Editorial

Proton Spectroscopic and Dynamic Contrast-Enhanced Magnetic Resonance: A Modern Approach in Prostate Cancer Imaging

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1. Introduction

At present, the evaluation of prostate cancer is more determined by the use of clinical nomograms including prostate-specific antigen (PSA) determination and by pathologic findings of the tumour at biopsy or after surgery. For a long time, a valid diagnostic imaging procedure has not been available for prostate cancer detection, staging, and follow-up during therapies. All three cross-sectional imaging modalities [computer tomography (CT), ultrasonography, and magnetic resonance (MR)] have been employed in patients with prostate cancer, and each have important limitations. In particular, reports on the value of magnetic resonance imaging (MRI) have been contradictory [1].

Recently a large number of studies [2–5] have shown that the addition of proton 1H-magnetic resonance spectroscopic imaging (1H-MRSI) and dynamic contrast-enhanced imaging to MR (DCEMR) could represent a powerful tool for the management of prostate cancer in most of its aspects: initial diagnosis, cancer localization and local staging, assessment of tumour aggressiveness, road-map for surgery and radiotherapy, and early detection of local recurrence.

2. Technical aspects

To obtain a combination of MRI with spectroscopic imaging, a magnet strength of at least 1.5 T is required, and the combination of an endorectal coil with a pelvic phased-array coil and the generation of faster imaging sequences are advisable [1]. In this way MRI and MRSI of the prostate can be performed in less than 1 h [1,2].

On T2-weighted MR images, the zonal anatomy of the prostate can be analysed. A decreased signal intensity within the high-intensity normal peripheral zone can be attributed to prostate cancer, but similarly to several benign conditions such as haemorrhage, prostatitis, hyperplastic nodes, or sequelae resulting from radiation or hormonal treatments [1,2]. The advantage of MRSI is that the spectroscopic analysis provides metabolic information regarding prostatic tissue by displaying the relative concentrations of chemical compounds within contiguous small volumes of interest (voxels). In addition, MRSI metabolic mapping of the entire prostate gland is possible with a resolution of 0.24 ml or smaller [1]. Choline, creatine, polyamines, and citrate are the metabolic peaks relevant to prostate cancer [5]. The spectral trace of prostate
cancer is characterized by raised choline (cell membrane constituent) or reduced citrate (conversion from a citrate-producing to citrate-oxidating metabolism), or both [1,5]. Therefore, an increased choline-to-citrate ratio is associated with prostate cancer. Because the creatine peak is very close to the choline peak, for practical purposes, the choline+creatine/citrate (Cho+Cr/Cit) ratio is used for the spectral analysis in clinical practice [1,5–7]. We must remember that this ratio includes also polyamines. The polyamine peak decreases in the presence of prostate cancer, and this is one of the reasons for going to higher magnetic field–strength MRI machines, in order to resolve these metabolites.

Dynamic contrast-enhancement can be used to improve MRI results in prostate cancer. DCEMR images can be acquired by using T1-weighted sequences so as to perform measurements in rapid succession, immediately following completion of an intravenous bolus injection of gadopentetate dimeglumine. The dynamic MR procedure can be performed in approximately 15 min per patient [2]. Functional dynamic imaging parameters are estimated as onset time of signal enhancement, time to peak, and peak enhancement and washout. DCEMR has shown to have a sensitivity of 73% and a specificity of 81% in defining prostate cancer [3].

At this time, more data in the literature are referred to MRSI than to the DCEMRI technique for the management of prostate cancer.

3. Role of MRSI in the initial diagnosis and cancer localization

Ultrasound-guided biopsy is considered the preferred method for prostate cancer detection and characterization. However, some studies have reported that sextant biopsies missed up to 30% of cancers, and biopsy results when compared with radical prostatectomy for tumour localization, showed a positive predictive value of 83.3% and a negative predictive value of 36.4% [1]. The term “virtual biopsy” has been coined to refer to the ability of MRSI to provide noninvasive tissue characterization of brain tumours. This optimistic terminology is not yet appropriate for prostatic MRSI, which is sustained by a limited number of validated studies [5].

MRSI may be used to stratify patients with a high and low probability of a subsequent positive biopsy. Although MRSI is not used at this time as a first approach to diagnose prostate cancer, it can be useful for directing targeted biopsies, especially for cases with PSA levels indicative of cancer and negative previous biopsy. The potential incremental benefit of MRSI could be attributed to the possibility of increased specificity for sextant localization of prostate cancer.

In this first step of prostate cancer management, the hope is that a combined use of MRI/MRSI may reduce the rate of false-negative biopsies, decrease the need for more extensive biopsies or repeat biopsy procedures, directing with a significant specificity and sensitivity a targeted biopsy.

4. Role of MRSI in local staging

The literature shows a wide range (50–92%) in the accuracy of local staging by MRI [1]. Because of a lower sensitivity and observer variability in identifying organ-confined and extracapsular diseases, the routine use of MRI in local staging of prostate cancer continues to be not recommended. Some studies have suggested that the addition of volumetric data from MRSI to the anatomic analysis of MRI significantly improves the evaluation of extracapsular extension and, in particular, MRSI analysis can reduce interobserver variability [1]. These suggestions must be better confirmed in larger validation studies.

5. Role of MRSI in the determination of tumour aggressiveness

The determination of prostate cancer aggressiveness is a very significant parameter for defining prognosis and treatment strategies. Biopsy specimens are not always accurate in the definition of Gleason grade, and significant percentages of downgrading between biopsy and radical prostatectomy have been reported [1,5].

MRSI has the potential to provide a noninvasive significant method for the clinical prediction of prostate cancer aggressiveness before treatment. Several studies [1,5,8] have indicated that the grade of elevation of choline and reduction of citrate can describe cancer aggressiveness, so that the Cho+Cr/Cit ratio correlates with the Gleason grade. A complication in the interpretation of Gleason grade could be the partial voluming of surrounding regions of healthy tissue when the cancer does not completely occupy the voxel used for MRSI [5]. Another limit in the MRSI prediction of prostate cancer aggressiveness is represented by a similar spectroscopic pattern between prostatic inflammation and low-grade tumours.
6. **Role of MRSI for treatment planning**

Currently, different clinical parameters are enclosed in nomograms to define an optimal treatment for each prostate cancer patient. A metabolic mapping of the prostate gland by MRSI may help to obtain a correct tumour-targeted therapy. The inclusion of MRSI in the actual nomograms may improve prediction of prostate cancer localization and extension, thereby improving patient selection for therapies. The possibility of mapping tumour volume or localizing more aggressive regions within the tumour is a relevant aspect. In the surgical plan, MRSI could help to define the preservation of periprostatic tissues (in particular neurovascular bundles) and to minimize the risk of positive surgical margins [1,5].

At this time, this role of MRSI is applied largely in patients selected for radiotherapy. MRSI can improve dose-volume planning in radiotherapy when compared to CT and MR, decreasing radiation dose to other sites [1,5].

7. **Role of MRSI and DCEMR in the definition of posttreatment local recurrence**

Some studies have shown that MRSI may be of value in the detection of locally recurrent prostate cancer after radiotherapy [5]. Coakley et al [9] suggested that the presence of three or more spectroscopic voxels with Cho+Cr/Cit ratio > 1.5 is associated with a sensitivity and specificity of 87% and 72%, respectively, for the presence of local recurrence after radiotherapy. On the contrary a complete metabolic atrophy was associated with a negative predictive value of 100% for the exclusion of local recurrence [9].

Recently Sciarra et al [2] analysed the accuracy of MRSI and DCEMR in the definition of local recurrence in patients with biochemical progression after radical prostatectomy. This work [2], first demonstrated that combined MRSI and DCEMR is a more accurate method (87% sensitivity and 94% specificity) than single MRSI or DCEMR analysis for identifying local prostate cancer recurrence in patients with biochemical progression after surgery. It is important to underline that in this study [2] the maximal transverse dimension of a mass representing local recurrence averaged 13.3 ± 4.5 mm in a first group validated by biopsy and 6.0 ± 0.5 mm in a second group validated by PSA restitution after radiotherapy. The study [2] sustains that combined DCEMR and MRSI are promising modalities for the correct definition and treatment planning of a biochemical progression after surgery for prostate cancer. After surgical removal of the prostate gland, spectroscopic and dynamic assessment of suspicious local recurrences can accurately distinguish between fibrotic/healthy prostate gland tissue (Cho+Cr/Cit ratio, < 0.5) and recurrent prostate cancer tissue (Cho+Cr/Cit ratio, > 0.5).

8. **Conclusions**

Several data underline an emerging role of MRI with MRSI and DCEMR as the most sensitive tool for the imaging of prostate cancer. The metabolic evaluation offered by the spectroscopic analysis and the functional dynamic evaluation offered by DCEMR significantly improve the accuracy of the anatomic imaging of prostate cancer obtained with MR [10].

This combination of MR techniques can substantially sustain the clinical management of patients with prostate cancer at different levels: in particular (1) in the initial assessment, reducing the need for more extensive biopsies and directing targeted biopsies; and (2) in the definition of a biochemical progression after primary therapies, distinguishing between fibrotic reaction and local recurrence from prostate cancer.

**Conflicts of interest:** The authors have nothing to disclose.

**References**


