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Artificial Intelligence in medical imaging and radiation oncology: opportunities and challenges

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Introduction: Artificial Intelligence (AI) and Machine Learning (ML) are increasingly ubiquitous in many areas of society, not least in medicine. AI offers the opportunity to harness computers to carry out more mundane tasks faster or better, e.g. more consistently, than humans. However it also has the potential to move beyond what humans can do. For example, AI can combine many and disparate data sources and types into decision-making (e.g. genomics, imaging, pathology), or can interrogate very large sets of retrospective data to learn patterns where manual investigation would not be feasible or would not readily identify them, e.g. in early sub-clinical disease detection. For decisions and predictions, humans are restricted in the number of pieces of information that can be considered and processed simultaneously (typically said to be around 5), whilst AI systems are not so limited and can integrate complex datasets efficiently. Human decisions can also be influenced by bias and noise, i.e. extraneous factors causing variation in decisions between individuals or at different times. Structured decision-making can improve this, e.g. at a simplest level using checklists to aid the decision process, or codifying and extending these into algorithms and computerisation. Algorithms

too can incorporate bias and must be carefully designed and tested to avoid this. Despite the potential of AI tools, they are just that, tools to supplement the clinical process and aid the clinician to be more efficient and effective. Therefore AI should be developed in ways that integrate it closely into clinical workflows, to enhance processes without adding unnecessary complexity or time. Furthermore, AI cannot provide the creative and critical thinking that is necessary in medicine, or the interpretation and responsibility for application to patients, or the patient care aspects, such as trust and reassurance.

This JMIR special issue on AI in Medical Imaging (MI) and Radiation Oncology (RO) brings together a range of reviews and overviews of aspects of this rapidly evolving and potentially disruptive technology and provides an indication of research and development work in Australian centres. AI, mainly in the form of ML, is already impacting image analysis and other applications in both MI and RO. This is only expected to increase, providing significant opportunities and potential practice changes, but also with associated risks and challenges that must be considered and managed.

Some concepts and terminology: There are many variants of definitions, but RANZCR¹ has adopted the following.:

- an AI system is *“a machine-based system that can, for a given set of human-defined objectives, make predictions, recommendations, or decisions influencing real or virtual environments. AI systems are designed to operate with varying levels of autonomy”*;
- and ML is *“a particular form of AI, which gives computers the ability to learn from and improve with experience, without being explicitly programmed. When provided with sufficient data, a machine learning algorithm can learn to make predictions or solve problems, ...”*

Most AI in medicine thus far is ML, using available datasets to train models to recognise patterns, or identify and develop representations of complex relationships between input data and output prediction, which can then be applied to classify or model new unseen data. A range of ML approaches and algorithms have been applied (e.g. linear regression, logistic regression, support vector machines, Bayesian networks, decision trees, random forest, neural networks). Most of these have used supervised learning, where the training examples (input)

are described not only by their features, but also by labelling the data with additional information that relates to the required learning task and applies domain knowledge. The model identifies relationships between features and class labels and the training examples provide the expected output (ground truth) of the model such that a comparison between these and actual model output can give a measure of the model accuracy. On the other hand, in unsupervised learning the data are described in terms only of their features and the learning can discover hidden structures from unlabelled data. Principal component analysis, clustering and self-organised neural networks are examples of unsupervised methods.

Research and development for medical applications have used a range of these approaches. However the focus is increasingly on artificial neural networks (ANN), i.e. adaptive networks of artificial neurons (information processing nodes) connected in layers and providing non-linear behaviour. Each node has multiple connections to nodes in the layer above, which provide data to it, and in the layer below, which receive data from it. Input connections are described and modified by weights, whilst outputs are by amplitude values. Weights, values and other network parameters are adjusted iteratively when the algorithm is trained, with the aim of optimising a particular cost-function defined for the application. For supervised learning, the overall NN outputs are compared to the training inputs and the variations are back-projected into the network until further similar data input provides consistent outputs. Deep Learning (DL) uses many hidden layers of artificial neurons and so has capacity for large numbers of parameters (hence, from these characteristics, termed 'deep'). Thus DL can provide a data-driven approach to deal with more complex problems and can support supervised or unsupervised learning. The DL network interconnections are complex, and the routes to decisions and outputs can therefore be obscure.

Training requires sufficiently large datasets, with enough diversity of examples for real-world application for the problem/s to be considered, thus avoiding bias and producing a model that is sufficiently accurate and also generalizable. One source of bias and uncertainty can arise from outputs being subjectively defined by one or more individuals, e.g. in imaging tasks, which can limit accuracy, since there may be no objective ground truth. Datasets require adequate completeness and quality for the specific purpose. In MI there are some large publicly available digital datasets that can be accessed for model training for a range of applications, as well as using locally curated hospital datasets. Typically, datasets in RO are smaller, although generally well-structured in oncology information systems. Thus although

ML is often intrinsically linked with the concept of Big Data, the amount of data in many clinical applications might not be so large! In practice it may be that where data is limited it can be augmented in order to increase the number and diversity of training examples, e.g. for image sets, by generating new data using transformations from existing images.

Two potentially significant modelling problems are poor fit and overfitting. Poor fit is where the model is too simple and won't match the training data. Overfitting occurs when the model contains more parameters than the data can justify, resulting in increased variance when fitting different training sets and the likelihood that the model will fail to fit additional data. Model complexity can be limited to prevent overfitting, termed regularization. Both problems increase modelling errors and a good model finds a trade-off between them, aiming to minimise errors when applied to new unseen data. Thus generated models must be carefully validated, using a validation dataset separate and ideally independent from the training data. If the available data is limited, resampling methods can be used, splitting the data into training and validation sets in different ways and cross validating between these divisions. For example the data can be divided into k equally sized subsets, with repeated training and validation on all the combinations of $k-1$ sets with the remaining set, (termed 'k-fold cross validation'). In the extreme when k equals the number of samples, this becomes the leave-one-out approach. Multiple re-sampling allows data points to be used more than once for testing, e.g. bootstrapping randomly draws data sets from the training data and estimates the model performance (statistical accuracy) from multiple trainings on different subsets.

In summary, safe and confident clinical use of ML requires models that are well-documented and clearly validated for application and performance accuracy, based on relevant datasets of adequate size, scope and quality. In addition, ML models should be interpretable, transparent, explainable and reproducible.

AI in Radiology and Radiation Oncology: MI and RO are medical specialties with existing infrastructure and characteristics that position them well to adopt and benefit from the potential of AI. For example, MI and RO are both technology-based with a long history of safe implementation of complex and potentially disruptive technologies and innovations, arising from both significant in-house development and commercial sources. They include multi-disciplinary teams encompassing not only clinical experts, but also physics, technical and computing/IT expertise, as well as having close links with technology manufacturers. They

have well-developed frameworks for technology assessment and evaluation, for new system commissioning, testing and on-going quality assurance, and for continuing technology development and quality improvement after implementation. They are strongly computer-integrated and data-rich, typically with well-structured digital datasets in comprehensive e-information systems, including extensive image sets in standardised formats.

There is already a wide and growing literature on AI in medicine in general²⁻⁴, including specifically in MI and RO. For MI, AI opportunities include applications in optimising acquisition parameters, reconstructing images, assessing image quality, and preprocessing and interpreting images. In turn this can improve detection, quantification and evaluation and hence improved diagnosis⁵⁻¹⁰. In addition AI can aid enhanced patient management and workflows and provide prognostic and predictive tools⁵⁻¹⁰. A number of MI examples are covered in this special issue, including applications in general radiology, chest x-rays, mammography and stroke, as well as reviews of AI in MRI image reconstruction for faster imaging and of image data augmentation methods for deep learning. In RO, many applications are also based on imaging data and its uses. Currently reported opportunities include in auto-segmentation of relevant structures, generation of synthetic CT for planning, radiomics applications, auto- (and knowledge-based) treatment planning, dose tracking and on-line adaptive radiotherapy, as well as in predictive modelling of treatment response and outcomes and their use in linked decision support, and a growing range of applications in process control and other quality assurance and safety areas¹⁰⁻¹⁶. This issue includes examples in auto-segmentation for treatment planning, motion tracking during treatment, the use of quantitative biomarkers to monitor response during and after treatment, and an overview of the Australian radiation oncology computer-assisted theragnostics network, using distributed (or federated) learning across centres to provide tools for outcome prediction and decision support.

Challenges and requirements: Despite all this activity and despite that some ML tools (such as linear regression, or atlas-based segmentation) have been available and used for some time, AI is still in its early days of clinical application in MI and RO and there are a range of issues and challenges still to be considered and solved^{3,4,6,9,12,14,17}. These include potential hazards and risks in clinical use, which require: clear and safe development of AI tools and applications and a responsibility on developers and researchers to provide sufficient detail in documentation and in research papers; rigorous validation and testing of both accuracy and limitations; risk

assessment and management of clinical implementation; on-going quality assurance; and appropriate evolving education and training. In this sense these are similar to other novel technology tools adopted into MI and RO, particularly software tools, and require similar structured approaches to their introduction and use and for further research and development.

Careful consideration must be given to the datasets used to generate models and their predictions, in order to avoid bias and to ensure accuracy in their application to patients. This necessitates clear clinical input into model purpose, design, optimisation and implementation and into understanding the source, scope and quality of data used. Model interpretability will affect user acceptance and confidence. These concepts lead to considerations of transparency around models and data and their possible application limitations, regardless of whether they are commercially supplied and certified or locally developed. Not least, this should focus attention on ensuring that models provide clinically relevant outcomes. In turn, this emphasises the need for local data (model inputs) to be high quality and the required data definition and collection to be clinically led.

Clear responsibilities and accountabilities must be defined for different aspects of AI applications, in order to underpin governance and management of their use. This includes well-defined relationships between different stakeholders at various levels, from developers and users to hospital managements and health authorities and up to government level. Furthermore, a range of robust frameworks are required, for example around: the ethics considerations of AI system use; standards of practice and standardisation of technical issues and terminology, up to the level of global harmonisation; regulatory considerations, both intra- and inter-jurisdiction, also up to international level; and the associated data privacy and security requirements. In order to link AI developments and support their translation into the clinic there have been specific calls for international efforts to bring stakeholders together within a clinical data science community to harmonise codes of conduct and shared visions¹⁷, as well as to support lower resourced healthcare systems.

As regards healthcare systems with lower resources, or remoter areas where other medical services and support are likely to be scarcer, it may be noted that AI can potentially offer increased impact in such situations. AI tools can supplement local expertise, providing access to wider resources and knowledge and providing feedback for training. While this has to be balanced against the technical costs and issues, servers could be situated elsewhere and AI

costs may be less than direct expertise costs. Such use must be implemented and managed within clear and careful standards and governance.

In the Australasian context, RANZCR has recognized the breadth of these concerns and the rapid development of AI applications in the field and has set up an AI committee to consider the implications (opportunities and risks) of AI in Radiology and RO and to make recommendations on topics such as ethics, standards, policy, education/training needs, etc.¹⁸. Some of this work is summarized in the paper in this issue on ethics and standards, whilst a number of the challenges mentioned above are touched upon in several of the included papers.

Last word: AI in MI and RO will continue to develop rapidly, with the potential to improve quality, efficiency and outcomes. It is likely to evolve and expand in complexity beyond current ML applications and towards wider 'more generalised artificial intelligence' functions and abilities and further disruptively transform these areas of practice. Manufacturers will be likely to develop and bundle applications that risk being more 'blackbox' in methods and data sources and thus potentially to have behaviour that is less predictable and understandable and hence be more challenging to validate and verify. The teams in MI and RO must have the resources and the mixed sets of expertise and training to be ready to adapt as this evolves, to harness and maximise the opportunities and also to recognise, manage and minimise the challenges. Strong clinical understanding of, and input to, these developments will help to ensure realistically assessed and balanced clinician trust in the AI applications in use. This in turn will underpin patient safety and maximum patient benefit as the technology expands in use and scope, as well as helping explainability of systems and decisions to patients. This special issue aims to support these objectives.

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References

1. RANZCR Standards of practice for artificial intelligence, 2020,
<https://www.ranzcr.com/college/document-library/standards-of-practice-for-artificial-intelligence>
2. Obermeyer Z, Emanuel EJ. Predicting the future—big data, machine learning, and clinical medicine. *N Engl J Med* 2016; 375: 1216. doi: [10.1056/NEJMp1606181](https://doi.org/10.1056/NEJMp1606181)
3. He J, Baxter SL, Xu J, Xu J, Zhou X, Zhang K. The practical implementation of artificial intelligence technologies in medicine. *Nat Med* 2019;25:30-36 doi: [10.1038/s41591-018-0307-0](https://doi.org/10.1038/s41591-018-0307-0)
4. Kelly, C.J., Karthikesalingam, A., Suleyman, M. *et al.* Key challenges for delivering clinical impact with artificial intelligence. *BMC Med* **17**, 195 (2019).
<https://doi.org/10.1186/s12916-019-1426-2>
5. Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJWL. Artificial intelligence in radiology. *Nat Rev Cancer* 2018;18:500–10. <https://doi.org/10.1038/s41568-018-0016-5>.
6. Thrall JH, Li X, Li Q, Cruz C, Do S, Dreyer K, Brink, J Artificial Intelligence and Machine Learning in Radiology: Opportunities, Challenges, Pitfalls, and Criteria for Success *J Am Coll Radiol* 2018;15:504-508. <https://doi.org/10.1016/j.jacr.2017.12.026>
7. Oren O, Gersh, BJ, Bhatt DL Artificial intelligence in medical imaging: switching from radiographic pathological data to clinically meaningful endpoints *Lancet Digital Health* 2020; 2: e486–488
8. Aggarwal R, Sounderajah V, Martin G, Ting DSW, Karthikesalingam A, King D, Ashrafian H, Darzi A, Diagnostic accuracy of deep learning in medical imaging: a systematic review and meta-analysis, *npj Digital Medicine* (2021) 4:65 ; <https://doi.org/10.1038/s41746-021-00438-z>
9. Artificial Intelligence in Medical Imaging: Opportunities, Applications and Risks, Eds: Ranschaert ER, Sergey Morozov S, Algra PR, Springer 2019, <https://doi.org/10.1007/978-3-319-94878-2> ISBN (hardcover) 978-3-319-94877-5 (eBook) 978-3-319-94878-2

10. El Naqa I, Haider MA, Giger ML, Ten Haken RK, Artificial Intelligence: reshaping the practice of radiological sciences in the 21st century *Brit J Radiol* 2020: 93 1106 <https://doi.org/10.1259/bjr.20190855>
11. Thompson RF, Valdes G, Fuller CD, Carpenter CM, Morin O, Aneja S, et al. Artificial intelligence in radiation oncology: A specialty-wide disruptive transformation? *Radiother Oncol* 2018;129:421–6. <https://doi.org/10.1016/j.radonc.2018.05.030>.
12. Huyn E, Hosny A, Guthier C, Bitterman DS, Petit SF, Haas-Kogan DA, Kann B, Aerts HJWL, Mak RH, Artificial intelligence in radiation oncology, *Nat Rev Clin Onc* 2020;17 771–781 <https://doi.org/10.1038/s41571-020-0417-8>
13. Francolini G, Desideri I, Stocchi G, Salvestrini V, Ciccone LP, Garlatti P, Loi M, Livi L, Artificial Intelligence in radiotherapy: state of the art and future directions, *Med Oncol* 2020: 37, 50 <https://doi.org/10.1007/s12032-020-01374-w>
14. Vandewinckele L, Claessens M, Dinkla MA, Brouwer CL, Crijns W, Verellen D, van Elmpt W, Overview of artificial intelligence-based applications in radiotherapy: recommendations for implementation and quality assurance *Radiother Oncol* 2020: 153 (2020) 55-66 <https://doi.org/10.1016/j.radonc.2020.09.008>
15. Machine Learning in Radiation Oncology: Theory and Applications, Eds: El Naqa I, Li R, Murphy MJ, Springer 2015
16. Big data in Radiation Oncology, Eds Deng J, Zing L, CRC Press 2019, ISBN 978-1-138-63343-8
17. Kazmierska J, Hope A, Spezi E, Beddar S, Nailon WH, Osong B, Ankolekar A, Choudhury A, Dekker A, Kathrine Røe Redalen KR, Traverso A, From multisource data to clinical decision aids in radiation oncology: The need for a clinical data science community, *Radiother Oncol* 2020;153 (2020) 43–54 <https://doi.org/10.1016/j.radonc.2020.09.054>
18. Artificial Intelligence in Radiology and Radiation Oncology: The State of Play 2019 <https://www.ranzcr.com/college/document-library/artificial-intelligence-the-state-of-play-2019>