

Towards Enhanced Reproducibility and Understanding of Prostate Cancer through Standardised MRI Acquisition, Analysis and Reporting

Standardised image acquisition and comprehensive automated analysis of multi-parametric Magnetic Resonance Imaging (mpMRI) are crucial in prostate cancer for optimal diagnosis and therapy and improving patient outcome. There is a clear need for computer-aided analysis and for software which can support clinical workflow to enable faster, more quality-controlled analysis and the extraction of both functional and anatomical information on suspicious lesions. The Dynamika software package, developed in collaboration with leading researchers, radiologists and urologists at UCL, London has been designed to meet this challenge and provide more accurate diagnosis, staging and monitoring of prostate cancer.

THE ROLE OF MRI IN PROSTATE CANCER

Prostate cancer (PCa) is the second most common cancer in men worldwide. The serum level of prostate-specific antigen (PSA) has been widely used for screening since the early 1990s. If after digital rectal examination, a cancer is suspected a biopsy is required. PSA, however, remains a controversial method of choice as it has poor sensitivity and an unacceptably low specificity [1]. In addition, the low-cost 12-core trans-rectal ultrasound (TRUS)-guided biopsy routinely misses and understages cancers [2]. As a consequence, too many patients are still being unnecessarily treated for indolent cancers.

The authors:

Dr. Diana Roettger, Rado Andrian, Dr. Olga Kubassova

Image Analysis Limited

London, UK

email: olga@imageanalysis.org.uk

www.imageanalysis.org.uk

Technological advances in MR sequences over the last few decades have resulted in significant improvements in MRI so that it is now a pivotal modality in prostate cancer management.

Multiparametric Magnetic Resonance Imaging (mpMRI) combines anatomical images from T2-weighted imaging (T2wI) with functional sequences:

- diffusion-weighted imaging (DWI), which quantifies the microscopic mobility of water molecules in tissues, and the apparent-diffusion coefficient (ADC) derived from it.
- dynamic contrast-enhanced (DCE) MRI, which is based on the permeability of blood vessels and extravasation of contrast agent into adjacent tissue.

While high-resolution T2wI provides the best assessment of the prostate's morphology, margins, and internal structure, DWI brings specificity, and DCE adds sensitivity, together making mpMRI especially effective in revealing anterior prostate cancer in men with negative random TRUS-biopsy [3].

MpMRI offers considerable information on prostatic lesions including the localisation, characterisation, size and volume, aggressiveness, and staging. Such an approach increases the positive predictive power of PCa diagnosis [4] and is becoming more and more integrated into the complete management of prostate cancer.

MpMRI is used today in the various stages of diagnosis and treatment pathway, helping clinicians to distinguish patients requiring treatment from those 'only' needing monitoring, and to define the most appropriate therapeutic strategy. Its role is spreading from detection to targeted (MRI-)guided biopsy, active surveillance (AS), focal/radiation therapy, and surgery — from planning to follow-up.

NEED FOR STANDARDS

Despite all the possibilities and potential that prostate mpMRI may offer, the broad and consistent adoption of the technique in clinical routine is not occurring without some difficulties.

Firstly this is because frequently from hospital to hospital the actual MRI sequences used can vary. In 2012, however, clinical guidelines for mpMRI of the prostate were published by prostate MRI experts such as those in the European Society of Urogenital Radiology (ESUR). Based on literature evidence and expert opinion, these guidelines aim to promulgate high quality mpMRI by providing consensus about the optimal requirements for acquisition, protocols for detection and staging, and evaluation with the correct indications for prostate cancer [5].

A second hurdle is the challenge of presenting a large amount of information and combining the various findings into a simple and comprehensive interpretation. Large or high-

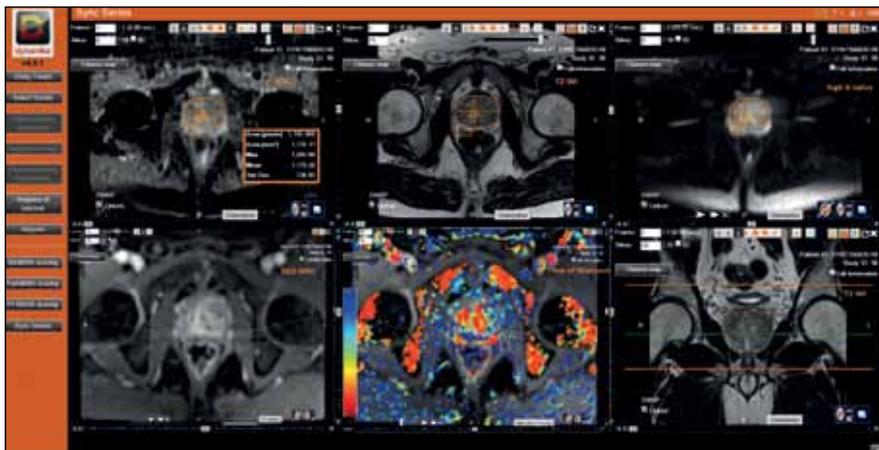


FIGURE 1. Advanced quantitative mpMRI analysis in Dynamika, from top left to right: 1. apparent diffusion coefficient (ADC) map with statistics for region of interest (ROI) for cellular density 2. axial T2-weighted image for anatomical volume information (ruler, 2D ROI and 3D ROI available) 3. diffusion weighted Image (DWI) of high b-value 4. DCE-MRI perfusion 5. Derived Time of Washout map overlaid on DCE data 6. coronal T2-weighted image for spatial slice localisation.

grade cancers tend to be well visualized on all sequences. Small, diffuse, or lower-grade lesions, on the other hand, may display discrepancies between different sequences, leading to a wide scope of possible interpretations, possible conflicting or inconsistent findings between different reporters and different diagnostic centers. Structured pathology reports, with standardised definitions for each component, have been shown to significantly enhance the completeness and quality of data provided to clinicians.

The introduction of the Prostate Imaging Reporting and Data System (PI-RADS) v1 by ESUR in 2012 and the updated v2 in 2014 by the joint steering committee formed by ESUR, the American College of Radiology (ACR) and AdMeTech Foundation, increases the potential for improved patient outcomes, through the establishment of standards for mpMRI acquisition, interpretation, and reporting, as well as enhancing the communication between practicing radiologists and clinicians [6].

NEED FOR SUPPORTIVE TECHNOLOGIES

Another problem is that prostate cancer management involves multiple health actors resulting in mpMRI being used at various stages of treatment: before biopsy; after biopsy; as an image guide for targeted biopsy; as a technique to monitor disease progression or the effect of treatment; or as a method to plan radiation and other focused energy therapies. Adequate infrastructure and supportive technologies are needed, to convey data and information, to facilitate analysis and structured reporting and communication in a fast, cost-effective and

easy manner between all persons involved, including the patients themselves.

Easing Complex Data Presentation and Review.

The understanding and interpretation of the different MRI volumetric sequences require a high level of expertise and is time-consuming. Conventionally, individual sequences are “mentally” fused and aligned to enable a joint assessment. For an untrained user, such process is very time consuming and prone to errors. The Dynamika software [7] addresses this challenge through a customisable user interface, in which individual mpMRI sequences can be laid out, registered and displayed in a spatially synchronized manner to provide the user with a view of the data where cancer can be easily assessed. In addition the software enables consistent reading across cases.

Processing tools are also available. These include image normalisation – particularly on T2wI, used to reduce interpatient variability of MR intensity values – and the computation of derived maps from raw data, displayed as overlays. For PCa, the recommended data presentation should include T2wI; high b-Value DWI (carcinomas display hyperintensity when $800 \leq b \leq 1000$ s/mm²); ADC map from DWI (carcinomas have reduced ADC, computed using preferably mono-exponential model) and DCE data (with at least signal intensity over time curve type classification map – for v1).

As shown in Figure 1, a coronal T2wI localiser – acquired or recomputed – is added to the T2wI, high b-value, ADC, DCE, and Washout-Time map overlaid on DCE, axial synched slices. The Dynamika software allows the computation of an ADC map from a DWI dataset if it is not already provided within the study. Furthermore, Regions-Of-Interest (ROIs) defined in a view are instantaneously propagated, mapped, and can be modified in the other views, with the relevant pixel value statistics being available.

Optimising (Structured) Reporting and Communication of Findings.

The benefits of proforma type reporting have been widely acknowledged, and the PI-RADS standardised graphic prostate scheme and scores aim to harmonise the reading and communication of the findings. Nevertheless, assessing multiple lesions by mapping subjective interpretations of different images into a standardised score and localising each one on pre-defined prostatic regions, requires both a high level of expertise and time.



FIGURE 2. Interactive PI-RADS eCRF: users can seamlessly report on custom or standardised PI-RADS (v1 or v2), switching between the form, the images and the ROIs instantly and synchronously, and input additional findings from specific advanced analysis.

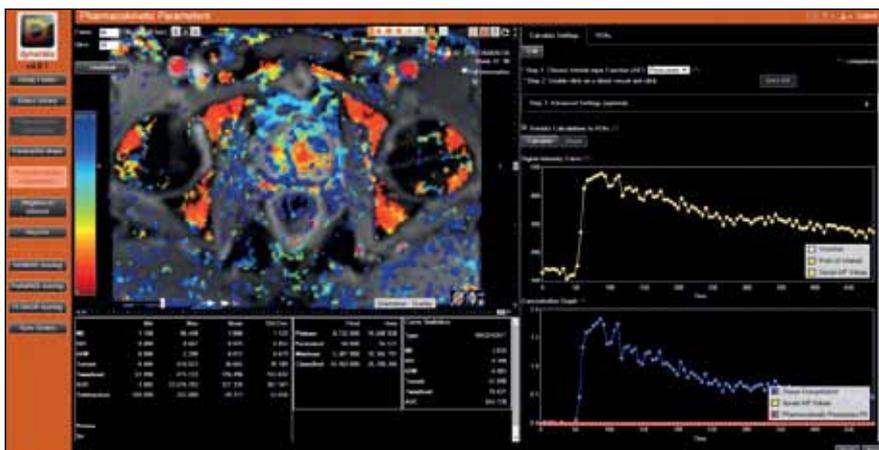


FIGURE 3. Dynamika Advanced Analysis of DCE data: Signal intensity curve over time, converted Gd concentration and derived pharmacokinetic parameters, displayed per pixel and statistics computed within the selected ROI.

The introduction of interactive PI-RADS report forms in the Dynamika software allows readers to experience a direct connection between the images and the reporting sheet. Images, ROIs and reports are no longer detached, and instant feedback in the report can serve a better understanding and analysis of the images.

As shown in Figure 2, not only are the scans within a study synchronized spatially, but Dynamika also links manipulations such as zoom and pan to retain a coherent presentation of information between the MR sequences. Upon review, the user can open a window of the interactive PI-RADS form, in which the synchronised ROIs are listed to be assigned to a specific sector defined by the standardised prostatic regions diagram. The PI-RADS form is regularly updated with the most recent research updates in line with PI-RADS v1 and v2 and include PSA, prostate and lesion volume, biopsy results, Gleason score, extracapsular extension, seminal vesicular invasion, lesion scores, DWI results, and 2D visualisations. In addition, the customisable user individual interface allows for adjustments for both PI-RADS updates as well as for user-specific preferences.

Advances in computer aided-diagnosis (CADx) could offer decreased reading time and consistent risk assessment of cancer presence. Evaluation of the principal current CADx systems for “Prostate Cancer Diagnosis” has unfortunately shown that they are not fully ready yet. Improvements will be made over the next decade and the wide deployment of prostate CADx systems in the clinical environment will eventually occur [8]. In the meantime, more focused applications for suspicious lesion detection, localisation and description, based on the

combination of T2wI, DWI and DCE, could help readers efficiently grade and report lesions in PI-RADS form. This is an area in which the company Image Analysis, developers of the Dynamika software package, is actively involved.

Enabling Advanced Quantitative Analysis.

Advanced quantitative analysis and colour maps based on DCE (parametric maps, pharmacokinetic parameters, subtraction, See Figure 3.) are also available and novel methods developed either by in-house research, collaborations, or external innovators – are continually integrated into the Dynamika software to aid lesion classification. These quantitative outcomes may be linked to PI-RADS scores for lesions and therefore allow a more precise monitoring for a specific lesion.

Facilitating Disease and Treatment Monitoring.

The ability to quantify ‘evolution’ over time is key in active surveillance or treatment monitoring. Imaging biomarkers are used to categorise lesions, measure disease progression or estimate doses for focal radiotherapy as well as guide biopsies. Multiple images of multiple time series need to be compared. This is difficult from a viewing perspective as well as from a timing aspect. The time-consuming task of comparison of a current image with a prior is automated. All datasets and reports are stored in one central database, easily and rapidly accessible from any computer connected to the internet. Further, the software organises the arrangement of the individual scans in an intuitive way and allows easy identification and propagation of ROIs between scans and studies.

CONCLUSION

MpMRI is growing in many areas of PCa management, as a result of the constant efforts of clinical research communities to promulgate and refine standards for acquisition, interpretation and reporting. The value and richness of the multi-parametric approach is undeniable in oncology, and mpMRI offers hopes and opportunities to further expand the understanding of PCa mechanisms, provide better detection and staging of lesions, evaluate therapeutic effects more efficiently and deliver more focused and personalised treatments.

Technology needs to adapt and offer better, easier and faster ways to present and analyse ever-larger and more complex clinical data. In the current era of evidence-based medicine, technology also needs to provide platforms to allow multi-disciplinary and multi-site/national collaborative research to investigate, evaluate and validate new treatments, quantitative imaging markers, or computer aided-diagnosis tools for PCa. Dynamika is such a dedicated cloud platform [9] developed for and in collaboration with researchers, radiologists and urologists. By incorporating the latest standards and keeping abreast of science, Image Analysis aims at improving quality and efficiency, and ensuring reliability and reproducibility of PCa diagnosis and treatment from more and more complex mpMRI data.

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