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LETTER TO THE EDITOR

Application of artificial intelligence (AI) in Radiotherapy workflow: Paradigm shift in Precision Radiotherapy using Machine Learning

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(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Letter to editor regarding "Applications and limitations of machine learning in radiation oncology"

Dear Editor,

We read with great interest the article by Jarrett et al titled "Applications and limitations of machine learning in radiation oncology" outlining the possible adaptation of machine learning into the radiotherapy workflow and the limitations of machine learning (ML) artificial intelligence (AI).[1] We agree with the author that (1) we need to understand the capabilities and limitations of ML and (2) the requirements of radiotherapy processes to benefit clinicians and cancer patients. The application of ML to radiotherapy pathway is more complex than in diagnostic imaging. In diagnostic radiology, ML only needs to be able to recognise similar patterns or structures such as in breast screening.

Radiotherapy pathway begins with the initial diagnosis and subsequently decision for radiotherapy. Next, patient undergoes imaging which allows clinician to "plan" radiotherapy on a virtual simulation of patient's body. Radiotherapy target delineation or contouring is where clinicians outline cancer volumes to deliver optimum radiotherapy doses and limit or avoid doses of radiotherapy to organ at risks (OARs). Additional margins are added to account for tumour spread and treatment delivery uncertainities.

In contouring, oncologist would apply *clinical judgement* by taking into account cancer pathology, potential tumour spread based on diagnostic imaging, patient performance status and others. Variation among clinicians in contouring exists and often peer review sessions are used by clinicians to reduce variations. Clinicians would interpret the variables; use their risk assessment and experience to define their interpretation of ground truth. Each clinician is essentially a natural intelligence itself and machine learning is replicating a summation of human (clinician) intelligence.

As such, as long as oncologists are interpreting patients' outlines and treatment plans, ML would struggle to meet individual patient needs. Even in daily clinical practice, day to day patient individual outlines differ, intra and inter observational differences exists and are difficult and cannot be easily reproducible. As such to say that "ground truth" of a tumour volume or OAR volume does not exist would imply that we have surveyed the entire cohort of oncologists which is not achievable. AI would have to be able to understand the whole radiotherapy pathway and although there are statistically significant differences in treatment volumes, in the end the actual deliverable doses are fairly consistent. A cancer of similar staging treated with similar technique would be treated in fairly consistent volumes.

There are roles for ML particularly in organ structures that are reproducible and have less likelihood of variation. Also, not all cancer volumes or OARs volumes are created equal with differences in organ constraints.[2] Besides, clinical practice also varies even within cancer centres nationally or internationally therefore a specific ML algorithm trained with a specific clinician cannot be used in another centre or directly translatable.[3]

"Garbage in, Garbage out" concept in computer science stills holds true to machine learning approaches. Often times, there is difficulty to access radiotherapy datasets. Therefore, before the authors give up on the adaptation of ML to radiotherapy, perhaps they can expand the cohort

of clinicians contributing to data to ensure their ML model is trained to a level truly representative of current UK clinical oncologists' practice.

We performed a review of literature review and have yet been able to identify ML being used clinically autonomously.[4] Therefore, ML technique when applied to radiotherapy process should not be aimed to replace clinicians but rather seen as an adjunct to aid clinicians. The current legal framework is not ready to allow this as well as only licensed clinicians can approve radiotherapy treatment plans.[5] ML algorithms should be benchmarked against the ability to produce clinically acceptable contours and the clinician time saved when using ML should be a standard performance metric.

There are areas of ML which can be used in radiotherapy which were not covered within this review. ML could be used in adaptive radiotherapy where treatment re-plan is required where due to changes either tumour volume or anatomy during treatment. The predictive capability of ML can also be utilised and researched to see if they could be used to assess patient's risks of cancer recurrence or stratify patient to separate cancer risks groups.

Cross-talk, collaboration and close consultations between all stakeholders such as clinician scientist, computer scientist, oncologists and patients are essential for successful implementation of ML to healthcare in line with aspirations for National Health Service to be a world leader in delivering AI in radiotherapy and oncology.[6]

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Response to letter: "Applications of artificial intelligence (AI) in Radiotherapy workflow: Paradigm shift in Precision Radiotherapy using Machine Learning"

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Dear Editor,

We are grateful to Boon et al, for their thoughtful comments on our article "Applications and limitations of machine learning in radiation oncology".

Their comments on variability in contouring were particularly insightful. As encouraged, we have no intention to "give up on adaptation of ML to radiotherapy". We firmly believe that there is substantial benefit to be derived using machine learning (ML). Any caution expressed in the original article was not intended to convey the impression that challenges, such as inter-observervariation in contouring, cannot be overcome but merely to set expectations that ML (or other technology) is not a solution in and of itself. We agree wholeheartedly that the route to successful implementation of ML in radiation oncology lies in "cross-talk, collaboration and close consultation between all stakeholders".

Therefore, we are keen to extend the multidiscipline group of stakeholders with whom we are already collaborating to ensure that the NHS is able to consolidate its position at the forefront of delivering AI in radiation oncology. To this end we would welcome direct approaches from UK institutions who share our desire to realise the patient benefit of integrating pragmatic ML solutions into the clinical pathway.