Informatics Opportunities and Challenges in Medical Imaging: A Journey

Theodoros N. ARVANITIS[a,1]

[a] *Institute of Digital Healthcare, WMG, University of Warwick, Coventry, UK*

Abstract. The role of the field of informatics in medical imaging is vital; novel or adapted informatics' core methods can be employed to realise innovative information processing and engineering of medical images. As such, imaging informatics can assist in the interpretation of image-based, clinically recorded evidence. This, in turn, leads to the generation of associated actionable knowledge to achieve precision medicine practice. The discipline of informatics has the power to transform data to useful clinical information patterns of observable evidence and, subsequently to generate actionable knowledge in terms of diagnosis, prognosis, and disease management. This paper presents the author's personal viewpoint and distinct contributions to innovations in the acquisition and collection of imaging data; storage, retrieval, and management of imaging information objects; quantitative analysis, classification, and dissemination of imaging observable evidence.

Keywords. Medical imaging, quantitative imaging informatics, image quality assurance, image exchange and interoperability

1. Introduction

Medical Imaging is a key and invaluable component of modern clinical medicine in the study of human health and disease. Imaging procedures, often being non-invasive and with limited side effects, generate rich data in terms of structural, compositional, and functional information of the human body [1], thus supporting the characterization and management of disease for an individual patient. The role of the field of informatics in medical imaging is pivotal; novel or adapted informatics' core methods can be employed to realise innovative information processing and engineering of medical images. As such, imaging informatics can assist in the interpretation of image-based, clinically recorded evidence and, consequently, generate associated actionable knowledge to achieve precision medicine practice [2].

The sub-discipline of medical imaging informatics presents, over the past three decades, a rapidly growing scientific endeavour within the field of biomedical and imaging informatics [3, 4], with many achievements and innovations. This paper discusses some of the important opportunities and challenges for the application of informatics in medical imaging, during this period. The author is presenting his personal

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[1] Corresponding Author, Theodoros N. Arvanitis, Institute of Digital Healthcare, WMG, University of Warwick, Coventry, CV4 7AL, United Kingdom; Email: t.arvanitis@warwick.ac.uk.

viewpoint and distinct contributions to innovations, achieved throughout this journey of progress in the medical imaging informatics field.

2. From Data to Actionable Knowledge - the role of medical imaging informatics

As early as the 1960s, the concept of automating the analysis of medical images, with the use of computers, was identified as a potential innovation to be explored by the community of clinical radiologists and associated scientists [5]. In 1959, during the Memorial Fund lecture of the forty-fifth annual meeting of the Radiological Society of North America, Lee B. Lusted (a radiologist and associate professor at the University of Rochester, at the time) elaborated on the potential of "electronic computers" in the analysis of radiographic images, by using "an electronic 'scanner-computer' to look at chest photofluorograms and to separate the clearly normal chest films from the abnormal chest films" [6]. This pioneering proposition recognizes that, bringing together medical imaging and informatics has been key, in the early reasoning of scientists and clinicians, on how to harness imaging information and use of computers into achieving medical diagnosis, and in extent making clinical decisions [7].

Modern imaging modalities can generate substantial amounts of data, rich on clinical information. The discipline of informatics has the power to transform data to useful clinical information patterns of observable evidence (imaging phenotypes) and, subsequently, to generate actionable knowledge in terms of diagnosis, prognosis, and disease management, thus achieving the current precision medicine goals [8, 9]. In this journey, from data to actionable knowledge, the discipline of informatics plays a vital role in the acquisition and collection of imaging data; storage, retrieval, and management of imaging information objects; quantitative analysis, classification, and dissemination of imaging observable evidence. In the following sections of this paper, we will discuss these topics in terms of challenges and opportunities from the author's personal perspective, as these themes developed over the past 30 years.

3. Capturing Imaging Observable Evidence

An information representation of the structure, composition and functioning of the human body, through imaging, requires the use of appropriate medical imaging modalities and associated protocols for the acquisition and collection of relevant data. To achieve this, the role of informatics has been complementary to that of medical imaging science. To harness the full utility of imaging data, imaging informatics provided, over the years, core quantitative and information management tools to capture, extract, organise and curate effective information from such data [10].

3.1. Imaging Protocols: capturing imaging information

At an early stage, the community has recognised that, the standardisation of imaging protocols is an essential component of digitally based image data collection during routine clinical patient assessment and of imaging-based clinical research [1]. Imaging protocols need to consider the subsequent analysis requirements of image data points, through informatics tools, and aim to normalise varying imaging capabilities without

compromising image quality. Protocol standardisation includes acquisition parameters (e.g., MR-pulse sequences, patient positioning, image reconstruction algorithm used, etc.) and quality assurance & control procedures (e.g., signal-to-noise acceptable levels, scanner calibration approaches, artifact reduction, etc. – discussed in the next subsection).

The author has contributed to the challenge of protocol standardisation, as part of his long-standing research programme on functional imaging-based characterisation of childhood brain tumours [11], together with his national and international collaborators. Standardisation of MR imaging acquisition is critical in enabling multicentre clinical research studies, related to childhood central nervous system tumours. Ensuring the adoption of a common imaging protocol facilitates the harmonisation of useful data collection (while preserving image quality). The availability of quality image data, collected by multiple clinical centres with varying imaging capabilities, is critical in clinical trial analysis work for CNS tumours. The European Society for Paediatric Oncology (SIOPE) Brain Tumour Imaging Working Group (in which the author has been a member of) has established such an imaging protocol. The Working Group has derived this protocol as a consensus, based on past clinical research experience/practice and research evidence (some of which will be discussed in the subsequent sections of this paper) from earlier clinical research studies [12, 13]. The protocol has provided recommendations to advanced imaging methods, including functional imaging approaches of MR spectroscopy (MRS), diffusion tensor imaging (DTI) and perfusion imaging. Various elements of the author's and his collaborators' work on MRS [14-19], DTI [20] and perfusion imaging [21], and the value of these approaches on childhood brain tumour imaging, has been instrumental in the accumulation of this evidence. Protocol consensus brings the opportunity of its application to specific clinical trials and studies; in the case of the aforementioned protocol, this includes the SIOPE Ependymoma II clinical study [22] and the SIOPE PNET V Medulloblastoma clinical programme [23].

3.2. Image quality assurance: the role of informatics

Dealing with imaging artifacts and applying imaging quality assurance & control, to ensure appropriate and acceptable image quality for reproducible imaging data, has also been an important challenge over the years (e.g., [24-26]). Informatics and analysis methods play a significant role in the management of this challenge. The author's beginnings, in the field of medical imaging and informatics, included his PhD work. In the early 1990's, the author's research focused on the understanding of the challenge of imaging artefacts in Magnetic Resonance Imaging and Spectroscopy. The author's thesis focused on the study of a particular example of motion related MR artifacts, the respiratory motion artifacts. With the aid of theoretical and simulation work, the source and appearance of these artifacts were carefully studied. This knowledge was used for the application of an informatics-based time-series analysis method (Lomb-Scargle periodogram), as an approach in the study of MR artifactual imaging data; thus, contributing to further opportunities for research in this area [27].

3.3. Curating Data and Imaging Evidence

The curation and management of the vast amounts of imaging data are essential functions, provided by medical informatics solutions. In clinical practice, the development of commercial Picture Archiving and Communication Systems (PACS) focused on

providing "economical storage, rapid retrieval of images, access to images acquired with multiple modalities, and simultaneous access at multiple [imaging] sites" [28]. PACS have brought opportunities for efficient management and exchange of digital imaging information as part of the clinical workflow. In section 6, a more detailed account of the informatics' challenges for PACS and associate standards, in terms of interoperability and image presentation, is given. Here, we address the challenge of developing curated data repositories, which can support the research imaging informatics community, in the development of innovations that relate to methodologies, models and tools.

Indeed, incorporating novel imaging techniques into clinical research studies and trials presents specific challenges due to the lack of standardisation in data collection, quality control and analysis. In addition, there is an ever-increasing need for expert analysis of novel imaging data, which may only be available at a remote location. The establishment of secure, internet-accessible research data repositories can provide a solution to the above-mentioned needs. The author and his national collaborators, as part of a Cancer Research UK – Engineering and Physical Sciences Research Council (CRUK-EPSRC) funded programme grant (2008-2013), and as part of the Children's Cancer and Leukaemia Group Functional Imaging Group in the UK, have developed an e-Repository of functional imaging data, to be used in clinical trials for children with brain tumours [29]. The e-Repository, which consists of a remote data entry system and associated database, seamlessly incorporates both clinical and functional imaging datasets in the context of multi-centre studies for childhood brain tumours. The data entry system (available at https://rde.cclgfig.bham.ac.uk/) is accessible through a secure shell connection on a web browser, allowing role-based access control for the addition, editing, and reviewing of data by principal investigators, study coordinators, data managers, and researchers, through remote access. Clinical and laboratory data, as well as conventional and functional imaging data are contained within the database. The current number of cases amount to more than 1500 cases from around 10 clinical centres, covering about three quarters of the UK population. Furthermore, all data are made available for both central and remote processing. The e-Repository also provides integrated automated data processing software tools. The overall design of the e-Repository has been made to be modular and expandable, to accommodate opportunity for future growth of imaging-based research in childhood brain tumours and other types of image-based clinical trial work [30].

4. Image Segmentation: an informatics challenge

A long-standing challenge of imaging informatics has been the accurate delineation of an imaging region of interest (ROI), as part of the process of characterizing health status and disease [1]. ROIs enable imaging specialists to focus on the extraction of relevant image features (qualitative and quantitative) that outline structural and functional human body components, to be used as part to the analysis that supports our understanding towards diagnosis, prognosis, and response to treatment for an individual patient. Image segmentation methods (semi-automatic or automatics), and their associated challenges, have been studied extensively over the past 30 years [31].

The author and his co-workers, as part of their work on brain tumours [11], have contributed to advance the community's understanding for this challenge. Image segmentation is a critical step in the analysis and subsequent diagnostic/prognostic characterisation of brain tumours, using MR-based functional imaging approaches. The

team has conducted a systematic review of 572 brain tumour segmentation studies, as reported during the period 2015–2020 [32]. The review assessed "physics or mathematics-based methods, deep learning methods, and software-based or semi-automatic methods, as applied to magnetic resonance imaging techniques" [32], including T1-weighted, T2-weighted, gadolinium-enhanced T1-weighted, fluid-attenuated inversion recovery, diffusion-weighted and perfusion-weighted MR imaging. The performance of each segmentation method was assessed through its median Dice score (initially proposed as image segmentation performance metric by Zijdenbos et al. [33]). The work found that the U-Net deep learning segmentation approach was cited the most and has reported high accuracy (Dice score 0.9), making U-Net a promising brain tumour segmentation on magnetic resonance images. Though substantial progress has been made for this challenge by the imaging informatics community, there remains an opportunity, in the future, to expand our knowledge in this area. The author and his team are currently continuing in the pursue of this quest.

5. Informatics Methods and Quantitative Imaging

As it was already argued, state-of-the-art imaging technology processes and the large-scale, novel, computational analysis of data sets, including the use of machine learning and artificial intelligence, are improving our understanding of human health function and disease. This, in turn, is creating a powerful driver to achieve precision medicine through quantitative imaging informatics. Computational quantitative analysis provides opportunities in aiding diagnosis, deriving diagnostic imaging biomarkers, providing prognostic biomarkers, aiding surgical decision-making and therapy planning, while offering clinicians with early indications of response to therapy [2, 34]. Although, many researchers and imaging specialists have worked, over the years, with different imaging technologies and have, most recently, successfully applied quantitative imaging informatics for different areas of disease, in this section, the author presents his own journey with quantitative imaging informatics.

The high-throughput identification, extraction, and analysis of quantitative functional imaging features, as well as the use of radiomics for the diagnostic and prognostic characterization of paediatric brain tumours, have been the main emphasis of the research work of the author and his co-workers. Clinical improvements have been made in diagnosis, management and predicting survivability, which deliver benefits directly to patients, healthcare providers, and the health service [16, 35].

While survival rates have steadily improved for childhood brain tumours, with approximately 75% of patients now living beyond five years [36], accurately predicting how the disease will progress in individual patients has remained a challenge. Over the past 15 years, the author's research attention has centred into developing quantitative imaging informatics methods in childhood brain tumours. This approach allows the investigation of tissue properties and the tumour's microenvironment, in a non-invasive manner, with the aim of answering clinical questions more directly, than can be achieved using conventional structural imaging. Noteworthy progress has been made in developing, implementing, and evaluating advanced MR-based functional imaging and associated computational quantitative analysis, leading to major advances in the field of quantitative imaging informatics. These include:

- Automated quantitation of metabolites [37, 38]; and discovering novel biomarkers [39, 40];
- Informatics-driven, quantitative textural analysis and radiomics [41-44];
- Advanced machine learning in multi-parametric functional imaging [45-48];
- Clinical verification and experimental validation of novel biomarkers [49];
- Development of imaging-based, clinical decision support tools [50, 51].

In particular, the emerging sub-field of radiomics, where the personal contributions of the author are recent, provides a solution for non-invasive tumour characterization, by converting medical images into mineable data, through the extraction of quantitative imaging features. When developing quantitative medical image analysis techniques, it is usual to consider attributes (e.g., intensity, morphology and texture) that radiologists explicitly or implicitly use in their assessment of a specified tissue appearance. Image texture can be defined as the spatial variation of pixel intensities within an image and is sensitive for the assessment of pathology. Visual assessment of texture is, however, particularly subjective. Additionally, it is known that human observers possess limited sensitivity to textural patterns, whereas computational texture analysis (TA) techniques can be significantly more sensitive to changes. Therefore, the radiomics area presents a new and exciting opportunity for the field of medical imaging informatics, with a lot of promise for achieving the objectives of precision medicine [52].

6. Image Interoperability and Presentation

The use of standards for image information exchange and interoperability has been central to the increased use of information systems for medical imaging. In particular, the increased use of Picture Archiving and Communication Systems (PACS), one of the most important informatics innovations in medical imaging, has been vital in the management and exchange of digital image information for clinical purposes. As early as 1981, during the first international meeting on PACS, it was recognized that internationally agreed digital image exchange standards would be essential for the successful development and deployment of imaging information systems [53]. In 1982, the American College of Radiology (ACR) and the National Electrical Manufacturers Association (NEMA) initiated a standardization effort on digital image exchange and communication, resulting in DICOM (Digital Imaging and Communications in Medicine) standard [54]. DICOM has enabled ubiquitous interoperability and connectivity of imaging equipment and PACS, over standard communication networks.

To develop such efficient, standardized PACS, it is important to appreciate the challenge of understanding the intricacies of clinically feasible network topologies and associated information system architectures. This challenge has been studied by many in the 1990s and beyond [55-58]. In the context of this challenge, and within the perspective of DICOM interoperability in PACS, the author and his team have investigated modelling and realistic simulation methodologies, to model a range of scenarios of DICOM session and application layer implementations over various network communication protocols [59, 60]. The work has demonstrated the importance in recognizing both the relevant clinical and technology requirements for a cost-effective the planning and deployment of PACS and associated imaging information systems.

In addition to the standardization of effective communication of raw imaging data over networks, DICOM has also evolved to facilitate appropriate image

display/presentation for interpretation and reporting, within the context of distributed radiological/clinical work. Appropriate presentation of image and related data can support clinicians to consistently visualize imaging findings and effectively communicate, between themselves, any manipulation and analysis of imaging data for clinical purposes. The DICOM Structured Reporting (SR) has provided a robust clinical documentation methodology to capture and display specific image and associated clinical data elements, in an interoperable format [61]. The DICOM SR can, therefore, relate imaging information to other clinical information, such as data from Electronic Healthcare Records and/or specialist Clinical Information Systems. The harmonization efforts [62] with other health informatics standards (e.g., HL7, FIHR) makes DICOM structured reporting a powerful informatics tool that provides consistency, scalable data capture, semantic interoperability, and robust information sharing between healthcare professionals [63].

The informatics community efforts to achieve such a ubiquitous information sharing of imaging data, included early challenges on display and presentation standardisation. In this journey, research has been focusing into developing uniform ways to specify the layout and image presentation parameters for imaging informatics. The author and his collaborators have originally looked at the development of a meta language, called Interscreen, to allow the recording of all information needed to reproduce a previously captured image representation/display on any PACS and associated device, while retaining the user's freedom to interact with the imaging data [64]. Inspired by the early DICOM SR work, and as part of the European Committee of Standardization (CEN/TC251 "Health Informatics" Technical Committee - Project Team 34), they have worked on the design and specification of Health Care Multimedia Reports [65] and have provided early implementation options for supporting the specification of presentation of electronic patient record content, including imaging data [66]. This work has offered opportunities for further developments of the DICOM SR standardisation effort.

Furthermore, the challenge of "economical" digital storage of images has also been an area of research and technology advancement for the imaging informatics community. Over the years, low-cost and high-capacity storage has been available to imaging facilities. However, image compression has been identified as a necessary technology for imaging, due to imaging data requiring substantial amounts of storage [67]. This, in addition to challenge of efficient transmission of large imaging datasets, has brought forward the necessity for investigating robust medical image compression algorithms (including both lossy and lossless image compression approaches) and their comprehensive evaluation [68]. The author's early work, in this area, has investigated different thresholding and quantization strategies for digital angiography image compression and, with co-workers, have developed a perceptual quality assessment method to assess any visible/invisible differences between original and compressed digital angiogram images. In particular, the work derived a multistage perceptual quality assessment (MPQA) model for compressed digital angiography images [68]. The research concluded that this model had better agreement on what is deemed to be a diagnostically acceptable lossy image reconstruction (by human experts) compared to objective error measurement methods; thus, contributing a useful addition to evaluation methods for assessing image quality reconstructed by different compression technologies, and opening new opportunities for further research on this challenge.

7. Concluding Remarks

In early 2015, the author was interviewed by the BQ Magazine (the UK's West Midlands leading business to business publication), reaching almost 24 000 readers [70]. He highlighted the power of imaging informatics and, more specifically, how informatics accurately diagnose and support the treatment of childhood brain tumours. The core innovation of the author's past and current work, in the field of imaging informatics, effectively supports the conversion of images from standard medical scans into data that can be mined and processed to identify useful characteristics, patterns, and disease markers, including for example MRI image texture. Gathering this data into one place (curated data repositories) and running it through complex software, incorporating computational and machine learning techniques, is aiding disease diagnosis (e.g., childhood brain tumours), and is providing more accurate prediction of disease progression, responsivity to treatments, patients' survival, and quality of life. This not only greatly improves the potential to advance clinical management of patients for successful therapy and cure, but supports more informed discussions between medical staff, patients, and their family on how to manage the challenges of the disease. Consequently, "imaging informatics" is emerging as a powerful 'weapon' in the arsenal of biomedical and health informatics technologies, for us to win the battle against disease.

This has been an amazing journey…and it continues, into the future!

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