Standards of Reporting for MRI-targeted Biopsy Studies
(START) of the Prostate: Recommendations from an International Working Group

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Abstract

Background: A systematic literature review of magnetic resonance imaging (MRI)-targeted prostate biopsy demonstrates poor adherence to the Standards for the Reporting of Diagnostic Accuracy (STARD) recommendations for the full and transparent reporting of diagnostic studies.

Objective: To define and recommend Standards of Reporting for MRI-targeted Biopsy Studies (START).

Design, setting, and participants: Each member of a panel of 23 experts in urology, radiology, histopathology, and methodology used the RAND/UCLA appropriateness methodology to score a 258-statement premeeting questionnaire. The collated responses were presented at a face-to-face meeting, and each statement was rescored after group discussion.

Outcome measurements and statistical analysis: Measures of agreement and consensus were calculated for each statement. The most important statements, based on group

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1. Introduction

There is growing interest in the use of prostate magnetic resonance imaging (MRI) to determine who should be offered prostate biopsy and how those biopsies should be taken. The aim of using MRI to refine the biopsy strategy is to maximise the detection of clinically significant prostate cancer (PCa) while reducing the burden of biopsy for men and the health care system. A systematic review to compare the accuracy of an MRI-targeted biopsy approach with standard transrectal biopsy for the detection of clinically significant disease has recently been published [1]. In 2003, the Standards for the Reporting of Diagnostic Accuracy (STARD) initiative published recommendations for the full and transparent reporting of diagnostic studies, including the use of a flowchart describing outcomes for each study participant and a checklist of items to be described [2]. The majority of studies of MRI-targeted biopsy in the systematic review did not conform well to these standards. In particular, most studies did not compare the detection of clinically significant PCa between MRI-targeted and standard approaches.

Thus, a consensus meeting composed primarily of urologists and radiologists with expertise in the field of MRI-targeted biopsy was set up to establish Standards of Reporting for MRI-targeted Biopsy Studies (START). Recommendations arising from a consensus meeting among experts in a field are useful when there is a lack of direct evidence from high-quality studies or conflicting data in the published literature [3]. The key features of the consensus methodology were two rounds of scoring of agreement with explicit statements; controlled feedback, where the first-round scores were fed back to the group prior to discussion and rescoring; presentation of statistical measures of the group’s agreement and a measure of the consensus within the group for each statement; and anonymised scoring, so that more vocal panel members did not dominate the outcome.

The objective of this paper is to define the standards required for the reporting of studies of MRI-targeted prostate biopsies to improve the quality of the published research in this field and allow comparison, data synthesis, and meta-analysis of future reports.
117 statements were scored with agreement and consensus, 3 statements with disagreement and consensus, and 114 statements with uncertainty (Table 1).

### 3.1. Preferred terminology

Several key definitions related to MRI-targeted biopsy of the prostate were discussed and agreed upon (Table 2). It was noted that the term *MRI-guided biopsy* has been used ambiguously in the literature to mean any biopsy targeted to a lesion first seen on MRI (including those that use real-time ultrasound imaging) and also to refer to the use of MR imaging to guide the needle during the biopsy procedure. Because of this ambiguity, the term was not included in the table of recommended definitions, and more precise alternatives have been given.

### 3.2. START checklist

The START checklist (Table 3) contains the panel's recommendations of statements to include in a report of MRI-targeted biopsy. The statements chosen were those scored with the greatest agreement and consensus, taking into account the panel discussion. This checklist would be useful for authors or reviewers to refer to when writing or reviewing studies of MRI-targeted biopsy of the prostate. A suitable case report form for data collection is given in Table 4.

The full questionnaire, with the panel's recommendation for each statement, is given in Supplementary Table A. Statements that scored with agreement and consensus but did not score highly enough to be included in the final checklist can be seen here. Noteworthy areas of uncertainty, where the panel did not reach consensus, are given in Table 5.

### 3.3. Reporting of study methodology and population

An important aspect in reporting of the study methodology is making clear whether any of the men have been included in previous reports of smaller cohorts (ie, whether it is an update of an on-going clinical cohort). Although it is useful...
to update published results over time, lack of clarity in this matter can make data synthesis or meta-analysis difficult, as each man should only be counted once.

The population from which the reported men originated (e.g., recruitment strategy and prior biopsy status) should be described. This is crucial, as it allows an assessment of the population’s spectrum of disease, which is likely to influence the diagnostic performance of MRI-targeted biopsies. In addition, it provides an indication of the applicability of the results in external populations.

Reporting the number of men who declined biopsy after MRI gives an indication of the number of men who may be inclined to do so if MRI were offered as the first test for men at risk of PCa. It is recognised that this is often difficult information to collect, especially if the cohort is generated from men who have undergone MRI-targeted biopsy rather than, for example, all men who have been referred with a suspicion of PCa.

3.4. Reporting magnetic resonance imaging conduct

Brief details of the MRI machine and the sequences are recommended for all reports of MRI-targeted biopsies. However, there was no consensus that detailed criteria...
giving rise to the score for each sequence or the individual results of each MRI sequence should be reported. Some reports, particularly those aimed at a radiologic audience, may choose to include these details.

It is well recognised that interpretation of multiparametric prostate MRI requires dedicated training and has a steep learning curve [11,12]. The simplest way to report the level of experience of the radiologists involved would be the number of years of their experience of prostate MRI reporting.

3.5. Reporting of the biopsy procedure

Targeted biopsies taken after standard biopsies may result in nonuniform prostate swelling, which could make image registration less accurate. It should, therefore, be made clear whether standard or targeted biopsies were taken first. If the operator taking the standard biopsies is aware of the MRI results, it may influence the conduct of the standard biopsy, thus influencing the detection rate of standard cores. It should therefore be reported whether the operator is aware of the MRI results. The anatomical approach used for biopsy (eg, transrectal or transperineal) and the type of registration used (visual or software assisted) should also be reported.

3.6. Reporting of magnetic resonance imaging–targeted biopsy results

There is great variation in the way histologic results of MRI-targeted biopsies are reported. There was strong agreement that when MRI-targeted and standard biopsies were carried out in the same group of men, the results should be reported separately, making it possible to determine the cancer yield of each approach in relation to that of the other, for both clinically significant and clinically insignificant PCa. Thus, in studies where only men with a positive MRI are included, a 3 × 3 table of agreement comparing clinically significant, clinically insignificant, and no cancer detection should be included. In studies that include men who also have a negative MRI but undergo a systematic biopsy, a 4 × 3 table should be used to present cancer detection (Table 6). In mixed populations, it may be useful to present additional tables presenting the diagnostic results by biopsy status (ie, no prior biopsy, prior biopsy positive, prior biopsy negative). There was no consensus that cancer detection should be reported according to location or zone of origin in the prostate.

Other results to report include the proportion of cores positive for clinically significant cancer in systematic cores alone and in targeted cores alone as well as measures of sampling efficiency, such as the mean number of cores...
meeting to propose such a definition, but agreement was reached on several related points. First, definitions of clinical significance in MRI-targeted biopsy studies should be limited to histologic definitions only and not include prostate-specific antigen, presence of a lesion on MRI, or choice of treatment, all of which have been reported in previous MRI-targeted biopsy studies as determinants of clinical significance. The definition of clinical significance used in the study should be clearly described, whether an established definition [13–15] or a new definition is used.

3.7. Clinically significant prostate cancer

There was much debate about the way in which clinically significant cancer diagnosed on MRI-targeted biopsy should be defined, and agreement was reached that a new definition based on an MRI-targeted sampling approach is needed. It was outside the scope of this consensus
Second, histologic information gained from MRI-targeted biopsies tends to show longer cancer core length and higher Gleason sum than standard transrectal ultrasound (TRUS)–guided biopsies [6]. This results from the intention to oversample areas of high suspicion rather than artefact of the sampling method and may prompt men and physicians to more radical treatment. The difference in risk stratification could also result from biopsy approaches with a high sampling density (eg, transperineal template-guided biopsy). The effect of targeted rather than standard or blind sampling may result in a drift towards higher risk classification that is an artefact of the sampling method and may prompt men and physicians to more radical treatment.

Finally, the group agreed that Gleason grade and maximum cancer core length are the most appropriate histologic parameters to report in studies of MRI-targeted biopsy, although there was no consensus on what the threshold for low-, intermediate-, or high-risk disease.
might be. One risk stratification system has been specifically developed to overcome the problems of multiple cores taken via the transperineal route and of targeted sampling and uses Gleason grade and maximum cancer core length to determine risk stratification, without using the number or proportion of positive cores [16].

4. Discussion

4.1. Summary of findings

The START checklist (Table 3) specifies key information that should be included in reports of studies evaluating MRI-targeted biopsies of the prostate.

4.2. Clinical and research implications

The ideal biopsy strategy for identifying PCa would successfully identify men with clinically significant cancer while overlooking men with clinically insignificant cancer and do so in a manner that minimises biopsy number and burden. MRI-targeted biopsy is a promising biopsy technique that may offer these advantages over standard TRUS-guided biopsy of the prostate. To assess this idea fully, it is important that the most relevant details of each study be reported in such a way they can be analysed and compared.

Studies evaluating MRI-targeted biopsies should contain all essential information for their validity, importance, and applicability to other patient groups to be assessed. The validity will be assessed from such items as whether the biopsy operator for standard cores was blinded to the MRI results, while the applicability of results will be assessed from details of the specific population studied. The START checklist sets out a list of details considered most relevant for this assessment.

Researchers may choose to design, conduct, and report studies with this checklist in mind, and it may also prove a useful tool for reviewers. It is hoped that the quality of research published in this field will be improved by adoption of these guidelines. Future work should be directed at establishing histologic definitions of clinically significant cancer from MRI-targeted biopsy.

4.3. Limitations

Expert group discussions are prone to bias, and groups consisting of those carrying out a particular procedure tend to emphasise the importance of that procedure [17]. The presence of a nonscoring chair, with no interest in the recommendation of any particular statement over another, helped to reduce this bias, as did the anonymous scoring method (rather than by a visible vote), with each score counting equally towards the group analysis.

As the objective of the meeting was well defined and within a newly emerging field, it was decided to have a scoring panel largely composed of urologists and radiologists with experience in this field. It might have been useful to have other interested parties, such as those who tend to refer patients for biopsy (family doctors or general urologists), who might have different priorities for the reporting of these diagnostic studies. To broaden the perspective, we included a pathologist and methodologist from two centres with MRI-targeted biopsy expertise.

It was not possible to invite all groups that have published on MRI-targeted biopsy, although centres using each of the main techniques (visual registration, software registration, and in-bore biopsy) were represented. The experience of each participating centre in MRI-targeted biopsy is summarised in the Supplementary Table C, available online.

5. Conclusions

Reporting of MRI-targeted biopsy according to the START checklist, as described here, would improve the quality of reporting and facilitate a comparison between standard biopsy and MRI-targeted approaches. Collation of data from studies fulfilling the START criteria may more easily allow the evaluation of MRI-targeted biopsy as a diagnostic strategy for the detection of clinically significant cancer.

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Study concept and design: Moore, Emberton.
Acquisition of data: Moore, Kasivisvanathan, Eggener, Emberton, Füttnerer, Gill, Grubb, Hadaschik, Klotz, Margolis, Marks, Melamed, Oto, Palmer, Pinto, Puech, Punwani, Rosenkrantz, Schoots, Simon, Taneja, Turkbey, Ukimura, van der Meulen, Villers, Watanabe.
Analysis and interpretation of data: Moore, Kasivisvanathan.
Drafting of the manuscript: Moore, Kasivisvanathan.
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**Appendix A. Supplementary data**

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**References**


