Will magnetic resonance imaging-guided biopsy replace systematic biopsy?

Jelle Barentsz[a], Jurgen J. Futterer[a] , Anwar R. Padhani[b]

[a] Radboud University Nijmegen Medical Centre, Department of Radiology and Nuclear Medicine, Nijmegen (NL) ; [b] Paul Strickland Scanner Centre, Mount Vernon Cancer Centre, Northwood (GB)

1. Introduction

The main disadvantages of the current diagnostic pathway in men with an elevated risk of prostate cancer (PCa) are that:

(1) systematic transrectal ultrasound (TRUS) biopsy misses a substantial proportion (20%) of significant PCa because of inherent systematic sampling errors, especially in the anterior gland [1,2]; (2) misclassifies pathologic status including Gleason score (GI) and tumour stage [3]; and (3) detects a high proportion of men with disease that is unlikely to be harmful (clinically insignificant), with subsequently overtreatments resulting in unintended harm [4]. The latter was the main reason for the U.S. Preventive Services Task Force recommendation against prostate-specific antigen-based screening for prostate cancer in 2012 [5].

2. Radiologic claims regarding multiparametric magnetic resonance imaging in suspected cancer patients

There is increasing evidence, such as two Level 1a systematic reviews [6,7], a Level 1a prospective clinical randomised trial [8], and multiple Level 1b studies [9,10], that multiparametric magnetic resonance imaging (mpMRI) is the best method of visualising primary significant PCa. It is, therefore, widely accepted that mpMRI has the performance characteristics to help manage men with suspected or proven PCa [11,12]. The clinical utility in terms of the ability to ''rule in'' and ''rule out'' the presence of significant disease depends on using the mpMRI approach, image quality, reading system, and reporter expertise [13–16]. The cancer detection ability of mpMRI is dependent on the anatomic location, tumour volume, and aggressiveness of the underlying cancer [3]. mpMRI detected lesions are not always significant malignant lesions [17]; false positive cancer/non-cancer cases do occur, thus adequate biopsy sampling is mandated for each lesion detected [18].

3. mpMRI-guided prostate biopsy

3.1. What technique should be used to sample mpMRI detected lesions?

There are a few available choices: prostate biopsy (PB) directly within the MR-scanner, MRI-TRUS fusion PB, and cognitive fusion PB via transrectal and transperineal routes. A recent systematic review showed, that the highest detection rate for significant PCa was with in-bore-PB (71%), followed by fusion-PB (59%), and finally cognitive-PB (54%). It should be remembered that not every patient needs to undergo in-bore-PB, because large, aggressive lesions can often be detected at TRUS-PB when mpMRI images are either reviewed or fused, and so can be adequately sampled.

3.2. What type of cancers does mpMRI-TB detect?

Literature indicates an improved ability of mpMRI-PB is to detect clinically significant cancers. A recent systematic review showed that the detection rate of clinical significant cancer is higher

(44–87%) than the rates reported for TRUS-PB [7], depending on the definition of clinical significance used for targeted biopsy; this ability applies equally to biopsy naıve and men with prior negative biopsies. Histologic grades on mpMRI-TB show high concordance (88%) with final pathology after prostatectomy, which is a sharp contrast to TRUS-PB (55% concordance rate) [3].

3.3. What is the performance of mpMRI-PB compared with systematic TRUS-PB when mpMRI is positive?

This question has been the subject of large prospective studies and systematic reviews. For example, a prospective study compared TRUS-PB in 225 biopsy naıve patients requiring biopsy with mpMRI-PB in mpMRI positive patients (n = 142). mpMRI-PB detected +13% more intermediate/high risk patients and -89% less low grade PCa than TRUS-PB [10]. Another large study in biopsy naıve men compared TRUS-PB in 391 men of whom 214 had positive mpMRI.mpMRI-PB was used, using a combination of cognitive, rigid, and elastic registration methods [19].

Overall, cancer detection rates were similar (despite fewer mpMRI-PB) but the mpMRI-PB approach had more significant cancers (Gl 7); less microfocal cancers (<5 mm Gl6) and greater cancer core length involvement.

A systematic analysis evaluated 16 studies that included 1926 men with positive mpMRI [6]. The data showed that the all cancer detection rates were similar with mpMRI-PB and TRUS-PB, missing 15% and 19% of cancers detected by the other technique (concordance cases 65%). This meta-analysis showed higher detection rates of significant disease with mpMRI-PB (91%) versus TRUS-PB (71%). Again, the insignificant cancer detection rates were lower for mpMRI-PB (44%) compared with TRUS-PB (83%) [6].

3.4. Does mpMRI-PB systematic miss clinically significant disease?

The key questions are: (1) what proportion of men with negative mpMRI harbour cancers that would require radical therapy if detected; and (2) what proportion of patients with significant disease would be detected by an additional backup TRUS-PB? The reported negative predictive value (NPV) of mpMRI-PB for significant disease has been reported to be high: 63–98% [7]. In a recent large prospective study in 391 patients, the NPV of mpMRI for high-grade PCa was 95.4%, the majority of missed PCas wereof low-grade and organ confined [20]. However, the NPV of mpMRI-PB is dependent on the definition of what constitutes significant disease on a targeted biopsy, the reference test employed for verification, with greater numbers of cores/prostatectomy inevitably finding more significant cancers than mpMRI-TB (vide infra) [7,9,21,22]. The consequences of missing potential significant lesions may be minimal. A recent large randomized study demonstrated that there were no men with negative mpMRI-PB who required radical therapy when saturation biopsies were used to verify mpMRI-PB results [8]. The central issue is the balance between benefits and limitations of mpMRI-TB when used alone compared with the strategy of combined mpMRI-TB with backup TRUS-PB in men with positive mpMRI findings. This was recently addressed in a very large prospective trial [9]. In 1003 men, there were additional cancers detected when mpMRI-TB was combined with TRUS-PB.