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Radiotherapy Treatment Planning in the Age of AI: Are We Ready Yet?

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Radiotherapy is an important treatment modality used for over half of all patients with cancer and a few benign conditions. Treatment planning, the design of radiotherapy for each individual case, is at the heart of radiotherapy and is thought of as both a science and an art. Due to the complex physics and mathematics involved, radiotherapy treatment planning is a pioneer among computationally supported medical processes. However, conventional treatment planning is still performed by humans—highly trained professionals called medical dosimetrists—using computer tools. The human planner interacts numerous times in the process of generating a plan with the treatment-planning system based on experience and skills to ensure satisfactory quality of each plan.

Like it has recently transformed and disrupted fields such as computer vision, natural language processing, and automobile autopiloting, artificial intelligence (AI) has promised to revolutionize radiotherapy treatment planning. In this special collection, we curated a series of articles reporting on the cutting edge of this important field at an exciting point of time. The review article of Wang *et al*¹ summarizes the current smart planning tools in 3 main categories: automated rule implementation and reasoning (ARIR), modeling of prior knowledge in clinical practice (KBP), and multicriteria optimization. The article systematically reviews the development history, clinical applications, and current progress on these main algorithms. Other recent progress, as well as emerging directions in AI-based treatment planning, are also reviewed, such as the applications of various deep learning algorithms, voxel-based dose prediction, and reinforcement learning. The challenges of AI in radiotherapy treatment planning are discussed alongside an outlook of the necessary requirements in regulation and collaboration.

As described in this review, one big impact of these AI algorithms is the potential improvement in the treatment planning workflow efficiency through automation. With such automation, human planners can be spared from many manual processes and therefore afforded more time to focus on further improving the plan quality. Wang *et al*'s study² shows such an

example in which a commercial ARIR algorithm, Pinnacle AutoPlan, was used to explore the dose-escalation limit of pancreatic stereotactic body radiotherapy (SBRT). Stereotactic body radiotherapy is an important treatment modality for borderline resectable and locally advanced pancreatic cancer that has shown promise but can be limited by normal tissue toxicity. Individualized target dose escalation within the normal tissue dose limit is potentially clinically meaningful but usually too time consuming to be practical. However, with the automation afforded by AI, this becomes feasible. Another study by Smith *et al*³ reports a rigorously designed comparison between 2 widely used commercial treatment-planning automation algorithms on prostate bed planning, including 1 ARIR-based algorithm (Pinnacle AutoPlan) and 1 KBP-based algorithm (Varian RapidPlan). Although clinicians and researchers are naturally interested in the performance comparison between these 2 fundamentally different algorithms, there has not been a good comparison reported, especially one that is well designed to rule out the human factors at play and ensure the comparison objectivity. The study by Smith *et al* nicely filled this important void. Using an established quantitative metric, the 2 algorithms were compared and found to yield similar performance. Interestingly, on one Plan Challenge case used for a human planner competition, both automation algorithms were able to achieve

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above-human average performances with marked efficiency improvement.

Our special collection also reports new applications in AI-based treatment planning. While conventional algorithms operate on inverse treatment planning and focus on dose optimization, Wang *et al*⁴ report a method to automate and optimize beam settings that can be followed by automatic fluence optimization for whole-breast radiotherapy. This typically requires a medical dosimetrist to spend substantial time on manual forward planning. In another study, Li *et al*⁵ investigate a collimator setting optimization algorithm for pancreatic SBRT treated with volumetric-modulated arc therapy (VMAT). This setting in conventional treatment planning is usually not optimized. Using this new algorithm to explore a new degree of freedom, significantly better sparing was achieved for organs at risk, important for this treatment modality.

Articles in this special collection also explore the practical challenges of current AI algorithms. Landers *et al*⁶ report an interesting study comparing 3 KBP dose prediction algorithms for both 4 π intensity-modulated radiotherapy (IMRT) and VMAT on a few disease sites including head and neck, lung, and prostate, each with limited patient data in terms of case numbers. Their comparisons illustrate an important finding: When patient data are limited for KBP, simple statistical learning is more robust to patient variability and hence better at dose prediction than more sophisticated machine learning methods. Addressing similar issues, Sheng *et al*⁷ propose a case-based reasoning method by judiciously combining the use of atlas-based and regression-based prediction to improve a model's overall robustness, particularly effective when dealing with novel anatomy. The applicability of their method was demonstrated on a cohort of patients having prostate cancer treated with IMRT.

An important issue in data science is data size—limited data increase the uncertainty of the data model. This is particularly critical for AI-based treatment planning because the data size in treatment planning is smaller than other big data applications in health care such as imaging. As mentioned earlier, the study of Landers *et al*⁶ highlights this problem and the importance of proper method selection. In another study conducted by Zhang *et al*,⁸ historical IMRT treatment plans of a large cohort of patients with head and neck cancer from a single institution ($n = 927$) were used to demonstrate the effectiveness of a knowledge-based statistical inference method for evaluating plan quality based on similar plans from the database. With this sufficiently large database, similar historical plans in terms of both geometry and dosimetry were selected to provide simple statistical predictions for new plans. This work developed useful infrastructures for automatic data extraction, anonymization, and analysis, which could also allow multi-institutional data integration to further increase data size. On the other hand, even from single institutional data, the challenges of data heterogeneity highlight the importance of proper data homogenization in data-based methods for AI-based treatment planning.

Finally, fully AI-based treatment planning requires automation of the entire treatment planning workflow. Artificial

intelligence-based segmentation is, therefore, an important branch of research as delineating regions of interest (ROIs) is an important and time-consuming step. The automatic segmentation of ROIs could greatly improve efficiency and possibly improve consistency. Conventionally, this has been done based on intensity thresholding, edge detection, and other mathematical methods. These algorithms mostly work on ROIs distinct from their backgrounds, such as lung, spinal cord, and brain but have limited accuracy to be clinically useful for other applications. With the advent of modern AI, machine learning—especially deep learning—approaches have demonstrated great potential in accurate ROI autosegmentation. In this collection, 2 noteworthy works on this topic are included.

In Li *et al* study,⁹ a deep learning U-Net model was used to autosegment the tumor target for nasopharyngeal radiotherapy. Using a large cohort of 502 patients divided into the training, validation, and testing data sets, they were able to train an algorithm to automatically segment the tumor targets in under a minute and achieve over 70% of agreement in terms of Dice similarity coefficient for primary tumors and over 60% agreement for involved lymph nodes compared against manual segmentation which takes a few hours to complete. While such performances are encouraging, it is also important to note that there remains much room for improvement before AI-based algorithms could completely replace humans on such challenging tasks. For the task investigated in this study, the remaining 30% to 40% inaccuracy compared to manual segmentation still takes hours of manual effort, so the semi-autosegmentation approach combining the AI algorithm and manual touch-up saved on average less than half an hour on each case compared to the completely manual approach.

To boost research in this important area, professional societies such as the Society of Photo-Optical Instrumentation Engineers, the American Association of Physicists in Medicine, and the National Cancer Institute have organized open competitions to use AI-based algorithms to solve specific clinical tasks. Chen *et al*'s work¹⁰ detailed the algorithms they developed for the Prostate-X Grand Challenge held by the abovementioned 3 organizations. In this challenge, the clinical task was to detect cancer on multiparametric magnetic resonance images from suspicious prostate lesions that included both cancer and benign lesions. They applied a transfer-learning approach to retune a deep convolutional neural network algorithm pretrained on ImageNet, a large data set of regular (nonmedical) images, based on the clinical task. Their best-performing model achieved the third best score among the 72 models submitted from 33 competing teams, and the performance was similar to radiologists following the standard clinical protocol. This work highlights the potential of using transfer learning to address the data size limitation in the medical problems and also demonstrates the importance of proper data processing and rigorous method design.

Artificial intelligence is rapidly propelling many revolutionary changes in our lives. Unmanned drones now share the sky with the piloted aircrafts for various tasks, and self-driving cars may completely reshape what “learning to drive” means for today's preteens. Like these other fields, radiotherapy

treatment planning also holds tremendous opportunities and challenges for AI-based automation. We hope the review article and the original research articles in this special collection provide our readers with an overview of current research and a glimpse of what the future holds.

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