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Re: Report on the PhD Thesis of Mr. Paul DUBOIS
To whom it may concern

Thesis title: Methods for automatization of radiotherapy dosimetry

This thesis explores innovative methodologies to enhance dosimetry, aiming to create a fully automated system adaptable to clinical constraints. The main contributions of the thesis can be summarized as follows:

Efficient Dosimetry Engine and Optimization Algorithms: The contribution refers to an efficient dosimetry engine alongside a detailed evaluation of open-source optimization algorithms. The development of clinically meaningful dose distances is commendable because it bridges a critical gap between theoretical optimization and practical application in clinical settings. By quantifying dose differences in a way that aligns with clinical relevance, this approach moves beyond abstract mathematical formulations to address real-world treatment objectives. It provides a robust framework for evaluating the quality and safety of radiation therapy plans, making it easier for clinicians to interpret and implement optimization results. However, while the groundwork is valuable, the thesis could delve deeper into the scalability and robustness of the proposed methodologies. The practical implications of integrating these improvements into existing workflows remain underexplored, particularly in terms of how they address the needs of diverse clinical environments with varying levels of resource availability.

Multi-Objective Optimization and Graph Theory: The second contribution of the thesis relates to multi-objective optimization and robust plan selection, utilizing graph theory to provide an advanced and systematic method for analyzing and managing the intricate relationships between various dose levels. By modeling the interactions and trade-offs among dose constraints as graph-theoretical structures, the framework enables a deeper and more nuanced understanding of how different treatment parameters influence each other, which is critical for optimizing outcomes in complex clinical scenarios. The use of graph theory in this context not only enhances the precision of optimization but also offers a powerful tool for decision-making, allowing clinicians to identify robust solutions that maintain effectiveness across varying treatment conditions. Despite its theoretical strengths, the framework's practical/clinical validation is limited. Without extensive validation in diverse clinical environments and a clear demonstration of its usability and efficiency, the framework's transition from theoretical innovation to practical utility remains uncertain.

Reinforcement Learning for Automation: The exploration of reinforcement learning (RL) in dosimetry automation is one of the thesis's most intriguing and impactful contributions, introducing two significant innovations that push the boundaries of automated treatment planning. The first innovation involves the development of a novel metric for training the RL agent, which evaluates the quality of generated treatment plans based on the similarity between RL-optimized dose distributions and clinically delivered doses. The second innovation is the adaptability of the RL algorithm to diverse clinical

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environments, a breakthrough that addresses one of the primary barriers to widespread adoption of automated dosimetry systems. While the idea of training an RL agent on historical data to optimize treatment plans is intriguing, it assumes that historical plans are optimal—an assumption that may not always hold. Additionally, the thesis does not fully address how the RL system handles deviations from historical trends or adapts to alternative clinical techniques.

Deep Learning for Dose Distribution Prediction: The thesis advances the application of deep learning for dose distribution prediction by using target Dose-Volume Histograms (DVHs) as structured guidance. This strategy is innovative, as it indirectly incorporates clinical priorities and enables the model to adapt to diverse clinical practices. However, reducing complex anatomical and radiological factors into one dimensional constraint from mathematical perspective may oversimplify critical aspects of treatment planning, potentially compromising precision in complex cases. Furthermore, the robustness of the method in handling conflicting or ambiguous one dimensional constraints/targets remains an open question, particularly in complex clinical scenarios.

This thesis raises several important questions, with the most critical centered on the need for robust validation. How can rigorous multi-center studies be designed and conducted to effectively demonstrate the proposed methodologies' reliability and applicability across diverse clinical environments? Addressing this question is pivotal for ensuring the broader adoption and practical utility of the research findings.

In conclusion, the thesis represents a significant contribution to the advancement of automation in cancer treatment, utilizing innovative computational techniques such as graph theory and deep learning to address critical challenges in dosimetry. The research demonstrates a high level of scientific rigor and creativity, with its findings presented at some of the most prestigious scientific events in the field, underscoring its relevance and impact. Given the substantial strides made and the strong foundation laid for future research, I have no reservations in recommending its acceptance as part of the requirements for the Ph.D. Furthermore, I fully endorse authorizing the candidate to proceed with the defense, confident in the quality and significance of his work.

Sincerely,

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