Clinically Meaningful Dose Clustering for Radiotherapy

Paul Dubois, Nikos Paragios, Paul-Henry Cournède

June 20, 2023

Abstract

Radiotherapy plays a crucial role in improving patient outcomes and has become more precise and tailored to individual patient needs with the advancements in technology. It is widely used for various cancer types either alone and/or in combination with surgery and chemotherapy. However, evaluating the quality of treatment plans and ensuring radiation delivery precision remain critical challenges in radiation therapy. This is especially important when comparing different treatment plans or techniques and assessing the influence of anatomical changes during treatment. Proper evaluation is necessary for determining treatment efficacy and optimizing patient outcomes.

This article presents a novel approach by clustering treatment plans, thereby reducing the reliance on human intervention for evaluating numerous potential plans and selecting the optimal course of action. This methodology effectively minimizes the duration required for optimizing patient treatment and enhances the overall efficiency of medical facilities.

1 Introduction

Radiotherapy is a prevalent intervention for treating cancer, utilizing ionizing radiation to eliminate malignant cells. Among the various radiotherapy approaches, intensity-modulated radiation therapy (IMRT) stands out as a technique that administers high radiation doses to the tumor while minimizing exposure to surrounding healthy tissues [4]. Traditional IMRT strategies employ several beams, usually 5, 7, or 9, originating from different angles around the patient (most of the time, equispaced angles) [1] [2]. Each beam's intensity is modulated to optimize radiation dose delivery to the tumor while reducing healthy tissue exposure. This technique surpasses the efficacy of the 3D-conformal radiotherapy (3D-CRT) approach [5] [9] [**?**]. The multi-leaf collimator (MLC), a computer-controlled device, shapes the radiation beam to match the tumor's contours, facilitating precise and efficient delivery of the therapy.

The efficacy of a radiotherapy treatment plan is contingent upon the optimization procedure, which encompasses multiple steps to guarantee the most favorable administration of radiation, adhering to the physician's directives. Computer software usually performs the optimization process, which incorporates the patient's anatomy, tumor/organs' location and size, and the radiation objectives defined by medical professionals.

Dose Optimization Inputs The initial phase of the optimization process involves the generation of a virtual representation of the patient's anatomy using medical imaging technologies such as CT or MRI scans. This model is subsequently exploited to identify the tumor's size and location and delineate the adjacent healthy tissues that require protection from radiation exposure. The subsequent step is to establish the requisite radiation dose for effective treatment, with physicians typically prescribing dose-volume objectives (e.g., 95% of PTV should receive a minimum of 75Gy). The dose is determined based on factors such as tumor size, location, and type, as well as the patient's medical history and general well-being. These steps are undertaken by medical professionals.

Dose Simulation In the radiation therapy optimization process, the next step involves computing the dose on the patient's volume by simulating one multi-leaf collimator (MLC) parametrization on the patient's body using medical imaging data. The computed dose is a map from the three-dimensional volume of the patient's body to a positive number of Grays, which is the unit used to measure the absorbed radiation energy. In practice, a discrete version of the dose is used, where the dose is calculated for each voxel of the patient's body.

Dose-Volume Histograms Doctors have delineated the various relevant structures in the patient's anatomy to allow calculation of the dose-volume histogram (DVH) for each structure based on a given dose. The dose-volume objectives are then represented as points on the DVH that should be maintained either above (in case of minimum dose constraints) or below (in case of maximum dose constraints).

Evaluation of Doses Doctors evaluate the quality of a dose using several criteria. First, they examine the 3D distribution of the dose on the patient's body, looking at the inter-structure distribution as well as the presence, number, and location of hot spots. Second, they analyze the DVH to determine if the curves match the predefined DVH objectives. This evaluation step is critical for ensuring that the surrounding healthy tissues are spared from unnecessary radiation exposure. By optimizing the treatment plan and verifying the quality of the dose, doctors can ensure the best possible outcome for the patient.

2 Methods

The assurance of accuracy and efficacy in radiation therapy necessitates the implementation of robust dose optimization process. This is achieved after the optimization of an inverse problem [10]; our specific implementation is described below.

2.1 Radiotherapy Dose Optimization

Mathematical Objective Function In order to capture the diverse dose goals specified within the TG-119 data-set [8], we designed a cost function that incorporates multiple objectives. The cost function employed in our study is a weighted sum of multiple objective functions, with each objective corresponding

to a specific dose goal. The construction of the cost function is defined as follows, using a square over/under-dose penalty function for each objective:

$$f(\mathbf{d}) = \sum_{o \in \mathcal{O}} w_o f_o(\mathbf{d})$$

$$f_o(\mathbf{d}) = \sum_{d \in \mathbf{d}[o_s]} (d - o_d)_+^2 \text{ if } o \text{ is a maximal dose-volume constraint}$$

$$f_o(\mathbf{d}) = \sum_{d \in \mathbf{d}[o_s]} (o_d - d)_+^2 \text{ if } o \text{ is a minimal dose-volume constraint}$$

with:

- $\mathbf{d}$ the voxel-wise dose; $\mathbf{d}[s]$ the dose on voxels of the structure s.
- $\mathcal{O}$ the set of objectives (dose-volume goals)
- w_o is the weight of the objective $o \in \mathcal{O}$ (ranges typically between 0 and 100)
- o_s, o_d & o_v respectively the structure, dose and volume goals of $o \in \mathcal{O}$ (e.g.: o_s: PTV; o_d: 80Gy; o_v: 95%)

MLC Fluence Discretization We approximated the fluence of each beam using bixels. Bixels[1] is a discrete element of the radiation beam that can be individually controlled to achieve spatially varying intensity levels. In our study, the width of these bixels was set to 5mm, corresponding to the width of leafs of the commonly used multi-leaf collimator.

Bixels Smoothness To promote smoothness and consistency in the distribution of bixel values, we introduced a regularization term in our optimization. This penalty term that penalizes variations between neighboring bixels. Specifically, a square penalty was applied to the differences between bixel values and their neighboring counterparts.

Simulation & Approximation The optimization process involved finding the optimal values for the bixels, denoted as $\mathbf{b}$, while considering the dose distribution voxel-wise $\mathbf{d}$ calculated based on the precomputed dose-influence matrix $\mathbf{L}$, which relates bixels to the corresponding voxels. Here, we make the assumption that bixels activation and dose deposition are linearly linked. This assumption is very commonly used.

Physical Limitations It is important to note that due to the physical constraints of radiation therapy, it is not possible to have negative energy rays. Consequently, each bixel value should be non-negative ($b \geq 0 \quad \forall b \in \mathbf{b}$). To ensure positive bixel values in practice, we applied an absolute value operation, computing $\mathbf{d} = \mathbf{L}|\mathbf{b}|$, where $|\mathbf{b}|$ represents the element-wise absolute value of $\mathbf{b}$.

[1] **be**am-**el**ement

Convexity The cost function employed in our study is constructed to be convex by design, ensuring desirable mathematical properties for optimization. As a result, regardless of the specific set of weights assigned to the objectives, minimizing this cost function is expected to consistently converge to the same optimal radiotherapy plan.

Multiple Plans Generation To generate diverse treatment doses for a given patient case and set of constraints, we employed a strategy of optimizing the cost function with different weight assignments for each constraint. Varying the weights associated with individual dose goals is how dosimetrists are now guiding optimization engines toward the best (clinically acceptable) solution. Playing with these weights allows to explore different trade-offs and prioritize certain aspects of the treatment plan over others.

Optimizer The optimization of the main objective function was performed using the open-source optimizer L-BFGS (Limited-memory Broyden-Fletcher-Goldfarb-Shanno). This optimizer has been demonstrated to exhibit superior performance compared to other open-source optimizers available [3].

2.2 Data

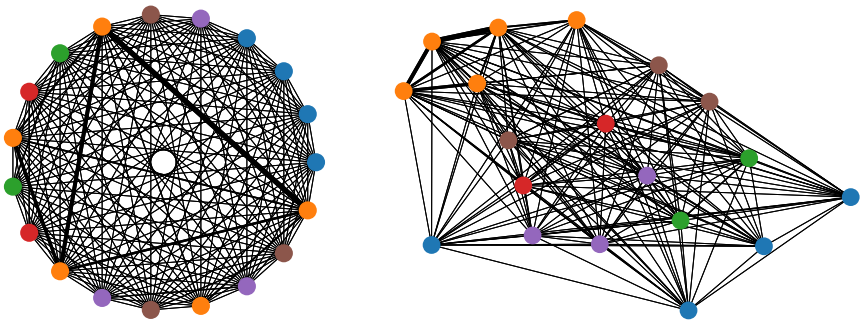
(Phantom) Patient The evaluation of our proposed method for clustering radiation doses was conducted using the TG-119 Prostate case [8], which is a well-established benchmark data-set commonly employed for assessing the quality of radiation therapy plans. The TG-119 data-set encompasses predefined dose goals, which were utilized in the formulation of our cost function.

Dose normalization We normalized the doses according to the "D50" normalization method, which is a common practice in the field of radiation therapy. It consists in normalizing the dose such that the median dose of the PTV is equal to the prescription dose.

2.3 Dose Clustering Techniques

Dose Distance To cluster the doses, we first need to define a distance between them. We used the Euclidean distance between the voxel-wise doses. We defined the weight of the edge between two doses as the inverse of the distance between them (since we want to maximize the weight of the edges between similar doses). Defining the weight of the edge as the inverse of the distance between the doses is quite standard in the field of graph theory [7] [6].

Community Detection We used the Louvain's method for community detection to cluster the doses. This method is a greedy optimization method that maximizes the modularity of the graph. The modularity of a graph is a measure of the quality of the partition of the graph into communities. We used the implementation of the Louvain's method in the python library networkx.



(a) (Circular Layout) (b) (Spring Layout)

Figure 1: Plot of the Network
edges width $\propto$ edge weight $\propto$ $1/\text{distance}$
node's color reflects community attribution

Evaluating Communities Split Evaluation of clustering quality was performed using dose-volume histograms (DVH) obtained from different doses. The mean and standard deviation of the DVH were computed for each cluster versus the entire data-set:

We conducted an analysis on the relative volume doses for the four distinct structures. A total of 101 dose values were sampled for each structure, with volume ranging from 0% to 100% equally spaced). These values were aggregated into a single vector, resulting in a vector length of 404 for each dose.

To assess the variability within these dose vectors, we calculated the standard deviation for the 404 elements of each vector. This statistical measure provides insight into the dispersion of the dose values within a given structure. By averaging the obtained standard deviations, we derived a scalar metric that quantifies the degree of separation among a group of doses.

3 Results

3.1 Doses Network

Graph Plots In figure 1, each node represents a dose. The communities are attributed using Louvain method and are identified by colors. Since the graph is clearly not planar, we choose to plot it in a circular layout (fig. 1a) and in a spring layout (fig. 1b).

In order to obtain a more precise understanding of the edge weights in the network, one can refer to the adjacency matrix of the edge weights, as depicted in Figure 2.

DVH Plot Figure 3 illustrates the Dose-Volume Histograms (DVHs), with the colors of the plots corresponding to the communities identified in the network analysis. To ensure clarity and prevent confusion, each structure is presented on a separate plot. Notably, our observations align with expectations, as doses

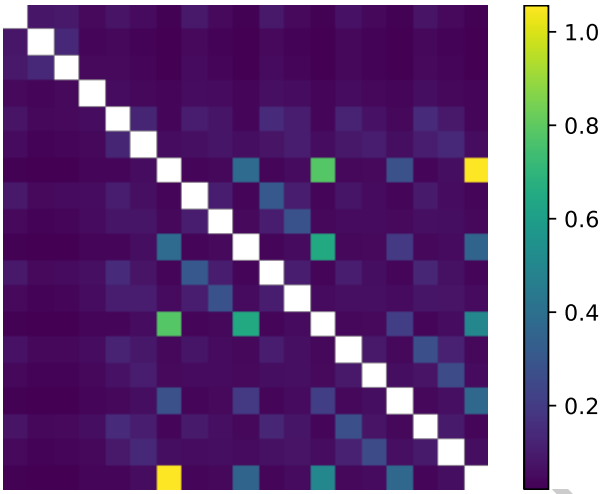


Figure 2: Weight Adjacency Matrix of the Network

Set	Set Size	Mean Standard Deviation
Cluster 1 **(blue)**	4	2.0542
Cluster 2 **(orange)**	5	0.4049
Cluster 3 **(green)**	2	0.3618
Cluster 4 **(red)**	2	0.4218
Cluster 5 **(purple)**	3	0.9702
Cluster 6 **(brown)**	3	1.2418
All	*19*	*3.5122*

Table 1: Clustering Quality

assigned to nodes within the same community (indicated by the same color) exhibit nearly overlapping DVHs.

The visualization of DVHs provides valuable insights into the distribution of doses received by different structures. The close correspondence between dose patterns and community assignment underscores the potential of network analysis in uncovering meaningful patterns within radiation therapy data. By associating the colors of the DVH plots with the communities identified in the network, we gain a deeper understanding of the relationship between dose assignments and structural characteristics. This analysis further supports the notion that nodes (doses) within the same community share similar profiles, suggesting they could be merged, as they will likely have the same clinical effect.

3.2 Dose Clustering Evaluation

As explained in 2.3, we use the mean standard deviation of doses at 101 equispaced values of volume to obtain a scalar value of how far apart are a set of doses; see table 1 for results.

The mean standard deviation of the clusters, with values of 2.0542, 0.4049, 0.3618, 0.4218, 0.9702, and 1.2418, averaging at 0.9091, is significantly lower (nearly 4 times lower) compared to the mean standard deviation of the full

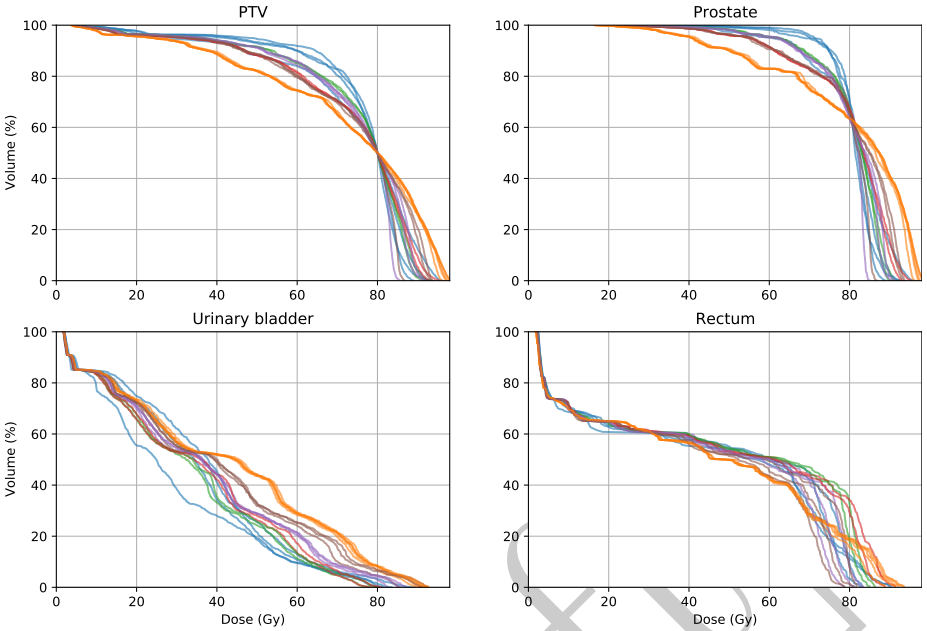


Figure 3: Dose-Volume Histogram

network, which is 3.5122 (see table 1). This notable reduction in standard deviation yells quantitatively that our clustering approach has favorable results. Our proposed clustering approach demonstrates strong performance in both qualitative and quantitative evaluations.

4 Discussion

The ability to regroup doses into communities provides opportunities for early stopping optimization, and valuable insights to understand clinical practices. However, the clustering of doses is a challenging task, as the dose space is high dimensional and the dose distribution is not smooth. The results presented here can not yet be used in clinical practice, they are promising and should be further investigated.

5 Conclusion

In conclusion, this study has presented a novel approach for clustering doses into communities based on dose distribution. This clustering was shown to be both quantitatively and qualitatively meaningful, suggesting the clinical effect of doses in the same cluster will be indistinguishable.

This could have the following use: First, we could run the clustering when performing the FMO[2], and stop the optimization process when the last few updates remain in the same cluster. Secondly, clustering doses coming from different patients would be another challenge, but if further research makes

[2]Fluence Map Optimization

it possible, one could be able to analyze the habits of clinical center. This could help understand why some centers perform better than others on specific anatomies.

Finally, dosimetrists nowadays usually submit more than one treatment plan for validation with the physicist. The physicist then has the responsibility of choosing the more appropriate one according to his past experience, patient's specificity, etc. We can think of optimizing doses with many different weights parameters for the constraints; this will lead to dozens of doses, which is unpractical for the physicist to search for the best one. However, clustering them could allow to reduce the number of doses to choose from, and therefore, make the process more efficient, needing less people in the dosimetry department.

As further research and validation are conducted, this approach holds great potential for enhancing treatment planning processes and ultimately improving patient outcomes.

References

[1] Thomas Bortfeld. Imrt: a review and preview. *Physics in Medicine and Biology*, 51(13):R363, jun 2006.

[2] Thomas Bortfeld. The number of beams in imrt—theoretical investigations and implications for single-arc imrt. *Physics in Medicine & Biology*, 55:83 – 97, 2009.

[3] Paul Dubois. Radiotherapy dosimetry: A review on open-source optimizer, 2023.

[4] Gary A. Ezzell, James M. Galvin, Daniel Low, Jatinder R. Palta, Isaac Rosen, Michael B. Sharpe, Ping Xia, Ying Xiao, Lei Xing, and Cedric X. Yu. Guidance document on delivery, treatment planning, and clinical implementation of imrt: Report of the imrt subcommittee of the aapm radiation therapy committee. *Medical Physics*, 30(8):2089–2115, 2003.

[5] Thomas P. Kole, Osarhieme Aghayere, Jason Kwah, Ellen D. Yorke, and Karyn A. Goodman. Comparison of heart and coronary artery doses associated with intensity-modulated radiotherapy versus three-dimensional conformal radiotherapy for distal esophageal cancer. *International Journal of Radiation Oncology*Biology*Physics*, 83(5):1580–1586, 2012.

[6] Zhengquan Li, Kuo Wang, Hao Ma, and Yaoxiang Wu. An adjusted inverse distance weighted spatial interpolation method. In *Proceedings of the 2018 3rd International Conference on Communications, Information Management and Network Security (CIMNS 2018)*, pages 128–132. Atlantis Press, 2018/11.

[7] Wojciech Maleika. Inverse distance weighting method optimization in the process of digital terrain model creation based on data collected from a multibeam echosounder. *Applied Geomatics*, 12(4):397–407, Dec 2020.

[8] Dinesh Kumar Mynampati, Ravindra Yaparpalvi, Linda Hong, Hsiang-Chi Kuo, and Dennis Mah. Application of aapm tg 119 to volumetric arc

therapy (vmat). *Journal of Applied Clinical Medical Physics*, 13(5):108–116, 2012.

[9] David Palma, Emily Vollans, Kerry James, Sandy Nakano, Vitali Moiseenko, Richard Shaffer, Michael McKenzie, James Morris, and Karl Otto. Volumetric modulated arc therapy for delivery of prostate radiotherapy: Comparison with intensity-modulated radiotherapy and three-dimensional conformal radiotherapy. *International Journal of Radiation Oncology*Biology*Physics*, 72(4):996–1001, 2008.

[10] S Webb. The physical basis of imrt and inverse planning. *The British Journal of Radiology*, 76(910):678–689, 2003. PMID: 14512327.