functional MRI could have a diagnostic role in patients with prostate cancer, identifying those patients who will have a negative work-up and those patients at high risk for a high Gleason score cancer of the prostate.

1. Introduction

Prostate cancer diagnosis still represents a clinical challenge, as currently available diagnostic methods remain suboptimal [1–3]. Moreover, there are both overdiagnosis and overtreatment risks [4,5]. Currently, prostate biopsy remains the only procedure that provides a definitive diagnosis.

However, the commonly used biopsy-based Gleason score might undergrade the disease [6–8]. It is also an invasive procedure that has a suboptimal sensitivity due to a lack of 10–20% in the rate of

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cancer detection on repeated biopsy after an initial negative biopsy [9]. Last but not least, transrectal biopsy is also associated to some complications, particularly urosepsis, with increasing cases of antibiotic resistant infections [10]. Infection rate is correlated to the number of biopsy cores [11].

Ideally, a reliable diagnostic test should provide an early cancer diagnosis, minimizing the occurrence of unnecessary biopsies. From this perspective, morphological MRI (mMRI) is a good candidate for prostate cancer investigation as it can provide excellent high contrast, high-resolution images of the prostate [8].

In recent years, functional techniques have been applied to improve the performance of MRI in the diagnosis of prostate cancer [12]. MR spectroscopic imaging (MRSI) can measure metabolites concentrations within the prostate, particularly choline and citrate, which are respectively increased and reduced in cancer. Diffusion Weighted Imaging (DWI) determines water diffusion properties, water diffusion is normally reduced in highly cellular cancer tissues [9]. Lastly, dynamic contrast enhanced (DCE) MRI can provide information on tissue angiogenesis.

Early promising data suggest that combined use of both morphological MRI and functional MRI (multi-parametric MR, mpMRI) such as MRSI, DWI and DCE may be of additional value for the localization of prostate cancer and its local staging [12].

The aim of this study is to evaluate the diagnostic performance of mpMRI in the detection of prostate cancer reporting preliminary results on 31 patients. Each patients underwent multi-parametric MRI, all data were aligned on a common spatial grid and several parameters were computed. Statistical analysis was then conducted in order to compare mpMRI with biopsy-based analysis.

2. Materials and Methods

2.1. Patient selection

Twenty-one consecutive male patients were screened to be enrolled in a single center prospective observational study (Table 1). The inclusion criteria was histologically proven prostate cancer. The exclusion criteria were as follows: inability to give informed consent; prior history of prostate cancer; prior pelvic irradiation; previous hormonal or surgical therapy; MRI contraindications (cardiac pacemakers, surgical clips and metallic hip implant); recent rectal surgery; severe hemorrhoids; or latex allergy.

All eligible patients underwent multi-parametric MRI and TRUS (Trans Rectal Ultra Sound) guided prostate biopsies. The study was approved by the review board of National Cancer Institute Pascale Foundation of Naples and written informed consent was obtained from each patient.

2.2. MR protocol

The mpMRI was performed before prostate biopsies. The MRI protocol included the insertion of an endorectal coil (EC) (Medrad, Pittsburg, PA), inflated with 60–90 mL of air, and subsequent imaging acquisition using both a 1.5 Tesla (T) MRI system (Siemens Symphony Tim, Erlangen, Germany) and a four-channel phased-array surface coil coupled to the endorectal coil. The MRI total acquisition time was of approximately 50 min. The multi-parametric MRI included mMRI, MRSI, DWI and DCE.

The morphological MRI comprised turbo spin echo (TSE) T2-weighted sequences in three perpendicular planes and coronal and transversal TSE T1-weighted sequence.

TSE T2-weighted sequence parameters were as follows: repetition time/echo time (TR/TE), 3800/104 ms (sagittal: 4660/96 ms; coronal: 5000/98 ms); slice thickness, 3 mm/gap 0 mm; flip angle, 180°; acquisition matrix, 320×288 (sagittal and coronal 320×256); field of view (FOV), 240×240 mm^2. T2-weighted images were obtained with and without fat saturation.

TSE T1-weighted were acquired in coronal to visualize lymph nodes, with the following sequence parameters: TR/TE, 550/12 ms; slice thickness, 3 mm/gap 0 mm; flip angle, 150°, acquisition matrix, 256×202; FOV, 448×512 mm^2. Transversal TSE T1-weighted sequence parameters were: TR/TE, 706/7.8 ms, slice thickness, 3 mm/gap 0 mm; flip angle, 150°; acquisition matrix, 356×192; FOV, 240×240 mm^2.

The MRSI parameters were: TR/TE, 690/120 ms; flip angle, 90°. The volume of interest (VOI) was composed by 32×32×16 voxel of 4.375×4.375×10 mm^3.

The transversal echo-planar DW-MRI pulse sequence parameters were: TR/TE, 2700/83 ms; slice thickness, 3.6 mm; flip angle, 90°; FOV, 136×160 mm^2; pixel spacing 1.67×1.67 mm^2; b value = 0, 50, 100, 150, 300, 600, 800 s/mm^2.

DCE-MRI sequence was as follows: 50 volumes, obtained without any gap after intravenous injection of 2 mL/kg of patient's weight of a positive, gadolinium-based paramagnetic contrast medium (Gadobutrol Gd-DTPA, Bayer Pharma AG, Berlin, Germany). The contrast medium was injected using Spectris Solaris® EP MR (MEDRAD Inc., Indianola, PA), with a flow rate of 2 mL/s, followed by a 10-mL saline flush at the same rate. T1-weighted Time-Resolved Angiography with Stochastic Trajectories (TWIST) 3-D transversal images were acquired in order to reduce temporal resolution. Acquisition parameters were: TR/TE, 3.01/1.09 ms; flip angle, 25°; slice thickness, 2 mm/gap 0 m; FOV, 300×300 mm^2; pixel spacing 1.17×1.17 mm^2; Temporal resolution, 10 s; pA: 0.20, pB: 0.20. The choice of pA and pB was based on the results of [13]. Antispasmodic drugs were not used.

Table 1
Patient characteristics.

	Patients with diagnosis of prostate cancer
Patients, n	31
Age, years	70.79 (5.85)
PSA, ng/mL	6.8 (2.4)
Positive biopsy core, n	3 (2.5)
Gleason score	6.4 (1.5) range 3–10

2.3. Volumes co-registration

All subsequent data analysis was performed using an in-house software written by Matlab R2007a (The MathWorks, Inc., Natick, MA, USA).

3D linear interpolation was performed in order to align DCE, DWI and MRSI data on a common spatial grid. Before alignment, the voxel size of DCE, DWI and MRSI were 1.17×1.17×2 mm^3, 1.67×1.67×3.6 mm^3 and 4.375×4.375×10 mm^3 respectively. After the alignment, the common spatial resolution was 4.375×4.375×10 mm^2. For the subsequent analysis, only voxels included in all datasets were considered.

2.4. DCE-MRI processing

We modeled the time intensity course (TIC) of contrast agent (CA) concentration within the tissue using the Eq. (1) [14]:

$$C_t(t) = v_p C_p(t) + C_p(t) * K^{trans} e^{-kept} \quad (1)$$

where $C_t(t)$ is the CA concentration at time t within the voxel of interest; $C_p(t)$ is the CA plasma concentration (AIF); K^{trans} is the volume transfer constant from plasma to Extracellular-Extravascular

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