Pareto Optimal Projection Search (POPS): Automated Treatment Planning by Direct Search of the Pareto Surface

Charles Huang, Yong Yang, Neil Panjwani, and Lei Xing

Abstract—Objective: Treatment planning is a time-consuming, iterative process with potentially high inter-planner variability. Fully automated treatment planning processes could reduce a planner’s active treatment planning time and remove inter-planner variability, with the potential to tremendously improve patient turnover and quality of care. In developing fully automated algorithms for treatment planning, we have two main objectives: to produce plans that are 1) pareto optimal and 2) clinically acceptable. Here, we propose the pareto optimal projection search (POPS) algorithm, which provides a general framework for directly searching the pareto front. Methods: Our POPS algorithm is a novel automated planning method that combines two main search processes: 1) gradient-free search in the decision variable space and 2) projection of decision variables to the pareto front using the bisection method. We demonstrate the performance of POPS by comparing with clinical treatment plans. As one possible quantitative measure of treatment plan quality, we adopt a clinical acceptability scoring function (SF) modified from the previously developed general evaluation metric (GEM). Results: On a dataset of 21 prostate IMRT cases collected at the Stanford Radiation Oncology Clinic (SROC), our proposed POPS algorithm produces pareto optimal plans that perform well in regards to clinical acceptability. Compared to the SF scores of manually generated plans, SF scores for POPS plans were significantly better ($p = 2.6 \times 10^{-7}$). Conclusion: Our proposed POPS algorithm provides a general framework for fully automated treatment planning that achieves clinically acceptable dosimetric quality without requiring active planning from human planners. Significance: Our fully automated POPS algorithm addresses many key limitations of other automated planning approaches, and we anticipate that it will substantially improve treatment planning workflow.

Index Terms— Automated treatment planning, POPS, Pareto optimal, Plan Optimization

I. INTRODUCTION

EXTERNAL beam radiation therapy involves the delivery of ionizing radiation with the intent to treat diseased tissue while minimizing dose to healthy organs [1], [2]. The goal of treatment planning is then to determine optimal beam angles, shapes, intensities, etc. that satisfy this overall clinical objective.

Prior to treatment, medical images are collected for the patient (e.g. CT, MRI, or PET scans), and physicians contour various anatomical structures on the collected images, including the planning target volume (PTV) and surrounding organs-at-risk (OARs) [3], [4]. For the case of intensity modulated radiation therapy (IMRT), planners determine the appropriate plan configuration (i.e. beam type, beam angle arrangement, etc.) and perform inverse planning to achieve a desired dose distribution or to satisfy various objectives and constraints [3], [4].

Traditionally, treatment planning has been regarded as a manual, iterative process to be performed by human planners. In this process, planners repeatedly adjust treatment planning parameters (TPPs), such as objective weights, dose constraint values, etc., until a clinically acceptable treatment plan solution is found. The iterative planning process is often conceptualized as a two-loop optimization process [5]. This iterative planning process is not only time-consuming and labour intensive, but the resulting plan quality highly depends on planner skill and experience [6]–[12], [5].

In developing automated methods for treatment planning, two main considerations are to produce plans that are pareto optimal and clinically acceptable. We also point out the distinction between automated methods (i.e. methods that reduce active planning from a human planner) and fully automated methods (i.e. methods requiring no active planning from a human planner). Pareto optimal plans are efficient—that is we cannot improve one aspect (e.g., reduce the dose in one OAR) without compromising at least one other aspect (e.g., reduce the PTV dose)[13], [14]. Plans that are not pareto optimal (i.e. dominated plans) are inefficient, and there exists a more optimal plan that, for instance, achieves better organ

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sparing for all OARs. Intuitively, producing efficient plans is a cornerstone of high-quality patient care, but not all pareto optimal plans are acceptable clinically. It is, therefore, critically important to produce plans that both efficient and clinically acceptable.

A. Related Works

Here, we provide a summary of various automated treatment planning approaches and point to a more in-depth review [15] for interested readers. Limitations with iterative treatment planning have spurred great interest in automated approaches, which can generally be categorized as knowledge-based planning (KBP) [16]–[19], protocol-based planning (PBP) [7], [8], [20]–[23], and multicriteria optimization (MCO) [6], [13], [24]–[27]. As each category of approach has its own benefits and drawbacks, no clear consensus has been reached on an approach that can replace manual planning, and, in practice, a combination of various approaches may be used in a case-by-case fashion.

KBP methods are a category of methods based on the premise that treatment planning results can be predicted from the geometric and anatomical information of a patient [16]. KBP typically follows the paradigm of training a supervised machine learning model on a dataset of previously generated treatment plans. Given input information in the form of a patient’s CT and structure segmentations, a knowledge-based model attempts to predict voxel-wise dose or the dose-volume histogram (DVH) [16]–[19]. Previous works report that knowledge-based models can accurately predict treatment planning results [16]–[18], but these results are often limited to a subset of the information in treatment plans (i.e. dose distribution, DVH, etc.) and are not equivalent to performing the treatment planning process. In cases where KBP performs poorly, lack of model interpretability limits the usability of KBP approaches. Moreover, because KBP is typically formulated as a supervised learning problem, it also does not guarantee that pareto optimal plans are produced and, instead, only attempts to produce plans that are similar to the ground-truth data used in training. Moreover, due to the potential overfitting of these trained models and their lack of interpretability (i.e. being regarded as black-box models due to complexity of model architectures), their practical usability in the clinic is currently limited.

PBP methods are a category of methods that employ rules or heuristics to mimic an experienced treatment planner performing iterative planning. Previous works have proposed various rules for adjusting treatment planning parameters (i.e. objective weights, constraint values, etc.) based on advice from consulted physicians [8], [20]–[23]. Others have followed a model-free approach, opting to use reinforcement learning to mimic human planners [7].

While protocol-based methods may offer a practical approach to automation, there are two main limitations that have yet to be addressed. First, the design of rules or heuristics for protocol-based planning highly depends on the perspective of the planner, leading to variable plan quality between institutions or even individual planners [8], [9]. Automated approaches, ideally, should remove inter-planner variability and provide a baseline method for producing high-quality treatment plans, but the issue of inter-planner variability remains very present in protocol-based approaches. Second, just as knowledge-based planning does not necessarily produce pareto optimal plans, protocol-based planning does not either.

Unlike KBP and PBP approaches, MCO approaches attempt to generate pareto optimal treatment plans. That is, treatment plans in which we cannot improve one aspect (e.g., reduce the dose in one OAR) without compromising at least one other aspect (e.g., reduce the PTV dose). Multicriteria optimization approaches can be further divided into a posteriori MCO [13], [24], [25] and a priori MCO [6], [26], [27].

In a priori MCO, a pareto optimal solution is found according to provided preferences. Such approaches require sufficient preference information to be provided by the planner, and some notable examples include scalarization (e.g. $\epsilon$-constraint method, achievement scalarization, etc.) [28], prioritized optimization [6], [26], [27], and the lexicographic method [29]. Translating physicians’ intuitions regarding ideal planning to a list of preferences, however, is no trivial task, and sometimes treatment plan solutions found from preference information may not align with a planner’s expectations. Where
The purpose of our fully automated POPS algorithm is to produce treatment plans that are both pareto optimal and optimal with respect to clinical acceptability. Alternative automated approaches like KBP and PBP have a key limitation in that they do not necessarily generate pareto optimal plans. Moreover, alternative MCO approaches discuss methods for generating the pareto front while delegating the task of selecting the acceptable plan to a human planner. Our approach provides a practical way to search the pareto front for clinically acceptable plans, producing plans that are both pareto optimal and clinically acceptable.

As previously mentioned, pareto optimal plans are non-dominated and further improvements to the plan in regards to one aspect are only made by trading-off in regards to other aspects. Intuitively, pareto optimal treatment plans lie on the front between the region of feasible and infeasible plans. As described previously, one valid way of formulating the problem is to perform multicriteria optimization with multiple weighted objective functions. Such an approach, however, involves a separate decision space and objective function space (as depicted in Figure 1a). Our proposed POPS algorithm instead formulates the iterative treatment planning problem as a feasibility search, which allows for a more direct relationship between the decision and constraint feasibility spaces (Figure 1b). We can then project points from the decision space to the constraint feasibility space and utilize any gradient-free searching algorithm to navigate to our desired treatment plan solution.

B. Quantifying Clinical Acceptability

By convention, the evaluation of treatment plans has been a manual, iterative, and qualitative process. In performing their qualitative evaluation, physicians ideally draw on their repository of clinical experience to judge various components of the plan. Previous works that explore various DVH constraints have attempted to operationalize the considerations made in a physician’s qualitative assessment [12], [30], [31]. Similarly, evaluation of treatment plans through various metrics.
has been used previously in knowledge based planning [16]–[18], as well as more broadly for data analytics [12], [30], [31].

To summarize the general intuition that can be followed in quantifying clinical acceptability of treatment plans, the overall quality of a treatment plan can be determined by assessing its performance in regards to individual metrics and criteria. We can first define a list of criteria, termed clinical acceptability criteria, that a physician might incorporate into their evaluation. As a foundation for our proposed list, we incorporate criteria from the list of DVH constraints discussed in Chen et al.[32]. While this particular list of criteria may not be agreeable to every physician, the entries can be readily changed to suit individual preferences or to follow various institutional protocol. Essentially each criteria represents a chosen control point on the DVH, and while we use the control points identified in Chen et al., other control points may certainly be used to similar effect. The main heuristic we follow in selecting these criteria is to provide relatively uniform sampling to the DVH for each organ. Based on advice from consulted physicians and our uniform sampling heuristic, we then incorporate additional criteria to judge sparing of the body, separate from sparing of surrounding OARs. The full list of criteria is included in Table 1.

From a list of criteria, we can then design individual scoring functions ideally tailored to the criteria and structure being judged. Previous works have proposed a variety of scoring functions [12], [30], [31]. While some of these scoring functions (e.g. step function, regret, etc.) are too broad and lack organ-specific considerations [12], [31], other scoring functions incorporate organ-specific considerations implicitly through the use of statistics that require a long history of treatment plan solutions [30].

Our adopted SF score, instead, attempts to incorporate interpretable, organ-specific scoring from literature [30] without requiring a lengthy history of treatment plan solutions. To that end, we modify the previously proposed generalized evaluation metric (GEM) score, replacing its gamma distribution probability term with piece-wise sigmoid functions.

\[
SF = \begin{cases} 
\frac{1}{\sum_{s \in S} 2^{-Priority_s} \cdot \sum_{i \in s} \sigma_i^{\pm}(PV_i - CV_i, \alpha_1, \alpha_2)} \, & \text{if solution is infeasible} \\
\frac{1}{\sum_{s \in S} 2^{-Priority_s} \cdot \sum_{i \in s} \sigma_i^{\pm}(PV_i - CV_i, \alpha_1, \alpha_2)} & \text{otherwise}
\end{cases}
\]

As shown in Equation 1 and 2, the intuition of organ-specific scoring is encapsulated by tailored piece-wise sigmoid functions (where \(\alpha_1\) and \(\alpha_2\) describe the steepness of the sigmoid functions and are chosen empirically) and a priority-based weighting (where the weighting scheme is adapted from Mayo et al. [30]). To select the steepness of the sigmoid functions, we adhere to the following heuristics:

1. Decreasing DVH values for each organ imply better sparing to that organ
2. Organ doses approaching 0 have diminishing returns, in regards to score
3. Not satisfying the listed clinical acceptability criteria is highly undesirable and intuitively results in a bad score

Following these heuristics, \(\alpha_1\) is selected to be small in order to abide by heuristic 2 and \(\alpha_2\) is selected to be large relative to \(\alpha_1\) in order to abide by heuristic 3. Priority values for each OAR were selected based on advice from consulted physicians.

Following the precedent of Mayo et al.[30], our clinical acceptability criteria do not include the target volume. For prostate IMRT, where the target volume is relatively large and the dose distribution to the target is relatively homogeneous (at least for the dose constraints used here), inclusion of target volume clinical acceptability criteria may be unnecessary. For other regions of the body or in particularly complex treatment planning cases, target volume criteria can certainly be incorporated without affecting POPS performance.

In Equation 2, \(s\) refers to a structure (OAR) in the structure set \(S\). The priority of a specific structure, \(Priority_s\), adjusts its exponential weighting. \(i\) refers to a clinical acceptability criteria (as listed in Table 1), \(N_o\) refers to the total number of clinical acceptability criteria for a specific structure, and \(\sigma^{\pm}\) refers to the structure score computed using a piecewise sigmoid function of the difference between the plan value \(PV_i\) and the criteria value \(CV_i\).

As an example, to compute the structure score for the second bladder criteria \((D(55%) \leq 47)\), we first compute the difference \(z_i = PV_i - CV_i\). Here, \(CV_i = 47\) Gy and \(PV_i\) is found as the corresponding dose on the bladder DVH for 55% volume. In this toy example, we use a plan value \(PV_i = 20\) Gy, \(\alpha_1 = 0.2\), and \(\alpha_2 = 3\). We would then compute the structure score \(\sigma^{\pm}(z_i, \alpha_1, \alpha_2) = 0.0045\). Assuming the solution is feasible, the scoring function then performs a weighted-average using OAR priorities. Our results use the priorities as listed in Table 1, which were determined based on advice from consulted physicians, but they may also be changed to better suit individual planner preferences.

Intuitively, our proposed SF scores treatment plans on a scale between 0 and 1, where lower scores are better. Plans that attain scores of 0.5 satisfy the listed clinical acceptability criteria, on
average. Plans that attain scores smaller than 0.5 achieve better OAR sparing, on average, than a plan that just satisfies the listed clinical acceptability criteria.

C. POPS Algorithm

The general methodology of our proposed POPS algorithm combines two search methodologies: 1) a projection from the decision variable space to the pareto front using the bisection method and 2) a gradient-free search (i.e. simplex search) of the decision variable space—and the corresponding points on the pareto front—for a clinically acceptable treatment plan. Our implementation utilizes Nelder-Mead simplex search due to its simplicity, but our methods can incorporate any gradient-free optimization approach. To allow for better reproducibility of our results, we implement our approach using the open-source MatRad software package.

To start, we define the coordinates of a point \( p \) in the decision variable space as \( (c_1, c_2, ..., c_n) \) (i.e. red circles in Figure 2), the coordinates of a projected point \( p' \) on the pareto front as \( (c'_1, c'_2, ..., c'_n) \) (i.e. blue circles in Figure 2), and the SF score of the projected point as \( f(p') \). We can then formulate the iterative treatment planning problem as a feasibility search using Equation 3. We note that POPS performs equally well if other constraints are chosen besides equivalent uniform dose (EUD) (i.e. mean, max, and DVH constraints).

For clarity, we provide visualizations for a hypothetical 2D case below (see Figures 2 and 3 for visualizations of the pareto front in 2D). However, our POPS algorithm generalizes to n-dimensional cases, and results are provided in later sections for 5D prostate IMRT cases.

POPS:

\[
\begin{align*}
\min_x & \quad \frac{1}{N_{\text{ptv}}} \sum_{j \in \text{ptv}} (d_j - \bar{d})^2 \\
\text{s.t.} & \quad x \geq 0 \\
& \quad c_{\text{EUD, rectum}} \leq c_1 \\
& \quad c_{\text{EUD, bladder}} \leq c_2 \\
& \quad c_{\text{EUD, FH R}} \leq c_3 \\
& \quad c_{\text{EUD, FH L}} \leq c_4 \\
& \quad c_{\text{EUD, body}} \leq c_5 \\
& \quad D_{\text{ptv}}(95\%) \geq 76 \\
& \quad D_{\text{ptv}}(\text{min}) = 74 \\
& \quad D_{\text{ptv}}(\text{max}) = 82
\end{align*}
\] (3)

1. Define the bounds \( p_{b,1}, p_{b,2}, ..., p_{b,n} \) for the decision variable search space by projecting a seed point \( p_s \) onto the pareto front.

Projection of the seed point can be performed using a variety of methods. In our implementation, we perform projections by conducting a one-dimensional search using the bisection method along a vector direction. When projecting the seed point to define the decision space bounds, we perform the one-dimensional search by tightening the EUD constraint in one OAR (while fixing all other constraints), and repeat this projection for each OAR (five times total for a 5D prostate case). The projected points will form the bounds for the decision space and can be visualized as a simplex (see Figure 2b).

As visualizations for n-D are too difficult, we instead provide visualizations in 2D where the feasibility search space is in \( R^2 \) while the decision space is the line bounded by the initial projected points. For a n-dimension treatment planning

![Figure 2](image_url). (a) Visualization of the POPS algorithm for a hypothetical 2D problem. (b) Starting from a seed point, we define the bounds for the decision variable space by projecting the seed point using the bisection method. (c) We then define the initial simplex and (d) project the initial simplex to the pareto front, while computing the SF score for each projected point. (e) We can then use a gradient-free search (i.e. simplex search) to search the pareto front for a clinically acceptable treatment plan.
problem, the constraint feasibility search space is in $R^n$ while the decision space is a simplex bounded by $n$ points that are found by projecting the seed point along orthogonal directions.

2. **Within the bounded decision space, define the initial simplex vertices $p_1, p_2, \ldots, p_n$.**

   For simplicity, we define our initial vertices by taking the weighted average of the boundary points.

   $\tau_{i,j} = \begin{cases} 
   0.3, & \text{if } i = j \\
   1, & \text{otherwise}
   \end{cases}$

   $p_i = \frac{\sum_{j=1}^{n} p_{b,i} \tau_{i,j}}{\sum_{i=1}^{n} \tau_{i,i}}$  \hspace{1cm} (5)

   Here, $\tau_{i,j}$ refers to the weights assigned to each boundary point $p_{b,i}$. Prior knowledge can also be incorporated in the form of better starting simplex vertices, but our implementation uses a more straightforward initialization for reproducibility.

3. **Project each of the simplex vertices $p_1, p_2, \ldots, p_n$ from the decision space to the pareto front to obtain the projected points $p'_1, p'_2, \ldots, p'_n$, again using the bisection method.**

   Here we describe the projection component that is an important recurring theme in the POPS algorithm. Projection of the simplex vertices to the pareto front is visualized for the 2D case in Figure 2d. In contrast to the projection of the seed point, all subsequent projections use the bisection method to perform a one-dimensional search along a fixed vector direction. To determine this vector direction, we empirically calculate the vector from the centroid of the initial simplex to the origin. Example visualizations for one-dimensional search along this vector direction are shown as solid black lines in Figure 2.

4. **Compute the function evaluation (i.e. SF score) for each of the projected simplex vertices to obtain $f(p'_1), f(p'_2), \ldots, f(p'_n)$.**

   We can compute the SF score for a particular treatment plan solution $p$ using Equations 1 and 2.

5. **Order the simplex points by their function evaluations such that $f(p'_1) \leq f(p'_2) \leq \ldots \leq f(p'_n)$.**

6. **Compute the centroid $p_c$ of the $n - 1$ best simplex points.**

7. **Reflection:**

   a. Compute the reflected point in the decision space as $p_r = p_c + \alpha(p_c - p_n)$. We follow the official MATLAB version and use $\alpha = 1$.

   b. Project the reflected point to the pareto front to obtain $p'_r$.

   c. Compute the function evaluation $f(p'_r)$.

   d. If $f(p'_1) \leq f(p'_2) < f(p'_{n-1})$, replace the worst simplex point with $p_r$ and start from 5.

8. **Expansion:**

   a. If $f(p'_i) < f(p'_r)$, compute the expansion point in the decision space as $p_e = p_c + \beta(p_e - p_n)$. We follow the official MATLAB version and use $\beta = 1$.

   b. Project the expansion point to the pareto front to obtain $p'_e$.

   c. Compute the function evaluation $f(p'_e)$.

   d. If $f(p'_e) < f(p'_r)$, replace the worst simplex point with $p_e$ and start from 5.

   e. Otherwise, replace the worst simplex point with $p_r$ and start from 5.

9. **Outside Contraction:**

   a. If $f(p'_{n-1}) \leq f(p'_r)$, compute the outside contraction point in the decision space as $p_{oc} = p_c + \gamma(p_r - p_n)$. We follow the official MATLAB version and use $\gamma = 0.5$.

   b. Project the outside contraction point to the pareto front to obtain $p'_{oc}$.

   c. Compute the function evaluation $f(p'_{oc})$.

   d. If $f(p'_{oc}) < f(p'_r)$, replace the worst simplex point with $p_{oc}$ and start from 5.

   e. Otherwise, continue to step 11

10. **Inside Contraction:**

    a. If $f(p'_n) \leq f(p'_r)$, compute the inside contraction point in the decision space as $p_{ic} = p_c + \gamma(p_n - p_r)$. We follow the official MATLAB version and use $\gamma = 0.5$.

    b. Project the inside contraction point to the pareto front to obtain $p'_{ic}$.

    c. Compute the function evaluation $f(p'_{ic})$.

    d. If $f(p'_{ic}) < f(p'_r)$, replace the worst simplex point with $p_{ic}$ and start from 5.

    e. Otherwise, continue to step 11

11. **Shrink:**

    a. Replace every point except the best point (i.e. $p_i$ where $i = 2, \ldots, n$) with $p_i = p_i + \rho(p_i - p_n)$. We follow the official MATLAB version and use $\rho = 0.5$.

    b. Start from step 5

III. RESULTS

A. Experimental Setup and Evaluation

To determine the proficiency of our automated POPS algorithm, we compare it to gold-standard treatment plans created as part of routine clinical workflow. While these human-created treatment plans are not necessarily pareto optimal, they provide a benchmarking baseline in terms of clinical acceptability. Our comparisons utilize the SF score, which is described previously in Materials and Methods, to evaluate treatment plans both from our POPS algorithm and from human planners. Using our SF score, we can evaluate treatment plans on a scale between 0 and 1, where lower is better. Equations 1 and 2 are used to compute the SF score and are further explained in the Methods section.
The dataset used in our experiment consists of 21 prostate IMRT cases acquired from the Stanford Radiation Oncology Clinic (SROC). Scanner details, acquisition dates, and treating physician varied across cases. Gold-standard human-created treatment plans were created using a treatment planning system from Varian Medical Systems. As part of routine clinical workflow, various OARs (including the rectum, bladder, left/right femoral heads, and body) were contoured, along with the PTV. In order to mitigate the effect of beam angle selection on plan quality, we use a plan setting of 11 equally spaced photon beams (from 20° to 360° in increments of 32.7°). Similarly, a prescription dose of 76 Gy delivered over 40 fractions, a bixel size of 5 \(mm\), and a dose voxel size of 3 \(\times\) 3 \(\times\) 3 \(mm^3\) were used as well. Our POPS algorithm additionally implements the open-source MatRad software package to perform inverse planning \[4\] which uses a pencil-beam dose calculation algorithm and IPOPT[33].

As our POPS algorithm outputs pareto optimal plans, we expect it to produce treatment plans that perform at least as well as the human-created plans, within a small margin of error. In comparing SF score performance, we can compute the relative difference as the following:

\[
\text{Rel. Dif.} = \frac{\text{SF}_{\text{POPS}} - \text{SF}_{\text{PHYS}}}{\frac{1}{2}(|\text{SF}_{\text{POPS}}| + |\text{SF}_{\text{PHYS}}|)}
\]

B. Comparison to Baseline and Initial Plans
As mentioned, we perform comparisons between initial plans, dosimetrist generated plans (the gold-standard), and

![Figure 3. Boxplot visualization for 5D prostate IMRT cases, comparing initial plans to physician generated plans to POPS.](image_url)

![Figure 4. Visual comparison of initial, intermediate, and final treatment plans generated for an example patient using POPS. Dose conformity and organ sparing significantly improve from the initial plan after running POPS.](image_url)
POPS generated plans. These treatment plans are evaluated using the proposed SF score that allows for a quantitative evaluation of DVHs on a scale between 0 and 1, where lower is better.

As demonstrated in Figure 3, our proposed POPS algorithm produces treatment plans that score better than the gold-standard dosimetrist generated plans for all 21 patients. Paired t-test results additionally demonstrate significant improvement in favour of POPS generated plans over dosimetrist generated plans ($p = 2.6 \cdot 10^{-7}$) and initial plans ($p = 4.0 \cdot 10^{-1}$). Unsurprisingly, both POPS generated and dosimetrist generated treatment plans outperformed the initial plans in terms of SF scores. Figure 3 additionally demonstrates that POPS produced better scoring plans for each of the 21 cases, as the relative differences are all negative.

A visualization of the differences in dose distribution between an example of a representative initial plan and the corresponding POPS generated plan is provided in Figure 4. We can visually appreciate the improvement to plan quality when comparing the final and initial plans. Moreover, we can visualize incremental improvements following iterations of the POPS algorithm. Upon arrival at the final plan, we observe substantial improvements to OAR sparing for all OARs as compared to the initial plan, as well as incremental improvement to sparing of the rectum when comparing the final plan to intermediate plans. Dose delivered to the PTV remains relatively homogenous throughout all iterations with dose conformity being noticeably improved in the final plan when comparing to the initial plan.

Figure 5 provides visualizations of three example cases: 1) where the POPS provided a large improvement over the dosimetrist generated plan, 2) where POPS provided a moderate improvement, and 3) a case where the POPS and dosimetrist generated plans scored similarly. It is clear from all three cases that POPS generated plans perform better in sparing the rectum, which is assigned the highest priority in our SF score following the advice of consulted physicians.

In the DVH for the large improvement case (row 2 column 1 of Figure 5), we can appreciate substantial improvements to DVH curves for both the rectum (purple line) and bladder (blue line), along with similar performing DVH curves for the femoral heads and body. Clearly, the dosimetrist generated plan is not pareto optimal. In these scenarios, POPS produces more efficient plans than the dosimetrist, highlighting the importance of pareto optimality in treatment plan quality. The dose distribution (row 1 column 1 of Figure 5) for this large improvement case additionally demonstrates that PTV dose is highly conformal and the algorithm performs well in regards to OAR sparing. In the DVH for the moderate improvement case (row 2 column 2 of Figure 5), we observe significant improvements over the dosimetrist plan in regards to rectum sparing (purple line) at the expense of sparing to bladder (blue line). We suspect this trade-off occurs because the dosimetrist plan is close to pareto optimal, and POPS—with our current scoring function—assigns greater priority to the rectum than the bladder. Finally, in cases where POPS generated plans and dosimetrist generated plans score similarly, it is likely that the
Automated treatment planning approaches have steadily grown in popularity due to their potential to drastically reduce active planning time [7], [8], [16], [20], [21], [23], [25], [28]. Following the iterative approach to treatment planning, human planners repeatedly adjust treatment planning parameters and perform inverse planning until a clinically acceptable solution is found. For IMRT cases, active planning time—planning time that directly utilizes a human planner’s decisions or actions—for human planners has been reported to be on the order of 135 minutes, with active planning time potentially increasing for more complex cases [25].

Endeavouring to reduce active planning time, a variety of automated approaches have been proposed, which can be generally categorized as knowledge-based planning, protocol-based planning, and MCO. As introduced earlier, knowledge-based planning approaches typically leverage “black-box,” supervised machine learning approaches to predict components of dosimetrist generated plans (i.e. the dose distribution, DVH, etc.) [16]–[18]. On one hand, such approaches, in theory, have the potential to reproduce dosimetrists’ plans with high accuracy at exceedingly low computation times. On the other hand, such approaches, in practice, may suffer from poor generalization, poor interpretability, and limited effectiveness in outperforming their ground-truth dosimetrist generated plans [34]–[36].

Protocol-based methods attempt to mimic human planners performing iterative planning using carefully designed rules or trained reinforcement learning agents [7], [8], [20]–[23]. While practical, these methods are potentially limited by inter-planner variability and, like KBP, do not necessarily produce pareto optimal plans.

MCO approaches, by contrast, attempt to produce pareto optimal solutions. Where a posteriori MCO (database MCO) approaches attempt to generate the entire pareto front (or at least approximate the pareto front) [13], [24], [25], a priori MCO approaches select a pareto optimal plan based on physician-defined preferences for objective weights and dose constraints [6], [26], [28], [29]. Both types of MCO approaches produce pareto optimal plans but delegate the task of selecting clinically acceptable plans to the physician, either explicitly (i.e. in the case of a posteriori MCO) or implicitly through preferences (i.e. in the case of a priori MCO).

While we do not have access to implementations of other MCO algorithms in the MatRad framework, we report their active planning times for rough comparison in Table 3. Our initial implementation of POPS requires no active planning

### Table 2. Comparison of DVH values for five uniformly selected control points (D(20%), D(40%), D(60%), D(80%), D(98%)) between dosimetrist generated and POPS generated plans. Lower dosage values are better as they imply better OAR sparing. The lowest values for each OAR are also bolded.

| OAR      | D(20%) (Gy) | D(40%) (Gy) | D(60%) (Gy) | D(80%) (Gy) | D(98%) (Gy) |
|----------|-------------|-------------|-------------|-------------|-------------|
| Human Planner |
| Rectum   | 53.9 (11.2) | 32.8 (8.1)  | 21.1 (7.3)  | **10.0 (5.3)** | 3.1 (1.1)  |
| Bladder  | **36.6 (21.7)** | **15.2 (12.0)** | **7.0 (7.1)** | **3.9 (5.1)** | **2.0 (2.7)** |
| FH R     | 24.9 (4.9)  | 20.3 (4.4)  | 15.2 (4.2)  | 7.5 (4.4)   | 2.3 (1.3)   |
| FH L     | 23.0 (4.7)  | 17.9 (3.5)  | 13.7 (3.3)  | 7.1 (4.4)   | 2.2 (1.2)   |
| Body     | **3.5 (1.7)** | 0.6 (0.2)   | 0.2 (0.1)   | 0.1 (0.1)   | 0*          |

*Values were vanishingly small
dosimetrist generated plans are close to pareto optimal, and the dosimetrist’s assignment of OAR priority agrees with the OAR priorities listed in Table 1.

Table 2 provides further quantitative comparison between dosimetrist generated plans and POPS generated plans. Here, five DVH control points were selected to provide an approximation of the DVH curve for each OAR. Dosage values are comparable between the two methods, demonstrating comparable OAR sparing. While POPS generally performs better for the rectum, femoral heads, and body, it performs slightly worse for the bladder. Overall, POPS produces pareto optimal plans that are highly comparable to dosimetrist generated plans with regards to clinical acceptability.

### IV. DISCUSSION

This present study introduced a fully automated treatment planning algorithm, POPS. POPS combines projections using the bisection method and a gradient-free search to produce treatment plans that are both pareto optimal and clinically acceptable. To evaluate clinical acceptability, we compare POPS performance to manual planning by dosimetrists, the current gold-standard. Quantitative results for the 21 prostate IMRT cases in our dataset demonstrate that in every case, the POPS generated plan in terms of SF score.

#### A. POPS vs Other Approaches

Automated treatment planning approaches have steadily grown in popularity due to their potential to drastically reduce active planning time [7], [8], [16], [20], [21], [23], [25], [28]. Following the iterative approach to treatment planning, human planners repeatedly adjust treatment planning parameters and perform inverse planning until a clinically acceptable solution is found. For IMRT cases, active planning time—planning time that directly utilizes a human planner’s decisions or actions—for human planners has been reported to be on the order of 135

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from human planners. Alternative \textit{a posteriori} MCO approaches, for reference, require a human planner to select clinically acceptable plans from a database of pareto optimal solutions, resulting in a longer active planning time.

One major benefit of having no active planning time is that many patients can be run in parallel, reducing the average time overall per patient and allowing for great scalability to servers or clusters. For our 5D prostate IMRT implementation, POPS utilizes 5 CPU threads. On our consumer-level desktop Ryzen 2700x CPU (16 threads), up to 3 patients may be run simultaneously, which scales to potentially 25 patients on a Ryzen 3990x workstation and even more when factoring in servers or a gpu-based implementation.

Overall, our proposed POPS algorithm directly searches the pareto front for clinically acceptable treatment plans, as defined by a scoring function. We note that the particular scoring function can be interchanged, as desired, without affecting the functionality of the POPS algorithm. In contrast to previous categories of MCO approaches, POPS automates the selection process of a clinically acceptable plan. In practice, POPS provides a general framework that allows for the direct search of the pareto front. Based on results for 21 prostate IMRT cases, POPS generated plans score better than dosimetrist generated plans for all cases. Our comparisons use the clinical acceptability criteria proposed in previous work [32]. As treatment plan evaluation can be subjective, we certainly acknowledge that physicians can choose criteria that may be somewhat different from what we adopted in the present study. To that end, Table 1 can be modified as desired to better suit individual preferences without affecting the performance of the POPS algorithm. Similarly, we found our heuristics to work well for prostate IMRT planning, but they may also be modified, resulting in different hyperparameter values, to suit different anatomies or physician preferences. The POPS framework allows for the implementation of alternative scoring functions or clinical acceptability criteria. For a given scoring function and set of criteria, POPS produces treatment plans that satisfy the overall objective of this study: to produce treatment plans that are both pareto optimal and clinically acceptable in a fully automated fashion.

**B. Limitations and Potential Improvements to Speed**

Based on the reported computation times from Craft et al., MCO approaches that utilize approximations of the pareto front typically have computation times less than 10 minutes. Our current implementation, which uses the MatRad software package to perform inverse planning and does not yet utilize pareto front approximations, has computation times around an hour. We would like to clarify that the computation time differences are not the result of POPS. Rather, they can be attributed to two main factors: inverse planning software implementation differences and the PGEN approximation method (or equivalent pareto front approximation method). Each time POPS makes an adjustment to the search variables, the vast majority of time is spent in computing function evaluations (i.e. performing inverse planning), so the bottleneck to sequential throughput is inverse planning speed. We have implemented our POPS algorithm using the open source MatRad package so that our findings can be more easily verified by other studies, but implementation of POPS in alternative treatment planning software packages like Eclipse or RayStation or ConRad [3] will speed up computation accordingly.

For our implementation, we make no additional assumptions or approximations in regards to dose constraints or objectives (beyond those made by the matRad software package), but recent works such as ConRad demonstrate dramatic improvements to inverse planning throughput if certain approximations are made [3]. Similarly, as reported by Craft et al. [24], [25], their implementation uses the PGEN approximation of the pareto front, requiring significantly fewer function evaluations to approximate the pareto front. We hope to apply both improvements to our POPS algorithm in the future and anticipate similarly large increases in speed as were observed in their works.

**V. CONCLUSION**

External beam radiation therapy is used for treatment of over 60% of cancer patients. Within the radiation therapy workflow, the treatment planning process represents a bottleneck to high quality patient care, due to the time-consuming nature of the iterative planning process and inter-planner variability. Previous works in automated planning can be generally categorized as KBP, PBP, and MCO approaches, each having key limitations. Our proposed POPS algorithm attempts to address these limitations and provides a fully automated framework for performing pareto optimal treatment planning.

Evaluation of treatment plan quality is an especially subjective and nuanced process. While we acknowledge that particular scoring of treatment plans may differ according to

**Table 3.** Comparison of average computation times and active planning times required for each patient.

| Method                                               | Active Planning Time/Patient |
|------------------------------------------------------|-----------------------------|
| Human Planner*                                      | 135 min                     |
| Approximated MCO (with RayStation implementation)*   | 12 min                      |
| POPS (with MatRad implementation)                    | 0 min                       |

* Based on reported average time from Craft et al. [25]
planner expertise and preferences, we adopt a scoring function (SF) for the purpose of evaluating prostate IMRT plan quality in regards to clinical acceptability criteria previously proposed in literature[32]. Using this proposed SF score, we demonstrate that our proposed POPS algorithm produces plans that are both pareto optimal and clinically acceptable, as compared to manually generated plans. Our results indicate that POPS can substantially improve treatment planning workflow.

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