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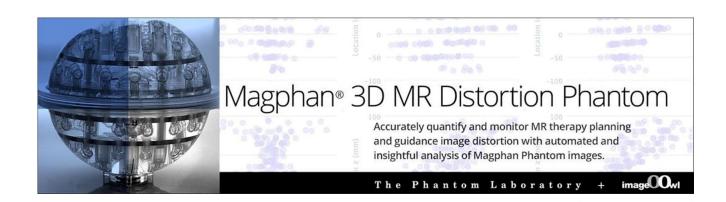
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Knowledge-based IMRT treatment planning for prostate cancer

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Purpose: To demonstrate the feasibility of using a knowledge base of prior treatment plans to generate new prostate intensity modulated radiation therapy (IMRT) plans. Each new case would be matched against others in the knowledge base. Once the best match is identified, that clinically approved plan is used to generate the new plan.

Methods: A database of 100 prostate IMRT treatment plans was assembled into an information-theoretic system. An algorithm based on mutual information was implemented to identify similar patient cases by matching 2D beam's eye view projections of contours. Ten randomly selected query cases were each matched with the most similar case from the database of prior clinically approved plans. Treatment parameters from the matched case were used to develop new treatment plans. A comparison of the differences in the dose–volume histograms between the new and the original treatment plans were analyzed.

Results: On average, the new knowledge-based plan is capable of achieving very comparable planning target volume coverage as the original plan, to within 2% as evaluated for D_{98} , D_{95} , and D_1 . Similarly, the dose to the rectum and dose to the bladder are also comparable to the original plan. For the rectum, the mean and standard deviation of the dose percentage differences for D_{20} , D_{30} , and D_{50} are $1.8\% \pm 8.5\%$, $-2.5\% \pm 13.9\%$, and $-13.9\% \pm 23.6\%$, respectively. For the bladder, the mean and standard deviation of the dose percentage differences for D_{20} , D_{30} , and D_{50} are $-5.9\% \pm 10.8\%$, $-12.2\% \pm 14.6\%$, and $-24.9\% \pm 21.2\%$, respectively. A negative percentage difference indicates that the new plan has greater dose sparing as compared to the original plan.

Conclusions: The authors demonstrate a knowledge-based approach of using prior clinically approved treatment plans to generate clinically acceptable treatment plans of high quality. This semiautomated approach has the potential to improve the efficiency of the treatment planning process while ensuring that high quality plans are developed. © 2011 American Association of Physicists in Medicine. [DOI: 10.1118/1.3574874]

Key words: treatment planning, IMRT, mutual information, knowledge-based

I. INTRODUCTION

Prostate cancer is the most common cancer among men of all races in the United States, accounting for 192 280 new cases in 2009. Most prostate cancer patients undergo intensity modulated radiation therapy (IMRT), which results in 90% disease-free rates after 5 years for early stage cases. IMRT has been shown to permit the delivery of higher therapeutic dose to the target volume while reducing dose to adjacent organs at risk, i.e., bladder, rectum, and femoral heads. The goal of radiotherapy treatments is to deliver effective treatment while maximizing patient survival and quality of

life. Given the prevalence of prostate cancer and the reliance on IMRT for treating it, any improvements to prostate IMRT can have an immediate and a substantial clinical impact.

Currently, each IMRT plan is developed *de novo* and optimized using a trial-and-error approach that is both time consuming and subjective and, more importantly, may not even be maximally optimal in sparing critical organs. The entire process of IMRT treatment planning can take several hours per case to achieve a clinically acceptable plan. ^{4,5} The iterative process involves striking a compromise between the conflicting constraints of providing homogenous coverage of the prostate target volume while simultaneously sparing dose to

the adjacent normal critical structures. While a plan can be deemed clinically acceptable, that plan can be far from clinically optimal if the dose to the normal tissue is not minimized to the best extent possible. Many community centers utilize dose constraints that are published in the literature as the limit below which there are no complications. However, since these limits are population-based, the best strategy for any individual patient would be to reduce the dose as much as possible by pushing the limits of dose sparing, which is the approach used at our institution. Unfortunately, this strategy can be time consuming and highly dependent on the skill and experience of the planner. A large multi-institution study reported that there is a wide variability across medical institutions between the prescribed radiation dose and the dose delivered, with 46% of the patients receiving a maximum dose that was more than 10% higher than the prescribed dose while 63% of the patients received a dose that was more than 10% lower than the prescribed dose. This implies that plans at centers with limited expertise may not be clinically optimal, in that they may not minimize the bladder and rectal doses to the maximum extent possible. We address this problem by developing a semiautomated approach to IMRT treatment planning, whereby we leverage the prior knowledge and experience about the treatment planning approaches used to achieve the greatest possible rectum/bladder sparing without compromising target coverage.

Knowledge-based approach in radiation oncology have been used to develop imaging informatics platforms for proton therapy and radiosurgery. Wu *et al.* also have used a database of plans for IMRT treatment plan quality control as well as for generating dose–volume histogram (DVH) objectives. ^{9,10} The challenges of addressing issues of the variability of manual contouring and segmentation, particularly in head and neck cancers, have been addressed with atlas-based solutions that utilize patient databases. ^{11–13}

In this study, we propose a knowledge-based approach of using similarity metrics to search a patient data reference library of previously generated and clinically approved plans. These existing plans represent a valuable expertise knowledge base that "understands" how best to treat the cancer while minimizing dose to normal tissues. If a new patient can be matched to a similar, existing patient, then the existing data from that match can be used to derive new treatment plans that meet prescription objectives and are patient specific. In other words, by utilizing a knowledge base of prior, clinically approved plans that have been manually optimized, we hypothesize that we can develop a semiautomated system to create new plans that are also clinically acceptable. If successful, this approach of assembling and utilizing a knowledge base of treatment plans can potentially be made available for use at other institutions and may lead to more consistent treatment planning quality across institutions.

II. METHODS AND MATERIALS

II.A. Knowledge-based reference library

In this initial study, we assembled a database of 100 prostate cancer IMRT cases, all of which were previously

planned using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA), reviewed, and delivered within our clinic. IRB permission was obtained for the use of these retrospective cases in this HIPAA-compliant study, and the cases were anonymized prior to use. Each treatment plan includes the CT dataset, tumor/target volume and normal structure contours, beam geometry specifications, beam intensity (fluence) maps, and dose distributions. At our institution, seven coplanar beam angles are typically used: at 25°, 75°, 130°, 180°, 230°, 280°, and 330°.

II.B. Case similarity algorithm

Our hypothesis is that if the relative spatial locations of target volume and normal structures for a new "query" case can be closely matched to a prior "reference" case within the knowledge base, then it may be possible to use the treatment plan parameters from the matched case as an improved starting point in the planning/optimization process. The algorithm for retrieving similar patient cases is based on matching of 2D images, specifically the beam's eye view (BEV) projections of the structure contours. Since each treatment beam "sees" a 2D projection of the 3D treatment volume along the angle of the radiation beam, the projections of the contours become the inputs that determine the aperture and fluence maps in IMRT treatment planning.

Within each BEV projection image, a unique index number is assigned to correspond to the projection of each structure or the overlapping regions of two or more structures. The goal of the image similarity algorithm is to match, to the best extent possible, the projection images for each of the seven beam angles of the query case to the corresponding seven beam angles of prior cases contained in the knowledge base. We use mutual information (MI) as the similarity metric for image matching:

$$MI(X;Y) = \sum_{x} \sum_{y} P(X,Y) \log_2 \frac{P(X,Y)}{P(X)P(Y)},$$
(1)

where P(X) and P(Y) are the marginal distributions and P(X,Y) is the joint probability distribution of two images X and Y. ¹⁴ Because mutual information relies only on the statistical properties of the image histograms, it is more robust at tasks such as image registration and matching compared to traditional linear approaches such as cross correlation. ¹⁵ MI has been widely and effectively used for image registration and fusion of multimodality images. ¹⁶ Additionally, MI has also been used to match 2D ROIs of mammography masses for computer-aided-detection. ^{17–20}

The mutual information for the query case and a reference case was calculated for each of the seven treatment angles. A single composite MI value was calculated from the simple average of the seven MI values corresponding to each of the treatment angle image pairs. The overall MI scores of all the query–reference pairs in the reference library were rank-ordered. A GUI was developed to review the query case images compared with the best matches, and visual inspection of each beam angle match confirmed that the similarity

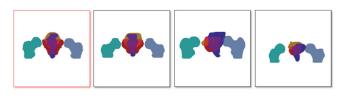


Fig. 1. Projection image matching example: (a) query image, (b) best match (MI=2.8), (c) poor match (MI=1.6), (d) worst match (MI=0.8). [Structures in the PA view shown include the planning target volume, bladder, rectum, and femoral heads.]

algorithm successfully retrieved cases with similar BEVs (Fig. 1).

II.C. Generating new treatment plans

Once the best-matching library reference case was found, the treatment parameters from that case were imported and utilized to develop a new treatment plan for the query case. Those treatment parameters included the beam geometry specifications, the fluence maps, and the final structure constraints and weights used to optimize the reference case during IMRT planning.

Elastix, a deformable registration toolkit using b-splines was implemented to perform minor scaling and translations to improve alignment of the imported fluence to the planning target volume (PTV) of the query case (see example in Fig. 2).²¹

After deformable fluence registration, the resulting dose distribution will likely still need further minor optimization. Under the assumption that the reference and query case are similar, the final constraints and priorities used to previously manually optimize the reference case would also likely almost optimally maximize the query case. Thus, the final step consisted of optimizing the query case using the constraints and priorities from the reference case. The optimization was initiated and allowed to run for a total of 50 iterations (approximately 2–3 min on the Eclipse treatment planning system) without any manual intervention. Note that the prescription doses and constraints from the reference case were appropriately scaled to match the query case.

II.D. Evaluating the treatment plan quality

Table I depicts the prostate IMRT protocol used at our institution to specify the dose-volume constraints for critical

Table I. Duke University's prostate IMRT protocol with dose–volume constraints. All constraints are based on a target dose of 78 Gy.

Critical structure	Dose (Gy)	% Volume	
Bladder	70	20	
Bladder	62.4	30	
Bladder	39	50	
Rectum	98% of Rx dose	0	
Rectum	70	20	
Rectum	56	30	
Rectum	39	50	
Lt femoral head	50	0	
Rt femoral head	50	0	
Penile bulb	30	15	
Small bowel	45	0	

structures. The protocol is similar to those established by the Radiation Oncology and Therapy Group (RTOG) for prostate IMRT clinical trials.²² The typical clinical practice strives to deliver a prescription dose (or higher) to at least 95% of the tumor volume while not exceeding normal structure dose constraints.

In this study, the quality of each of treatment plan was evaluated by comparing the dose-volume histograms of the new semiautomated plan to that of the original plan developed manually by an expert (human) planner for the query case. We considered a plan to be "high quality" if it both (i) met the 95% dose to PTV prescription, and (ii) reduced normal structure dose to the maximum extent possible even below guidelines set forth for bladder, rectum, and femoral heads. That is, any further reduction would compromise the PTV coverage. A comparison of the various DVH cut-points considered the dose to percent volume coverage (D_r, which is the dose to the highest x% of volume) for the PTV and two normal structures (i.e., bladder and rectum). The cutpoints for the PTV were D₉₈, D₉₅, and D₁. Specifically, D₁ was used to quantify the maximum target dose. For both the bladder and the rectum, the respective cut-points at D_{50} , D_{30} , and D_{20} were evaluated.

In this initial study, 10 query cases were randomly selected from the knowledge base of 100 cases. Only the constraints for five major structures were selected and imported, including PTV, bladder, rectum, and the two femoral heads. Each plan was normalized to deliver the

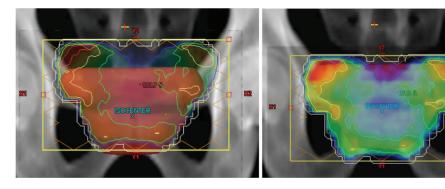


Fig. 2. Imported fluence: (a) before registration (fluence map is shown as contours), (b) after registration (fluence map is shown as colorwash).

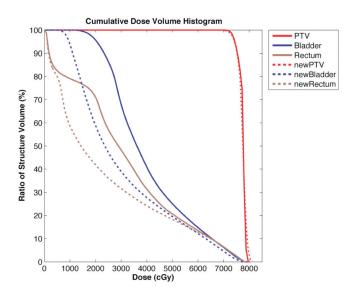


Fig. 3. A comparison of DVHs for the new plan (dashed line) as compared to the original plan (solid lines). As one of the best of ten cases, case 8 demonstrates comparable PTV coverage and considerably greater dose sparing to both rectum and bladder.

prescription dose to approximately 97%–98% of the planning target volume. Using the most similar matched case for 10 query cases randomly selected from the knowledge base of 100 cases, a total of ten new treatment plans were developed in this manner.

III. RESULTS

While the results of all ten query cases are summarized, three of the ten cases have been selected to illustrate, in greater detail, the comparison between the new semiautomatically generated plan and original manual plan DVHs. Treatment plans were evaluated based on the relative percentage differences at specific DVH points:

% diff =
$$100 * (D_{\text{vol-new plan}} - D_{\text{vol-original plan}})/D_{\text{vol-original plan}}$$
. (2)

A negative percentage difference indicates that the new plan has reduced dose as compared to the original plan. For a critical structure, such a negative percentage difference indicates an improvement, that is, greater dose sparing. The DVH of the femoral heads are not plotted to make it easier to visualize the PTV, bladder, and rectum. Figure 3 is the DVH for case 8, which is one of the best of ten cases, in that it shows a very comparable PTV dose distribution between the new plan (dashed lines) and the original plan (solid lines) and considerably greater dose sparing to both bladder and rectum

For case 8, the PTV coverage in the new plan is approximately equal to the original plan; relative percentage differences at D_{98} , D_{95} , and D_1 were -0.5%, -0.1%, and 1.4%, respectively. For the rectum, the new plan consistently demonstrated large additional dose sparing, as shown by the dashed curve of the new plan consistently shifting to the left of the solid line of the original plan. For example, the new plan cut dose at D_{50} in half from 39.1% to 19.3%. Similar dose savings were also demonstrated in the bladder. Detailed

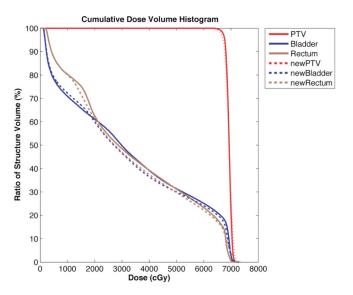


Fig. 4. A comparison of the DVH for case 7, which is representative of the majority of the ten cases. This plot shows that dose to the PTV, rectum, and bladder in the new plan (dashed) are very comparable to the original plan (solid).

cut-point values for all cases are reported below in tables. In summary, case 8 illustrates that the new plan has very comparable PTV coverage and substantial dose sparing to both the bladder and the rectum.

The DVH plot for case 7 is shown in Fig. 4 and is representative of the majority of the ten cases, with very comparable dose distributions for the PTV, bladder, and rectum.

Nine of the ten new plans had comparable DVH results relative to the original clinical plan. Figure 5 illustrates the only case (case 5), which had comparable PTV coverage but higher dose to both bladder and rectum as compared to the original plan. The PTV results are very comparable, with relative percentage differences of -0.5%, -0.2%, and 1.0% at

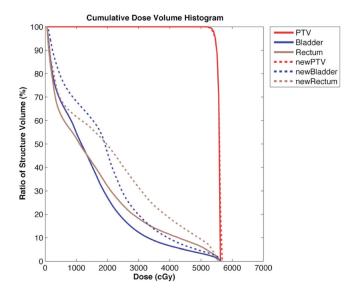


Fig. 5. A comparison of DVH for the PTV, rectum, and bladder of the original plan (solid) and the new knowledge-based plan (dashed) illustrates comparable PTV coverage, but higher dose to both bladder and rectum. However, these normal structure doses are still clinically acceptable since they are far below the dose–volume constraints set forth in the protocol.

Table II. Percentage difference in PTV coverage between new and original plan. (%diff= $100*(D_{\rm vol-new\ plan}-D_{\rm vol-original\ plan})/D_{\rm vol-original\ plan}$).

Case	D_{98}	D_{95}	D_1
1	4.3	4.6	5.6
2	-1.4	0.6	7.7
3	-0.8	0.1	0.6
4	-0.4	-0.1	0.6
5	-0.5	-0.2	1.0
6	-0.4	-0.3	1.0
7	1.8	2.2	4.2
8	-0.5	-0.1	1.4
9	1.0	1.2	1.8
10	-3.5	-1.7	1.4
Mean	-0.03	0.62	2.5
Stdev	2.1	1.7	2.4

Table IV. Percentage difference in bladder dose between new and original plan. (%diff= $100*(D_{\text{vol-new plan}} - D_{\text{vol-original plan}})/D_{\text{vol-original plan}}$).

Case	D_{20}	D ₃₀	D ₅₀
1	4.8	4.9	1.8
2	-15.1	-28.0	-50.2
3	2.8	2.6	-3.2
4	-10.6	-19.6	-32.0
5	25.9	31.2	64.5
6	-27.7	-37.8	-57.3
7	1.6	-1.3	-6.6
8	-9.5	-18.5	-34.7
9	1.2	-4.0	-11.0
10	-0.2	-8.4	-31.0
Mean	-5.9	-12.2	-24.9
Stdev	10.8	14.6	21.2

 D_{98} , D_{95} , and D_1 . However, the bladder dose at D_{20} , D_{30} , and D_{50} values indicated decreased sparing by 25.9%, 31.2%, and 64.5%, respectively. Similarly, the dose to the rectum indicated decreased sparing by 36.4%, 46.5%, and 78.0%, respectively. Although there is substantially higher relative percentage dose to both the rectum and the bladder dose in the new plan, note that in terms of absolute dose-to-volume cut-points, the critical structure doses would still be clinically acceptable since they are far below the dose constraints set forth in the protocol (refer to Table I).

A detailed comparison of the relative percentage differences [Eq. (2)] at specific dose-to-volume values to the PTV for all ten new plans versus the original plans is shown in Table II. A negative value indicates that the new plan has less PTV coverage as compared to the original plan. The average percentage differences for the ten cases (mean \pm standard deviation) at D₉₈, D₉₅ and D₁ are -0.03% \pm 2.1%, 0.62% \pm 1.7%, and 2.5% \pm 2.4%, respectively. On average, the new knowledge-based plan is capable of achieving very comparable PTV coverage to the original plan (within 2% as evaluated for

Table III. Percentage difference in rectum dose between new and original plan. (%diff= $100*(D_{\rm vol-new\ plan}-D_{\rm vol-original\ plan})/D_{\rm vol-original\ plan}$).

Case	D_{20}	D ₃₀	D ₅₀
1	5.9	5.0	-4.0
2	-11.1	-22.1	-35.8
3	2.4	2.7	-19.8
4	-3.2	-14.4	-35.5
5	36.4	46.5	78.0
6	16.3	14.1	23.7
7	1.5	-0.8	-1.6
8	-7.6	-22.1	-50.6
9	10.1	13.3	6.7
10	1.7	1.7	-8.2
Mean	1.8	-2.5	-13.9
Stdev	8.5	13.9	23.6

both D_{98} and D_{95} , as well as for D_1 , the dose to the highest 1% of the PTV volume).

Table III shows the percentage differences between the new and the original plan for the rectum dose at D_{20} , D_{30} , and D₅₀ for the ten cases. For the normal structures, a negative value indicates an improvement, in which the new plan has a greater dose sparing to the rectum as compared to the original plan. For the ten cases, the mean and standard deviation for the rectum dose percentage differences for D₂₀, D₃₀, and D_{50} are $1.8\% \pm 8.5\%$, $-2.5\% \pm 13.9\%$, and $-13.9\% \pm 23.6\%$, respectively. Three of the ten new plans (cases 2, 4, and 8) have greater rectal dose sparing as compared to the original plan, while five (cases 1, 3, 7, 9, and 10) are quite comparable to the original plan. Although the percentage differences for D_{20} , D_{30} , and D_{50} for cases 5 and 6 appear high, the absolute dose values are still clinically acceptable since they fall below the dose constraints set forth in the original protocol (refer to Table I).

Lastly, Table IV shows the percentage differences between the new and the original plan for the bladder dose at D_{20} , D_{30} , and D_{50} for the ten cases. A negative value indicates an improvement, in which the new plan has greater dose sparing to the bladder as compared to the original plan. For the ten cases, the mean and standard deviation for the bladder dose percentage differences for D_{20} , D_{30} , and D_{50} are $-5.9\% \pm 10.8\%$, $-12.2\% \pm 14.6\%$, and $-24.9\% \pm 21.2\%$, respectively. Five of the ten new plans (cases 2, 4, 6, 8, and 10) have substantially less dose to the bladder, while four (cases 1, 3, 7, and 9) are very comparable to the original plan. As previously mentioned, for case 5, the percentage differences for D_{20} , D_{30} , and D_{50} may appear to be high, but the absolute dose values are still clinically acceptable since they fall below the dose constraints set forth in the original protocol (refer to Table I).

IV. DISCUSSION

We have found that a new IMRT treatment plan can be developed semiautomatically by importing the set of

fluences from a prior optimized case selected from a knowledge-based reference library, without having to start anew from a blank slate, as is typically done in manual planning.

IV.A. Size of knowledge base

To demonstrate the feasibility of using the knowledgebased approach to develop new treatment plans, our initial study randomly selected 10 test cases from a database of 100 prior cases. Recognizing that the relatively small number of test cases may have limited statistical power, we are still encouraged by the potential of utilizing a knowledge-based treatment planning approach to produce clinically acceptable treatment plans. We hope to observe useful trends as we expand our database and continue to develop more treatment plans. As we continue to increase the size of the database, we intend to study the effect of the knowledge-base diversity on the overall system performance. For example, we did not include boost plans in our initial database; although we could construct a separate database of boost plans and develop treatment plans specific to boost treatments. Additionally, we intend to collect cases from outside institutions to investigate interinstitutional variability of treatment planning, as well as the appropriateness of utilizing our knowledge base across institutions.

IV.B. Contouring consistency across institutions

We recognize that inconsistencies in structure contouring, particularly across different institutions, may present some challenges in the implementation of our specific algorithm across institutions. For example, some institutional practices include nodal involvement when defining the PTV will result in larger PTV contour regions, which in turn may not appear in the knowledge base constructed at an institution that does not share that practice. Similarly, the contouring protocols are related to the dose prescription of that institution (i.e., posterior PTV margin adjacent to rectum is related to dose escalation protocols). However, we believe that the general framework for knowledge-based treatment planning can still be implemented across institutions using site-specific guidelines concerning structure definition and margins. Further adoption of RTOG contouring and prescription protocols as well as increasingly robust atlas-based solutions may also help reduce the practice variability across institutions, and thus, it would be quite feasible to implement a national archive of knowledge cases for use across institutions.

IV.C. Improving case similarity retrieval

In this initial study, our algorithm identified the single best-matched case based on the simple sum of the seven individual MI values for each beam angle. We investigated whether the simple average of seven individual MI scores could mask the extent of individual geometric matching information at each beam angle. Empirically, we found that by using the GUI to visually review the top five matched cases (based on the average MI score) from the entire database nearly always yielded individual beam-angle MI scores that

were also high. In the future, we plan to explore alternative methods of improving the case-similarity matching, such as weighting schemes based on beam angle. It may also be possible to improve case similarity retrieval through matching the full 3D volumetric dataset, rather than simply using the beam's eye view projection images.

Our study implemented MI as a case-similarity approach to search for a small set of best-matched cases from the entire database but does not rely on MI as the sole determinant of dose-constraint satisfaction. Since the primary objective of treatment planning is to provide adequate PTV coverage, we have found that by further applying deformable registration to align the imported fluences of the matched case to the PTV of the query case, it effectively aids the optimizer by providing a good starting point to help successive optimization to proceed. We found that if we were to leave out the deformable registration of the fluence map with the PTV, the treatment plan does not yield adequate PTV coverage. The third and last step involves importing the optimization weights from the matched case, which the optimizer then utilizes to satisfy the dose constraints. We found that by using this three-step process, the optimizer required very few steps to converge.

IV.D. Assessing DVH plan quality

We intend to investigate methods to correlate the similarity metric with the overall treatment plan quality. Currently, we chose to evaluate the plan quality based on the DVH cut-points specified by the protocol at our institution. We compared each new semiautomated plan with the original manually developed plan at these specified normal structure constraints. There is still considerable disagreement about the specific values for dose/volume limits for normal tissue.²³ The RTOG Prostate Group Consensus recently reported for the rectum, 50 Gy \leq 50% and 70 Gy \leq 20%, and for the bladder, 55 Gy \leq 50% and 70 Gy \leq 30%. The limits for the femoral heads were set at <5% for 50 Gy and for the small bowel at 0% for 52 Gy.²⁴ Similar dose/volume limits were recently reported in the recent QUANTEC study, for the rectum: 50 Gy < 50%, 60 Gy < 35%, 65 Gy < 25%, 70 Gy < 20%, and 75 Gy < 15%. 25,26 For the bladder, the reported limits are 65 Gy < 50%, 70 Gy < 35%, 75 Gy < 25%, and 80 Gy < 15%. The protocol at our institution specifies even more conservative normal tissue constraints (refer to Table I). Thus, we chose not to assess DVH plan quality based on absolute differences from the normal tissue constraints, as these limits are typically already very generous, are population-based, and are related to the clinical end-points corresponding to late tissue toxicities. Rather, we assessed the individual DVH plan quality of a new plan by a comparison with the original plan, as that best reflects the extent to which the new semiautomated plan can strive to meet the (human) achievable limits of dose sparing.

IV.E. Reduction in treatment planning time

We found that the knowledge-based treatment planning approach can significantly reduce planning time by skipping past all but the last few iterations of the planning process. For each of the 10 test cases, approximately 50 iterations were required to meet the optimization objectives, taking approximately 2–3 min on the Eclipse treatment planning workstation. Additionally, these iterations were allowed to proceed automatically, with no human input other than initiating the optimization. It is foreseeable that several treatment plans optimized for different clinical objectives (i.e., rectal sparing) can be quickly generated in this manner and made available for the clinician to choose from. Knowledge-based treatment planning offers the potential to improve the efficiency of the treatment planning process while maintaining high quality.

IV.F. Other disease sites

We initially selected prostate cancer in order to investigate the feasibility of a knowledge-based treatment planning approach for two reasons: (i) the high volume of prostate cancer cases presenting in radiation oncology, and (ii) the relative ease of IMRT treatment planning for prostate cancer as compared to more challenging disease sites such as head and neck. It may be possible to extend this approach to other disease sites (i.e., head and neck) that are more challenging and time consuming to plan. Additionally, since head and neck cases typically arise less frequently than prostate cases, many sites with limited experience and planning expertise could benefit from the expertise of a knowledge-base system based on cases assembled from multiple institutions.

V. CONCLUSIONS

The IMRT treatment planning process is an iterative time consuming process that is highly dependent on the skill and experience of the planner. It has been reported that there is wide variability across medical institutions between the prescribed radiation dose and the dose delivered, which is suggestive of the potentially significant variability in the quality of treatment plans across institutions. We demonstrate the potential of using a knowledge base of prior optimized treatment plans to generate clinically acceptable prostate IMRT treatment plans for new cases. This approach involves identifying the most similar patient case in the database and adapting its parameters to the new case. Knowledge-based treatment planning demonstrates the feasibility for a semiautomated treatment planning solution to improve the efficiency of the treatment planning process while ensuring that high quality plans are developed.

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- ¹A. Jemal, R. Siegel, E. Ward, Y. Hao, J. Xu, and M. J. Thun, "Cancer statistics, 2009," CA Cancer J. Clin. **59**, 225–249 (2009).
- ²O. Cahlon, M. Hunt, and M. J. Zelefsky, "Intensity-modulated radiation therapy: Supportive data for prostate cancer," Semin. Radiat. Oncol. 18, 48–57 (2008).
- ³S. Webb, *Intensity-Modulated Radiation Therapy* (Institute of Physics Publishing, Bristol/Philadelphia, 2001).
- ⁴D. Djajaputra, Q. Wu, Y. Wu, and R. Mohan, "Algorithm and performance of a clinical IMRT beam-angle optimization system," Phys. Med. Biol. **48**, 3191–3212 (2003).
- ⁵A. Pugachev, J. G. Li, A. L. Boyer, S. L. Hancock, Q. T. Le, S. S. Donaldson, and L. Xing, "Role of beam orientation optimization in intensity-modulated radiation therapy," Int. J. Radiat. Oncol., Biol., Phys. **50**, 551–560 (2001).
- ⁶I. J. Das, C. W. Cheng, K. L. Chopra, R. K. Mitra, S. P. Srivastava, and E. Glatstein, "Intensity-modulated radiation therapy dose prescription, recording, and delivery: Patterns of variability among institutions and treatment planning systems," J. Natl. Cancer Inst. 100, 300–307 (2008).
- ⁷B. J. Liu, "A knowledge-based imaging informatics approach for managing proton beam therapy of cancer patients," Technol. Cancer Res. Treat. **6**, 77–84 (2007).
- ⁸K. J. Lee, D. C. Barber, and L. Walton, "Automated gamma knife radiosurgery treatment planning with image registration, data-mining, and Nelder-Mead simplex optimization," Med. Phys. **33**, 2532–2540 (2006).
- ⁹B. Wu, F. Ricchetti, G. Sanguineti, M. Kazhdan, P. Simari, M. Chuang, R. Taylor, R. Jacques, and T. McNutt, "Patient geometry-driven information retrieval for IMRT treatment plan quality control," Med. Phys. **36**, 5497–5505 (2009).
- ¹⁰B. Wu, F. Ricchetti, G. Sanguineti, M. Kazhdan, P. Simari, R. Jacques, R. Taylor, and T. McNutt, "Data-driven approach to generating achievable dose-volume histogram objectives in intensity-modulated radiotherapy planning," Int. J. Radiat. Oncol., Biol., Phys. 79, 1241–1247 (2010).
- ¹¹X. Han, M. S. Hoogeman, P. C. Levendag, L. S. Hibbard, D. N. Teguh, P. Voet, A. C. Cowen, and T. K. Wolf, "Atlas-based auto-segmentation of head and neck CT images," Med. Image Comput. Comput. Assist. Interv. 11, 434–441 (2008).
- ¹²L. J. Stapleford, J. D. Lawson, C. Perkins, S. Edelman, L. Davis, M. W. McDonald, A. Waller, E. Schreibmann, and T. Fox, "Evaluation of automatic atlas-based lymph node segmentation for head-and-neck cancer," Int. J. Radiat. Oncol., Biol., Phys. 77, 959–966 (2010).
- ¹³G. Strassmann, S. Abdellaoui, D. Richter, F. Bekkaoui, M. Haderlein, E. Fokas, N. Timmesfeld, B. Vogel, M. Henzel, and R. Engenhart-Cabillic, "Atlas-based semiautomatic target volume definition (CTV) for head-and-neck tumors," Int. J. Radiat. Oncol., Biol., Phys. 78, 1270–1276 (2010).
- ¹⁴T.M. Cover and J. A. Thomas, *Elements of Information Theory* (Wiley, New York, 1991).
- ¹⁵W. Li, "Mutual information functions versus correlation functions," J. Stat. Phys. **60**, 823–837 (1990).
- ¹⁶C. Studholme, D. L. Hill, and D. J. Hawkes, "Automated three-dimensional registration of magnetic resonance and positron emission tomography brain images by multiresolution optimization of voxel similarity measures," Med. Phys. 24, 25–35 (1997).
- ¹⁷G. D. Tourassi, R. Vargas-Voracek, D. M. Catarious, Jr., and C. E. Floyd, Jr., "Computer-assisted detection of mammographic masses: A template matching scheme based on mutual information," Med. Phys. 30, 2123–2130 (2003).
- ¹⁸G. D. Tourassi, E. D. Frederick, M. K. Markey, and C. E. Floyd, Jr., "Application of the mutual information criterion for feature selection in computer-aided diagnosis," Med. Phys. 28, 2394–2402 (2001).
- ¹⁹G. D. Tourassi, B. Harrawood, S. Singh, J. Y. Lo, and C. E. Floyd, "Evaluation of information-theoretic similarity measures for content-based

- retrieval and detection of masses in mammograms," Med. Phys. 34, 140–150 (2007).
- ²⁰G. D. Tourassi, B. Harrawood, S. Singh, and J. Y. Lo, "Information-theoretic CAD system in mammography: entropy-based indexing for computational efficiency and robust performance," Med. Phys. 34, 3193–3204 (2007).
- ²¹M. S. S. Klein, K. Murphy, M. A. Viergever, and J. P. W. Pluim, "Elastix: A toolbox for intensity based medical image registration," IEEE Trans. Med. Imaging 29, 196–205 (2010).
- ²²RTOG 0126-A Phase III Randomized Study of High Dose 3D-CRT/IMRT versus Standard Dose 3D-CRT/IMRT in Patients Treated for Localized Prostate Cancer, 2008.
- ²³M. T. Milano, L. S. Constine, and P. Okunieff, "Normal tissue tolerance dose metrics for radiation therapy of major organs," Semin. Radiat. Oncol. 17, 131–140 (2007).
- ²⁴C. A. Lawton, J. Michalski, I. El-Naqa, M. K. Buyyounouski, W. R. Lee, C. Menard, E. O 'Meara, S. A. Rosenthal, M. Ritter, and M. Seider, "RTOG GU Radiation oncology specialists reach consensus on pelvic lymph node volumes for high-risk prostate cancer," Int. J. Radiat. Oncol., Biol., Phys. 74, 383–387 (2009).
- ²⁵A. Jackson, L. B. Marks, S. M. Bentzen, A. Eisbruch, E. D. Yorke, R. K. Ten Haken, L. S. Constine, and J. O. Deasy, "The lessons of QUANTEC: recommendations for reporting and gathering data on dose-volume dependencies of treatment outcome," Int. J. Radiat. Oncol., Biol., Phys. 76, S155–S160 (2010).
- ²⁶L. B. Marks, E. D. Yorke, A. Jackson, R. K. Ten Haken, L. S. Constine, A. Eisbruch, S. M. Bentzen, J. Nam, and J. O. Deasy, "Use of normal tissue complication probability models in the clinic," Int. J. Radiat. Oncol., Biol., Phys. 76, S10–S19 (2010).