Use of Multiparametric MRI in T-Staging of Prostate Cancer

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Abstract

Prostate cancer is one of the most common malignancies in men, generally with a slow growth rate and early detection is essential for a complete treatment. Multiparametric magnetic resonance imaging (MP MRI) lead to a better choice of therapy by improving detection and staging of prostate cancer. Conventional sequences are useful to evaluate prostate cancer in the peripheral zones; functional acquisitions, represented by DWI and DCE, extent the MR diagnostic accuracy particularly in central and anterior fibromuscular stroma zones. This technique also improves the differential diagnosis of prostate cancer.

Keywords: MP MRI, prostate cancer, staging

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**Introduction**

Prostate cancer is the most frequently diagnosed cancer in males and the second most common cause of death from cancer in men [1].

The choice of therapy and prognosis for prostate cancer has been based mainly on the following factors, serum prostate specific antigen (PSA) level, digital rectal examination (DRE) and transrectal ultrasonography (US)-guided systematic random prostate biopsies [1-6].

The PSA level provides a higher detection rate of prostate cancer than digital rectal examination, but its specificity is low (36%) with false-positive results in benign conditions, such as benign prostatic hyperplasia (BPH), acute and chronic prostatitis [4, 7, 8].

The biopsy sample analysis provides informations on Gleason score, which correlates with prostate cancer prognosis, but Gleason score is underestimated in 46% of cases [4, 9-11]; 35% of cancers are missed on first biopsy because of its location outside the routine biopsy zone [4, 6, 12, 13].

The MRI examinations lead to a better choice of therapy by improving detection and staging of prostate cancer; currently, the treatment modalities include active surveillance for low-grade and small-volume tumors, surgery, radiation therapy and hormone therapy [2].

**MP MRI - Principles**

MP MRI examination includes an anatomic T2-wi acquisition and at least two functional acquisitions[6, 14, 15]; based on our experience, we will refer to these functional acquisitions, diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MR Imaging [6].

For a correct and easy analysis, it is important to use the standardize MR planes for the evaluation of prostate cancer: axial plane, coronal plane, slice in the seminal vesicle plane, slice in the prostate long axis and slice perpendicular to the rectal-prostatic interface [16]. In addition, the slices used in T2-wi, DWI, DCE T1 after Gd injection must have the same plane, slices number, slice thickness and identical interslice space [16].

**Pitfalls and limitations**

Andrew B. Rosenkrantz and Samir S. Taneja [17] identified ten pitfalls that may limit the characterization of the prostate tissue, grouped into three categories:

1. normal anatomic structures that may be mistaken for tumor - central zone, thickening of surgical capsule, periprostatic venous plexus and neurovascular bundle;
2. noncancerous abnormalities that can mimic tumor - postbiopsy hemorrhage, stromal BPH nodule, inflammatory and postinflammatory changes (acute and chronic prostatitis, postinflammatory scars and atrophy) and granulomatous prostatitis;
3. technical challenges related to DWI - anatomic distortion of high-b-value DWI, lack of suppression of benign prostate tissue on standard high-b-value DWI and suboptimal windowing of the ADC map.

**Local staging of prostate cancer with MP MRI**

The most widely used staging system of prostate cancer is the TNM system proposed by the American Joint Committee on Cancer which incorporated prognostic information from the Gleason score and preoperative PSA levels [18, 19].

T-staging of prostate cancer is shown in fig. 1.

**Primary tumour staging (T) [19]:**

- **T1:** not palpable via DRE or seen using TRUS
  - **T1a:** tumor incidental histologic finding in 5% or less of tissue resected
  - **T1b:** tumor incidental histologic finding in more than 5% of tissue resected
  - **T1c:** cancer found by needle biopsy for a raised PSA

- **T2:** palpable on DRE, but confined to the prostate - fig. 2
  - **T2a:** less than half of one lobe
  - **T2b:** more than half of one lobe
  - **T2c:** cancer in both lobes of the prostate

- **T3:** spread outside the prostate
  - **T3a:** extracapsular extension (one or both sides) - fig. 3
  - **T3b:** tumour invades the seminal vesicles - fig. 4

- **T4:** spread into the adjacent tissues (other than seminal vesicles) - fig. 5
  - e.g. bladder sphincter, rectum, levator ani or pelvic side wall
Editorial

For adequate therapy planning it is important to differentiate between organ-confined (stages T1 and T2) and non-organ-confined disease (stages T3 and T4) [4, 18, 21].

When prostate cancer is localized near the distal sphincter, it requires the presence of an area of non-cancerous prostate tissue with a thickness of at least 5 mm between tumoral nodule and distal sphincter; this aspect is important in therapeutic decision, urological treatment vs. radiotherapy [20].

Jelle O. Barentsz et al. proposed a scoring system regarding extra-prostatic involvement, similar to the PI-RADS scoring system [14]. Extraprostatic disease include extra-capsular extension, seminal vesicle infiltration, distal sphincter, rectal wall, neurovascular bundles and bladder neck [14]. The scoring system uses a five-point scale as follows [14]:

- score 1: clinically significant disease is highly unlikely to be present;
- score 2: clinically significant cancer is unlikely to be present;
- score 3: clinically significant cancer is equivocal;
- score 4: clinically significant cancer is likely to be present;
- score 5: clinically significant cancer is highly likely to be present.

The criteria for each extra-prostatic involvement are present in schematic form as follows: extra-capsular extension (fig. 6), seminal vesicles invasion (fig. 7), distal sphincter involvement (fig. 8) and bladder neck involvement (fig. 9).
Fig. 6 Prostate cancer - extracapsular extension; adapted from Barentsz JO, Richenberg J, Clements R et al. European Radiology 2012 [14] and Portalez D. JFR 2014 [20].

Fig. 7 Prostate cancer - seminal vesicle invasion; adapted from Barentsz JO, Richenberg J, Clements R et al. European Radiology 2012 [14] and Portalez D. JFR 2014 [20].

Fig. 8 Prostate cancer - distal sphincter involvement; adapted from Barentsz JO, Richenberg J, Clements R et al. European Radiology 2012 [14] and Portalez D. JFR 2014 [20].

Fig. 9 Prostate cancer - bladder neck involvement; adapted from Barentsz JO, Richenberg J, Clements R et al. European Radiology 2012 [14] and Portalez D. JFR 2014 [20].

**N and M staging**

N1 indicates metastasis in loco-regional lymph nodes and M1 indicates distant metastases [18, 19].

The sensitivity and specificity in the detection of pelvic lymph nodes is approximately 40% and 80%, respectively, for both CT and MRI exams [20].

The imaging criteria are the following, short axis greater than 10 mm for oval lymphadenopathy and a diameter greater than 8 mm for round lymphadenopathy, but in these cases histopathological confirmation is required [20].

Regarding skeletal metastases from prostate cancer, bone scintigraphy remains the “gold standard” in detection and localization [20].

**T2-w MRI**

Conventional T2-w MR imaging has remained the most widely used imaging in local staging of prostate cancer [18].

MRI findings suggestive for extracapsular spread are irregular capsular bulge, broad contact with the capsule (>12 mm), disruption of the prostatic capsule, extension into the periprosthetic fat, obliteration of the rectoprostatic angle and asymmetry of the neurovascular bundle [4, 18, 20, 22, 23].

MRI findings suggestive for seminal vesicle invasion include loss of normal seminal vesicle architecture, seminal vesicle enlargement, focal or diffuse areas of low signal intensity within the seminal vesicle with or without mass effect, ejaculatory duct enlargement, thickening of the ductus deferens and obliteration of the angle between the prostate and seminal vesicle [18, 20, 24-27]. Several different routes of invasion were identified, tumor extension through the ejaculatory duct, direct extension from the base of the prostate or extension from the fat tissue and isolated tumor deposition [24, 26]. For an optimal characterization of seminal vesicle it is necessary to exclude hematic content appears in high signal intensity on T1-w images and low signal intensity on T2-w images [18].

**Diffusion-weighted MRI**

Due to anatomic distortion, artifacts and poor spatial resolution, DWI and ADC maps are not useful to characterize extracapsular extension in prostate cancer, but recent technical advancements in this area may improve the performance of these acquisitions, regarding the local staging of prostate cancer [18]. When the seminal vesicles are invaded by prostate cancer, the images will show diffusion restriction appearing in high signal intensity on the high b-value images, respectively low signal intensity on the apparent diffusion coefficient (ADC) maps [18].

**DCE MRI**

These techniques require high temporal resolution to the detriment of spatial resolution; therefore, these techniques will require thick sections with decreased accuracy rates for prostate cancer staging [18, 28, 29]. Early, rapid and strong enhancement with quick washout of contrast material in the seminal vesicle on dynamic T1-weighted images is highly suggestive for...
seminal vesicle invasion [18, 30]. Jurgen J. Fütterer et al. demonstrated that DCE MRI significantly improves staging performance for the less experienced readers [18, 31], but had no benefit for the experienced reader in staging prostate cancer [31].

Discussions

**T3a tumors — extracapsular extension**

The most important predictive factors for extracapsular extension are asymmetry of the neurovascular bundle and obliteration of the rectoprostatic angle [18, 22]. Tempany et al. reported that the sensitivity of MR imaging was 68%, specificity was 59% and overall accuracy was 64% for neurovascular bundle invasion by prostate cancer [18, 32].

Nicolas Bloch B. et al. demonstrated that the combination of high-spatial-resolution DCE MRI and T2-w MRI improved characterization of extracapsular extension with better results compared with either technique independently [18, 33, 34]; the overall sensitivity, specificity, positive predictive value and negative predictive value for ECE were 75 %, 92 %, 79 % and 91 %, respectively, with the combined data sets for all readers [34].

Patients with extracapsular extension have a greater risk for positive surgical margins, decreasing the chance of long-term control [18, 35, 36].

**T3b tumors — seminal vesicle invasion**

Areas of low signal intensity on T2-wi in the seminal vesicle are highly predictive for invasion, if tumor with extracapsular extension is seen at the base of the prostate [24, 26]. MRI studies using an endorectal coil has been shown to be most accurate in evaluating seminal vesicle invasion by prostate cancer [26]. Dae Chul Jung et al. reported that the sensitivity of MR imaging was 71.4% and specificity was 96.6% for predicting seminal vesicle invasion [37]; two uroradiologists retrospectively analyzed the MR images of 217 patients who had undergone retropubic radical prostatectomy and 14 of these had evidence of seminal vesicle invasion at histopathologic evaluation [37].

Chan Kyo Kim et al. reported that T2-wi with DWI showed a better diagnostic performance than T2-wi alone for predicting seminal vesicle invasion and the accuracy of the less experienced reader using T2WI with DWI showed a significant improvement [18, 38]; for the experienced reader, the specificity for T2-wi with DWI and for T2-wi alone was 96% and 81%, respectively, and accuracy was 90% and 77%, respectively [38]. Ogura et al. reported that early enhancement in the seminal vesicles on DCE MRI has an accuracy rates of 97% for seminal vesicle invasion [18, 30].

Patients with seminal vesicle invasion have a high incidence of lymph node metastasis and a poor prognosis [18, 39] with a high probability of progression to distant metastases [18, 40, 41].

**T-staging**

However, there is no "gold standard" for T-staging of prostate cancer considering the sensitivity and specificity reported in the literature, but the diagnostic accuracy is significantly improved when integrate functional acquisitions DWI/ADC map and DCE MRI [20].

Conclusions

A correct staging of prostate cancer is essential for an appropriate treatment plan. T2-wi acquisitions is considered the best sequence used in the local staging of prostate cancer, but DCE MRI and DWI extent the MR diagnostic accuracy in transitional and anterior fibromuscular stroma zones and improve the differential diagnosis. It is essential to make a correct evaluation of the tumor location, of the risk of tumoral infiltration of the prostate capsule, of the tumoral involvement of the seminal vesicles, distal sphincter and of the bladder neck. The MRI findings and the MR final report must be confronted to the histopathological results.

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