Automated radiation therapy treatment planning generation combining prior data and novel optimization techniques

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Abstract

Modern radiotherapy uses reverse planning to find a single patient-specific treatment plan.[1] The field modulation is optimized by manual adjustment technology, and the priority between the target and normal tissue dosimetry is determined according to historical experience. The current radiotherapy plan relies on the professional knowledge of human beings and the experimental determination of achievable radiation dosimetry. Highly specialized training for physicians, physicists, dosimetrists, and radiation therapists can ensure high-quality radiation therapy. Using the power of artificial intelligence and big data to predict the achievable radiation dose, and has the ability to improve the treatment efficiency, improve the treatment quality, and overcome the limitations of humans in the implementation of advanced technology. Current technologies do not provide real-time patient-specific dosimetry and trade-off analysis. To this end, the project will create an analytical real-time dose (RTD) calculator to generate radiation doses outside the target area in real-time. Compared with the clinical dose distribution in Oncospace database of big data and the predicted metering distribution of RTD, the obtained results lead to the following conclusion that RTD uses data-driven artificial intelligence method to increase the ability to avoid human errors, improve the quality of patients' specific plans, and finally effectively improve the treatment results.

Introduction

The quality and ultimate success of cancer treatment around the world depends on the available technology and human ability to harness it. However, we believe that artificial intelligence may be able to improve treatment efficiency, improve treatment quality, and overcome the limitations of human beings in implementing advanced technologies. The key obstacle to be overcome is to provide an in-depth understanding of patient-specific achievable dosimetry and the inherent tradeoff of radiation dose delivery. The ability to accurately characterize dose and dose substitutes have not been developed, such as dose-volume histogram (DVH), which takes into account the tradeoff between target coverage, normal tissue dosimetry, and different delivery methods.[8,10,11] This defect is mainly due to the variability of the anatomical structure between patient and doctor preference models. Selected treatment plans for specific patients are driven by doctors' experience and clinical trial knowledge, and rarely include a comprehensive analysis of competitive trade-offs between different treatment plans. Patient-specific variables are initially communicated in the radiation therapy prescription through the specifications of the therapy machine, beam delivery techniques, dosimetry targets, and desired target dosimetry.[12] Our proposition is that these specifications should be based on achievable patient-specific dosimetry knowledge. The obstacles to providing such information to clinicians are efficiency and accuracy. Current technologies do not provide real-time patient-specific dosimetry and trade-off analysis.

Modern radiotherapy uses reverse planning in intensity-modulated radiotherapy (IMRT) to formulate a specific treatment plan for a single patient,[5] and predict the specific radiation dose of the patient. The quality of the IMRT treatment plan depends on the planner's level of experience and the amount of time the planner spends making the plan.[2] By providing estimates of radiation dose, planners can find similar or better plans faster.[4] For treatment consistency, data-driven artificial intelligence methods will inherently compare treatment plans with acceptable prior treatment data and increase the ability to avoid human errors.[13] Finally, a comprehensive understanding of patient-specific dose tradeoffs will inherently improve the quality of patient-specific plans, independent of training and experience, and ultimately improve treatment outcomes. To this end, the project will create an analytical real-time dose (RTD) calculator. In order to deliver a uniform dose to a target with a mass, there is a constant integrated dose-related to non-target tissues. Variables that determine the overall radiation dose to non-target tissues are

radiation characteristics (including variables such as radiation energy), the size of target tissues, and the number of normal tissues to pass through. Through the preservation of integral doses and the management of dose cores, RTD calculator will allow analysis and real-time redistribution or "rescheduling" of doses outside the target area. The breakthrough of this goal is to generate radiation dose in real-time. The RTD calculator is applied to patient data to obtain the predicted radiation dose distribution and compared with the clinical dose distribution in the big data Oncospace database to evaluate the accuracy of the RTD calculator. RTD calculator is hypothesized that can improve the ability to avoid human errors, improve the quality of patients' specific plans, and ultimately effectively improve the therapeutic effect due to the use of data-driven artificial intelligence methods.

Methods / Materials

OVH and DVH

The overlap volume histogram (OVH) is a one-dimensional function that describes the distribution of distances of the organ volume relative to target volume. The OVH is generated by comparing the sparing relationships of organs at risk between new patients and previous patients in the database.[3,9] OVH graphs can show the volume percentage change between different OARs and targets at different degrees of target expansion and contraction. It also can be seen from the OVH graph that their overlapping volumes change correspondingly when the distance between the target and OARs change. According to the spatial relationship between different OARs and targets, the corresponding overlapping volume percentage is calculated and plotted into a graph. By comparing the spatial relationship between organs at risk and targets of new patients with the data of previous patients in the database, it can contribute to generate dose volume histogram (DVH) and estimate the accuracy of delivered dose distribution. By using a database of previous patient geometry and dosimetric information, the intensity-modulated radiation therapy (IMRT) planning method can generate achievable DVH objectives. According to OVH analysis, the database generates DVH objectives (Dv) at a specific percent volume for patients, and the minimum value of Dv in previous patient groups can be generated. DVH takes into account the tradeoff between target coverage, normal tissue dosimetry, and different delivery methods.

Kernel estimation:

The kernels are computed for varying beam energy, varying volume phantoms, and varying target sizes. Dose kernels computational methods have been developed to determine the integral radiation dose of outside target tissue. The dose falloff in different core radius can be found by selecting different target sizes. The resulting kernels demonstrate dose falloff as a function of these variables. As mentioned before, target size could have a significant influence on LDS function thus changing the whole dose falloff, various target sizes are chosen finding the dose falloff in different kernel radius. The range of diameters of patients' target is from 5mm to 140mm. First, the data we exported from DICOM is a 4D matrix including x, y, z, dose volume. We choose one of the slices and change it to a 3D matrix which can be visualized. Then, we cut the 3D image in 4 different directions to create the averaged dose spread function. Since we only need the falloff part of the curve, 90 percent of the max dose volume is chosen to be the ceiling and ignore the data above it. Last but not least, we found the maximum value for dose in the patient's data and normalized the dose falloff curve.

Dose estimation in phantoms:

For each voxel outside the target, we need to calculate the r1 and r2. As shown in Figure 1, r1 is the distance from the center of the target to the intersect of the boundary and the line connected center and voxel and r2 is the distance from the intersect to the voxel. In order to calculate r1 and r2 in matlab, we need to find the boundary of the target first, which is a list of points. Then, we use matlab built in function

to find the center of the target. For each voxel outside the target, we calculate the distance between the voxel to every point in the boundary and find the minimum value which will be assigned as r2. Moreover, we calculate the distance between the center and the voxel and then use it to subtract r2 to get the value of r1.

Target size may have an important impact on dose falloff, so ellipse, irregular shape and targets of various shapes can be used as the basis for future clinical scientific applications. We have a 2D table containing R1 (column) and R2 (row) value, since the R1 value in the original table is diameter rather than radius, the value of R1 in the table needs to be changed to radius first to ensure the consistency of the whole unit. According to the data of R1, R2 and dose falloff table, the dose falloff corresponding to R1 and R2 are found by interpolating the table data. Because linear interpolation on a set of data points is used for curve fitting, values that do not belong to this table may appear within a set of known data points. By using Matlab to convert the values of table R1, R2, and dose falloff into 3D colormap, the corresponding doses can be found more efficiently by looking up R1 and R2 for each voxel. We need to rebuild this table to become a new three-dimensional table with input r1+r2 where r1+r2 represents the relationship between organ at risk (OAR) and the target. This means that we can now calculate overlap volume histogram between OAR and target from r1+r2 and find the most similar previous patient data in the database. When the similar patients data is obtained, we have constant integral dose and normalized the dose volume to change and rebuild the dose distribution to protect the orgain at risks. This enables analysis and real-time dose redistribution outside the target area. We also evaluate the accuracy of the RTD calculator via comparison with delivered dose distribution with big-data, Oncospace. Based on an input patient CT image, patients structures, and a radiation therapy prescription we will compare predicted dose to clinically delivered dose. The dose comparison needs to start from a single dose distribution delivered clinically by each patient to a series of dose distributions based on several similar patients and similar organs at risk.

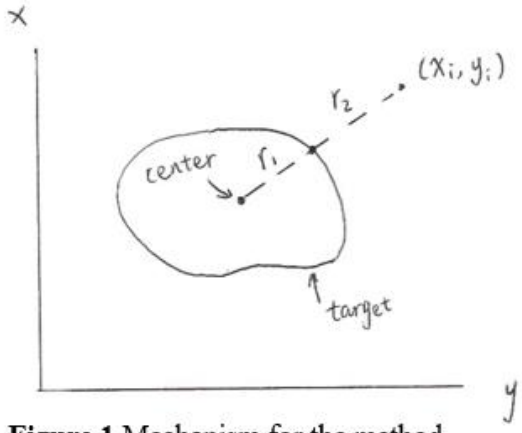

Figure 1 Mechanism for the method

Dose estimation in patient anatomy:

As we have finished the computational modeling, we start to apply our code to real patients. We have 30 patients who have pancreatic cancer. Each of them have irregular and different numbers targets through which we could further prove the success of RTD calculator.At the final step, we will evaluate the accuracy of RTD calculator by comparing the predict dose distribution to the clinical distribution.

Results

Kernels change as a function of phantom size

For top to bottom, the diameter of the target increases. As shown in the figure, there is a threshold for target size which is around 60mm for diameter. The falloff curve for target size above the threshold is concave up and for target size below the threshold is concave down. We also decided to expand the range to 300mm in case the target is larger than the example. The dose falloff function that we created from DICOM dose is shown in Figure 1.

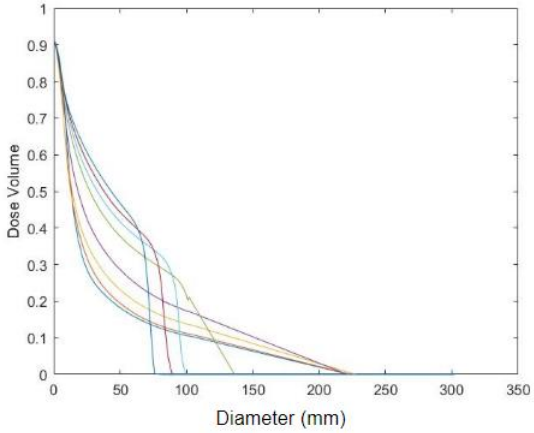

Figure 2 Dose falloff for different target size

Dose distribution for circular and elliptic model

We have plotted integral dose as a function of target size. In order to get a more accurate delivery dose volume, we created a look-up table for each voxel based on the dose distribution from prior patients'. First, the data we exported from DICOM is a 4D matrix including x, y, z, dose volume. We choose one of the slices and change it to a 3D matrix which can be visualized. Then, we cut the 3D image in 4 different directions to create the table. Since we only need the fall off part of the curve, 90 percent of the max dose volume is chosen to be the ceiling and ignore the data above it. For each cut, the radius for the line is identical which means they have the same R1 value. Each cut is a row in the table. The first column is R1 values and the bar above the first row are R2 values. The inputs for this table are R1, which is the distance from the center of the target to the intersect of the boundary and the line connected center and voxel, and R2, which is the distance from the intersect to the voxel. The outputs are dose distribution as shown on figure 3 and the overall dose volume. It works perfectly for every ellipse model we apply and no matter what the shape is and the dose spread is sharper falloff when r1 is smaller. The unit of the table is millimeter and the unit of the model is voxel. Since there is a conversion between mm and voxel, the table could not include every voxel in the model. We use interpolation to address this problem. Because linear interpolation on a set of data points is used for curve fitting, values that do not belong to this table may appear within a set of known data points. By using Matlab to convert the values of table R1, R2 and dose falloff into 3D colormap, the corresponding does can be found more efficiently by looking up R1 and R2 for each voxel.

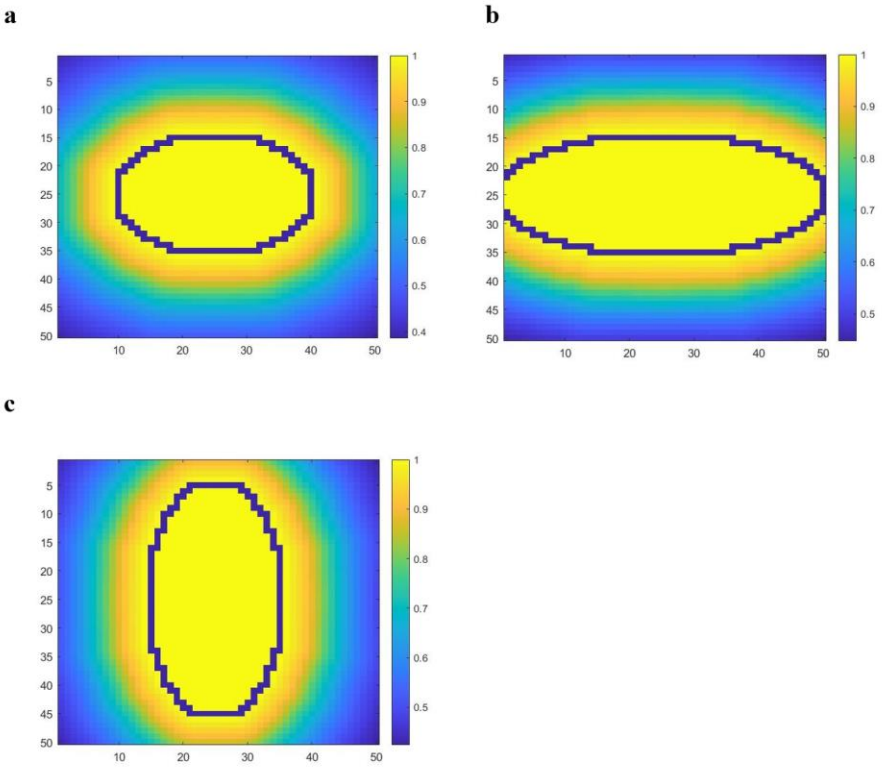

Figure 3 Dose distribution in different shapes of ellipse

Application on real patients and Evaluation of accuracy

As shown in the last section, the code we created by matlab works perfectly in the circular and elliptical model. Therefore, the next step is to apply the code to the real patient case. We have thirty patients' data total. We have run 5 patients data out of these 30 patients. The results are really promising. Unexpectedly, this improvement is not as easy as it might look like. Since there are more than 60 slices for every patient, the time we spent on running the code is much longer than we expected. As shown in figure 4, the left image of each part is a clinical dose distribution and the right image is a predicted dose distribution that we created. This is one of many patient data that we analyzed. The reason we choose this specific patient as an example is because not only its outcome could show both the advantages of our tool and the limitations which could give us a direction for future development, but also it covers many cases that our tool might deal with in clinical trials. First of all, the predicted dose distribution is different from clinical dose distribution since the tool we developed will assume the spread function is uniform in every direction. There are three total targets in this patient which could be seen in figure 4 d and these three targets are not very parallel in space. The first three images show two targets and the last three images have all three targets displayed. This suggests that our code works very well no matter how many targets there in the patients. However, despite the promising results we got from the RTD calculator, there are still some problems waiting to be solved in our project. As displayed in figure 4, a,b and d, the code malfunctions in part of the area and just assume the dose values are one which is the same as the voxels inside the target. If there are more than one target in the patient, this situation will happen when the slices chosen just include one of the targets. This drawback won't affect our final results but hopefully we could fix it in the future.

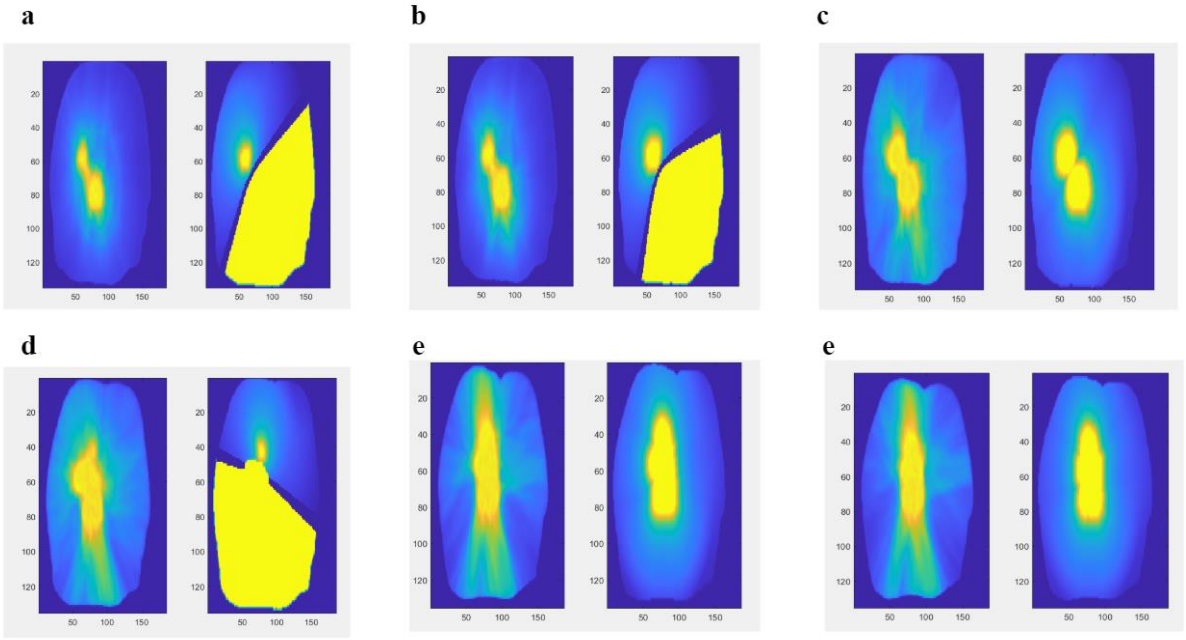

Figure 4 Comparison between clinical dose distribution and predict dose distribution

Figure 5 shows the comparison between the integral dose of clinical data and predict data. We applied the code to 10 patients out of 30 patients due to lack of time caused by the COVID-19 situation. The solid line is for the predict integral dose and the dash line is for the clinical integral dose. Most of the curves start to increase after the first 20 slices because the first slices don't contain the voxels that have positive dose values and thus the integral dose remains zero. As shown in Figure 5, the solid lines are really close to the dash lines suggesting the success of the RTD calculator.

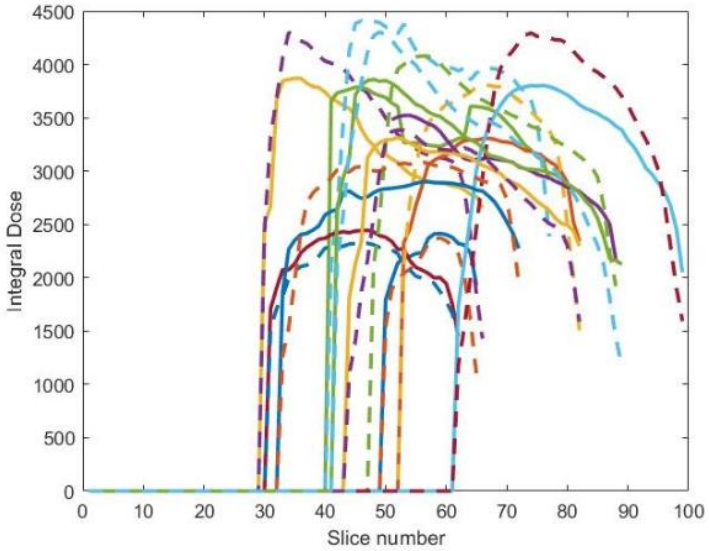

Figure 5 Integral dose for clinical data and predict data

Discussion

Manual methods used in radiotherapy planning would be replaced by automation. In order to ensure consistency of quality and retain necessary doctor decisions, automation should provide a patient-specific plan set, including theoretically achievable DVH values and trade-offs. We introduced an automated algorithm to perform this key step of clinical radiation oncology artificial intelligence integration. We created a dosimetry prediction model that allowed a priori estimation of three-dimensional dosimetry, dose rate and dose tradeoff space, organ risks, and different administration strategies. We also evaluated the accuracy of the RTD calculator and results show that RTD calculator is accurate. However, as we mentioned above, there are some limitations in this calculator which requires further development. Based on the high gradient and low gradient dose distributions from previous dosimetry, the 3D dose distribution of the patient was estimated.[7] This method was applicable to challenges posed by the anatomy of a specific patient while maintaining the doctor's decision through nuclear variation in the target region. We can find the DVH of each voxel in the region of interest, and our program should solve the problems caused by the irregular shape of organs and the overlap between organs. Therefore, when clinicians query the previous patient data, they would have a more accurate and precise similarity between the data and the current patient.

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