A Collimator Setting Optimization Algorithm for Dual-arc Volumetric Modulated Arc Therapy in Pancreas Stereotactic Body Radiation Therapy

by

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Chunhao Wang

Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University

2019
ABSTRACT

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Abstract

This project aims to develop an automatic collimator setting optimization algorithm to improve dosimetric quality of pancreas Volumetric Modulated Arc Therapy (VMAT) plans for Stereotactic Body Radiation Therapy (SBRT).

Fifty-five pancreas SBRT cases were retrospectively studied. Different from the conventional practice of initializing collimator settings manually, the proposed algorithm simultaneously optimizes the collimator angles and jaw positions which are customized to the patient geometry. This algorithm includes two key steps: an iterative optimization algorithm via simulated annealing that generates a set of collimator settings candidates, and a scoring system that choose the final collimator settings based on organs-at-risk (OARs) sparing criteria and dose prescription. The scoring system penalizes 3 factors: 1) jaw opening ratio on Y direction to X direction; 2) unmodulated MLC area within the jaw aperture in a dynamic MLC sequence; 3) OAR shielding capability by MLC with MLC aperture control constraints. For validation, the other 16 pancreas SBRT cases were analyzed. Two dual-arc plans were generated for each validation case, an optimized plan (Plan_{opt}) and a conventional plan (Plan_{conv}). Each plan was generated by a same set of auxiliary planning structures and dose-volume-histogram (DVH) constraints in inverse optimization. Dosimetric results were analyzed and compared. All results were tested by Wilcoxon signed-rank tests.
Statistic results showed that both plan groups had no statistical differences in target dose coverage V95% (p=0.84) and Root Conformity Index (p=0.30). Mean doses of OARs were improved or comparable. In comparison with Plan\textsubscript{conv}, Plan\textsubscript{opt} reduced maximum dose ($D_{0.03\text{cc}}$) to stomach (-49.5cGy, $p=0.03$), duodenum (-63.5cGy, $p<0.01$), and bowel (-62.5cGy, $p=0.01$). Plan\textsubscript{opt} also showed lower modulation complexity score ($p=0.02$), which implies its higher modulation complexity of the dynamic MLC sequence.

In conclusion, the proposed collimator settings optimization algorithm successfully improved dosimetric performance for dual-arc VMAT plans in pancreas SBRT. The proposed algorithm was demonstrated with great clinical feasibility and readiness.
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1. Introduction

1.1 Radiation Therapy

Radiation therapy is the most common treatment of cancer. Cancer is an umbrella term of hundreds of diseases, whose nature is unregulated malignant cell proliferation. These cells could invade into neighboring tissues and remote organs, which is the main reason of cancer metastasis and mortality [1]. A mass of tissue formed by cancer cells is called malignant tumor, or malignant neoplasm.

As a primary treatment of cancer, radiation therapy eliminates cancer cells by damaging their DNA using ionizing radiation, which is high energy electromagnetic waves or particles. Based on the type of radiation used, radiation therapy can be divided into electron beam therapy, photon beam therapy, proton therapy, neutron therapy, and other heavy particle therapy (including helium, neon, silicon, argon, and carbon ions) [2]. Based on the distance between radiation source and tumor, radiation therapy can be divided in two major categories: External Beam Radiation Therapy (EBRT) and Internal Radiation Therapy (also called Brachytherapy). In EBRT, radiation beams come from the outside of the patient body and reach the tumor. While in brachytherapy, the radioactive seeds are placed into the patient body, close to or inside of the tumor. On one hand, brachytherapy can deliver higher dose (delivered energy or unit mass) to the tumor and have better normal tissue sparing; On the other hand, EBRT is non-invasive and more compatible to different treatment sites.
EBRT is the most common type of radiation therapy. Most of the time EBRT refers to external photon beam radiotherapy, so without further explanation, EBRT in this thesis refers to photon based EBRT. Few popular techniques used in EBRT includes: three-dimensional conformal radiation therapy (3D-CRT), intensity modulated radiation therapy (IMRT), and volumetric modulated arc therapy (VMAT).

1.2 Pancreatic cancer

Pancreatic cancer is the fourth leading cause of death of cancer in the United States in 2015, caused 41615 death in 2015 and 44330 death projected in 2018. The five-year survival rate of pancreatic cancer is 8% from 2007 to 2013; moreover, over 50% of the patients who were diagnosed when they had developed metastasis reported a five-year survival rate of only 3% [3]. Without intervention, the median survival is 2.5 months for patients diagnosed as pancreatic cancer [4]. Pancreatic cancer is predicted to be the second leading death among all kinds of cancers by 2030, and the incidence is expected to be doubled by then [5].

The pancreatic tumor is located at the upper part of retroperitoneal space, surrounded by duodenum, jejunum, stomach, kidneys, spleen and other important organs. The rich lymphatic and vessel system connected pancreas to nearby lymph nodes, organs and even more distant organs like the liver, lungs, and pleura [6]. Pancreatic adenocarcinomas constituted Almost 90% of pancreatic cancer and is the focus of most of the discussions [7]. Diagnose of pancreatic cancer at early stage is not
practical in clinics for that pancreatic cancer is rare, and its symptoms is so common and indistinguishable that no designated examination has been proven to be sufficiently effective [8].

1.3 Treatment of pancreatic cancer

The only practical curative treatment for pancreatic tumor is surgical resection [9, 10], while 85-90% of the patients exhibited local advanced tumor or metastasis were ineligible for pancreatectomy [6]. Furthermore, among the patients underwent successful resection, more than 20% of them developed local recurrence and more than 70% experienced systemic recurrence [11]; Meanwhile, the five-year survival rate after resection remains 10-25% [12].

The additional treatments including radiotherapy, adjuvant therapy, neoadjuvant therapy [13]. Adjuvant chemotherapy, radiotherapy and chemoradiotherapy aims at preventing recurrence after resection [14], whereas neoadjuvant chemotherapy, radiotherapy and chemoradiotherapy helps with shrinking the borderline resectable tumor before the surgery [11].

Conventional neoadjuvant or adjuvant radiotherapy delivers 45-50 Gy (1.8-2.0 Gy/d) in total and conventional definitive radiotherapy for unresectable tumors delivers 50-60 Gy (1.8-2.0 Gy/d) [9]. In contrast, SBRT delivers 35-50 Gy (5.0-7.0 Gy/d) to the region of vessel involvement and 25-30 Gy (5.0-6.0 Gy/d) to the other region of the PTV (planning target tumor) [15]. The tolerances of the nearby GI OARs constraint the total
prescription dose of the PTV [16]. Earlier studies tested delivering all 25 Gy in one fraction, which yielded satisfying local control but acute complications [17].

1.4 **Pancreatic SBRT**

Stereotactic Body Radiotherapy (SBRT) is an emerging radiotherapy technique. Typically, SBRT delivers 35-50 Gy (5.0-7.0 Gy/fx) to the region of vessel involvement and 25-30 Gy (5.0-6.0 Gy/fx) to the rest of the planning target volume (PTV) [15]. Several advantages of SBRT over neoadjuvant conventionally fractionated chemoradiation exist (1.8-2.0 Gy/fx, 45-60 Gy in total [9]), including: 1) SBRT can kill tumor cells through hypofractionated dose by direct cytotoxicity as well as other mechanisms such as stromal and vascular damage [18-20]; 2) SBRT avoids the delay of full-dose chemotherapy as the treatment time is reduced from up to 6 weeks to 1 week [21]; 3) Acute complications are rare and toxicity levels acceptable [22, 23]. Recent data showed that local recurrence dropped from up to 86% to around 20% after receiving SBRT for a year [22]. SBRT was also proven to benefit patients with unresectable tumors [24, 25] or isolated locally-recurring tumors after resection [16, 26].

1.5 **Deliver pancreatic SBRT by VMAT**

Volumetric Arc Modulated Therapy (VMAT) has a higher delivery efficiency and improved dose conformity compared to static IMRT in delivering SBRT [27]. The improved dose conformity of VMAT over IMRT could be due to the combination of an increased number of angular positions for irradiation and the additional modulations in
dose rate and gantry rotation speed. Challenges of VMAT-based pancreas SBRT include the complex tumor/OAR geometry and the proximity of surrounding OARs with prioritized dose limits allotted to the Gross Tumor Volume (GTV). Moreover, target motion and deformation induced by respiratory motion requires an additional margin for the treatment target region. This additional margin further reduces the distance between target and OARs, or may even create or enlarge target/OAR overlapping. SBRT treatment planning for the pancreas requires considerable efforts: while meeting maximum dose constraints to proximal GI (gastrointestinal) OARs (stomach, large/small bowel, and duodenum) is prioritized, improvements of target coverage may need a few trials from experienced planners before reaching the ideal balanced dosimetric results [16].

1.6 Research Objective

Of the many factors that can affect dosimetric outcomes in VMAT planning, collimator settings (including collimator angles and jaw positions) have drawn our attention. Collimator angles and jaw (carriage) positions have an impact on OAR sparing, especially when the PTV projections in beam-eye-views (BEVs) were non-convex or contained separated subvolumes [28-31]. Previous studies proved that dose coverage and DVH statistics were related to collimator angle selections in VMAT [32-35]. However, in clinics, collimator parameters are commonly set following institutional guidelines and conventions. One common practice is employing dual arcs with
symmetric collimator angles (for example, 30 and 330 degrees). Jaw apertures are set
manually or semi-automatically to include all PTV segments in all BEVs. Collimator
settings determined based on individual anatomy and dose constraints may facilitate the
balance of target coverage and OAR sparing, thus improving treatment plan quality
with reduced human efforts.

1.7 Outline of the Thesis

In this work, a collimator setting optimization algorithm was developed for dual-
arc VMAT pancreas SBRT. For each individual case, a group of dual-arc collimator
settings candidates was derived using simulated annealing iterative optimization. This
iterative optimization was built upon a thorough analysis of patients’ anatomy and dose
constraints in a previous pancreas case library. The final collimator setting was
determined by a scoring system that evaluates MLC modulation capability in both target
shaping and OAR shielding.
2. Literature Review

Soon after the invention of VMAT, the effect of collimator rotation on the dose distribution in VMAT has been investigated for a variety of treatment site. In many related papers, the authors would pick a couple of collimator angles most frequently used in clinics. For each of these pairs of collimator angles, VMAT plans were made and the dose distribution was quantitatively compared. The best pair of collimator angles was thus decided for the treatment site. This kind of decision of collimator angles is not patient specific, time consuming, and it confidence level could be affected by the limited patient cohort size and collimator angle selections. However, these kind of research convinced all that collimator angles have an impact on plan quality, and efforts have been made to optimize this parameter for different treatment sites.

Most of the former collimator angle optimization was focused on colli-VMAT, which can be regarded as VMAT whose collimator angles are different in different angular sections. Optimization of collimator angle in full arc VMAT was rare. Few popular mindsets of optimization were: 1) Reduce the MLC aperture size; 2) Align the direction of leave movement with the spinal cord. The first method was usually used for head and neck cases, where there could be multiple PTVs or the shape of PTV is non-convex. The second method was usually used for vertebral cases. Both of these methods cannot be directly applied to colli-VMAT of pancreas SBRT. Meanwhile, colli-VMAT requires extra Quality Assurance (QA) tests that the collimator rotation should be
sufficiently fast and accurate. The time intervals waiting for the collimator to rotate to the assigned angle undermine the advantage of the high delivery efficiency of VMAT. Therefore, in pancreas cases, specific collimator optimization algorithm for full arc VMAT is necessary.

2.1 Dosimetric effects of collimator angles in VMAT

In 2010, Mancosu et al. [36] studied the relationship between dosimetric outcomes and collimator angles of dual arc VMAT and single arc VMAT for vertebral metastases. $80^\circ$-$280^\circ$ for dual arc VMAT and $80^\circ$ for single arc VMAT results in the best plans in terms of target coverage and OAR sparing (spinal cord). They drew conclusions that the plan quality is better when the direction of MLC movement is parallel to the spinal cord.

In 2012, Treutwein et al. [37] concluded that $45^\circ$ of collimator angle in single arc VMAT is best balanced between plan quality and delivery efficiency for pancreas cancer.

In 2015, Kim et al. [38] discovered that the gamma passing rate is related to the collimator angles of dual arc VMAT.

In 2016, Tas et al. [32] decided that $75^\circ$-$285^\circ$ for dual arc VMAT yielded the best dose coverage and OAR sparing for prostate cancer.

In 2018, Li et al. [33] further incorporated modulation complexity score ($MCS_v$) into the consideration of collimator angles, and claimed $45^\circ$ is the optimal for dual arc VMAT for prostate cancer.
In summary, most of these research focused on vertebral cases and prostate cases, whose PTV or OAR has a more regular shape than other treatment site, and the anatomy geometry is relatively uniform between different patients. Pancreas cancer meets neither of these traits, and thus need more sophisticated optimization method.

### 2.2 Practices of collimator angle optimization

In 2010, Zhang et al. [39] proposed colli-VMAT for paraspinal SBRT. At each gantry angle, the optimal collimator angle would be the one that MLC moves along the main orientation of spinal cord. The colli-VMAT plans were optimized by an in-house program and compared with the conventional VMAT plans. Colli-VMAT resulted in better PTV V95%, PTV D95%, and spinal cord D05% compared with conventional VMAT and IMRT.

In 2010, Kang et al. [31] developed a optimization method of couch and collimator angles in dual arc dual isocenter VMAT for multi-PTV brain metastases. The optimal couch and collimator angles would be the one that the projections of multiple targets on y axis in BEV least overlapped with each other. The optimized VMAT plans yielded improved dose homogeneity and reduced $V_{12Gy}$.

In 2017, Ahn et al. [30] proposed a method to optimize collimator angles in colli-VMAT of head and neck cases. The optimal collimator angles would be the ones yield the smallest MLC opening areas in that angular section. It was proven that smaller angular sections resulted in better plan quality and less total MUs.
In summary, these proposed methods either were tailored for multi-target treatment site, paraspinal cases, or colli-VMAT. None of these can be directly applied to dual arc VMAT pancreas cases.
3. Method

3.1 Materials

55 pancreas cases were included in this study. 39 of these cases were analyzed by exhausting search and helped with the selection of the initial settings of the collimator setting simulated annealing optimization; the 16 remaining cases were replaned using the optimized collimator settings and the template collimator settings, respectively, to validate the improvement of the plan quality.

In this study, treatment planning was performed using Eclipse™ v13.7 software (Varian Medical System, Palo Alto, CA). Dose calculations were carried out by the AAA (Anisotropic Analytical Algorithm) with 1mm grid resolution.

3.2 Theorem and workflow

Figure 1 summarizes the workflow of the developed algorithm, which has two core components: 1) an iterative optimization that generates a group of collimator settings candidates; and 2) an MLC modulation efficiency evaluation that finalizes the collimator settings using a scoring system.
Figure 1: Flowchart of the proposed collimator angle optimization algorithm.

### 3.3 Determination of initial collimator angles

To determine the optimal collimator setting of an individual case, the proposed algorithm started from 10 pre-determined collimator angle pairs to search for the optimal collimator setting. Specifically, these initial collimator angles (CSa,i, i = 1,2,..10) were used as starting points in the iterative optimization in Figure 1. To determine CSa,i, a case library that consists of 39 dual-arc VMAT pancreas SBRT cases were analyzed. Critical planning structure contours, including PTV, boost PTV (if prescribed), large/small bowel, duodenum, and stomach, were exported to an in-house software.
package written in MATLAB (MathWorks, Natick, MA). Digital Reconstruction Radiographs (DRRs) of all BEVs pertaining to each structure were generated. For each case, an exhaustive search was performed to find all possible dual-arc collimator settings (CS) under the condition that each PTV voxel must be included in all BEVs by at least one arc (Condition A). The optimal CS was selected as the one with the smallest value of $X_d$, which is the larger jaw opening value in the X direction (parallel to MLC motion direction) of dual arcs. Ten collimator angle pairs were selected as the representatives of the optimal ones in all library cases and were used as the initial collimator angles $CS_{a,i}$ for individualized collimator setting optimization.

### 3.4 Determination of collimator setting candidates

As shown in the left section of Figure 1, a group of collimator settings candidates were generated, and these candidates would be evaluated to generate the finalized collimator setting. To determine these collimator setting candidates, an iterative search using simulated annealing was designed to find the subset of potential collimator setting candidates from the initial angle pool. Inspired by a classic thermodynamic method in Monte Carlo simulation, simulated annealing applies unfavorable perturbation under regulation during the optimization to avoid local minimum trapping [40].

The iterative optimization started from each of the 10 initial starting points $CS_{a,i}$. At each iteration step, a random perturbation ($< \pm 4$mm for jaw positions and $< \pm 2$ degrees for collimator angle) was added to the current results. If Condition A was
violated, the program would continue to the next loop; otherwise, the $X_d$ (defined above) would be calculated and compared with the one from the last loop. If $X_d$ decreases, the perturbed collimator setting would be accepted; otherwise, the perturbed collimator setting would be accepted with an annealing probability $P$:

$$P = \exp(-k \cdot i \cdot \Delta X_d)$$

(1)

where $i$ is the iteration number, $k$ is a constant that controls the speed of annealing, $\Delta X_d$ is the increase of the $X_d$. 10 candidate collimator settings (candidate $CS_j$, $j = 1, 2, 3, \ldots, 10$) were calculated from the 10 initial collimator settings, respectively. Constraints were added to avoid unreasonable settings, such as identical collimator angles in dual-arc pair and extremely small jaw aperture.

### 3.5 Determination of optimal collimator setting

To determine the optimal collimator setting, a Collimator Setting Score (CSS) was designed to evaluate the generated collimator setting candidates. Collimator Setting Score focused on MLC modulation capability in terms of target shaping and OAR shielding. Starting with each candidate, a dynamic MLC sequence of dual-arc pairs ($DS$) was generated to conform to 3D non-OAR PTV volumes (i.e., PTV minus proximal GI OARs) in all BEVs. Collimator Setting Score was calculated based on the MLC sequences. Specifically, a Collimator Setting Score consists of three parts:
3.5.1 Jaw Ratio Score

Jaw Ratio Score (JS) penalizes the ratio of jaw openings in the X and Y directions, and is defined as:

\[ JS = 1 - \exp\left(-\frac{FR_a}{FR_i}\right) \] (2)

where \( FR_a \) is the ratio of jaw opening in the Y direction to the X direction after optimization, and \( FR_i \) is the corresponding value in the initial collimator setting before optimization. Jaw Ratio Score was calculated separately for each of the two arcs and then averaged.

3.5.2 Modulation Area Score

Modulation Area Score (MS) penalizes the ‘dead’ MLC area in a dynamic MLC sequence when the MLC remains static within the jaw aperture during modulation. It is defined as:

\[ MS = \frac{A_j - A_s}{A_j} \] (3)

where \( A_j \) is the area of jaw aperture, and \( A_s \) is the area of the static MLC area. Modulation Area Score was calculated separately for each of the two arcs and then averaged.

3.5.3 GI OAR Sparing Score

GI OAR Sparing Score (GS) evaluates MLC’s potential of OAR dose sparing. GI OAR Sparing Score relies on the presumption that the maximum dose sparing of each
OAR is proportional to the 2D area of its DRRs shielded by the MLC in all BEVs. GI OAR Sparing Score is then defined as:

$$GS = 1 - \exp\left(-\frac{1 - SP_p}{1 - SP_O} \times \frac{D_c}{D_R}\right)$$ (4)

where $SP_{PO}$ is the percentage of PTV/OAR 2D projections shielded by the generated $DS$, $D_S$ is the dose prescription, and $D_c$ is the expected maximum dose of the OAR. GI OAR Sparing Score was calculated for each OAR and each arc, and then averaged.

### 3.5.4 Collimator Setting Score

Collimator Setting Score was designed as the multiplication of these three scores:

$$CSS = JS \cdot MS \cdot GS$$ (5)

The final collimator settings would be the candidate with the highest Collimator Setting Score.

### 3.6 Validation

To validate the proposed algorithm in pancreas SBRT planning, a dosimetry study was conducted to compare key dosimetric results of the plans generated with the optimized collimator setting and with the conventional collimator setting. In this part, 16 pancreas SBRT cases that were not included in the previously mentioned case library were studied. Dual-arc VMAT plans were generated with the optimized collimator settings ($Plan_{opt}$) and the conventional collimator settings ($Plan_{conv}$), respectively. In each case, an identical set of planning structures and DVH dose constraints for VMAT optimization determined by an experienced planner was used in the generations of both
plans to minimize human planning bias. Dosimetric outcomes of Plan\textsubscript{opt} and Plan\textsubscript{conv} were compared primarily by the target dose coverage and the maximum dose ($D_{0.03cc}$ and $D_{0.1cc}$) delivered to each proximal GI OAR. Target conformity index root (CI\textsubscript{r}) [41] and mean dose to all OARs were also compared. In addition, Plan\textsubscript{opt} and Plan\textsubscript{conv} were evaluated by Modulation Complexity Score (MCS) [42] and weighted MLC opening ($A_w$) as quantitative assessments of plan modulation intensity. $A_w$ was defined as:

$$A_w = \sum_i F_{w,i} \times \sum_j \text{MU}_{w,j,i} \times \text{MO}_{j,i}$$

where $F_{w,i}$ is the field weight of the arc number $i$ ($i = 1, 2$), $\text{MU}_{w,j,i}$ is the MU weight of the arc number $i$ and control point number $j$ ($j = 1, 2, \ldots, 178$), and $\text{MO}_{j,i}$ is the MLC opening of the arc number $i$ and control point number $j$. $A_w$ measures the weighted average of beam aperture size shaped by the dynamic sequence, and its value is considered to be inversely correlated with modulation strength.

Wilcoxon signed-rank tests were performed to compare these parameters between Plan\textsubscript{conv} and Plan\textsubscript{opt}, and the statistical significance level was set to 0.05.
4. Results

4.1 Plan comparison

Figure 2 shows an example plan comparison of Plan\textsubscript{opt} (left) and Plan\textsubscript{conv} (right) from a selected study case. Primary PTV is illustrated by the cyan segment (prescribed with 500 cGy × 5 fx) in (a), and boost PTV is illustrated by the red segment (660 cGy × 5 fx) in (b). Isodose distributions in both plans showed decent target coverage and reasonable gradient distribution. Specifically, dose coverages were similar between Plan\textsubscript{opt} (V25Gy = 97.9\% to PTV, V33Gy = 96.7\% to PTV boost) and Plan\textsubscript{conv} (V25Gy = 98.0\% to PTV, V33Gy = 96.7\% to boost PTV). The maximum dose constraints (3300 cGy) to the proximal GI OARs, stomach (yellow), duodenum (dark blue), and large bowel (dark green), were met in both plans. In a detailed comparison with Plan\textsubscript{conv}, Plan\textsubscript{opt} demonstrated improved boost PTV dose conformity in the axial view (a) (as shown by yellow arrows). In addition, Plan\textsubscript{opt} also demonstrated better primary PTV dose conformity in the sagittal view (b). In terms of OAR sparing, Plan\textsubscript{opt} achieved better maximum dose sparing of large bowel (dark green) in (c). Indicated by blue arrows, the 3300cGy (max dose limit) isodose line in Plan\textsubscript{opt} abutted the large bowel’s concavity space and stayed apart from the protruding segment. In contrast, the same isodose line in Plan\textsubscript{conv} did not spared large bowel. (d) also indicated improved stomach (yellow) sparing by Plan\textsubscript{opt}: while While both plans met the max dose limit (3300cGy) of stomach, Plan\textsubscript{opt} spared more stomach volumes from high isodose levels (3135cGy, brown;
3000cGy, white) in the sagittal view. In terms of quantitative results, Plan_{opt} reduced the maximum dose (at 0.1 cc) to the large bowel (3199 cGy), stomach (3130 cGy), and duodenum (3199 cGy) in comparison to Plan_{conv} (3247 cGy, 3217 cGy and 3218cGy, respectively). In addition, the mean dose to bilateral the kidneys and liver was slightly improved in Plan_{opt}.

Figure 2. Dose distribution comparison of Plan_{opt} (left) and Plan_{conv} (right) from a selected case.
4.2 Comparison of dosimetry outcomes

Figure 3 shows the comparison of key dosimetric outcomes of Plan$_{conv}$ and Plan$_{opt}$ of all 16 cases. As illustrated, dose coverage and dose conformity to primary PTV and boost PTV (if prescribed) of Plan$_{conv}$ and Plan$_{opt}$ were comparable. In contrast, $D_{0.1cc}$ and $D_{0.03cc}$ of all proximal GI OARs decreased in Plan$_{opt}$ compared with Plan$_{conv}$, and these reductions were statistically significant except for stomach $D_{0.1cc}$. Median value of OAR mean dose results of 16 studied cases are also reported in Table I. Generally, mean dose results in Plan$_{opt}$ and Plan$_{conv}$ were comparable with minimal differences.

Table 1. Dose statistic results of Plan$_{conv}$ and Plan$_{opt}$ as shown in Figure 3.

<table>
<thead>
<tr>
<th>OAR</th>
<th>Parameters</th>
<th>Plan$_{conv}$</th>
<th>Plan$_{opt}$</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>$D_{mean}$ (cGy)</td>
<td>642.0</td>
<td>605.5</td>
<td>0.01*</td>
</tr>
<tr>
<td></td>
<td>$D_{0.1cc}$ (cGy)</td>
<td>3078.0</td>
<td>3037.5</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>$D_{0.03cc}$ (cGy)</td>
<td>3108.0</td>
<td>3058.5</td>
<td>0.03*</td>
</tr>
<tr>
<td>Duodenum</td>
<td>$D_{mean}$ (cGy)</td>
<td>1276.5</td>
<td>1256.5</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>$D_{0.1cc}$ (cGy)</td>
<td>2904.5</td>
<td>2838.0</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td></td>
<td>$D_{0.03cc}$ (cGy)</td>
<td>2970.0</td>
<td>2906.5</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Bowel</td>
<td>$D_{mean}$ (cGy)</td>
<td>705.0</td>
<td>669.5</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>$D_{0.1cc}$ (cGy)</td>
<td>2776.0</td>
<td>2713.0</td>
<td>0.03*</td>
</tr>
<tr>
<td></td>
<td>$D_{0.03cc}$ (cGy)</td>
<td>2792.0</td>
<td>2729.5</td>
<td>0.01*</td>
</tr>
<tr>
<td>Kidney</td>
<td>$D_{mean}$ (cGy)</td>
<td>449.5</td>
<td>458.5</td>
<td>0.01*</td>
</tr>
<tr>
<td>Liver</td>
<td>$D_{mean}$ (cGy)</td>
<td>316.0</td>
<td>301.0</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>
Figure 3. Comparison of the dose statistics (normalized to prescription dose value) in $Plan_{conv}$ and $Plan_{opt}$. 

- **Target coverage**
- **Root Conformity Index**
- **Bowel $D_{0.1cc}$**
- **Bowel $D_{0.03cc}$**
- **Duodenum $D_{0.1cc}$**
- **Duodenum $D_{0.03cc}$**
- **Stomach $D_{0.1cc}$**
- **Stomach $D_{0.03cc}$**
4.3 Comparison of modulation complexity

Figure 4 shows the comparison of MCS (Modulation Complexity Score) and Aw (Weighted MLC opening). As illustrated, both MCS and Aw showed lower values in Plan<sub>opt</sub> than Plan<sub>conv</sub> with statistical significance. This observation suggests that Plan<sub>opt</sub> generally has stronger MLC modulation. In addition, the median MU values of Plan<sub>opt</sub> in the studied cases was 1775.0, which was higher than the corresponding values of Plan<sub>conv</sub> (1534.2). This MU result is consistent with MCS and Aw studies.

Figure 4. Comparisons of the Modulation Complexity Score and weighed MLC opening between Plan<sub>conv</sub> and Plan<sub>opt</sub>.
5. Discussion

Pancreas SBRT plans generated using our proposed jaw-angle optimization algorithm demonstrated improved dosimetric outcomes when compared to the plans with current clinical collimator settings. In addition, the proposed technique does not require extensive computation, so it can be easily integrated into the current treatment planning workflow.

5.1 Selection of initial collimator angles

The rationale of library analysis was to provide reasonable starting points for the simulated annealing optimization (Figure 1). These library cases were analyzed by an exhaustive search as described in the Methods section. To explain the selection of these initial settings, Figure 5 shows the summarized results of the library analysis and the 10 initial collimator angles pairs. In this figure, all accepted collimator settings were mapped to a 2D plane composed of two collimator angle parameters of dual arc pairs as independent variables represented by gray scale value, and the 10 initial collimator angle pairs were represented by red dots. The 2D map was symmetric to the plane center (90°, 90°) because angles with 180° difference were equivalent (i.e., X1/X2 and Y1/Y2 were exchangeable). The upper-left quadrant showed a scattered distribution with latent linear trends along the quadrant’s positive diagonal. Though not substantial, these trends may suggest that orthogonal or near-orthogonal collimator angles in dual arc pairs might be favored. This deduction also agrees with common sense in clinical
practice that orthogonal collimator angles enables MLC modulation in two directions, which brings additional modulation capabilities on inter-plane (Superior-Inferior) direction. As illustrated by red dots in Figure 5, the 10 settings covered the region with high occurrences and were distributed at a rather even interval in the 2D plane following the latent trend in the exhaustive search results. Hence, these 10 initial settings would suffice as initial values in iterative optimization.

Figure 5. Illustration of the initial collimator settings in the dual collimator angles plane.

5.2 Coincidence of exhausting search and simulated annealing optimization

The proposed iterative optimization workflow utilizes simulated annealing to optimize collimator settings for each case. The advantages of simulated annealing include higher computation efficiency compared to exhaustive search and decreased possibility of local minima trapping compared to gradient search. Two adaptations were
made to the classic simulated annealing algorithm in this study: 1) the initial collimator settings were selected from an analysis of 39 prior cases; 2) the perturbations added to the collimator settings in each iteration varied with the number of iteration steps. On our workstation (Intel Xeon E5-2640 v4, 64G RAM), the exhaustive search method required 2-6 hours (depending on the target geometry complexity) to find optimal jaw settings for each case. In contrast, the proposed iterative optimization took an average of 7 seconds. Such efficiency improvement suggests the feasibility of the proposed method in clinics. In addition, the accuracy of the results in the simulated annealing optimization was not compromised by the improved computation efficiency. Figure 6 shows the experiment results comparing the annealing optimization and exhaustive search of studied cases. As demonstrated in (a), the optimized collimator angle pair results from the proposed simulated annealing algorithm clustered on a positive diagonal region. The exhaustive search results, illustrated as red dots in (b), agreed well with the results in (a). A few red dots scattered at boundary regions in (b) representing the results with extreme jaw positions, and these results could be excluded using current clinical paradigms. In short, the proposed optimization posed both high accuracy and high efficiency.
5.3 Future research

The proposed algorithm focused on the dual-arc VMAT regime, which were the most commonly used technique for pancreas SBRT at our institution. Inclusion of additional arcs may further improve the dosimetric outcomes, but may not be desired due to longer treatment time, especially for patients who need a breath-hold motion management and who have problems lying flat on the treatment couch. With further development, the proposed algorithm can be extended to multiple-arc (>2) VMAT. Another possible future research direction is the further tuning of the MLC efficiency scoring system. The designed scoring scheme in this work was determined by our extensive clinical experience. However, the exact quantitative relationships between each score and the selected dosimetric outcomes were unknown. Further studies with a
larger cohort size would facilitate the modeling of such correlations and enable the extension to other treatment sites.
6. Conclusion

In this work, a collimator setting optimization algorithm for dual-arc VMAT pancreas SBRT was successfully developed. The plans generated with the collimator settings from the proposed algorithm had improved dosimetric quality in comparison with the plans generated with the default collimator settings. The proposed algorithm was demonstrated with great clinical feasibility and readiness.
Reference


