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Prostate MR image quality of apparent diffusion coefficient maps versus fractional intracellular volume maps from VERDICT MRI using the PI-QUAL score and a dedicated Likert scale for artefacts

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ABSTRACT

Purpose: This study aimed to assess the image quality of apparent diffusion coefficient (ADC) maps derived from conventional diffusion-weighted MRI and fractional intracellular volume maps (FIC) from VERDICT MRI (Vascular, Extracellular, Restricted Diffusion for Cytometry in Tumours) in patients from the INNOVATE trial. The inter-reader agreement was also assessed.

Methods: Two readers analysed both ADC and FIC maps from 57 patients enrolled in the INNOVATE prospective trial. Image quality was assessed using the Prostate Imaging Quality (PI-QUAL) score and a subjective image quality Likert score (Likert-IQ). The image quality of FIC and ADC were compared using a Wilcoxon Signed Ranks test. The inter-reader agreement was assessed with Cohen's kappa.

Results: There was no statistically significant difference between the PI-QUAL score for FIC datasets compared to ADC datasets for either reader ($p = 0.240$ and $p = 0.614$). Using the Likert-IQ score, FIC image quality was higher compared to ADC ($p = 0.021$) as assessed by reader-1 but not for reader-2 ($p = 0.663$). The inter-reader agreement was 'fair' for PI-QUAL scoring of datasets with FIC maps at 0.27 (95% confidence interval; 0.08–0.46) and ADC datasets at 0.39 (95% confidence interval 0.22–0.57). For Likert scoring, the inter-reader agreement was also 'fair' for FIC maps at 0.38 (95% confidence interval; 0.10–0.65) and substantial for ADC maps at 0.62 (95% confidence interval; 0.39–0.86).

Conclusion: Image quality was comparable for FIC and ADC. The inter-reader agreement was similar when using PIQUAL for both FIC and ADC datasets but higher for ADC maps compared to FIC maps using the image quality Likert score.

Abbreviations: VERDICT, Vascular, Extracellular, and Restricted Diffusion for Cytometry in Tumor; INNOVATE, CombIning advaNces in imagiNg With biOmarkers for improVed Diagnosis of Aggressive prosTate cancer; mpMRI, multiparametric MRI; FIC, intracellular volume fraction; ADC, apparent diffusion coefficient; PI-RADS, Prostate Imaging Reporting and Data System.

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1. Introduction

Image quality has an important impact on the diagnostic accuracy of magnetic resonance imaging (MRI) and its interpretation by radiologists in the detection of prostate cancer. Suboptimal diagnostic quality can reduce accuracy and confidence in diagnosis, leading to indeterminate scores [1,2]. Therefore, assessing image quality for novel imaging sequences and comparing them to conventional imaging is important. Vascular, Extracellular, and Restricted Diffusion for Cytometry in Tumors (VERDICT) is a non-invasive diffusion-weighted MRI (DWI) technique which estimates histological parameters from the prostate to better characterise prostate cancer [3–6]. The technique combines a customised multi-b-value acquisition and a mathematical model of the three different diffusion environments in prostate tissue: a) Intracellular water, b) water in the extracellular extravascular space and c) water in vessels. From fitting the acquired data to the mathematical model, estimates of parameters in the three compartments can be derived. Recent studies have shown that fractional intracellular volume (FIC) derived from the intracellular diffusion environment is increased in prostate cancer compared to normal prostate tissue and has the potential to reduce false positives compared to multiparametric MRI [7]. However, for this technique to be used clinically, image quality needs to be compared to multiparametric MRI.

Recently a scoring system has been developed called Prostate Imaging Quality (PI-QUAL) which aims to assess the quality of multiparametric MRI against objective technical criteria and subjective criteria for visual assessment [8]. The PI-QUAL score is based on a 1-to-5 scale where the lowest score of 1 indicates all sequences are below the standard of diagnostic quality and the highest score of 5 implies that all sequences are of optimal quality [5,8,9]. Image quality can also be assessed by a Likert scale (Likert-IQ) used in published studies which is more subjective [10,11]. This scale is also a 5-point Likert scale which can be applied to each image type.

In this study, two readers assessed the image quality of MRI datasets which either had an apparent diffusion coefficient (ADC) map or a fractional intracellular volume (FIC) map using both PI-QUAL and the more subjective 5-point image quality Likert (Likert-IQ) score. The cases were randomly selected from the INNOVATE trial, which is the largest prospective evaluation of VERDICT MRI so far [12]. The clinical outcomes of the study have been published [13]. The objectives of this study were: i) to determine whether the image quality is equivalent for FIC and ADC maps, and ii) to assess inter-reader agreement for PI-QUAL and image quality Likert scoring systems in VERDICT MRI.

2. Methods

2.1. Participants

A random sample of 57 patients was taken from the INNOVATE cohort of 303 (registration no. NCT02689271)[14]. This sample size was based on reader availability and the time taken to read each dataset. Randomisation was performed on Microsoft Excel (version 16.49, Microsoft Corporation, 2021).

ADC maps were derived from four different *b*-values (b = 0,150,500 and 1,000 s/mm^2) from two MR scanners; 1.5 T Avanto (Siemens, Erlangen Germany) and 3 T Achieva (Philips, Best, Netherlands). VERDICT-MRI was performed on one scanner (Achieva) and using six different *b*-values (0, 90, 500, 1500, 2000, 3000 s/mm^2). The acquisition parameters have been published in previous studies [3]. The acquired data were fitted to the VERDICT model using in-house software to generate parametric maps including fractional intracellular volume (FIC), fractional vascular volume (FVASC) and fractional extravascular extracellular space (FEES) maps representing the three different diffusion environments. The maps are produced as a colour heatmap with high FIC shown in warm colours (red) and lower FIC values in cooler (blue) colours.

2.2. Study Design

The study cohort was divided into two separate groups: A and B.

For cohort A, datasets were compiled with T2W coronal, T2W axial, high *b* value (1,400 or 2,000 s/mm^2), dynamic contrast-enhanced imaging and ADC map (Fig. 1).

For Cohort B, datasets were compiled with FIC maps instead of ADC maps.

Two readers highly experienced in prostate MRI reporting (i.e., reporting more than 1,000 prostate MRI scans per year and more than 5 years of reporting experience at a specialist centre) assessed and scored each image type individually in a locked sequence starting with T2W axial and coronal, followed by either ADC or FIC, high *b* value and dynamic contrast enhancement (DCE). An equal number of datasets from Cohort A and Cohort B were taken for each reading session. This was to ensure that readers had equal exposure to the two maps rather than imbalance, which may affect results.

Image quality was assessed using the PI-QUAL and Likert-IQ scoring systems (Table 1, Fig. 2). The PI-QUAL score is assessed using a dedicated checklist of technical parameters and visual inspection to determine whether each image type is diagnostic or non-diagnostic (Fig. 2). The locked sequential read is shown in Fig. 3. The reporting pro-forma is shown in Fig. 4.

After a washout period of one month, cohort A datasets were presented with FIC maps and Cohort B datasets with ADC maps. This meant that each patient had either their FIC or ADC maps read by both readers but separated by a month to avoid recall. Images were displayed using the DICOM viewer: Horos (Horos Project, Annapolis, MD, USA).

The overall PI-QUAL score depends on how many image types are rated as diagnostic in a dataset for a participant. Although PI-QUAL does not specifically include the assessment of VERDICT maps, it does have specific criteria for diffusion-weighted imaging (Fig. 2). These criteria were applied by readers to assess VERDICT maps.

2.3. Statistical analysis

Image quality was compared for FIC and ADC maps using the Wilcoxon Signed Ranks non-parametric test for categorical data. Overall, PI-QUAL scores for datasets with FIC were compared to datasets with ADC using the same test. To account for differences in image quality due to the different field strengths of the two scanners, a subgroup analysis of image quality was carried out for ADC maps acquired at 1.5 T and 3 T. Median scores and 95% confidence intervals were presented as descriptive statistics.

The inter-reader agreement was assessed using weighted Cohen's kappa (K) at two levels.

For PI-QUAL scoring:

- PI-QUAL 1, 2 and 3 scores were designated to one group (not possible to rule out all significant lesions).
- PIQUAL 4 and 5 scores were assigned to the other group (possible to rule in and out all significant lesions).

For Likert scoring:

- Scores of 1, and 2 were designated one level (non-diagnostic image quality).
- Scores of 3, 4 and 5 were designated to the other group (diagnostic image quality).

The level of agreement was inferred as: $\leq$0 indicating no agreement, 0.01–0.20 as none-slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, 0.81–1.00 as almost perfect agreement [8].

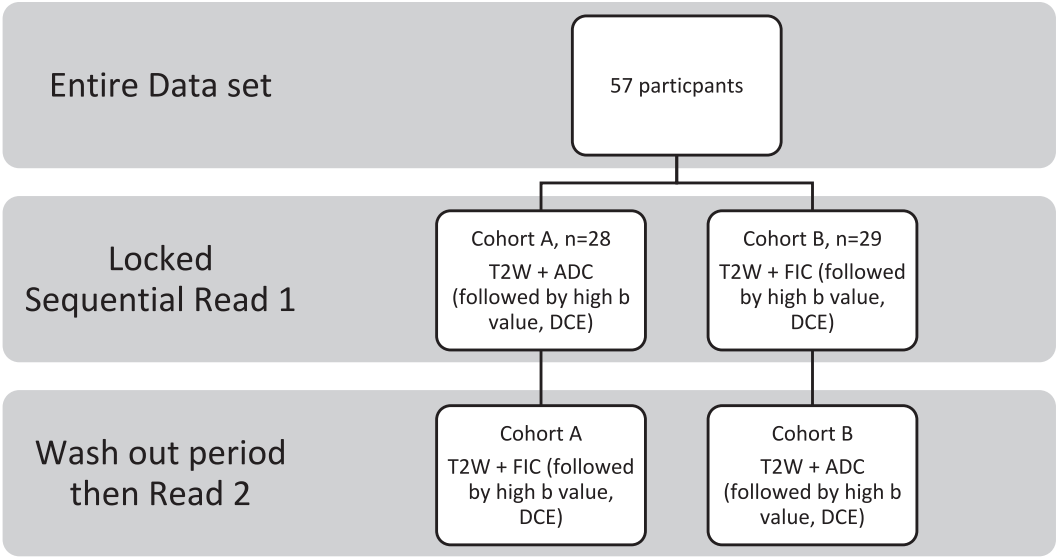


Fig. 1. Study Design T2W, T2 Weighted; ADC, apparent diffusion coefficient; DCE, dynamic contrast-enhanced; FIC, fractional intracellular volume.

Table 1
PIQUAL and Likert Image Quality Scoring.

Score	PIQUAL	Likert
1	All mpMRI sequences are below the minimum standard of diagnostic quality	very poor quality, considered non-diagnostic (artefacts on all slices, scans uninterpretable)
2	Only one mpMRI sequence is of acceptable diagnostic quality	poor quality with some impairment of diagnostic quality (substantial artefacts, but still interpretable)
3	At least two mpMRI sequences taken together are of diagnostic quality	satisfactory quality without impairment of diagnostic quality (some artefacts present),
4	Two or more mpMRI sequences are independently of diagnostic quality	good quality (hardly any artefacts),
5	All mpMRI sequences are of optimal diagnostic quality	excellent quality (no artefacts present).

Legend PIQUAL, Prostate Imaging Quality Score; mpMRI, multiparametric MRI.

3. Results

3.1. Participants

The demographics of the INNOVATE cohort have been mentioned previously [13]. The random sample of 57 participants had a median age of 64 (range 47–78) and a median prostate-specific antigen (PSA) of 5.98 ng/ml (range 0.83–37.4) comparable to the full cohort. A total of 32/57 (56%) participants underwent a biopsy of MRI lesions. Fifteen out of 32 (47%) participants had clinically significant cancer (defined as Gleason score $\geq 3+4$, with 12 biopsies showing Gleason $3+4$ disease and 3 biopsies showing Gleason $4+3$ disease respectively. Three out of 32 participants (9%) had Gleason $3+3$ disease and fourteen (44%) had a negative biopsy.

3.2. Image quality

Fig. 5 shows representative images from the study cohort for each Likert-IQ score where both readers had identical image quality scores. The frequencies of scores are charted in Figs. 6 and 7.

The median Likert-IQ score for ADC for reader-1 was 3, 95% confidence interval (CI) [3,4] and for reader-2 it was 4, 95% CI [3,4]. For FIC, the median quality score for reader-1 was 4, 95% CI [3,4] and also 4 for reader-2, 95% CI [3,4]. There was a statistical difference between FIC quality and ADC quality for reader-1 ($p = 0.021$) but not for reader-2 ($p = 0.663$). For PI-QUAL scoring, the median PI-QUAL score for ADC datasets was 3, 95% CI [3,4] for reader-1 and 4 for reader-2, 95% CI [4,4]. The median score for FIC datasets was 3, 95% CI [3,4] for reader-1 and 4 for reader-2, 95% CI [4,4]. There was no statistical difference between FIC and ADC PI-QUAL scores ($p = 0.240$ and $p = 0.614$).

There were a similar number of cases that were rated as poor quality or non-diagnostic on Likert-IQ for FIC and ADC by both readers. For instance, the first reader rated 9 FIC cases as 2/5 for image quality and 9 ADC cases as 2/5 on the Likert scale. In addition, the first reader rated 4 cases as 1/5 for ADC maps and no cases as 1/5 for FIC maps. The second reader rated 14 FIC and 14 ADC cases as 2/5 on the Likert quality scale. One FIC and one ADC case were rated 1/5 by the second reader.

Likert rating given by both readers, for example, '5′ was rated Likert 5 (excellent quality), '4′ (good quality), '3′ (satisfactory quality), '2′ (poor quality), and '1′ (very poor quality). Red arrows show susceptibility artefacts from rectal gas, which are worse for lower-quality scores.

3.3. 1.5T subgroup

For participants who had ADC maps derived from 1.5 T data ($n = 18$), the median ADC Likert-IQ rating and the median FIC quality score for both readers was 3. There was no difference between ADC and FIC quality scores in the subgroup for reader-1 ($p = 0.542$) and reader-2 ($p = 0.263$).

The median PI-QUAL score for ADC datasets was 3 for reader-1 and 4 for reader-2. The median PI-QUAL scores for FIC datasets for reader-1 and reader-2 were 3 and 4, respectively. There was no difference between PI-QUAL scores for FIC compared to ADC for reader-1 (0.579) and reader-2 ($p = 0.083$).

3.4. 3T subgroup

For participants with ADC maps derived from 3 T data ($n = 39$), the median ADC quality rating for reader-1 was 3 and for reader-2 was 4. The median FIC quality score was 4 for both readers. For reader-1, the FIC quality score was higher than ADC ($p = 0.022$). There was no difference between ADC and FIC quality scores in this subgroup for reader-2 ($p = 0.72$).

The median PI-QUAL score for ADC datasets was 3 for reader-1 and 4 for reader-2. The median PI-QUAL score for FIC datasets was 4 for both readers. There was no difference between PI-QUAL scores for FIC compared to ADC for reader-1 ($p = 0.324$) and reader-2 ($p = 0.549$).

Scan & site number:

PRECISION

Prostate Imaging QUALity control (PI-QUAL) scoring sheet

PI-QUAL score	Criteria	Clinical implications
1	All mpMRI sequences are below the minimum standard of diagnostic quality	It is NOT possible to rule in all significant lesions § It is NOT possible to rule out all significant lesions §
2	Only one mpMRI sequence is of acceptable diagnostic quality	
3	At least two mpMRI sequences taken together are of diagnostic quality	It is possible to rule in all significant lesions It is NOT possible to rule out all significant lesions
4	Two or more mpMRI sequences are independently of diagnostic quality	It is possible to rule in all significant lesions It is possible to rule out all significant lesions
5	All mpMRI sequences are of optimal diagnostic quality	

§ Therefore reports should not include PI-RADS or Likert scores

Please (✓) if present: (note: '*adequate*' means compliant with the technical specifications reported in PI-RADS v. 2 guidelines) *

T2-WI		DWI		DCE	
Technical parameters		**Technical parameters**		**Technical parameters**	
Axial plane		Axial plane matching T2-WI		Axial plane matching T2-WI	
Sagittal or coronal plane		Adequate field of view		Adequate field of view	
Adequate field of view		Adequate in-plane resolution		Adequate in-plane resolution	
Adequate in-plane resolution		Adequate slice thickness		Adequate slice thickness	
Adequate slice thickness		Multiple [> 2] *b* values acquired		Pre-contrast T1-WI available	
Z-axis correctly positioned		High *b* value (synthesised or acquired)		Fat suppression/subtraction	
Visual assessment		**Visual assessment**		Adequate temporal resolution [≤ 10 sec]	
Capsule clearly delineated		Adequate ADC map		Adequate total observation rate [≥ 2min]	
Seminal vesicles clearly delineated		Absence of artefacts (e.g. rectal air)		**Visual assessment**	
Ejaculatory ducts clearly delineated				Capsular vessels clearly delineated	
Neurovascular bundles clearly delineated				Vessels in the Alcock's canal clearly delineated	
Sphincter muscle clearly delineated				Absence of artefacts (e.g. movement)	
Absence of artefacts (e.g. movement)					

Is T2-WI of diagnostic quality? ☐ Yes ☐ No

Is DWI of diagnostic quality? ☐ Yes ☐ No

Is DCE of diagnostic quality? ☐ Yes ☐ No

PI-QUAL score: 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Comments:

Date:

Reporting Radiologist:

Signed:

* *Weinreb JC, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. Eur Urol 2016;69:16–40.*

Fig. 2. PI-QUAL Scoring Sheet Legend: T2-WI, T2-weighted imaging; DWI, diffusion-weighted imaging; DCE, dynamic contrast–enhanced; ADC, apparent diffusion coefficient. Reprinted with permission from Giganti et al. 2020.

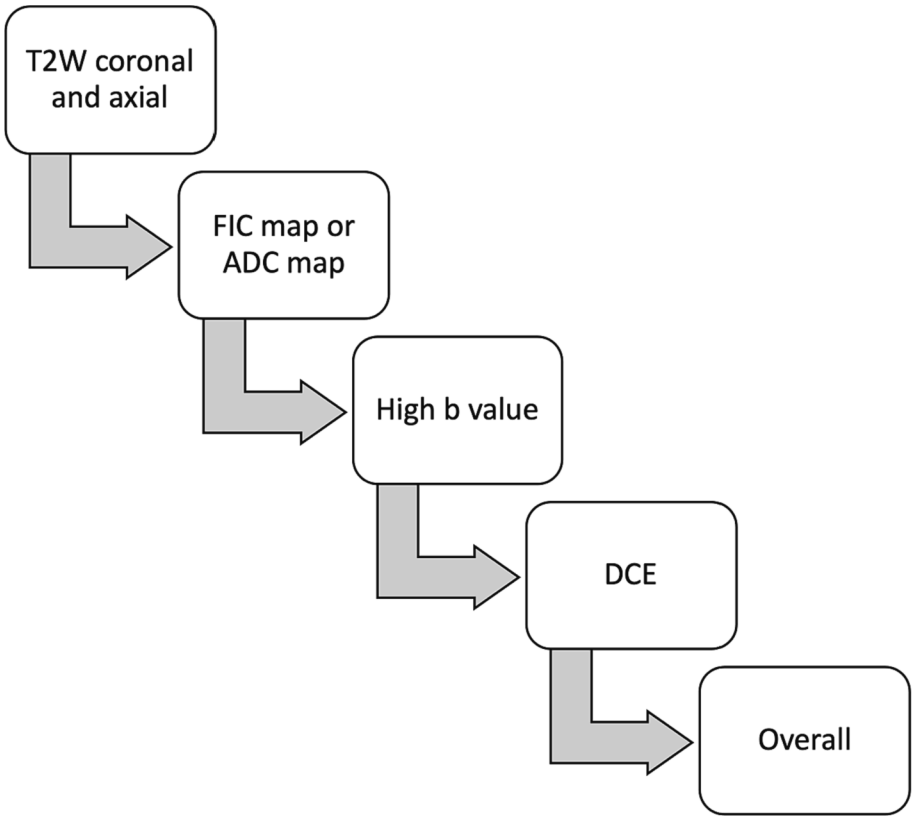


Fig. 3. Locked Sequential Read scheme Image quality was assessed in a locked sequence. FIC = fractional intracellular volume, ADC = apparent diffusion coefficient, DCE = dynamic contrast enhancement. The highlighted 'Likert score' and 'PI-RADS 2.1 score' are the scores that were assessed for the primary and secondary outcomes.

There was no difference in image quality between scanners for ADC maps as rated by reader-1 ($p = 0.131$) or reader-2 (0.405).

3.5. Inter-Reader agreement

The inter-reader agreement was 'fair' for PI-QUAL scoring of datasets with FIC maps at 0.27 (95% CI; 0.08–0.46) and ADC datasets at 0.39 (95% CI 0.22–0.57). For Likert scoring, the inter-reader agreement was also 'fair' for FIC maps at 0.38 (95% CI; 0.10–0.65) and substantial for ADC maps at 0.62 (95% CI; 0.39–0.86).

4. Discussion

The major findings of this study are that the image quality and inter-rater agreement of FIC were comparable to the ADC as rated by two experienced genitourinary radiologists using two different scoring systems. Using the PI-QUAL image quality score, the inter-reader agreement was fair for both FIC and ADC datasets. Using the Likert-IQ scoring, the inter-reader agreement was fair for FIC and substantial for ADC.

Similar image quality is expected as both acquisitions use echo planar imaging, which is prone to susceptibility artefacts from rectal air or peristalsis. The slightly lower inter-rater agreement for FIC maps using the Likert-IQ scoring could be due to the unfamiliarity of the readers with FIC maps.

Recent studies have shown that FIC maps can characterise prostate cancer better than ADC maps, which in turn could potentially spare unnecessary biopsies in patients with suspicion of prostate cancer [3]. For this promising imaging technique to be translated into the clinic, image quality must be comparable to the current ADC maps if being assessed qualitatively. The quality of prostate MRI is important, especially in the MRI-derived targeted biopsy paradigm of prostate cancer diagnosis [3]. The ability to rule out significant lesions in a patient with a favourable PSA profile could avoid an immediate unnecessary biopsy due to the high negative predictive value of prostate MRI [15].

This is the first study where readers have assessed the image quality of FIC maps using PI-QUAL, therefore results cannot be directly compared to other literature. However, two recent studies have assessed inter-rater agreement for PI-QUAL of mpMRI and shown higher kappa values of up to 0.82 [16,17]. The lower kappa values seen in our study could be due to the different levels of familiarity of the two readers in using the PIQUAL score. One author had greater familiarity with using PIQUAL compared to the other. Interestingly in this study by Giganti et al., the percentage agreement was lowest for conventional diffusion-weighted imaging and there was substantial disagreement when assessing the adequacy of ADC maps. ADC maps tend to be more susceptible to artefacts and noisier compared to T2 weighted and post-contrast imaging which could explain this variation.

The relatively small number of patients included in this analysis is a limitation of the study. However, taking a random sample from the study cohort should be representative of the larger cohort. Another limitation of the study is that FIC maps were derived from VERDICT acquisition on a 3 T scanner whereas some ADC maps ($n = 18$) were derived from 1.5 T and this could be a confounding factor in assessing image quality. However, subgroup analysis of participants who had both datasets derived from 3 T, did not show any differences in image quality between FIC and ADC. A further limitation is that the PI-QUAL scoring system was not designed to be used for VERDICT maps. All the technical and visual assessment criteria are however applicable to any diffusion-weighted sequence. For instance, the field of view, in-plane resolution, slice thickness and the number of b values for VERDICT MRI are comparable to mpMRI DWI. The use of PIQUAL for VERDICT was therefore judged to be appropriate by the study authors before the start of the study. The overall PIQUAL score is a global image quality score for the whole MRI dataset and therefore any differences between ADC and FIC

INNOVATE VERDICT

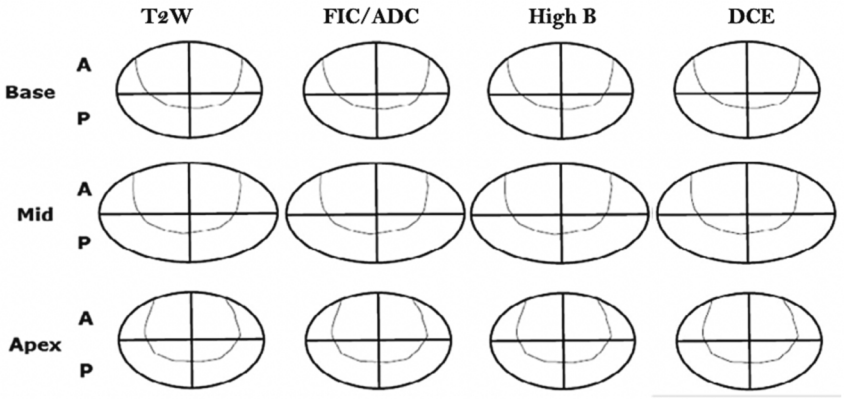
Radiologist name:

Study ID:

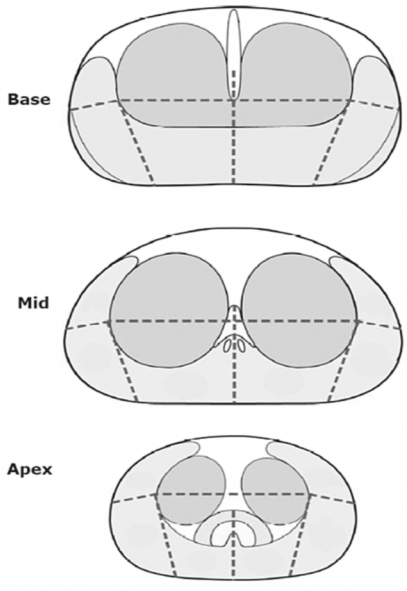
Date:

T2W image quality:	1☐; 2☐; 3☐; 4☐; 5☐	PIQUAL Non-diagnostic ☐
FIC image quality:	1☐; 2☐; 3☐; 4☐; 5☐	PIQUAL Non-diagnostic ☐
ADC image quality:	1☐; 2☐; 3☐; 4☐; 5☐	PIQUAL Non-diagnostic ☐
DWI high b value image quality:	1☐; 2☐; 3☐; 4☐; 5☐	PIQUAL Non-diagnostic ☐
DCE image quality:	1☐; 2☐; 3☐; 4☐; 5☐	PIQUAL Non-diagnostic ☐
Overall PIQUAL score:	1☐; 2☐; 3☐; 4☐; 5☐	

1. **Prostate Volume =** ☐☐☐ cc (…….AP x …….TV x …….CC x 0.52)
2. **Sector scores**



3. **Individual Lesions – draw, number and score lesions below**



4. **Overall Likert Score =** 1☐; 2☐; 3☐; 4☐; 5☐
5. **Overall PIRADS 2.1 =** 1☐; 2☐; 3☐; 4☐; 5☐
6. **Time taken**
   a. **T2W + FIC/ADC =**
   b. **Whole dataset =**

Fig. 4. Reporting Pro-forma Legend: T2-W, T2-weighted imaging; FIC, fractional intracellular volume; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; DCE, dynamic contrast–enhanced; PIQUAL.

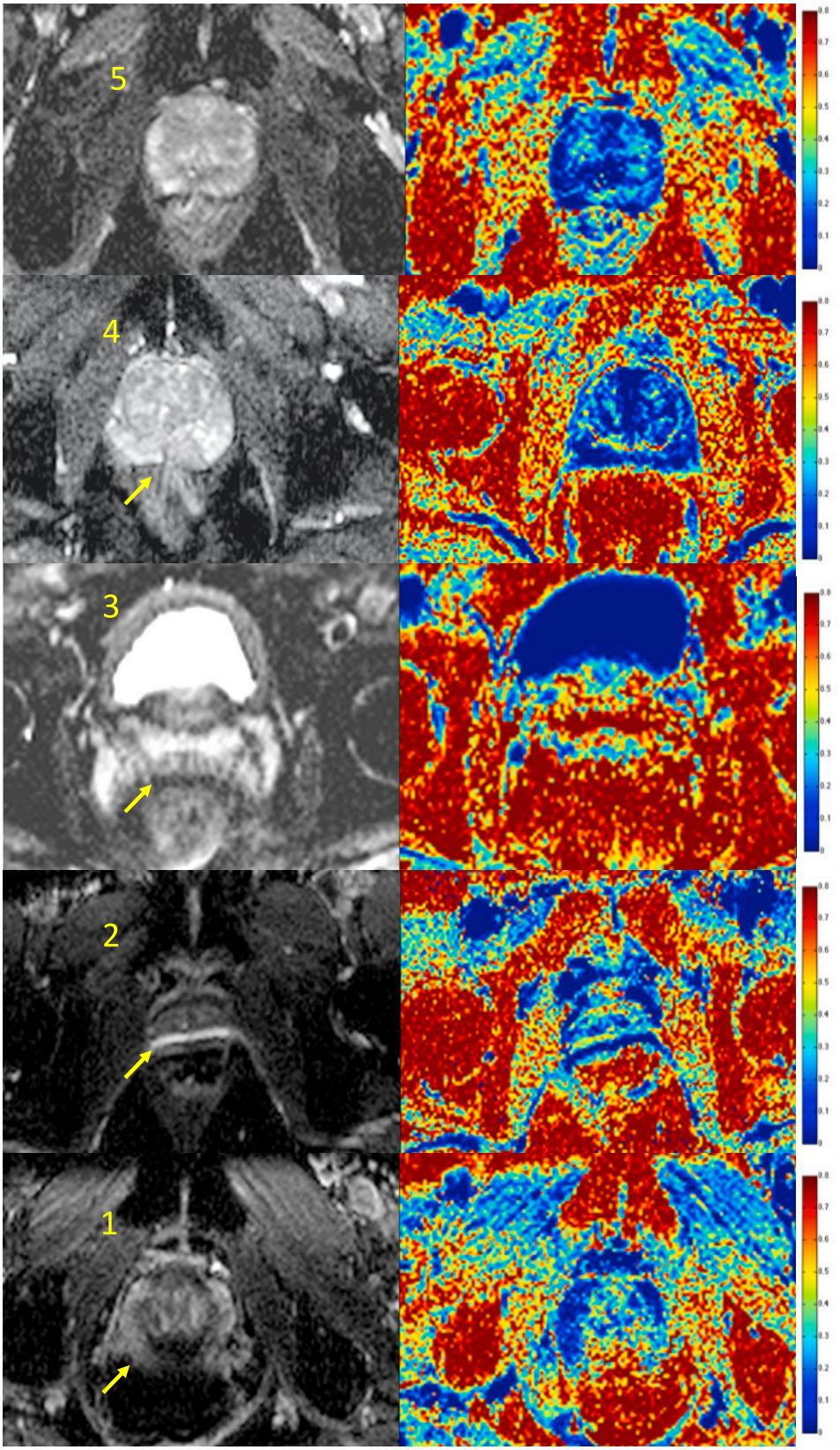


Fig. 5. Apparent Diffusion Coefficient (ADC) maps (left) and Fractional Intracellular Volume (FIC) maps (right) from 5 participants.

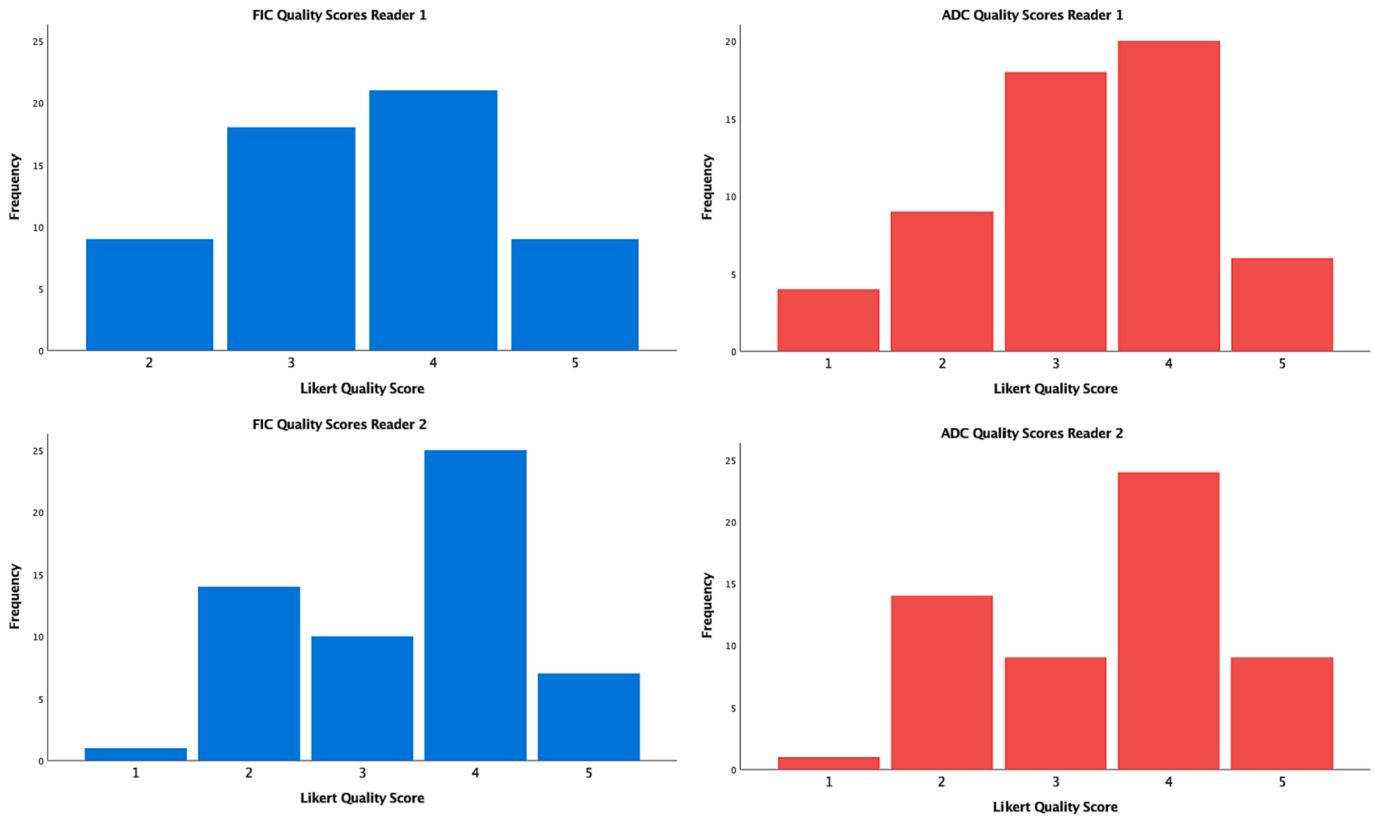


Fig. 6. Likert Quality Scores for both readers; FIC on left, ADC on right.

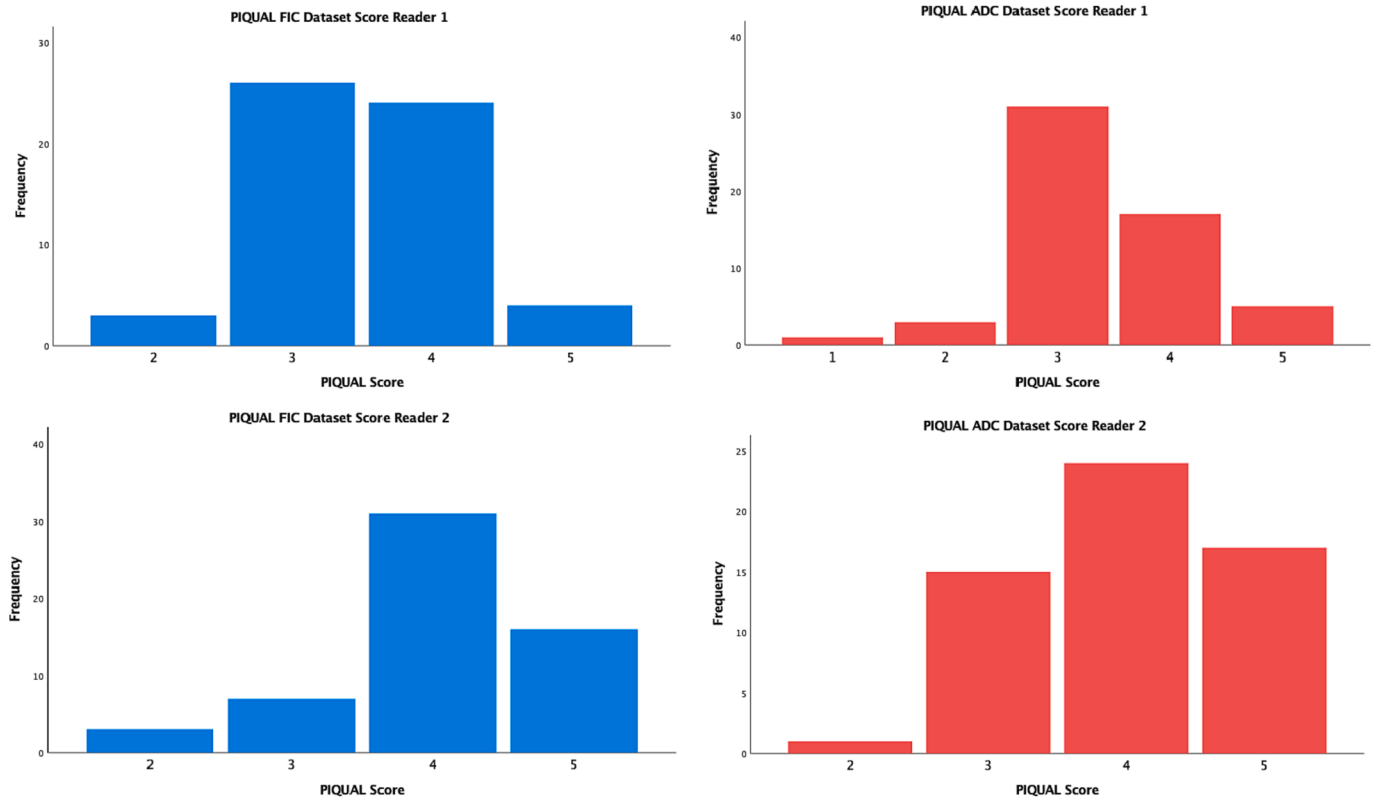


Fig. 7. PI-QUAL scores for both readers.

quality for a given patient, may not be reflected in the overall score. The use of Likert-IQ allowed for individual comparison of ADC and FIC maps.

5. Conclusion

Image quality and inter-reader agreement of two scoring systems for image quality (PI-QUAL score and Likert-IQ) were comparable for FIC maps compared to ADC maps.

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CRediT authorship contribution statement

Saurabh Singh: . **Francesco Giganti:** Writing – review & editing, Validation, Supervision, Investigation, Data curation, Conceptualization. **Louise Dickinson:** Writing – review & editing, Supervision, Investigation, Data curation. **Harriet Rogers:** Writing – review & editing, Visualization, Software, Methodology, Investigation, Data curation. **Baris Kanber:** Writing – review & editing, Resources, Investigation, Data curation. **Joey Clemente:** Writing – review & editing, Resources, Project administration, Investigation. **Hayley Pye:** Writing – review & editing, Project administration, Investigation, Data curation. **Susan Heavey:** Writing – review & editing, Resources, Investigation, Data curation. **Urszula Stopka-Farooqui:** Writing – review & editing, Investigation, Data curation. **Edward W. Johnston:** Writing – review & editing, Project administration, Methodology. **Caroline M Moore:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Alex Freeman:** Writing – review & editing, Investigation. **Hayley C Whitaker:** Writing – review & editing, Project administration, Investigation, Data curation. **Daniel C Alexander:** Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Eleftheria Panagiotaki:** Writing – review & editing, Supervision, Software, Investigation, Formal analysis, Data curation, Conceptualization. **Shonit Punwani:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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