Prostate Cancer

Reporting Magnetic Resonance Imaging in Men on Active Surveillance for Prostate Cancer: The PRECISE Recommendations—A Report of a European School of Oncology Task Force

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Article info

Article history:
Accepted June 9, 2016

Keywords:
Prostate cancer
Prostate MRI
Active surveillance

Abstract

Background: Published data on prostate magnetic resonance imaging (MRI) during follow-up of men on active surveillance are lacking. Current guidelines for prostate MRI reporting concentrate on prostate cancer (PCa) detection and staging. A standardised approach to prostate MRI reporting for active surveillance will facilitate the robust collection of evidence in this newly developing area.

Objective: To develop preliminary recommendations for reporting of individual MRI studies in men on active surveillance and for researchers reporting the outcomes of cohorts of men having MRI on active surveillance.

Design, setting, and participants: The RAND/UCLA Appropriateness Method was used. Experts in urology, radiology, and radiation oncology developed a set of 394 statements relevant to prostate MRI reporting in men on active surveillance for PCAs. Each statement...
1. Introduction

The use of multiparametric magnetic resonance imaging (MRI) to inform the detection of prostate cancer (PCa) has grown rapidly in the last few years. Numerous publications have sought to standardise the conduct and reporting of prostate MRI [1–3]. Most recently the European Society of Uroradiology and the American College of Radiology [4] have sought to standardise the conduct and reporting of MRI to inform the detection of prostate cancer (PCa) has grown rapidly in the last few years. Numerous publications were calculated for each statement. The most important statements, derived from both group discussion and scores of agreement and consensus, were used to create the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) checklist and case report form.

Outcome measurements and statistical analysis: Measures of agreement and consensus were calculated for each statement. The most important statements, derived from both group discussion and scores of agreement and consensus, were used to create the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) checklist and case report form.

Results and limitations: Key recommendations include reporting the index lesion size using absolute values at baseline and at each subsequent MRI. Radiologists should assess the likelihood of true change over time (ie, change in size or change in lesion characteristics on one or more sequences) on a 1–5 scale. A checklist of items for reporting a cohort of men on active surveillance was developed. These items were developed based on expert consensus in many areas in which data are lacking, and they are expected to develop and change as evidence is accrued. Conclusions: The PRECISE recommendations are designed to facilitate the development of a robust evidence database for documenting changes in prostate MRI findings over time of men on active surveillance. If used, they will facilitate data collection to distinguish measurement error and natural variability in MRI appearances from true radiologic progression.

Patient summary: Few published reports are available on how to use and interpret magnetic resonance imaging for men on active surveillance for prostate cancer. The PRECISE panel recommends that data should be collected in a standardised manner so that natural variation in the appearance and measurement of cancer over time can be distinguished from changes indicating significant tumour progression.

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2. Materials and methods

2.1. Study design

We used the RAND/UCLA Appropriateness Method [7]. A core group (C.M.M., I.G.S., A.K., C.A., and F.G.) developed a draft set of 350 statements and sent them to all panel members for modification. Statements could be revised, removed, or added at this stage. A revised set of 394 statements was scored by each panel member on a scale of agreement from 1 to 9, in which 1 indicated strongest disagreement and 9 indicated strongest agreement. These scores were collated, and a summary of agreement, uncertainty, or disagreement (derived from the group median score) was calculated for each statement. Calculations to determine consensus or lack of consensus for each statement were performed using the RAND/UCLA classical criteria that take into account the proportion of panelists scoring within a given category of agreement (7–9), uncertainty (4–5), or disagreement (1–3). For a statement to have consensus, a clear majority scoring in that category is needed.

A chair (P.A.) who did not participate in scoring convened a panel meeting. A graphic representation of the group response was presented for each statement that included the group median score and the degree of consensus (Fig. 1). Each statement was discussed. Some statements were modified or removed; others were added as a result of the discussions. Following discussion, each statement was rescored anonymously by each panel member. Following the meeting, the individual panelist scores were collated, and the degree of agreement and consensus was calculated for each statement. The collated scores and the content of the discussion were used to develop the PRECISE checklist of reporting criteria for studies of MRI in men on active surveillance and
the PRECISE case report template form to report MRI at baseline or follow-up in these men.

The checklist provides a guide for authors in preparing a manuscript for publication and for reviewers and editors when assessing manuscripts. The case report template form is suitable for clinical use allowing communication of imaging findings and their likely relevance to referring clinicians, and it will also allow data collection to inform the reporting of cohorts of men.

2.2. Setting and participants

The panel included 10 experts in urology, 8 in radiology, and 1 in radiation oncology (Supplementary Table 1 summarises panellist experience). Faculty attending the 2nd European School of Oncology Active Surveillance February 2016 workshop in Milan, Italy, were initially approached to join the panel. Additional members not attending the workshop were invited to ensure a balance of expertise. Two panel members were unable to travel to the meeting and participated by online conference (B.T. and P.P.) with audio participation and desktop viewing so they could see all of the presentations.

3. Results

To avoid ambiguous statements and to identify consensus if it existed, 38 statements were deleted, 56 statements modified, and 11 statements added during the panel meeting, giving a final set of 367 statements that were scored.

During the first round, 201 of 394 statements were scored with consensus and agreement. Table 1 shows the scoring during the meeting.

3.1. The PRECISE case report form for reporting a magnetic resonance study in an individual man on active surveillance

The PRECISE case report form (Fig. 2) includes each item that should be reported for an individual man having an MRI at baseline or follow-up during active surveillance.

3.2. The PRECISE checklist for reporting cohorts of men having magnetic resonance imaging in active surveillance

The PRECISE checklist (Table 2) shows the panel recommendations for reporting a cohort of men who have a
prostate MRI during active surveillance. All statements in the checklist were scored with consensus and agreement. Items were not included in the checklist if they were scored with disagreement or lack of consensus at the meeting. Items were grouped together, and all definitively agreed statements were included. Supplementary Table 2 describes the full list of items and their scores. The intention was to develop a comprehensive but not restrictive set of statements, balancing the need for clarity and brevity and recognising the variations in current reporting practice, both in histologic and radiologic data.

3.3. Reporting the conduct of magnetic resonance imaging

The PRECISE guidelines are not intended to replace or compete with the comprehensive guidelines on the conduct of prostate MRI developed by the Prostate Imaging Reporting and Data System (PI-RADS) group[4]. The panel agreed that publications should state whether study MRI scans were conducted in accordance with contemporary guidelines and should cite the guidelines used. We recognise that the conduct of MRI may change over the reporting period of a study because of the longitudinal nature of active surveillance cohorts.

3.4. Reporting of magnetic resonance imaging

The number of radiologists reporting scans in the study cohort should be stated. If an individual scan was reported by more than one radiologist, the use of separate or consensus reporting should be clarified. When scans were reported separately, the method used to combine results should be used (eg, mean of absolute size values at each time point, mean change in size between scans per reporter). The format of the radiology report should be stated (eg, prose, template, and/or diagrammatic reporting, with and without embedded or annotated MRI images). The PRECISE case report form was designed to facilitate the routine collection of clinical and imaging data in a manner that will allow cohort comparison of men on active surveillance in a standardised manner. It should be stated whether the MRI readings were done retrospectively, with one reading of a set of MRIs from previous time points, or whether scans were reported contemporaneously, with or without reference to previous images or reports.
Table 2 – The PRECISE checklist

<table>
<thead>
<tr>
<th>Item</th>
<th>Section of paper</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Title</td>
<td>The study should be identified as reporting results from MRI in men on active surveillance, either to identify men as suitable for AS or as a tool for repeat assessment on AS.</td>
</tr>
<tr>
<td>2</td>
<td>Introduction</td>
<td>The introduction should include a clear statement of the research question or study aim (e.g., correlation of pathologic outcomes with radiologic change, assessment of radiologic change on repeat MRI) and background information such as the take-up of AS in men deemed suitable.</td>
</tr>
<tr>
<td>3</td>
<td>Study design and population</td>
<td>The setting, location, and recruitment period and study design (prospective/retrospective) should be reported. It should be made clear (and citation given) if the report is an update of a previously published cohort. The inclusion and exclusion criteria with the maximum Gleason score, maximum PSA, and the name, version, and citation of an established AS protocol or risk classification system (where relevant) should be reported. The requirement for confirmatory biopsy, frequency of PSA testing, and the indication and frequency for biopsy, MRI, and any additional test (e.g., genomic classifiers) should be specified.</td>
</tr>
<tr>
<td>4</td>
<td>Conduct of the MRI</td>
<td>Whether or not the MRI conduct met the minimum criteria set by the European Society of Uroradiology and the American College of Radiologists [4] or other stated guidelines.</td>
</tr>
<tr>
<td>5</td>
<td>Reporting of the MRI</td>
<td>The number of radiologists reporting scans in the study should be stated. The availability (or not) of clinical information and previous MRI images to the reporting radiologist should be stated. When more than one radiologist reports a scan, it should be stated whether this is done separately or in consensus. When done separately it should be stated how a summary value was derived (e.g., mean absolute values or mean change between scans per reporter). The reporting method used (e.g., prose vs diagrammatic report, name and version of scoring system) should be given.</td>
</tr>
<tr>
<td>6</td>
<td>Conduct of the biopsy</td>
<td>The anatomic approach (transrectal/transperineal) and method of targeting MRI lesions; the use of separate pots for targeted and systematic cores (if applicable). The time interval between MRI and biopsy (median and range). Whether systematic cores are taken in all, and the intended number of systematic cores per prostate and targeted cores per lesion; whether systematic biopsy was performed blind to MRI findings. The criteria for choosing a lesion to be targeted, whether the biopsy operator had direct access to the MR images, Where software assistance was used for registration of MRI and ultrasound images, the manufacturer and model should be stated.</td>
</tr>
<tr>
<td>7</td>
<td>Patient characteristics</td>
<td>The age range, baseline PSA, and MRI-derived prostate volume, distribution of Gleason score, and risk categories across the group and the MCCL. The number of men taking drugs that would affect the hormonal environment of the prostate (e.g., 5α-reductase inhibitors, testosterone) should be recorded. A flowchart of participants showing numbers of men eligible, offered and enrolled in the study, with those who continue on AS and the treatment status of those who are not on AS.</td>
</tr>
<tr>
<td>8</td>
<td>Individual patient baseline MRI report</td>
<td>The baseline MRI report should contain the prostate volume measured on T2 W imaging and a likelihood of clinically significant cancer on a scale of 1–5 for the whole prostate and for each lesion. The likelihood of extraprostatic extension and seminal vesicle involvement should be reported on a 1–5 scale. The index lesion size should be reported using volume (by planimetry or derived from three diameters) or measurement of 1 or 2 diameters.</td>
</tr>
<tr>
<td>9</td>
<td>Follow-up MRI</td>
<td>In addition to features reported at baseline, any subsequent MRI report should include the following: • A score on a 1–5 scale for the likelihood of significant change, along with a description of the change that has given rise to the score (e.g., change in size, change in conspicuity on one or more sequences) • Any change in likelihood of significant cancer (1–5 scale) • An increase in suspicion due to extension into seminal vesicles or a suspicious lymph node or bone lesion • Absolute values of lesion size at baseline and each subsequent scan • The appearance of any new lesion • Any lesion becoming nonvisible.</td>
</tr>
<tr>
<td>10</td>
<td>Reporting of follow-up biopsy findings</td>
<td>Separate reporting of systematic and targeted cores with a MCCL and Gleason grouping per patient irrespective of whether this was derived from targeted or systematic cores; mean/median number of cores per prostate and per lesion; mean/median number of lesions per patient where targeted cores were taken.</td>
</tr>
<tr>
<td>11</td>
<td>Statistical analysis</td>
<td>The effect of interreader variability; whether any effect depends on the size of the baseline lesion; whether outliers (very large or very small lesions) were excluded; how the disappearance of a lesion is handled in the statistical analysis. Where there is adequate power to do so, univariate and multivariate analysis should be used to assess the added value of a reporting statement to baseline clinical data; the odds ratio for a single and a combination of unfavourable factors should be given.</td>
</tr>
<tr>
<td>12</td>
<td>Discussion</td>
<td>The clinical applicability of the findings should be discussed, along with the correlation of the observed MRI changes with traditional tools to measure disease progression (DRE, PSA kinetics, biopsy findings).</td>
</tr>
</tbody>
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AS = active surveillance; DCE = dynamic contrast-enhanced; DRE = digital rectal examination; DWI = diffusion-weighted imaging; MCCL = maximum cancer core length; MRI = magnetic resonance imaging; PSA = prostate-specific antigen; T2W = T2-weighted.

3.5. Reporting of the biopsy at entry to active surveillance

There was agreement and consensus on the use of the Gleason score, but uncertainty and no consensus on the use of maximum cancer core length (MCCL) and maximum number and proportion of cores. Panel members felt that many cohorts of men on active surveillance will not have had an MRI-targeted biopsy at study entry and that the number or proportion of positive cores would be strongly influenced by the strategy used to perform the biopsies (standard or targeted to MRI lesions). Reporting the maximum number of positive cores is a helpful indicator in a standard random biopsy, but it is less helpful when oversampling is intended during a targeted biopsy of a
lesion seen on MRI. It was acknowledged that it is helpful for the radiologist in the clinical setting to know the location of positive biopsies, although this information would not be known in a blinded study.

3.6. Reporting of magnetic resonance imaging at baseline and follow-up

Prostate volume on T2-weighted sequences and PSA density should be reported. Determination of an assessment of the likelihood of clinically significant disease on a 1–5 scale is required for each MRI. The use of the term assessment was chosen to include both those groups who use PI-RADS (v.1 or v.2) and those who use a 1–5 scale based on overall clinical impression without predefined characteristics per sequence (commonly called a Likert scale). The scale used should be identified.

The highest likelihood of clinically significant cancer of all separate lesions should provide the likelihood of clinically significant cancer for the whole prostate. For men with a visible lesion, the key metric is the size of the index lesion on the baseline MRI and at each time point thereafter. The term index lesion can be used to denote the largest lesion, or the one with the highest Gleason grade, or the one of highest suspicion based on MRI criteria [6]. It was noted that not all men with PCs suitable for active surveillance will have a visible lesion on MRI. It was agreed that size can be measured using volume (by planimetry or calculated from three diameters), by biaxial measurement of maximum diameters on an axial slice, or by a single measurement of maximum diameter. The panel felt that as yet there was insufficient evidence to determine which of the methods for measuring size was optimal for distinguishing between natural fluctuation in tumour volume, measurement errors over time, or true disease progression. Some believed that planimetry volume would be most accurate; others were concerned that this was too time consuming. For lesions best seen on functional image sequences (eg, high b-value images), a single diameter may be more reproducible than a volume because of the need to use larger voxel sizes in sequence acquisitions. Comparative data from the same cohort on the reproducibility of different size measurements (eg, planimetry volume and biaxial diameter) would be of great value in exploring this further.

All parameters reported on the baseline MRI should be reported again on follow-up MRI. In addition, any MRI report after the baseline MRI report should include an assessment of the likelihood of significant radiologic progression from the baseline MRI scan, on a 1–5 scale, along with a description of the change that has given rise to that assessment (eg, change in size or change in conspicuity on one or more sequences). Table 3 shows further details. It should be noted that there are no robust data on which to base the threshold for a significant change in size or conspicuity. The intention is that data collection using the suggested format will allow such data to be acquired, and that, in time, thresholds can be set.

3.7. Clinically significant disease in men on active surveillance

It was agreed that Gleason grading and MCCls were important determinants of clinically significant disease in men on active surveillance, but no cut-off could be agreed upon. It was agreed that Gleason ≥4+3 or ≥T3a disease or any involvement of lymph nodes or bone metastases is clinically significant. Some panelists deemed any Gleason pattern 4 as significant; others felt that small-volume secondary pattern 4 disease alone was not necessarily of clinical significance in all men. PSA and PSA derivatives such as PSA density and PSA doubling time were deemed of interest in determining clinically significant disease, although again no threshold was identified.

It was acknowledged that clinical significance of MRI lesions is also influenced by patient factors such as age and comorbidities; a lesion may be deemed significant in a younger man aged 50 yr but not in an older man with several comorbidities.

3.8. Noteworthy areas of uncertainty

There was no agreement on the best way to present change in lesion size or appearance over time across a cohort of men. It was acknowledged that some lesions become nonvisible during follow-up, and there was uncertainty over how best to deal with this when aggregating results across a cohort. Concern was expressed that use of percentage change of lesion volume across a cohort could yield a large percentage change in small lesions (eg, a 0.1-cm³ lesion increasing to a 0.3-cm³ lesion) and thereby skew results across the cohort. It was also noted that the measurement errors of small lesions could be larger than any change, even if significant in percentage terms.

Table 3 – Assessment of likelihood of radiologic progression on magnetic resonance imaging in men on active surveillance

<table>
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<th>Likert</th>
<th>Assessment of likelihood of radiologic progression</th>
<th>Example</th>
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<tbody>
<tr>
<td>1</td>
<td>Resolution of previous features suspicious on MRI</td>
<td>Previously enhancing area no longer enhances</td>
</tr>
<tr>
<td>2</td>
<td>Reduction in volume and/or conspicuity of previous features suspicious on MRI</td>
<td>Reduction in size of previously seen lesion that remains suspicious for clinically significant disease</td>
</tr>
<tr>
<td>3</td>
<td>Stable MRI appearance: no new focal/diffuse lesions</td>
<td>Either no suspicious features or all lesions stable in size and appearance</td>
</tr>
<tr>
<td>4</td>
<td>Significant increase in size and/or conspicuity of features suspicious for prostate cancer</td>
<td>Lesion becomes visible on diffusion-weighted imaging; significant increase in size of previously seen lesion</td>
</tr>
<tr>
<td>5</td>
<td>Definitive radiologic stage progression</td>
<td>Appearance of extracapsular extension, seminal vesicle involvement, lymph node involvement, or bone metastasis</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging.
The panel did not reach consensus on whether repeat standard biopsy and/or targeted biopsy should be performed on men with MRI changes. Some felt that a man eligible for treatment at the start of the surveillance period (e.g., small-volume Gleason 3 + 4 disease) would not require additional biopsy confirmation for a minor radiologic change. Although some expressed a wish for biopsy verification of suspected MRI-depicted disease progression, it was recognised that patients and clinicians may reasonably opt for treatment without further biopsy.

4. Discussion

4.1. Summary of results

The PRECISE checklist outlines key information that researchers should report in a study of a cohort of men having an MRI on active surveillance for PCa. The PRECISE case report form is designed for clinical radiologists to report an individual MRI at baseline or follow-up. Use of the case report form will ensure that appropriate data are collected to inform cohort reporting.

The number of statements scored with agreement and consensus reduced from pre-meeting scoring to scoring at the meeting. The purpose of the face-to-face element of a formal consensus meeting is to allow detailed discussion and interaction of the panellists to fully explore a topic. This can reduce or increase consensus. The reduced number of statements with agreed consensus showed that many challenging topics were discussed in an area in which data are emerging.

4.2. Clinical and research implications

MRI is being used more frequently in men on active surveillance to assess for clinically significant disease missed at initial biopsy or to reduce the need for repeat biopsy [8]. There are data to suggest that stability on MRI can predict Gleason score stability [9].

The use of MRI in men on active surveillance varies between countries and health systems, with a lower use of MRI outside of academic centres [10]. Some centres exclude men with visible lesions on MRI from an active surveillance programme to reduce the likelihood of unfavourable pathology [11,12]. It is known that some small lesions on prostate MRI can be pathologically benign or of a low-grade tumour only [13]. However, others recognise that it is likely that long established active surveillance series would no doubt have included men who would have had visible lesions on MRI had it been available at that time, and treatment of all men with MRI-visible disease is likely to lead to significant overtreatment. Data have shown that men with a visible lesion (positive MRI) are more likely to receive treatment than men with a negative MRI. The extent to which clinical decisions may have been influenced by this factor is not easy to determine because there are few studies in which clinicians were blinded to MRI results.

We hope that use of the PRECISE checklist will allow the natural history of MRI changes in men on active surveillance to become clearer, allowing appropriate significance thresholds for radiologic disease to be set both at baseline and during surveillance. The correlation of radiologic findings with PSA and histologic data, and treatment-free survival will also be of great value. The use of the PRECISE recommendations to analyse large data sets such as those from the Movember Global Action Project on Active Surveillance [14] would allow rapid assessment and refinement of the recommendations based on data from multiple centres worldwide.

4.3. Limitations

The greatest limitation of these recommendations is the lack of published data on which they are based. The intention of these recommendations is that they will allow robust data collection in those areas deemed most important by expert opinion, so that further iterations will be based on those data. The areas most in need of research are the optimal way of measuring lesion size to allow repeatability over time and both the change in size and absolute size that should prompt clinical action. Although there is a possibility of bias in the groups selected for the consensus meeting, only a small number of centres declined the invitation to participate.

5. Conclusions

The PRECISE recommendations were developed to facilitate robust data collection and thus assess the natural history of MRI findings in men on active surveillance. If widely used, the data derived will facilitate the determination of thresholds that identify radiologically significant disease and important radiologic changes on MRI. It is likely that initial validation work will lead to refinement of the recommendations in due course.

Author contributions: Caroline M. Moore had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Moore, Valdagni, Schoots, Allen, Kirkham.

Acquisition of data: Giganti, Schoots, Albertsen, Allen, Bangma, Briganti, Carroll, Haider, Kasivisvanathan, Kirkham, Klotz, Ozzzane, Padhiani, Panebianco, Pinto, Puech, Ranniko, Renard-Penna, Touijer, Turkbey, van Poppel, Valdagni, Walz, Moore.

Analysis and interpretation of data: Giganti, Moore.

Drafting of the manuscript: Moore.

Critical revision of the manuscript for important intellectual content: Giganti, Schoots, Albertsen, Allen, Bangma, Briganti, Carroll, Haider, Kasivisvanathan, Kirkham, Klotz, Ozzzane, Padhiani, Panebianco, Pinto, Puech, Ranniko, Renard-Penna, Touijer, Turkbey, van Poppel, Valdagni, Walz, Moore.

Statistical analysis: Giganti, Kasivisvanathan, Moore.

Obtaining funding: Moore, Valdagni.

Administrative, technical, or material support: Kasivisvanathan.

Supervision: Moore.

Other (specify): None.

Financial disclosures: Caroline M. Moore certifies that all conflicts of interest, including specific financial interests and relationships and
affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Sponsor and role of the sponsor:** European School of Oncology (ESO), supported by educational grants from Siemens Healthcare GmbH and the ProADAMO Foundation, funded the research. The organisations cited had no role in the data collection or analysis, or in manuscript preparation. The paper was developed by the ESO-PRECISE Task Force, and the initiative was supported by the ESO and through unrestricted educational grants provided by Siemens Healthcare and the ProADAMO Foundation.

**Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at [http://dx.doi.org/10.1016/j.eururo.2016.06.011](http://dx.doi.org/10.1016/j.eururo.2016.06.011).

**References**


