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UROONCOLOGY
Mini Review

MRI apparent diffusion coefficient (ADC): A biomarker for prostate cancer after radiation therapy

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ABSTRACT

Prostate specific antigen (PSA) remains the most used test to assess the response after therapies including the radiation therapy (RT). Apparent diffusion coefficient (ADC) derived from the conventional diffusion-weighted imaging (DWI), as a part of noncontrast or biparametric MRI (bpMRI) (T2-weighted and DWI), offers diagnostic accuracy and cancer detection rate equivalent to that of multiparametric MRI. Cellular changes induced by RT can be quali-qualitatively demonstrated as early as 3 months after RT as an increase in the signal intensity of the tumor on the ADC map. ADC, in association with PSA, represents a potential biomarker imaging for evaluating treatment efficacy in PCa both during and shortly after RT.

Keywords: Apparent diffusion coefficient; biparametric magnetic resonance imaging; prostate cancer radiation therapy; prostate cancer therapies

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Prostate cancer (PCa) is the second most common cancer diagnosis in the United States, the third of cancer death with estimates about 248,530 new cases and about 34,130 deaths in 2021.[1]

Prostate specific antigen (PSA) remains the most used test to assess the response after therapy including the radiation therapy[2]; however, it is often a deleted tool for the follow-up of these patients especially if considered alone:

1. PSA is often less produced in more aggressive and undifferentiated cancers.
2. PSA increase, after treatment, may become evident only when the disease is already progressing.
3. Follow-up based only on PSA dosage can significantly delay treatment decisions.

Apparent diffusion coefficient (ADC), derived from the conventional diffusion-weighted imaging (DWI), is a short scan widely available on commercial MR scanners. It is a part of noncontrast or biparametric MRI (bpMRI) including T2-weighted and DWI/ADC that requires less than 9 minutes of examination and offers diagnostic accuracy and cancer detection rate equivalent to multiparametric MRI.[3–5]

Moreover, the no-use of gadolinium-based contrast medium and thus the elimination of the risk of immediate hypersensitivity reactions[6] and depositions in the brain must be considered.[7]

ADC measures the diffusive movement of water molecules within the tissue, which is often influenced by microstructure, cell density, and other histological components present in the tissue at a microenvironmental level. ADC is commonly clinically calculated using MRI with DWI[8] and the following formula based on a monoexponential model:

$$Sb/S0 = \exp(-b \cdot ADC),$$

where Sb and S0 are the signal intensity with and without the application of the diffusion gradient, respectively.

Table 1. Time of Increase in the Signal Intensity of the PCa on the ADC Map After Radiotherapy

Author/Year	Type of RT	Time After RT (Months)	MRI Scanner	ADC Maps Analysis
Takayama et al[17]	Carbon-ion radiotherapy	3-9	1.5 T	Qualitative
Song et al[18]	EBRT	1-5	3.0 T	Quali-quantitative
Park et al[19]	Radiotherapy	1	3.0 T	Quali-quantitative
Decker et al[20]	Intensity-modulated EBRT	3	3.0 T	Quali-quantitative
Wu X et al[21]	Radiotherapy	3-12	3.0 T	Quali-quantitative

RT: radiotheraphy; MRI: magnetic resonance imaging; ADC: apparent coefficient diffusion; EBRT: external beam radiation therapy.

High signal intensity (white) on DWI at high b-values and low signal intensity (black) restricted diffusion on ADC map reflect cellularity in PCa malignant tissue; ADC values are inversely proportional to tumor cellularity and correlate well with tumor aggressiveness (i.e., Gleason score) improving specificity of prostate MRI.[9–12]

The potential applications of DWI as a biomarker are manifold. DWI has further improved the performance of MRI in detection[13,14] of primary and recurrent PCa and has allowed a more accurate characterization, localization, and local staging of prostatic lesions.[15,16]

Thanks to DWI introduction, prostate MRI has gained increasing interest for the pretreatment assessment of PCa, in the radiotherapeutic planning and in follow-up of patients after radical prostatectomy or radiation therapy to detect local cancer recurrence.

Several studies demonstrated that PCa ADC value can increase significantly after radiotherapy (Table 1):

1. after carbon-ion radiotherapy[17];
2. in both peripheral and transitional zones 1-5 months after completion of external beam radiotherapy (EBRT)[18];
3. during and 1 month after radiotherapy in patients treated for PCa[19];
4. during, immediately, and 3 months after intensity-modulated EBRT, but the ADC value of healthy prostate tissue did not change significantly after irradiation[20];
5. 3 months after irradiation compared to that pretherapy status, and it increased further at 12 months after treatment.[21]

Main Points

- Apparent diffusion coefficient (ADC), as a part of biparametric MRI, represents an accurate tool for both diagnosis and follow-up of prostate cancer.
- Cellular changes induced by radiation therapy can be quali-quantitatively demonstrated by ADC maps.
- ADC can be considered a biomarker to evaluate prostate cancer response after radiotherapy.

Our experience, with an MRI scanner at 3.0T, also demonstrates that radiation therapy-induced cellular change can be showed qualitatively already 3 month after radiation therapy. A reduction in the volume of the prostate gland and an increase in the signal intensity of the tumor on the ADC map are shown (Figure 1).

The detection and targeting of local recurrence after radical prostatectomy and/or radiotherapy represent an additional potential use of DWI and could have important applications in the treatment of recurrent diseases. Morgan et al.[22] reported that ADCs derived from DWI used as an adjunct to T2-weighted MRI for detecting local tumor recurrence within the prostate had a 93.8% sensitivity and 75% specificity for identifying lesions larger than 0.4 cm^2. Recent studies evaluated the efficacy and safety of re-irradiation in recurrent PCa patients using stereotactic body radiotherapy and showed an excellent 3-year disease control with an acceptable toxicity.[23]

In conclusion, bpMRI is a valid technique not only for diagnosis but also for radiation therapy planning in patients with PCa. It provides anatomical and functional information of high spatial resolution and allows to improve the definition of target volumes in radiation therapy. Moreover, ADC derived from DWI as a part of bpMRI in association with PSA represents a potential tool for evaluating treatment efficacy in PCa during and shortly after irradiation; the role of this functional imaging in patients underwent to reirradiation is suitable to further investigations.

Informed Consent: Written informed consent was obtained from the participant who participated in this study.

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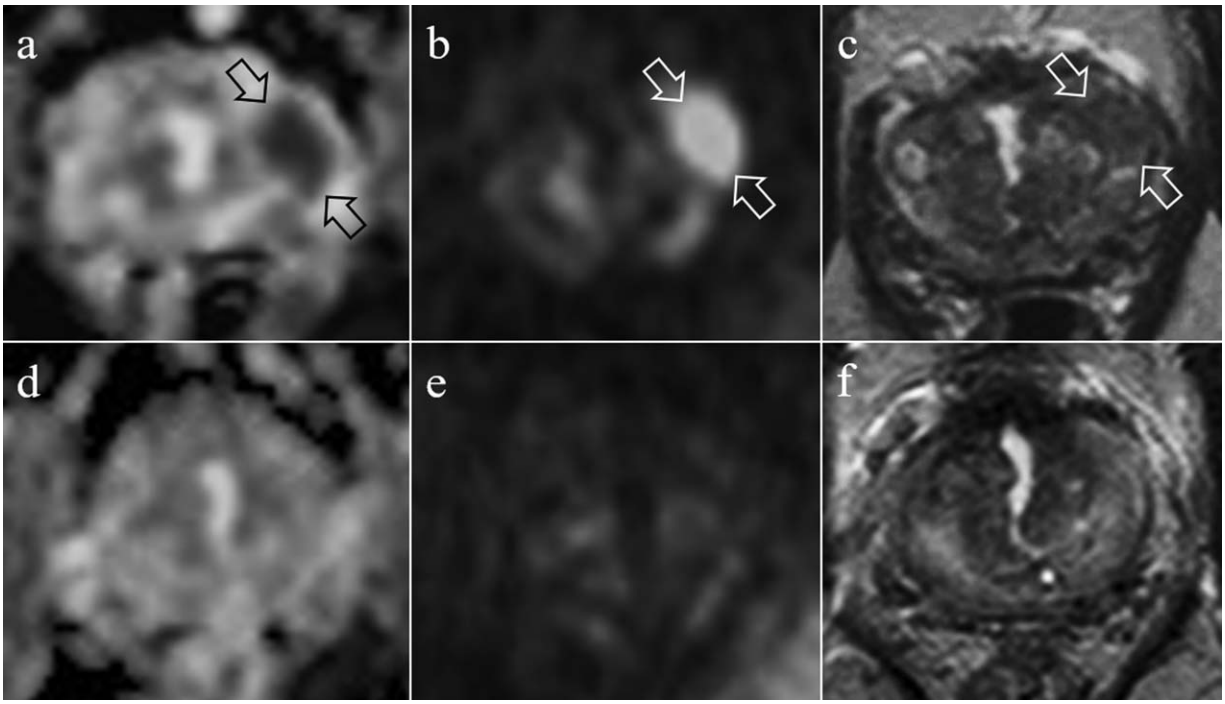

Figure 1. Apparent coefficient diffusion (ADC) (a), corresponding DWI at high b-values (1,500 s/mm^2) (b) and T2-weighted (c) biparametric MRI at 3.0T in an 82 year-old patient with increase in serum PSA level = 7.6 ng/mL showed an ovalar lesion located in the left anterior transition zone at the middle part with marked hypointensity indicative of marked restricted diffusion on ADC map (arrows in a) and hyperintensity on corresponding DWI at high b-values (1,500 s/mm^2) (arrows in b) and hypointense on T2-weighted imaging (arrows in c). Gleason score 3 + 4 = 7 adenocarcinoma at histology after targeted biopsy. ADC map (d), corresponding DWI at high b-values (1,500 s/mm^2) (e) and T2-weighted (f) biparametric MRI obtained 6 months after radiation therapy showed an increase in tumor signal intensity on ADC map (d) reflecting its complete resolution and on T2-weighted imaging (f) the reduction of the prostate gland size.

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