Accepted Manuscript

Sequential prostate MRI reporting in men on active surveillance: initial experience of a dedicated PRECISE software program



Francesco Giganti, Clare Allen, Jonathan W. Piper, David Mirando, Armando Stabile, Shonit Punwani, Alex Kirkham, Mark Emberton, Caroline M. Moore

S0730-725X(18)30335-7
doi:10.1016/j.mri.2018.10.013
MRI 9084
Magnetic Resonance Imaging
29 July 2018
8 October 2018
18 October 2018

Please cite this article as: Francesco Giganti, Clare Allen, Jonathan W. Piper, David Mirando, Armando Stabile, Shonit Punwani, Alex Kirkham, Mark Emberton, Caroline M. Moore, Sequential prostate MRI reporting in men on active surveillance: initial experience of a dedicated PRECISE software program. Mri (2018), doi:10.1016/j.mri.2018.10.013

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Sequential prostate MRI reporting in men on active surveillance: initial experience of a dedicated PRECISE software program

Francesco Giganti, MD ^{1,2}, Clare Allen, MD ¹, Jonathan W Piper ³, David Mirando ³, Armando Stabile, MD ^{2,4,5} Shonit Punwani, MD ^{1,6}, Alex Kirkham, MD ¹, Mark Emberton, MD ^{2,5}, Caroline M Moore, MD ^{2,5}

- 1. Department of Radiology, University College London Hospital NHS Foundation Trust, London, UK
- 2. Division of Surgery & Interventional Science, University College London, London, UK
- 3. MIM Software Inc, Cleveland, OH
- 4. Department of Urology, Vita-Salute San Raffaele University, Milan, Italy
- 5. Department of Urology, University College London Hospital NHS Foundation Trust, London, UK
- 6. Centre for Medical Imaging, University College London, London, UK

Corresponding author:

Francesco Giganti, MD

Division of Surgery and Interventional Science, University College London, 3rd Floor, Charles Bell House, 43-45 Foley St., London, United Kingdom W1W 7TS email: f.giganti@ucl.ac.uk

Abstract

Background and objectives: There is interest in using sequential multiparametric magnetic resonance imaging (mpMRI) to assess men on active surveillance (AS) for prostate cancer. The Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) recommendations propose standardised reporting mpMRI data for these men. This includes accurate size measurements of lesions over time, but such approach is time consuming for the radiologist and there is a strong need of dedicated tools to report serial scans in a systematic manner. We present the results from an initial validation cohort using dedicated PRECISE reporting software to allow automated comparison between sequential scans on AS.

<u>Materials and methods</u>: We retrospectively analysed baseline and followup scans of 20 men randomised to 6 months of daily dutasteride (n=10) or placebo (n=10) from the MAPPED trial. Men underwent 3T mpMRI at baseline and after 6 months, and a dedicated radiologist reported the scans using both a widespread commercially-available platform (Osirix[®]) and a semi-automated dedicated PRECISE reporting tool (MIM[®]). Tumour volume by planimetry in all sequences and conspicuity on diffusionweighted imaging were assessed. Reporting time was recorded, and we used the Wilcoxon test for statistical analysis.

2

<u>Results</u>: Median tumour volumes and conspicuity were similar using both approaches. The reporting time of the follow-up scan was quicker using the PRECISE reporting workflow both in the whole population (12'33'' vs 10'52''; p=0.005) and in the dutasteride arm (15'50'' vs 12'59''; p=0.01). A structured report including clinical and imaging data was generated according to the PRECISE recommendations and a comparison table between lesion characteristics at baseline and follow-up scans was also included.

<u>Conclusion</u>: We conclude that a dedicated PRECISE reporting tool for sequential scans in men on AS results in a significant reduction in the reporting time and allows the radiologist to easily compare scans over time. This tool will help with our understanding of the natural history of mpMRI changes during AS.

tool will help with our unden nges during AS.

Sequential prostate MRI reporting in men on active surveillance: initial experience of a dedicated PRECISE software program

Francesco Giganti, MD ^{1,2}, Clare Allen, MD ¹, Jonathan W Piper ³, David Mirando ³, Armando Stabile, MD ^{2,4,5} Shonit Punwani, MD ^{1,6}, Alex Kirkham, MD ¹, Mark Emberton, MD ^{2,5}, Caroline M Moore, MD ^{2,5}

- 7. Department of Radiology, University College London Hospital NHS Foundation Trust, London, UK
- 8. Division of Surgery & Interventional Science, University College London, London, UK
- 9. MIM Software Inc, Cleveland, OH
- 10. Department of Urology, Vita-Salute San Raffaele University, Milan, Italy
- 11. Department of Urology, University College London Hospital NHS Foundation Trust, London, UK
- 12. Centre for Medical Imaging, University College London, London, UK

Corresponding author:

Francesco Giganti, MD

Division of Surgery and Interventional Science, University College London, 3rd Floor, Charles Bell House, 43-45 Foley St., London, United Kingdom W1W 7TS email: <u>f.giganti@ucl.ac.uk</u>

Sequential prostate MRI reporting in men on active surveillance: initial experience of a dedicated PRECISE software program

> Scr

Abstract

Background and objectives: There is interest in using sequential multiparametric magnetic resonance imaging (mpMRI) to assess men on active surveillance (AS) for prostate cancer. The Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) recommendations propose standardised reporting mpMRI data for these men. This includes accurate size measurements of lesions over time, but such approach is time consuming for the radiologist and there is a strong need of dedicated tools to report serial scans in a systematic manner. We present the results from an initial validation cohort using dedicated PRECISE reporting software to allow automated comparison between sequential scans on AS.

<u>Materials and methods</u>: We retrospectively analysed baseline and followup scans of 20 men randomised to 6 months of daily dutasteride (n=10) or placebo (n=10) from the MAPPED trial. Men underwent 3T mpMRI at baseline and after 6 months, and a dedicated radiologist reported the scans using both a widespread commercially-available platform (Osirix[®]) and a semi-automated dedicated PRECISE reporting tool (MIM[®]). Tumour volume by planimetry in all sequences and conspicuity on diffusionweighted imaging were assessed. Reporting time was recorded, and we used the Wilcoxon test for statistical analysis.

6

<u>Results</u>: Median tumour volumes and conspicuity were similar using both approaches. The reporting time of the follow-up scan was quicker using the PRECISE reporting workflow both in the whole population (12'33'' vs 10'52''; p=0.005) and in the dutasteride arm (15'50'' vs 12'59''; p=0.01). A structured report including clinical and imaging data was generated according to the PRECISE recommendations and a comparison table between lesion characteristics at baseline and follow-up scans was also included.

<u>Conclusion</u>: We conclude that a dedicated PRECISE reporting tool for sequential scans in men on AS results in a significant reduction in the reporting time and allows the radiologist to easily compare scans over time. This tool will help with our understanding of the natural history of mpMRI changes during AS.

Key words: Active surveillance; Magnetic resonance imaging; Prostatic neoplasms; Computer-aided diagnosis

Abbreviations:

PCa: prostate cancer

AS: active surveillance

MpMRI: multiparametric magnetic resonance imaging

PRECISE: Prostate Cancer Radiological Estimation of Change in Sequential

Evaluation

ADC: apparent diffusion coefficient

PI-RADS: Prostate Imaging Reporting and Data System

PSA: prostate specific antigen

T2-WI: T2-weighted imaging

DWI: diffusion-weighted imaging

DCE: dynamic contrast-enhanced

IQR:interquartile ranges

Introduction

Men with low and intermediate risk prostate cancer (PCa) are offered active surveillance (AS) to defer or avoid radical treatment and its potential side effects, without missing the opportunity for cure [1,2].

There is evidence that multiparametric magnetic resonance imaging (mpMRI) shows potential in identifying AS candidates, who may have little benefit from therapy but still need to be continuously monitored to allow prompt curative treatment if the disease shows signs of becoming more aggressive [3]. However, the use of mpMRI in men on AS varies between countries and health systems, with a lower use of mpMRI outside of academic institutions [4].

As a result, many men have more frequent and invasive testing than needed, at a cost to them and the health care system, and a small number of men will eventually have significant disease detected too late, increasing the likelihood of metastatic spread. Additionally, there are few published data to inform us on any specific radiological change to define the progression of the disease (e.g. volume, change in lesion size or appearance over time, quantitative parameters like the apparent diffusion coefficient -ADC-, etc.) that should prompt biopsy or active treatment [5– 7].

Morgan et al. [5] reported the results of 151 men on AS undergoing mpMRI at two time points (median interval 1.9 years). They showed that tumour volume increased measurably in 34.4% of men after 2 years of

AS, and that change in ADC could be used to identify tumours with measurable growth ($-6.8\% \pm 12.3\%$ for men with measurable growth vs $0.23\% \pm 10.1\%$ for those without, p=0.0005). Our group [7] has recently investigated changes in the mpMRI appearance of lesions on AS and showed the variability of volume measurements on serial scans, assessing change in lesion size according to grade. From a total of 86 men, 43/86 men did not have a visible lesion on the initial scan; of these, 5/43 had developed a suspicious focus at a median follow up of 3.6 years. There was a significant increase in volume by a median of 10% (p < 0.01), more specifically by a median of 6% for Gleason 3+3 and 18% for 3+4 (p = 0.058).

A recent meta-analysis by Schoots and colleagues [9] has shown that cancer upgrading occur almost three-times more often in men with a visible lesions (35%, confidence intervals -CI- 27-43%) in contrast to a negative scan (12%; CI 8–18%) with a relative risk of 2.77 (CI 1.76–4.38).

Gallagher and colleagues [8] reported the outcomes from a mpMRI based AS programme that did not involve protocol biopsies after the first confirmatory biopsy. In 211 men (median follow up of 4.2 years) progression to radical therapy was significantly higher at all stages in men with visible lesions than in men with initially negative scans (47/125 vs 11/86; p<0.001).

Whilst there is a well-established reporting system for reporting mpMRI in the diagnostic setting (Prostate Imaging Reporting and Data System – PI- RADS v.2 and 2.1) [10,11], the challenge of assessing change over time needs addressing [12].

An international consensus panel has published the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) recommendations [13], which establish the reporting standards for mpMRI in men with PCa on AS.

These guidelines propose that mpMRI data should be collected and analysed in a standardised manner, including accurate size measurements of lesions over time. Moreover, a standardised, structured report should be generated for each scan, as well as the comparative reports over time. Given the increasing burden in prostate mpMRI reporting that the radiologist faces, reporting according to the PRECISE recommendations can be time-consuming during daily clinical practice. There is a strong need of specific tools to allow reading, archival and analysis of mpMRI in a timely and accurate way.

The aim of this paper is to provide initial evidence of the utility of a specific tool to report according to the PRECISE recommendations, and to show the importance of automated comparison between sequential mpMRI in the individual man with PCa on AS.

11

1. Materials and methods

This is a retrospective analysis of a prospective, double-blind, randomised clinical trial (MAPPED) approved by the Hammersmith & Queen Charlotte's & Chelsea Research Ethics Committee (UK) (09/H0707/84), and the Medicines & Health Regulatory Agency and registered on the European Clinical Trials register (EudraCT 2009-102405-18) [14].

All patients gave written informed consent to participate in this study.

2.1 Patient selection

The initial population comprised 42 men with biopsy-proven PCa on AS randomised to 6 months of 0.5 mg daily dutasteride (a 5-alpha reductase inhibitor widely used for the treatment of lower urinary tract symptoms) or placebo, undergoing 3T mpMRI scans at baseline and 6 months. The MAPPED study used mpMRI-determined PCa volume as a primary endpoint, and the detailed protocol has been previously published [15]. From the initial database, we randomly identified 20 men (ten in the dutasteride and ten in the placebo arm) and retrieved the baseline and the 6-month mpMRI scans for each patient.

2.2 MR imaging technique

All patients underwent mpMRI using a 3T system (Magnetom Verio, Syngo MR B17; Siemens Healthcare, Erlangen, Germany) and a pelvic phased-array coil. All examinations included unenhanced axial, sagittal

and coronal turbo spin-echo T2 weighted imaging and axial diffusionweighted imaging (*b* values of 0, 100, 800 s/mm² and dedicated 0, 1400 s/mm² used for calculation of the ADC map), and dynamic-contrast enhanced sequences during intravenous injection of 0.1mmol/kg of body weight of gadoterate meglumine (Dotarem®, Guerbet,Roissy, France) at a rate of 2 mL/s, in accordance with standard guidelines [16]. In the absence of contraindications, an intramuscular injection of 20 mg of scopolamine butylbromide (20 mg, Buscopan, Boehringer Ingelheim, Ingelheim, Germany) was administered.

2.3 Image analysis

A specialist radiologist (FG, with 5 years of experience in PCa mpMRI reporting) - blinded to prostate specific antigen (PSA) values and treatment allocation - analysed the images using two different software programs: a widespread commercially-available platform (Osirix[®] v. 4.1.2 - Geneva, Switzerland) and a dedicated, customised semi-automated PRECISE reporting tool (MIM[®] Symphony Dx v. 6.8.3 - Cleveland, OH, USA).

To avoid any recall bias, the radiologist started each reporting session using one software program (for 10 patients) or the other (for 10 patients) as the first platform.

Tumour volume by planimetry in all sequences (T2-weighted, diffusionweighted -DWI- and dynamic contrast enhanced -DCE- imaging) and lesion conspicuity on DWI (i.e. the mean ADC of the peripheral zone

13

divided by the mean ADC of the tumour) were assessed at each time point, as previously reported (10,12). Reporting time for each scan using both platforms was also recorded (this included the time to hand-draw the diagram by the radiologist and the time to check PSA levels and Gleason Grade at the end of the reporting session, performed by an independent operator to avoid recall bias).

The PRECISE reporting tool provided a dedicated workflow that led the radiologist to report according to the PRECISE recommendations using a step-by-step procedure. After an overall look at the different sequences on the same window (Fig. 1), the radiologist was asked to contour the prostate by planimetry and then any visible lesion(s) on T2-weighted, DWI and DCE sequences independently (Fig. 2). At the end of each workflow, clinical and imaging data (such as PI-RADS or Likert score, PRECISE score, extracapsular/seminal vesicles extension, parameters changed from the previous scan, etc.) were manually inserted and included in the final structured report. At the beginning of the reporting session for follow-up scans (6 months), the contours of the prostate volume were rigidly transferred from the baseline scan, with the radiologist being able to edit them if needed. Conversely, only a single dot indicating the location of the previous lesion was transferred onto the new images to ensure an unbiased calculation of the new volume.

The conspicuity of each lesion was calculated after the reporting session, and therefore this was not included in the reporting time.

14

2.4 Statistical methods

Data are presented as medians and interquartile ranges (IQR) and were compared using a two-tailed Wilcoxon test. P values were then adjusted for False Discovery Rate and were considered to indicate a significant difference when < 0.05.

All statistical analyses were performed by using SPSS (version 20.0; SPSS, Chicago, Illinois, USA).

A CERTING

2. Results

The median age of the 20 men analysed in this study was 63.45 years (IQR: 60.16 – 66.61), and median PSA at baseline was 6.3 ng/mL (IQR: 5.44 – 8.16). Twelve men (60%) had Gleason 3+3 and eight (40%) Gleason 3+4 PCa at entry biopsy.

All lesions (apart from one in the dutasteride arm that was not visible on DWI) were visible both at baseline and 6-month scans.

Table 1 reports median tumour volumes, ADC values and conspicuity calculated using the two software programs in the whole population (n = 20), both at baseline and after 6 months.

There were no significant differences between the two methods for all parameters.

There was a significant reduction in the reporting time at 6 months using the dedicated PRECISE reporting tool (12'33'' vs 10'52'', respectively; p = 0.005) (Table 1).

Similar results were found analysing the placebo (n=10) and the dutasteride (n=10) arms independently, with no significant differences between the two methods for all parameters (Table 2 and Table 3).

A significant difference in the reporting time was observed in the dutasteride arm using the PRECISE reporting tool (15'50'' vs 12'59''; p = 0.01).

Additionally, a structured report including baseline and follow-up scans was generated using the dedicated tool, as advocated in the PRECISE recommendations [13] (Fig. 3).

Data obtained from the comparison between two-time points (including the increase or decrease rate) were also reported (Fig. 3).

A prose and a diagrammatic report from the same patient are shown in Fig. 4.

A CLER MAN

3. Discussion

The PRECISE recommendations were built to allow robust data collection of prostate mpMRI on AS and highlighted the areas most in need of research [13].

Our initial study indicates that a dedicated PRECISE software program is a promising tool to assist the radiologist in the reporting of serial prostate scans in men on AS for PCa.

Quantitative data extracted using the two platforms were comparable, as the volumes, ADC values and conspicuity were not significantly different (Table 1). Conversely, there was a significant reduction in the reporting time at follow-up scans using the dedicated PRECISE workflow, both for the whole population (p=0.005) and in the dutasteride arm (p=0.01). The main reason lies in the capability of the PRECISE tool to transfer prostate volume contours from one scan to the other and to show the previous location of any lesion, with a considerable drop in the time required for contouring in the follow-up scan.

A closer look at the results in the dutasteride arm (Table 3) shows that dutasteride was associated with increased tumour ADC and reduced conspicuity on DWI using both platforms. This is in line with our previous findings [17] and could also explain why the reporting time at 6 months was quicker using the PRECISE tool in this arm compared to the placebo

(i.e. the lesion was less visible, and therefore less time was required to report the scan).

In addition to this, the PRECISE tool generated a structured report that compares data at different time points, including clinical and quantitative findings (Fig. 3).

This preliminary study suggests that the use of dedicated reporting tools in line with the PRECISE recommendations [13] could be of help to report and analyse data from prostate mpMRI on AS and would allow to transfer contours and regions of interest to serial scans for quick comparison.

Moreover, specific tools to analyse data from different cohorts on AS could pave the way to the creation of a cloud-based platform for multiple centres with multiple readers, as advocated by the panel of experts who drafted the PRECISE recommendations [13].

Another key point that emerges from the PRECISE guidelines is the quality and standardisation of the mpMRI reports for men on AS. At present, many centres worldwide are still using a narrative report, often without including any images (Fig. 4). Such reports can vary from centre to centre and from radiologist to radiologist, resulting in a huge variability that can be sometimes difficult to interpret.

At this regard, the PRECISE recommendations suggest that the ideal report should be easily readable by different operators and should include

the essential snapshots of the lesion on different mpMRI sequences, and a visual diagram that could assist the operator during biopsy procedures. Our study provides a first attempt to address this issue, as we generated a structured report according to the PRECISE recommendations (Fig. 3).

It is clear from this study that dedicated platforms developed within the industry hold promise to analyse large data sets from men on AS for PCa allowing a quicker assessment and refinement of the PRECISE recommendations from multiple centres worldwide. Additionally, such platforms would aid quantitative analysis and structured reporting using fully automated and semi-automated algorithms in line with the PRECISE guidelines.

The correlation of radiological findings (both qualitative and quantitative) obtained from the PRECISE reporting tool with PSA and histologic data (e.g. Gleason score) has been also advocated, and this has been included in the structured report that we obtained using our tool (Fig. 3).

The main finding of this study is that the use of a dedicated PRECISE reporting tool would facilitate the determination of thresholds that identify radiologically important changes on mpMRI on a large-scale, allowing men at lowest risk to have less frequent testing (with a positive impact on cost effectiveness for health systems) but at the same time ensuring that any signs of higher risk disease based on mpMRI phenotype can be carefully investigated (e.g. targeted biopsy). The comparison table (including the

20

rate of increase or decrease of each parameter) shown in Fig. 3 represents a first answer to define these thresholds, which could be then compared with the histological outcomes from targeted biopsy if radiological progression is suspected.

Various methodological limitations apply to our study. First is the small cohort of men.

Second, we analysed only two mpMRI scans within a relatively short time frame (6 months), therefore we cannot comment on the medium/longterm natural history of PCa on mpMRI.

Third, a single radiologist was involved in this retrospective analysis and this does not allow to assess the inter-reader variability.

The same mpMRI machines were used for baseline and follow-up scans; therefore, we cannot comment on the variability between different systems and vendors.

Finally, we carried out our analysis using only two platforms, but we acknowledge that there are other commercially available platforms. It will be interesting to compare our results with those from other dedicated reporting platforms.

4. Conclusions

In conclusion, there is compelling evidence to support the use of mpMRI in men with PCa suitable for AS. However, there is still need of robust data from large cohorts that can provide a deeper insight into the huge amount of data that can be extrapolated from a single mpMRI scan. As such, there is a strong need of novel tools and reporting software programs to assist the radiologist in the reporting of sequential mpMRI scans according to the PRECISE recommendations [13]. If these recommendations will be widely used, the data derived will facilitate the determination of thresholds that identify radiologically significant disease and important radiologic changes on mpMRI.

To achieve this, automated comparisons across a patient over time using dedicated reporting tools would help with our understanding of the natural history of mpMRI changes on AS.

Our initial results support this idea and demonstrate how specific reporting programs can be of huge help to analyse large data sets, allowing a quicker assessment and refinement of the PRECISE recommendations.

Acknowledgements

The authors are indebted to all the men who greatly contributed to the realisation of this study.

Funding

The original study was investigator-led and sponsored by University College London. The study was supported financially by GlaxoSmithKline (GSK) who also provided supplies of both drug and placebo. GSK had no input into the design, conduct and analysis of the study.

Francesco Giganti is funded by the UCL Graduate Research Scholarship and the Brahm PhD scholarship in memory of Chris Adams.

Jonathan W Piper is a stockholder and employee for MIM® Software Inc Cleveland, Ohio, USA. David Mirando is an employee for MIM® Software Inc Cleveland, Ohio, USA. Mr Piper and Mr Mirando did not have any financial or business interests in this study.

Alex Kirkham receives research support from the UCLH/UCL NIHR Biomedical Research Centre.

Mark Emberton is a UK National Institute of Health Research (NIHR) Senior Investigator. He receives support from the UCLH/UCL NIHR Biomedical Research Centre.

References

- Tosoian JJ, Carter HB, Lepor A, Loeb S. Active surveillance for prostate cancer: Current evidence and contemporary state of practice. Nat Rev Urol 2016;13:205–15. doi:10.1038/nrurol.2016.45.
- [2] NICE. Prostate cancer: protocol for active surveillance.Implementing the NICE guideline on prostate cancer (CG175) 2014.
- [3] Schoots IG, Petrides N, Giganti F, Bokhorst LP, Rannikko A, Klotz L, et al. Magnetic resonance imaging in active surveillance of prostate cancer: A systematic review. Eur Urol 2015;67:627–36. doi:10.1016/j.eururo.2014.10.050.
- [4] Loeb S, Walter D, Curnyn C, Gold HT, Lepor H, Makarov D V. How Active is Active Surveillance? Intensity of Followup during Active Surveillance for Prostate Cancer in the United States. J Urol 2016;196:721–6. doi:10.1016/j.juro.2016.02.2963.
- [5] Morgan VA, Parker C, MacDonald A, Thomas K, DeSouza NM. Monitoring tumor volume in patients with prostate cancer undergoing active surveillance: Is MRI apparent diffusion coefficient indicative of tumor growth? Am J Roentgenol 2017;209:620–8. doi:10.2214/AJR.17.17790.
- [6] Dianat SS, Carter HB, Pienta KJ, Schaeffer EM, Landis PK, Epstein JI, et al. Magnetic resonance-invisible versus magnetic resonancevisible prostate cancer in active surveillance: A preliminary report on

disease outcomes. Urology 2015;85:147–53. doi:10.1016/j.urology.2014.06.085.

- [7] Giganti F, Moore CM, Punwani S, Allen C, Emberton M, Kirkham A. The natural history of prostate cancer on MRI: lessons from an active surveillance cohort. Prostate Cancer Prostatic Dis 2018. doi:10.1038/s41391-018-0058-5.
- [8] Gallagher KM, Christopher E, Cameron AJ, Little S, Innes A, Davis G, et al. 4-year outcomes from an MP-MRI based active surveillance programme - PSA dynamics and serial MRI scans allow omission of protocol biopsies. BJU Int 2018:0–1. doi:10.1111/bju.14513.
- [9] Schoots IG, Nieboer D, Giganti F, Moore CM, Bangma CH, Roobol MJ. Is magnetic resonance imaging-targeted biopsy a useful addition to systematic confirmatory biopsy in men on active surveillance for low-risk prostate cancer? A systematic review and meta-analysis.
 BJU Int 2018. doi:10.1111/bju.14358.
- [10] Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging Reporting and Data System: 2015, Version 2. Eur Urol 2016;69:16–40.
 doi:10.1016/j.eururo.2015.08.052.
- [11] Padhani AR, Weinreb J, Rosenkrantsz AB, Villeirs G, Turkbey B, Barentsz J. Prostate Imaging-Reporting and Data System Steering Committee: PI-RADS v2 Status Update and Future Directions. Eur Urol 2018. doi:10.1016/j.eururo.2018.05.035.
- [12] Vargas HA, Hötker AM, Goldman DA, Moskowitz CS, Gondo T,

Matsumoto K, et al. Updated prostate imaging reporting and data system (PIRADS v2) recommendations for the detection of clinically significant prostate cancer using multiparametric MRI: critical evaluation using whole-mount pathology as standard of reference. Eur Radiol 2016;26:1606–12. doi:10.1007/s00330-015-4015-6.

- [13] Moore CM, Giganti F, Albertsen P, Allen C, Bangma C, Briganti A, et al. 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. Eur Urol 2017;71:648–55. doi:10.1016/j.eururo.2016.06.011.
- [14] Robertson NL, Moore CM, Ambler G, Bott SRJ, Freeman A, Gambarota G, et al. MAPPED study design: A 6month randomised controlled study to evaluate the effect of dutasteride on prostate cancer volume using magnetic resonance imaging. Contemp Clin Trials 2013;34:80–9. doi:10.1016/j.cct.2012.10.003.
- [15] Moore CM, Robertson NL, Jichi F, Damola A, Ambler G, Giganti F, et al. The Effect of Dutasteride on Magnetic Resonance Imaging Defined Prostate Cancer: MAPPED—A Randomized, Placebo Controlled, Double-Blind Clinical Trial. J Urol 2017;197:1006–13. doi:10.1016/j.juro.2016.11.090.
- [16] Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs
 G, et al. ESUR prostate MR guidelines 2012. Eur Radiol
 2012;22:746–57. doi:10.1007/s00330-011-2377-y.
- [17] Giganti F, Moore CM, Robertson NL, McCartan N, Jameson C, Bott

SRJ, et al. MRI findings in men on active surveillance for prostate cancer: does dutasteride make MRI visible lesions less conspicuous? Results from a placebo-controlled, randomised clinical trial. Eur Radiol 2017;27:4767–74. doi:10.1007/s00330-017-4858-0.

[18] Giganti F, Gambarota G, Moore CM, Robertson NL, McCartan N, Jameson C, et al. Prostate cancer detection using quantitative T2and T2-weighted imaging: The effects of 5-alpha-reductase inhibitors in men on active surveillance. J Magn Reson Imaging 2018;47:1646– 53. doi:10.1002/jmri.25891.

CCC RANK

Table 1 – Median tumour volumes, ADC values, conspicuity and reportingtime calculated using $Osirix^{®}$ and $MIM^{®}$ for each time point for 20patients.

Table 2 – Median tumour volumes, ADC values, conspicuity and reporting time calculated using $Osirix^{®}$ and $MIM^{®}$ for each time point in the placebo arm (n=10).

Table 3 – Median tumour volumes, ADC values, conspicuity and reporting time calculated using $Osirix^{®}$ and $MIM^{®}$ for each time point in the Dutasteride arm (n=10).

Figure 1 – Initial overview of the multiparametric MR scan using the PRECISE workflow.

Figure 2 – Prostate volume (A) and lesion (B-E) contours by planimetry using the PRECISE workflow of a 59-year-old man with presenting PSA of 9.69 ng/mL and a Gleason 3+3 tumour at biopsy. This patient was in the placebo arm.

The whole prostate is contoured on each slice from base to apex on axial T2-weighted sequences (A). The lesion in the right peripheral zone (arrows) is then sequentially contoured on each slice on T2-weighted (B), dynamic-contrast enhanced (C) and diffusion-weighted imaging + apparent diffusion coefficient map (D and E show the contours on the apparent diffusion coefficient map, in baseline (D) and follow-up (E) scans, respectively).

Figure 3 – Structured reports using a dedicated reporting tool according to the PRECISE recommendations of the same patient shown in Fig. 2. The images show data from baseline and follow-up scans together with a comparison table (including the rate of increase/decrease) of the key

parameters of the lesion from each scan and a diagram showing lesion location and PI-RADS v.2 score (in red).

Figure 4 – Examples of a traditional prose (A) and hand-drawn diagrammatic (B) report of the same patient shown in Fig. 2.

A CERTING

Table 1 – Median tumour volumes, ADC values, conspicuity and reportingtime calculated using $Osirix^{®}$ and $MIM^{®}$ for each time point for 20patients.

		Baseline		6 months				
	Osirix®	MIM®	р	Osirix®	MIM®	р		
T2-WI volume (cc)	0.29 (0.17- 0.57)	0.32 (0.14- 0.66)	0.72	0.23 (0.15- 0.51)	0.30 (0.18- 0.54)	0.28		
DWI volume (cc) *	0.23 (0.14- 0.35)	0.27 (0.16- 0.45)	0.28	0.27 (0.12- 0.48)	0.30 (0.11- 0.49)	0.29		
DCE volume (cc)	0.31 (0.26- 0.60)	0.39 (0.24- 0.68)	0.28	0.27 (0.10- 0.64)	0.34 (0.12- 0.60)	0.96		
ADC lesion * (x 10 ⁻³ mm ² /s)	0.90 (0.86- 1.04)	0.84 (0.76- 1.06)	0.29	1.01 (0.87- 1.07)	0.93 (0.81- 1.18)	0.49		
ADC PZ * (x 10 ⁻³ mm ² /s)	1.53 (1.41- 1.64)	1.56 (1.48- 1.70)	0.78	1.49 (1.39- 1.61)	1.49 (1.42- 1.62)	0.72		
Conspicuity [§]	1.59 (1.37- 1.83)	1.73 (1.4-2)	0.28	1.49 (1.33- 1.83)	1.60 (1.27- 2.10)	0.29		
Reporting time (mins and sec)	14'47'' [10'20'' – 17'37'']	14'34" [11'45"- 16'42"]	0.66	12'33" [09'14" – 16'18"]	10'52" [08'41" – 13'56"]	0.005		

Note – Data are medians and 1st and 3rd interquartile ranges (parentheses); T2-WI: T2-weighted imaging; DWI: diffusion-weighted imaging; DCE: dynamic contrast enhanced; ADC: apparent diffusion coefficient; PZ: peripheral zone. * Data from 19 patients.

 $\ensuremath{^\$}$ Conspicuity was defined as the mean ADC of the peripheral zone divided by the

Stephenson Sold and a second secon **Table 2** – Median tumour volumes, ADC values, conspicuity and reporting time calculated using $Osirix^{\mathbb{R}}$ and $MIM^{\mathbb{R}}$ for each time point in the placebo arm (n=10).

		Baseline		6 months		
	Osirix®	MIM®	р	Osirix®	MIM®	р
T2-WI volume (cc)	0.29 (0.13- 0.44)	0.27 (0.15- 0.44)	0.58	0.24 (0.17- 0.41)	0.30 (0.22- 0.44)	0.28
DWI volume (cc)	0.19 (0.15- 0.27)	0.20 (0.16- 0.33)	0.36	0.26 (0.12- 0.33)	0.27 (0.14- 0.35)	0.58
DCE volume (cc)	0.30 (0.27- 0.52)	0.34 (0.24- 0.58)	0.36	0.19 (0.10- 0.46)	0.34 (0.09- 0.45)	0.88
ADC lesion (x 10 ⁻³ mm ² /s)	0.89 (0.86- 1.04)	0.91 (0.72- 1.16)	0.81	0.94 (0.87- 1.07)	0.98 (0.78- 1.06)	0.68
ADC PZ (x 10 ⁻³ mm ² /s)	1.58 (1.34- 1.63)	1.59 (1.55- 1.71)	0.46	1.50 (1.41- 1.61)	1.50 (1.44- 1.68)	0.66
Conspicuity [§]	1.59 (1.33- 1.77)	1.65 (1.43- 1.82)	0.56	1.55 (1.45- 1.97)	1.61 (1.38- 1.98)	0.69
Reporting time (mins and sec)	11′59″ (10′06″ – 15′09″)	12'53" (10'55"- 15'24")	0.36	10'47'' (08'46'' – 12'38'')	9'28'' (08'30'' – 11'59'')	0.36

Note – Data are medians and 1st and 3rd interquartile ranges (parentheses); T2-WI: T2-weighted imaging; DWI: diffusion-weighted imaging; DCE: dynamic contrast enhanced; ADC: apparent diffusion coefficient; PZ: peripheral zone.

[§] Conspicuity was defined as the mean ADC of the peripheral zone divided

by the mean ADC of the tumour on DWI.

 Table 3 – Median tumour volumes, ADC values, conspicuity and reporting time calculated using $Osirix^{®}$ and $MIM^{®}$ for each time point in the Dutasteride arm (n=10).

		Baseline		6 months				
	Osirix®	MIM®	р	Osirix®	MIM®	р		
T2-WI volume (cc)	0.43 (0.25-0.7)	0.48 (0.19- 0.68)	0.93	0.33 (0.16- 0.57)	0.31 (0.17- 0.54)	0.93		
DWI volume (cc) *	0.27 (0.14- 0.52)	0.44 (0.21- 0.5)	0.24	0.47 (0.08- 0.49)	0.37 (0.11- 0.59)	0.58		
DCE volume (cc)	0.46 (0.26- 0.75)	0.53 (0.28- 0.79)	0.40	0.42 (0.16- 0.64)	0.42 (0.18- 0.59)	0.93		
ADC lesion * (x 10 ⁻³ mm ² /s)	0.91 (0.86- 1.04)	0.84 (0.78- 0.88)	0.24	1.01 (1- 1.06)	0.92 (0.84- 1.18)	0.39		
ADC PZ * (x 10 ⁻³ mm ² /s)	1.51 (1.43- 1.65)	1.50 (1.48- 1.56)	0.71	1.49 (1.41- 1.58)	1.46 (1.39- 1.51)	0.93		
Conspicuity [§]	1.59 (1.46- 1.83)	1.77 (1.54-2)	0.24	1.41 (1.32- 1.52)	1.50 (1.27- 1.70)	0.39		
Reporting time (mins and sec)	17'52" (13'25" – 19'59")	16'35" (13'28"- 19'48")	0.57	15'50" (11'44" – 19'02")	12'59" (09'28" – 16'03")	0.01		

Note – Data are medians and 1st and 3rd interquartile ranges (parentheses); T2-WI: T2-weighted imaging; DWI: diffusion-weighted imaging; DCE: dynamic contrast enhanced; ADC: apparent diffusion coefficient; PZ: peripheral zone.

* Data from 9 patients.

[§] Conspicuity was defined as the mean ADC of the peripheral zone divided by the mean ADC of the tumour on DWI.

SR'







Baseline scan

Reporting Radiologist						e of so	an		Date of report	08/05/201			
PSA 9.69 ng						A Date					12/01/2012	PSA density	0.28 ng/m
Prostate volume on T2-weighted imaging				33.8	3 Mag	Magnet strength 3.0T						Coll used	SIEMENS Veri
Likelihood of clinically significant disease (1-5)					5 PI-F	PI-RADS 2 score (maximal) 4						TNM stage	T2aN
Likelihood of extrapr	rostatic	extension (T3a) (1-5)		3 Like	elihood	d of se	minal	vesicle inva	sion (T3b) (1-	-5) 1		
Lesion Appeared Lesion T since last (focal/diff scan?			lype fuse)	Not risible	D1	D2	D3	Volume (D1 x D2 x D3 x 0.52)	Volume by planimetry	Likelihood of clinically significant disease (1-5)*	PI-RADS-2 score		
	1	n/a	foca	1		1.12	0.69	0.81	0.33	0.19	5	4	
	2	n/a											

	Sequence where lesion best seen	Volume where lesion best seen	Volume on T2- weighted imaging
Lesion 1 - Right Posterior Mid	DWI_b	0.15	0.19
Lesion 2			
Lesion 3			

Follow-up scan

	Reporting Rec	diologist				Date	of sc	an					27/07/	2012	Date of report	09/05/2018	
	PSA				11.47 ng	PSA	Date						26/07/3	2012	PSA density	0.32 ng/mL	
	Prostate volu	me on T2-weig	hted ima	ging	35.30	Mag	net st	rength					-	3.0T	Coll used	SIEMENS Verio	
	Likelihood of clinically significant disease (1-5)) 5	PI-R	ADS 2	score	e (max	imal)				4	TNM stage	T2aN0		
	Likelihood of extraprostatic extension (T3a) (1-5)			-5) 3	Like	lhood	of se	minel	vesicle inv	asion (T3b)	(1-5)		1				
			Lesion	Appeared since test scan?	Lesion Type (focalidiffuse)	Not visible	D1	02	83	Volume (D1 x D2 x D3 x 0.52)	Volume by planimetry	Likelih clini signil clacese	cod of cally icant c (1-5)*	PLRAS	9		
			1	No	focal		1.25	0.75	0.72	0.35	0.22			4			
			2	No													
			3	No													
						Sequ	ence	where	lesio	n best seen	Volume lesion b seen	where	Volun weigt imagi	ne on 1 Ited ng	r2-		
			Lesion	1 - Right I	Posterior Mid			DW	ЛLЬ		0.2	5		0.22			
				Lesion	12												
				Lesion	13												
		Date of pr MRI	evious	Likelik	nood of cha ius MRI (1-	ange 1 5)*	rom	Par PI-I	rame RAD	ter whicl S score,	has ch T3a or T	anged 3b dis	(e.g. ease)	volu	me on T2W-I	, visibility on E	WI, Likert score
Lesion 1 - Right Pos	terior Mid	13/01/2	012		4								Volum	e, Co	inspicuity (D	WI)	
Lesion 2		13/01/2	012														
Lesion 3		13/01/2	012														

Comparison table

Lesion 1 - Right Poste	rior Mid							
		13/01/201	2	27/07/2012				
	Change	%Change	Rate (1/y)) Change %Change Rate (1/y)				
T2 Volume (mL)		0.19			0.22			
w.r.t. Previous				0.03	16.48	0.06		
w.r.t. Baseline								
DWI Volume (mL)		0.15			0.25			
w.r.t. Previous				0.1	64.49	0.18		
w.r.t. Baseline								
DCE Volume (mL)		0.15			0.23			
w.r.t. Previous				0.23	8	0.43		
w.r.t. Baseline								
ADC Mean		1280.98		1011.94				
w.r.t. Previous				-269.04	-21	-503.59		
w.r.t. Baseline								
ADC Median		1262		976				
w.r.t. Previous				-286	-22.66	-535.33		
w.r.t. Baseline								
ADC Minimum		532		647				
w.r.t. Previous				115	21.62	215.26		
w.r.t. Baseline								
D1 (Sagittal) (cm)		1.12		1.25				
w.r.t. Previous				0.13	11.61	0.24		
w.r.t. Baseline								
D2 (Coronal) (cm)		0.69			0.75			
w.r.t. Previous				0.06	8.7	0.11		
w.r.t. Baseline								
D3 (Transverse) (cm)		0.81			0.72			
w.r.t. Previous				-0.09	-11.11	-0.17		
w.r.t. Baseline								









SV + Base

Midgland

Apex + sphincter

Indication: Gleason 3+3; PSA: 9.69 ng/ml.

A multiparametric MRI was performed using T1-weighted, T2weighted, diffusion-weighted and dynamic contrast enhanced images.

The prostate measures 3.6 x 4.3 x 4.5 (total volume: 36 cc).

The transition zone has a typical nodular appearance, and there is a low risk of clinically significant cancer (Likert score: 2/5).

In the right peripheral zone (mid-gland to apex) there is a 0.3 cc lesion (Likert score 5/5; PI-RADS score 4/5) that shows low signal on T2-weighted images, early enhancement on the dynamic sequences and restricted diffusion on the high b value sequences (ADC: $0.86 \times 10^{-3} \text{ mm}^2/\text{s})$. The lesion abuts the capsule and microscopic extracapsular extension cannot be ruled out (3/5).

No pelvic lymphadenopathy or seminal vesicle involvement.

Conclusion: PZ lesion on the right side of the prostate (5/5). Equivocal extracapsular extension (3/5).



Please number and draw in the regions/lesions of interest on diagram below

27 sectors scheme

R

