Split Common Coincidence Point Problem: A Formulation Applicable to (Bio)Physically-Based Inverse Planning Optimization

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Abstract: Inverse planning is a method of radiotherapy treatment planning where the care team begins with the desired dose distribution satisfying prescribed clinical objectives, and then determines the treatment parameters that will achieve it. The variety in symmetry, form, and characteristics of the objective functions describing clinical criteria requires a flexible optimization approach in order to obtain optimized treatment plans. Therefore, we introduce and discuss a nonlinear optimization formulation called the split common coincidence point problem (SCCPP). We show that the SCCPP is a suitable formulation for the inverse planning optimization problem with the flexibility of accommodating several biological and/or physical clinical objectives. Also, we propose an iterative algorithm for approximating the solution of the SCCPP, and using Bregman techniques, we establish that the proposed algorithm converges to a solution of the SCCPP and to an extremum of the inverse planning optimization problem. We end with a note on useful insights on implementing the algorithm in a clinical setting.

Keywords: coincidence point; inverse planning; convex optimization; fixed point; iterative algorithm; tumor control probability; radiobiological criteria; pseudocontraction

1. Introduction

The grail of modern radiotherapy is to ensure sufficient and conformal irradiation of tumor cells devoid of normal tissue(s) complications. This is achieved through a process known as radiotherapy treatment planning (RTP). A core component of RTP is the fluence map optimization, which involves determining a beam intensity (fluence) profile that would yield a dose distribution closest to a desired clinical outcome. In intensity-modulated radiation therapy (IMRT), for instance, radiation beams from an external source are split into smaller fields called beamlets, whose individual intensities can be regulated (modulated) [1]. To obtain an optimized treatment plan, the inverse problem of finding a set of beamlet intensities that would result in a dose distribution satisfying a set of prescribed clinical objectives is solved. The quality of any treatment plan is usually measured by how well the set of objectives are achieved. Therefore, the objective functions used in describing clinical requirements for treatment plan optimization are an important index in plan quality evaluation.

To this end, several authors have, on the one hand, proposed and analyzed different objective functions for optimizing treatment plans based on physical criteria (such as maximum dose, minimum dose, mean dose, etc.) and/or biological criteria (such as equivalent uniform dose (EUD), tumor control probability (TCP), normal tissue complication probability (NTCP), etc.) [2–9]. On the other hand, other studies have focused on the comparative analysis of objective functions using clinical

data [10–17]. From these studies, specific merits and limitations of physically- and biologically-based objectives can be identified. While target coverage enforced by physical criteria is desirable, it has also been reported that better critical organ sparing is achieved using biological criteria. Other results, however, favor hybrid (combination of biological and physical) criteria over just physical or biological criteria. Hence, it is safe to say that no particular objective function can be described as "the best", that is, better in all respects.

Consequently, inverse planning optimization has been a subject of extensive research. This has led to the development of several optimization formulations based on different objective functions [3,4,9,18], the most widely used being the linear programming approach, largely due to its simplicity and speed. However, this framework has a major drawback: lack of flexibility. Only a relatively limited number of objective functions and constraints can fit into the linear framework. Hence, "with any particular linear programming formulation, it is unlikely that a physician could always achieve an acceptable result" [19]. On the contrary, with nonlinear optimization formulations, a wide range of possible objective functions and constraints including mathematical models for predicting radiobiological responses can be accommodated. This is no doubt advantageous to RTP, even though the uncertainty in determining input parameters of some radiobiological models poses some difficulties.

Therefore, in this paper, we introduce and discuss a nonlinear optimization formulation called the split common coincidence point problem (SCCPP). We propose an iterative algorithm for approximating the solution of the SCCPP, and using Bregman techniques, we establish that the proposed algorithm converges weakly to a solution of the SCCPP. Furthermore, using some biological and/or physical objective criteria recommended for RTP optimization, we show that the SCCPP is a suitable formulation for inverse planning optimization and that the proposed algorithm converges to an extremum of the (bio)physically-based inverse planning optimization problem. It will be interesting to illustrate the performance of the algorithm under conditions obtainable in a clinical setting. Thus, we provide useful computational insights for implementation of the algorithm in such setting.

2. Preliminaries

In this section, we provide some useful definitions and results. We shall denote a reflexive real Banach space and its dual by E and E^*, respectively.

Definition 1. *A function* $\psi : E \longrightarrow \overline{\mathbb{R}}$ *is said to be:*

(a) *convex if for any* $\lambda \in [0,1]$ *and points* $u, v \in E$,

$$\psi(\lambda u + (1-\lambda)v) \leq \lambda \psi(u) + (1-\lambda)\,\psi(v)$$

(b) *strictly convex if the inequality in (a) is strict*
(c) *totally convex if there exists a function* $\varphi : [0, +\infty) \longrightarrow [0, +\infty)$ *varnishing only at zero such that:*
 $\psi(u) - \psi(v) \geq \langle v^*, \ u - v \rangle + \varphi(\| u - v \|), \ v^* \in \partial \psi(v)$

The set dom $(\psi)\{u \in E : \psi(u) < +\infty\}$ *is called the effective domain of* ψ. *When dom* (ψ) *is nonempty, is said to be proper.*

Definition 2. *Let* $\psi : E \longrightarrow \overline{\mathbb{R}}$ *be convex, and* $u \in dom(\psi)$. *The set*

$$\partial \psi(u) := \{u^* \in E^* : \langle u^*, \ v - u \rangle \leq \psi(v) - \psi(u), \ \forall \ v \in E\},$$

is called the subdifferential of ψ *at* u. *If* $\partial \psi(u)$ *is nonempty, then an element* $p \in \partial \psi(u)$ *is called the subgradient of* ψ *at* u.

Remark 1. *It is well known that if* ψ *is a proper, lower semi-continuous convex function, then for any* $u \in dom(\psi)$, $\partial \psi(u)$ *is nonempty. Moreover,* $0 \in \partial \psi(u)$ *iff* u *is a minimizer of* ψ.

Definition 3. *A function $\psi : E \longrightarrow \overline{\mathbb{R}}$ is said to be Legendre, if*

(a) $\partial\psi$ *is both locally bounded and single-valued on its domain*

(b) ψ *is strictly convex on every subset of $dom(\psi)$ and $(\partial\psi)^{-1}$ is locally bounded in its domain.*

Definition 4. *(See [20]) Let $\psi : E \longrightarrow \overline{\mathbb{R}}$ be a proper, lower semi-continuous convex function. Then:*

(a) *the generalized Bregman distance with respect to ψ and a subgradient p is defined as:*

$$B_\psi^p(u,v) = \psi(u) - \psi(v) - \langle p, \ u - v \rangle, \ p \in \partial\psi(v)$$

It is immediate that $B_\psi^p(u,v) \geq 0 \ \forall \ u, v \ \in dom(\psi)$. Furthermore,

$$B_\psi^p(u,w) = B_\psi^q(u,v) + B_\psi^p(v,w) + \langle u - v \ , \ q - p \rangle, \ p \in \partial\psi(w), \ q \in \partial\psi(v)$$

when $\partial\psi(u)$ is a singleton, we shall denote $B_\psi^p(.,.)$ simply by $B_\psi(.,.)$.

(b) *the Bregman projection relative to ψ of a point $uu \in dom(\psi)$ onto a nonempty, closed, and convex subset K, is defined as the unique vector $\prod\limits_{\psi}^{K}(u)$ satisfying $B_\psi\left(\prod\limits_{\psi}^{K}(u),u\right) = inf\left\{B_\psi(v,u) : v \in K\right\}$. If ψ is totally convex and Gateaux differentiable, then $\prod\limits_{\psi}^{K}(u)$ is the unique solution contained in K of the following variational inequalities (see [21]);*

(i) $\langle \nabla\psi(u) - \nabla\psi(z), z - w \rangle \geq 0 \ \forall \ w \in K$

(ii) $B_\psi(w,z) + B_\psi(z,u) \leq B_\psi(w,u) \forall \ w \in K$

Definition 5. *A mapping $M : E \longrightarrow 2^{E^*}$ is said to be:*

(a) *monotone, if $\langle m - n, \ u - v \rangle \geq 0 \ \forall \ u,v \in dom(M), \ m \in M(u), \ n \in M(v)$*

(b) *maximal monotone if M is monotone, and the graph of M is not contained in the graph of any other monotone map*

(c) *φ-strongly monotone if there exists a non-negative function φ which varnishes only at zero such that:*

$$m - n, \ u - v \geq \varphi(u - v), \ \forall \ u,v \in dom(M), \ m \in M(u), \ n \in M(v)$$

If φ is the function $\varphi(x) = k_0 x^2$, $k_0 > 0$, M is called strongly monotone. Note that $dom(M) := \{z \in E \ : M(z) \text{is nonempty}\}$.

Definition 6. *A mapping $\phi : E \longrightarrow X$ (X is a normed space) is said to be Lipschitz if there exists $L > 0$ such that:*

$$\| \phi(u) - \phi(v) \|_X \leq L \| u - v \|_E \ \ \forall \ u,v \in E.$$

Definition 7. *(See [22]) Let $\phi_1, \ \phi_2 : \ E \longrightarrow E$ be two mappings. A point $u \in E$ is called a coincidence point of ϕ_1 and ϕ_2 iff $\phi_1(u) = \phi_2(u)$.*

Lemma 1. *[23] (a) If ψ is a lower semi-continuous, proper convex function on E, then $\partial\psi$ is a maximal monotone operator from E to E^*. (b) Let $T : E \longrightarrow E^*$ be a multivalued mapping. In order that there exists a lower semi-continuous proper convex function on E such that $T = \partial\psi$, it is necessary and sufficient that T be a maximal cyclically monotone operator. Moreover, in this case, T determines ψ uniquely up to an additive constant.*

Proposition 1. *[24] Let ψ be a lower semi-continuous convex function, such that $int(dom(\psi))$ is nonempty. Then, the function ψ is differentiable at $u \in int(dom(\psi))$ iff $\partial\psi(u)$ is a singleton. If ψ is differentiable on $int(dom(\psi))$, then the derivative is norm to weak* continuous on $int(dom(\psi))$.*

Proposition 2. *[24] Let ψ be a convex function such that $int(dom(\psi))$ is nonempty. Then, the following are equivalent:*

(i)   The function ψ is locally bounded from above on $int(dom(\psi))$

(ii)   The function ψ is locally bounded on $int(dom(\psi))$

(iii) The function ψ is locally Lipschitz on $int(dom(\psi))$

(iv)   The function ψ is continuous on $int(dom(\psi))$.

Moreover, if ψ is lower semi-continuous, then all these conditions are satisfied.

Lemma 2. *[25] Let ψ be uniformly convex on every nonempty, bounded and convex subset of $dom(\psi)$. Then, given two sequences $\{u_k\}_{k=1}^{\infty}$ in $dom(\psi)$ and $\{v_k\}_{k=1}^{\infty}$ in $int(dom(\psi))$ satisfying*

$$\lim_{k\to\infty} B_\psi(u_k,\ v_k) = 0,$$

if one of these sequences is bounded, then, the other is bounded too. Moreover,

$$\lim_{k\to\infty} \| u_k - v_k \| = 0$$

3. Main Results

3.1. Split Common Coincidence Point Problem (SCCPP)

Definition 8. *(Generalized Coincidence Point) Let T, S : $E_1 \longrightarrow E_2$ be two multivalued mappings. A point $u_0 \in E_1$ will be called a coincidence point of T and S iff there exists $\eta_0 \in T(u_0) \cap S(u_0)$. The problem of finding a coincidence point of T and S is called a generalized coincidence point problem.*

Remark 2. *A multivalued version of Definition 7 is obtained immediately by setting $E_1 = E_2$. If in addition, the map T or S is the identity operator, then the coincidence point problem reduces to the fixed point problem. It is worthy of mention that a particular case of the generalized coincidence point problem resulting when E_1 is a normed space, $E_2 = E_1^*$, T is monotone and $S = J$ (the normalized duality map) was introduced and studied by Chidume and Idu [26] as the J-fixed point problem. As a tool for solving optimization problems, the J-fixed point problem has awaken further research in that direction (See [27–29]).*

The split common coincidence point problem follows naturally from Definition 8 as Definition 9.

Definition 9.　Let T, S　be as in Definition 8, let $P, Q : E_3 \longrightarrow E_4$ be two multivalued mappings. Let $A : E_1 \longrightarrow E_3$ be a bounded linear map. Denote by $C_0(T, S)$ and $C_0(P, Q)$, the set of coincidence points of T and S, and the set of coincidence points of P and Q, respectively. Then, the SCCPP is

$$find\ u_0 \in E_1\ such\ that\ u_0 \in C_0(T, S)\ and\ Au_0 \in C_0(P, Q).$$

It follows that by setting $S = \mathbb{I}_{E_1}$, $Q = \mathbb{I}_{E_2}$ ($\mathbb{I}$ is the identity map), the split common fixed point problem (SCFP) introduced by Censor and Segal [30] and studied extensively (see e.g., [31–35]), is a sub-class of the SCCPP. The SCFP formalism, and its variant introduced and studied by Moudafi [36], has been used in modelling significant real-world inverse problems (see for example [37,38]).

3.2. Optimization by Generalized Coincidence Point Problem

Here, we establish an interconnection between optimization problems and coincidence point problems for a special class of operators, T and S. For this purpose, we shall assume that E_1 in Definition 8 is a reflexive Banach space, and simply denote it as E, and $E_2 = E^*$.

Definition 10. *(S-pseudocontraction) Let T and S be as in Definition 8. Then, T will be called S-pseudocontraction (or pseudocontractive with respect to S) if for every $u, v \in E$,*

$$\langle t_1 - t_2, u - v \rangle \leq \langle s_1 - s_2, u - v \rangle \; \forall \; t_1 \in Tu, \; t_2 \in Tv, \; s_1 \in Su, \; s_2 \in Sv$$

The concept of S-pseudocontraction generalizes that of J-pseudocontraction studied in [26].

Lemma 3. *Let T and S be as in Definition 10; then, the following are equivalent:*

(i)   *T is monotone.*
(ii)   *$S - T$ is S-pseudocontractive.*

Proof. Let $\Gamma := S - T$

$$\text{(i)} \implies \text{(ii)}$$

Let $u, v \in E$ be arbitrary; then, for every $t_u \in Tu$, $t_v \in Tv$, $s_u \in Su$, $s_v \in Sv$ and $\gamma_u \in \Gamma u$, $\gamma_v \in \Gamma v$ such that $\gamma_u = s_u - t_u$ and $\gamma_v = s_v - t_v$, we have that

$$\begin{aligned}
\langle \gamma_u - \gamma_v, \; u - v \rangle &= \langle s_u - t_u - (s_v - t_v), \; u - v \rangle \\
&= \langle s_u - s_v, u - v \rangle - \langle t_u - t_v, u - v \rangle \\
&\leq \langle s_u - s_v, \; u - v \rangle.
\end{aligned}$$

Thus, $\Gamma := S - T$ is S-pseudocontractive.

$$\text{(ii)} \implies \text{(i)}$$

We first note that $T = S - \Gamma$.

Now, let $u, v \in E$ be arbitrary, let $t_u \in Tu$ and $t_v \in Tv$, then $t_u = s_u - \gamma_u$ and $t_v = s_v - \gamma_v$ for some $s_u \in Su$, $s_v \in Sv$, $\gamma_u \in \Gamma u$, and $\gamma_v \in \Gamma v$. Thus,

$$\langle t_u - t_v, \; u - v \rangle = \langle s_u - \gamma_u - (s_v - \gamma_v), \; u - v \rangle = \langle s_u - s_v, \; u - v \rangle - \langle \gamma_u - \gamma_v, \; u - v \rangle \geq 0.$$

Therefore, T is monotone. $\square$

It is easily deducible from Lemma 3 that if T is S-pseudocontractive, then a coincidence point of T and S corresponds to a zero of the monotone map $S - T$. Hence, well known existence results for zeros of monotone operators naturally carry over for coincidence points of operators of this class. The crucial role of zeros of monotone operators in the analysis of solutions to minimization problems (see for example [39–42]) underscores the interplay between coincidence point problems and optimization problems.

3.3. Examples of S-Pseudocontraction

(1)   Let $E = \mathbb{H}$, a real Hilbert space, $S = \mathbb{I}$, the identity map on $\mathbb{H}$. Then, any pseudocontraction on $\mathbb{H}$ is S-pseudocontraction.
(2)   Every J-pseudocontraction is S-psuedocontraction with $S = J + M$, where M is any single-valued monotone map.

(3)   Let E be a smooth real Banach space, fix $p > 1$. Define $T_p : E \longrightarrow E^*$ and $S_p : E \longrightarrow E^*$ by:

$$T_p(u) = pJ(u)$$
$$S_p(u) = (p + \mu)J(u) + \parallel u \parallel^{p-2} J(u), \ \mu > 0.$$

Then, T_p is S_p-pseudocontractive and $0 \in C_0(T_p, S_p)$.

We remark that the map, T_p, failed to be pseudocontractive in the usual sense for $E = \mathbb{H}$. Furthermore, T_p is not J-pseudocontractive. In fact, for every mapping $T : E \longrightarrow E^*$, there exists a mapping $S : E \longrightarrow E^*$ such that T is S-pseudocontractive (Take $S = T + A$, where A is any monotone map on E).

Lemma 4. *Let $T : E \longrightarrow E^*$ be a single valued map. Let $S : E \longrightarrow 2^{E^*}$ be such that $\Psi := S^{-1} \circ T$ is well defined and single valued. If T is S-pseudocontractive, then for every $u, v \in E$,*

$$T(\Psi(u)) - T(\Psi(v)), \ \Psi(u) - \Psi(v) \leq T(u) - T(v), \ \Psi(u) - \Psi(v)$$

Proof. Let $u, v \in E$. By definition of Ψ, we have that

$T(u) \in S(\Psi(u))$ and $T(v) \in S(\Psi(v))$. Since T is S-pseudocontractive, then $\langle T(\Psi(u)) - T(\Psi(v)), \ \Psi(u) - \Psi(v) \rangle \leq \langle T(u) - T(v), \ \Psi(u) - \Psi(v) \rangle$ as required.   □

3.4. Approximation of Coincidence Points

Theorem 1. *Let E_1 and E_2 be reflexive real Banach spaces, with dual spaces E_1^* and E_2^* respectively. Let $T_1 : E_1 \longrightarrow E_1^*$ and $T_2 : E_2 \longrightarrow E_2^*$ be single-valued cyclically maximal monotone maps. Let $S_1 : E_1 \longrightarrow E_1^*$ and $S_2 : E_2 \longrightarrow E_2^*$ be mappings such that T_1 is S_1-pseudocontractive, T_2 is S_2-pseudocontractive and $g_1 := S_1^{-1} \circ T_1$, $g_2 := S_2^{-1} \circ T_2$ are well defined and single-valued. Let $A : E_1 \longrightarrow E_2$ be a bounded linear map with adjoint A^*. Assume that T_1^{-1} exists and generate inductively the sequence:*

$$
\begin{cases}
w_0 \in E_1 \\
v_n = T_1^{-1}(T_1(w_n) - rA^*(T_2(Aw_n) - T_2(g_2(Aw_n)))) \\
w_{n+1} = T_1^{-1}(\alpha T_1(v_n) + (1 - \alpha)T_1(g_1(v_n))) \\
r > 0, 0 \leq \alpha < 1.
\end{cases}
\tag{1}
$$

Suppose that the set $sol(SCCPP)$ is nonempty, where

$$sol(SCCPP) = \{z \in E_1 : z \in C_0(T_1, S_1) \text{ and } Az \in C_0(T_2, S_2)\}.$$

Then, given $z \in sol(SCCPP)$,

$$
\begin{aligned}
B_{\psi_1}(z, w_{n+1}) \leq{} & B_{\psi_1}(z, w_n) - B_{\psi_1}(v_n, w_n) - \alpha B_{\psi_1}(g_1(v_n), v_n) \\
& - r\Big[B_{\psi_2}(g_2(Aw_n), Aw_n) - B_{\psi_2}(Av_n, Aw_n)\Big]
\end{aligned}
$$

$\psi_1, \ \psi_2$ are convex functions guaranteed by Lemma 1 for T_1, T_2, respectively.

Proof. Let $z \in sol(SCCPP)$ and $\psi_1, \ \psi_2$ as in Lemma 1, using (1), definition of $B_\psi(.,.)$ and property of adjoint, we have that

$$B_{\psi_1}(z, v_n) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(v_n, w_n) + rT_2(Aw_n) - T_2(g_2(Aw_n)), \ Az - Av_n$$

Applying the fact that $z \in sol(SCCPP)$, simple arithmetic, Lemma 4, and second property of $B_\psi(.,.)$ in Definition 4(a), we obtain

$$B_{\psi_1}(z, v_n) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(v_n, w_n) - rB_{\psi_2}(g_2(Aw_n), Aw_n) - rB_{\psi_2}(Av_n, g_2(Aw_n)) + rB_{\psi_2}(Av_n, Aw_n)$$
$$\leq B_{\psi_1}(z, w_n) - B_{\psi_1}(v_n, w_n) - rB_{\psi_2}(g_2(Aw_n), Aw_n) + rB_{\psi_2}(Av_n, Aw_n) \tag{2}$$

Next, observe from (1) that

$$w_{n+1} = T_1^{-1}(T_1(v_n) - (1-\alpha)[T_1(v_n) - T_1(g_1(v_n))])$$

Then, applying same steps used in the above argument yield

$$B_{\psi_1}(z, w_{n+1}) \leq B_{\psi_1}(z, v_n) - \alpha B_{\psi_1}(w_{n+1}, v_n) - \alpha B_{\psi_1}(g_1(v_n), v_n) \tag{3}$$

Thus, combining (2) and (3) gives

$$B_{\psi_1}(z, w_{n+1}) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(v_n, w_n) - \alpha B_{\psi_1}(g_1(v_n), v_n) - rB_{\psi_2}(g_2(Aw_n), Aw_n) + rB_{\psi_2}(Av_n, Aw_n) \tag{4}$$

□

Corollary 1. *Under the conditions of Theorem 1, let $T_1 = T_2$, $S_1 = S_2$, $A = \mathbb{I}$ and $\alpha = 0$, then direct substitution gives*

$$B_\psi(z, w_{n+1}) \leq B_\psi(z, w_n) - (1-r)B_\psi(w_{n+1}, w_n) - B_\psi(g(w_n), w_n)$$

Theorem 2. *Under the conditions of Theorem 1, assume that T_1 is strongly monotone with constant k_1 and weakly sequentially continuous, and T_2 is k_2-Lipschitz and φ-strongly monotone on bounded sets. Take $r < \frac{k_1}{k_1 + k_2 \|A\|^2}$ and $\alpha > 0$, if $\mathbb{I}_{E_1} - g_1$ and $\mathbb{I}_{E_2} - g_2$ are demi-closed at zero, then, the sequence $\{w_n\}$ generated by (1), converges weakly to a point $z_0 \in sol(SCCPP)$.*

Proof. The added properties of T_1 and T_2, (4) and the fact that $0 < r < \frac{k_1}{k_1 + k_2 A^2}$ give the following:

- $B_{\psi_1}(z, w_{n+1}) \leq B_{\psi_1}(z, w_n) - v_n - \| w_n \|^2$
- $\lim_{n \to \infty} B_{\psi_1}(z, w_n)$ exists
- $\{w_n\}$ is bounded
- $\lim_{n \to \infty} \| v_n - w_n \| = 0$ and $\{v_n\}$ is also bounded.

   Also from (4), we deduce that

$$\lim_{n \to \infty} B_{\psi_1}(g_1(v_n), v_n) = \lim_{n \to \infty} B_{\psi_2}(g_2(Aw_n), Aw_n) = 0$$

Hence, the boundedness of the sequences $\{v_n\}$ and $\{Aw_n\}$ together with Lemma 2 gives the following:

- $\{g_1(v_n)\}$ and $\{g_2(Aw_n)\}$ are bounded
- $\lim_{n \to \infty} \| g_1(v_n) - v_n \| = \lim_{n \to \infty} \| g_2(Aw_n) - Aw_n \| = 0$

   Next, denote the set of weak limit points of $\{w_n\}$ by $W(w_n)$. The boundedness of $\{w_n\}$ guarantees that $W(w_n)$ is nonempty. To conclude our proof, it suffices to show the following:

(i) $W(w_n) \subseteq sol(SCCPP)$
(ii) $W(w_n)$ is a singleton

Now, for (i), pick $p_0 \in W(w_n)$ arbitrarily, then there exists $\{w_{n_j}\} \subseteq \{w_n\}$ such that $w_{n_j} \rightharpoonup p_0$. Thus, $v_{n_j} \rightharpoonup p_0$ and $Aw_{n_j} \rightharpoonup Ap_0$. Since $\| g_1(v_{n_j}) - v_{n_j} \| \longrightarrow 0$ and $\| g_2(Aw_{n_j}) - Aw_{n_j} \| \longrightarrow 0$, we have by demi-closedness that $p_0 = g_1(p_0)$ and $Ap_0 = g_2(Ap_0)$.

This gives that $T_1(p_0) \in S_1(p_0)$ and $T_2(Ap_0) \in S_2(Ap_0)$. Therefore, $p_0 \in sol(SCCPP)$.

Next, we show that $W(w_n)$ is a singleton. For a contradiction, suppose that there exists u_0, $u_1 \in W(w_n)$ such that $u_0 \neq u_1$, then, there exists $\{w_{n_k}\}$, $\{w_{n_i}\}$ subsequences of $\{w_n\}$ such that $w_{n_k} \rightharpoonup u_0$ and $w_{n_i} \rightharpoonup u_1$. Now we know that

$$\lim_{n \to \infty} \Big[\psi_1(u_0) - \psi_1(u_1) + B_{\psi_1}(u_1, \, w_n) - B_{\psi_1}(u_0, \, w_n) \Big] = \lim_{n \to \infty} \langle u_0 - u_1, \, T_1(w_n) \rangle$$

exists. Hence,

$$\lim_{k \to \infty} \langle u_0 - u_1, \, T_1(w_{n_k}) \rangle = \lim_{i \to \infty} \langle u_0 - u_1, \, T_1(w_{n_i}) \rangle$$

By weak sequential continuity of T_1, we have that

$$\langle u_0 - u_1, \, T_1(u_0) - T_1(u_1) \rangle = 0 \longrightarrow u_0 = u_1 \text{contradicting that } u_0 \neq u_1$$

Therefore $W(w_n)$ is a singleton. □

Corollary 2. *Let K_1 and K_2 be nonempty, closed, and convex subsets of reflexive spaces E_1 and E_2 respectively. Let $A : E_1 \longrightarrow E_2$ such that $A(K_1) \subseteq K_2$. Let T_1, T_2, S_1, S_2, g_1, g_2, r and α satisfy the assumptions of Theorem 2 on K_1 and K_2. Then, the sequence $\{w_n\}$ inductively generated by*

$$\begin{cases} w_0 \in K_1 \\ y_n = \prod_{\psi_1}^{K_1} \Big(T_1^{-1}(T_1(w_n) - rA^*(T_2(Aw_n) - T_2(g_2(Aw_n)))) \Big) \\ w_{n+1} = \prod_{\psi_1}^{K_1} \Big(T_1^{-1}(\alpha T_1(v_n) + (1-\alpha)T_1(g_1(v_n))) \Big), \end{cases} \tag{5}$$

weakly converges to a solution of the K_1, K_2 constrained SCCPP.

Proof. By simple computation using the definition of $B_{\psi_1}(.\,,\,.)$ and characterization of y_n as in Definition 4(b), we have for $z \in sol(SCCPP)$ that

$$B_{\psi_1}(z, y_n) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(y_n, w_n) + r\langle T_2(Aw_n) - T_2(g_2(Aw_n)), \, Az - Ay_n \rangle$$

By $z \in sol(SCCPP)$, simple arithmetic, Lemma 4, and second property of $B_{\psi_1}(.\,,\,.)$ in Definition 4(a), we obtain that

$$\langle T_2(Aw_n) - T_2(g_2(Aw_n)), \, Az - Ay_n \rangle$$
$$\leq B_{\psi_2}(Ay_n, Aw_n) - B_{\psi_2}(g_2(Aw_n), Aw_n) - B_{\psi_2}(Ay_n, g_2(Aw_n))$$

Hence,

$$B_{\psi_1}(z, y_n) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(y_n, w_n) + rB_{\psi_2}(Ay_n, Aw_n) - rB_{\psi_2}(g_2(Aw_n), Aw_n)$$

Similarly,

$$B_{\psi_1}(z, w_{n+1}) \leq B_{\psi_1}(z, y_n) - \alpha B_{\psi_1}(g_1(y_n), y_n) - \alpha B_{\psi_1}(w_{n+1}, y_n)$$

Thus,

$$B_{\psi_1}(z, w_{n+1}) \leq B_{\psi_1}(z, w_n) - B_{\psi_1}(y_n, w_n) + rB_{\psi_2}(Ay_n, Aw_n) - rB_{\psi_2}(g_2(Aw_n), Aw_n) - \alpha B_{\psi_1}(g_1(y_n), y_n) \tag{6}$$

It follows from (6) that

- $\lim\limits_{n\to\infty} B_{\psi_1}(z, w_n)$ exists
- $\{w_n\}$ is bounded
- $\lim\limits_{n\to\infty} \| y_n - w_n \| = 0$ and $\{y_n\}$ is also bounded.
- $\lim\limits_{n\to\infty} B_{\psi_1}(g_1(y_n), y_n) = \lim\limits_{n\to\infty} B_{\psi_2}(g_2(Aw_n), Aw_n) = 0$, thus $\{g_1(y_n)\}$ and $\{g_2(Aw_n)\}$ are bounded. Moreover, $\lim\limits_{n\to\infty} \| g_1(y_n) - y_n \| = \lim\limits_{n\to\infty} \| g_2(Aw_n) - Aw_n \| = 0$

Finally, using a similar argument as in Theorem 2, we deduce that

$$W(w_n) \subseteq sol(SCCPP) \text{ and } W(w_n) = \{u_0\}$$

$\square$

4. Application to Inverse Planning Optimization

4.1. An Inverse Planning Optimization Problem (IPOP)

Prior to treatment optimization, the patient's volume (usually a 3D representation of the patient's anatomy obtained from medical images such as computed tomography (CT) and magnetic resonance imaging (MRI) scans) is discretized into sub-volumes called voxels. The anatomy is further outlined into various structures grouped as planning target volume (PTV) and organs at risk (OAR). Individual voxels may belong to several structures, but for simplicity, it is usual to associate each to one structure.

Now suppose there are N number of voxels indexed by $i = 1, 2, \ldots, N$ and M candidate beams (beamlets) indexed by $j = 1, 2, \ldots, M$. Then, the total dose absorbed in the ith voxel is given by

$$d_i = \sum_{j=1}^{M} a_{ij} u_j$$

where a_{ij} is the $(i \times j)$th entry of the dose influence matrix $A : \mathbb{R}^M \longrightarrow \mathbb{R}^N$ and u_j is the intensity of the jth beam (beamlet) [19].The IPOP is formulated as

$$\text{find } u^* \in \mathbb{R}_+^M \text{ such that } Au^* \in \min(f)$$

where $f : \mathbb{R}^N \longrightarrow \mathbb{R}$ is a dose dependent objective function modeled based on clinical goals, and $\min(f)$ denotes the set of minimizers of f. For analysis of some convex reformulation of commonly used objective criteria in RTP, we refer the reader to [9,43].

4.2. SCCPP Reformulation of IPOP

We begin with the following assumptions:

(a) f is convex
(b) f is "partly" differentiable, that is, f can be written as a sum of two convex functions f_1 and f_2 such that f_1 or f_2 is differentiable. Without loss of generality, we shall always assume f_2 to be differentiable.
(c) There exists a differentiable convex function h and a positive constant θ, such that $\theta h - f_2$ is Legendre, totally convex, cofinite, and has Lipschitz continuous gradient

Now, let $E_1 = \mathbb{R}^M$, $E_1 = \mathbb{R}^N$, $K_1 = \bigcap_{l=1}^{\rho} \{u \in \mathbb{R}_+^M : \sigma_l(u) \leq \rho_l\}$ for some convex constraint functions σ_l and scalars $\rho_l \in \mathbb{R}$ and $K_2 = \mathbb{R}_+^N$. Let A be the dose influence matrix, then $A(K_1) \subseteq K_2$.

Let $f : E_2 \longrightarrow \overline{\mathbb{R}}$, a dose dependent objective function modeled based on clinical goals, satisfy assumptions (a)–(c). Define the following operators

$$
\begin{aligned}
T_1 &:= \tau \mathbb{I}_{E_1} = S_1, \tau > 0 \\
T_2 &:= \kappa \left(\nabla h - \tfrac{1}{\theta} \nabla f_2 \right), \ \kappa > 0 \\
S_2 &:= \kappa \left(\nabla h + \tfrac{1}{\theta} \partial f_1 \right), \ \kappa > 0
\end{aligned}
$$

Then, it can easily be shown that

(i) T_1 is strongly monotone, cofinite, sequentially continuous, and T_1 inverse exists
(ii) T_1 is S_1-pseudocontractive, and T_2 is S_2-pseudocontractive.
(iii) T_2 is Lipschitz continuous and φ-strongly monotone
(iv) the mappings $g_1 := S_1^{-1} \circ T_1$ and $g_2 := S_2^{-1} \circ T_2$ are well defined and single-valued [44]. Also $\mathbb{I}_{E_1} - g_1$ and $\mathbb{I}_{E_2} - g_2$ are demi-closed at zero.
(v)   a solution of the constrained SCCPP associated with T_1, S_1 and T_2, S_2 solves the constrained IPOP (see Lemma 3 and Remark 1). (i)–(iv) verifies all the assumptions of Corollary 2; hence, by (v), (5) converges to a solution of the IPOP.

4.3. Common Biological and/or Physical Objective Criteria in RTP

We now demonstrate that the reformulation presented in Section 4.2 accommodates *several* important physical and/or biological objective functions applied in RTP. We consider five examples. In each example, we provide f_1, f_2, h, and θ for which assumptions (a)–(c) in Section 4.2 are satisfied. We adopt the following notations:

$$
\begin{aligned}
\mathbb{T} &:= \ \text{number of voxels in the target volume (or PTV)} \\
\mathbb{O} &:= \ \text{number of voxels in Organs at Risk (OAR)}
\end{aligned}
$$

for a total of N voxels, we index voxels in OAR by $\mathbb{T}+1$, $\mathbb{T}+2$, ..., $\mathbb{T}+\mathbb{O} = N$.

Example 1. *(Physical criteria)*

$$
f(w) = \sum_{j=1}^{\mathbb{T}} a_j \left(w_j - D_p^j \right)^{q_1} + \sum_{j=\mathbb{T}+1}^{N} b_j \left(w_j - D_{max}^j \right)_+^{q_2}
$$

where $(.)_+ := \max\{., 0\}$, D_p^j *is the dose prescription for voxel j,* D_{max}^j *is the maximum dose allowed for voxel j,* a_j *and* b_j *are positive weighting factors, and the exponents* q_1 *and* q_2 *are even. Clearly, f is convex.*

$$
\begin{aligned}
f_1 &:= 0 \\
f_2 &:= f \\
h &:= f + \tfrac{\lambda}{2} \| \, . \, \|^2, \ \lambda > 0 \\
\theta &= 1
\end{aligned}
$$

A very similar objective function was studied in [4]. Part of the results obtained indicates that with choice of exponents greater than 2, dose homogeneity inside the target can be effectively improved.

Example 2. *(Biological criteria)*

$$
f(w) = -\ln \left(TCP_{LQ}(w) \right) - \ln(1 - NTCP_{AN}(w))
$$

where

$$TCP_{LQ}(w) = \exp\left[-N_0 \sum_{j=1}^{\mathbb{T}} v_j \exp\left(-\alpha w_j - \frac{\beta w_j^2}{n_f}\right)\right]$$

$$NTCP_{AN}(w) = 1 - \exp\left[-\sum_{j=\mathbb{T}+1}^{N} v_j \left(\frac{\alpha w_j + \frac{\beta w_j^2}{n_f}}{\alpha \Delta}\right)^a\right], \ 1 \le a < +\infty$$

N_0 *is the initial number of clonogenic cells,* v_j *is the relative volume of voxel* j *,* α *and* β *are radiobiologic parameters of the linear quadratic (LQ) cell survival model such that* $\alpha^2 n_f > 2\beta$*, and* n_f *is the number of treatment fractions. Clinical* α*,* β *,* n_f *values in this category for prostate, brain, breast, and liver tumors can be found in [45–49].* Δ *and* a *are structure-dependent scalars.*

We remark that f is a negative log transform of an uncomplicated tumor control model derived from the LQ-Poisson TCP and a biological effective dose (BED) version of the Alber and Nusslin NTCP model [50]. The convexity of f follows from Appendix A and E in [43].

$$\begin{aligned} f_1 &:= 0 \\ f_2 &:= f \\ h &:= f + \frac{\lambda}{2} \|.\|^2, \ \lambda > 0 \\ \theta &= 1 \end{aligned}$$

Example 3. *(Biological criteria)*

$$f(w) = -\ln\left(1 - (NTCP_{RS}(w))^s\right), \ s > 0$$

where

$$NTCP_{RS}(w) = \left[1 - \prod_{j=1}^{N}\left(1 - \exp\left(-sN_0 \exp\left(-\alpha w_j - \frac{\beta w_j^2}{n_f}\right)\right)\right)^{v_j}\right]^{\frac{1}{s}}$$

s is the relative parameter characterizing the internal organization of a structure (or organ). Other parameters are the same as in Example 2.

f is a negative log transform of the well known relative Seriality NTCP model. Its convexity was analyzed in [43].

$$\begin{aligned} f_1 &:= 0 \\ f_2 &:= f \\ h &:= f + \frac{\lambda}{2} \|.\|^2, \ \lambda > 0 \\ \theta &= 1 \end{aligned}$$

In [4], a related objective function (weighted sum of NTCPs evaluated with Lyman NTCP model), and subjected to physical constraints specifying the "admissible minimum and maximum dose to targets", was proposed and implemented.

Example 4. *(Hybrid criteria)*

$$f(w) = \sum_{j=1}^{\mathbb{T}} a_j \left(w_j - D_p^j\right)^{q_1} - \ln(1 - NTCP_{AN}(w))$$

where the symbols have the same meaning as in Examples 1 and 2. The convexity of f follows easily from [43].

$$\begin{aligned}
f_1 &:= 0 \\
f_2 &:= f \\
h &:= f + \tfrac{\lambda}{2} \|\,.\,\|^2, \ \lambda > 0 \\
\theta &= 1
\end{aligned}$$

Example 5. *(Physical criteria)*

$$f(w) = \sum_{j=1}^{\mathbb{T}} a_j \left(w_j - D_p^j\right)^{q_1} + \sum_{j=\mathbb{T}+1}^{N} b_j \left(w_j - D_{max}^j\right)_+$$

where the symbols have the same meaning as in Example 1. f is clearly convex.

$$\begin{aligned}
f_1 &:= \sum_{j=\mathbb{T}+1}^{N} b_j \left(w_j - D_{max}^j\right)_+ \\
f_2 &:= \sum_{j=1}^{\mathbb{T}} a_j \left(w_j - D_p^j\right)^{q_1} \\
h &:= f_2 + \tfrac{\lambda}{2} \|\,.\,\|^2, \ \lambda > 0 \\
\theta &= 1
\end{aligned}$$

4.4. Insights on Algorithm Implementation

The algorithm labeled (5) has been carefully designed. Its efficiency in terms of speed and accuracy can easily be demonstrated by a simple numerical example. However, this may not be truly valuable. In this instance, what may truly be of high value and practical usefulness is to demonstrate those, when the algorithm is implemented for the reformulated IPOP, in a clinical setting.

Implementation in a clinical setting involves a series of steps beginning with the selection of a clinical case (for example, a prostate cancer case), and obtaining the relevant clinical datasets. These clinical datasets may include the original Digital Imaging and Communications in Medicine (DICOM) CT scan image, the DICOM radiotherapy structure files containing the contours of targets and organs at risk, and the dose prescriptions as well as treatment schedule. Furthermore, we require optimization data such as size, resolution, and number of voxel grids in each geometrically contoured structure, and beam information such as beam energy, couch, and gantry angles, number of beamlets, and the geometric location of each beamlet, required for the computation of the dose influence matrix, which is then coupled into the optimization algorithm (in this case, (5)) to generate the optimized fluence map. These processes are far from trivial. Thus, we refrain from illustrating and analyzing this implementation in this paper. Nevertheless, for the RTP objective functions presented in Section 4.3, we give explicit forms of the operator g_2 appearing in (5) (for Examples 1 and 4) and an approximate form of g_2 (for Example 2), to aid in executing (5) during clinical implementation.

Forms of g_2.

For Example 1, with $\kappa = 1$, $q_1 = 4$ and $q_2 = 2$,
$S_2^{-1}(x) = u \in \mathbb{R}^N$ such that:

if $j \leq \mathbb{T}$:

$$u_j = D_p^j + \left(\frac{x_j - \lambda a_j D_p^j}{8a_j} + \sqrt{\left(\frac{x_j - \lambda a_j D_p^j}{8a_j} \right)^2 + \left(\frac{\lambda}{12a_j} \right)^3} \right)^{\frac{1}{3}} + \left(\frac{x_j - \lambda a_j D_p^j}{8a_j} - \sqrt{\left(\frac{x_j - \lambda a_j D_p^j}{8a_j} \right)^2 + \left(\frac{\lambda}{12a_j} \right)^3} \right)^{\frac{1}{3}}$$

else if $x_j > \lambda D_{max}^j$:

$$u_j = \frac{2b_j D_{max}^j + x_j}{2b_j + \lambda}$$

else:

$$u_j = \frac{x_j}{\lambda}$$

Hence, $g_2(x) = S_2^{-1}(\lambda x)$

For Example 4, with $= 1$, $q_1 = 4$, $a = 2$, and $\nabla^2 \lambda > 1$
$S_2^{-1}(x) = u \in \mathbb{R}^N$ such that:

if $j \leq \mathbb{T}$:

$$u_j = D_p^j + \left(\frac{x_j - \lambda a_j D_p^j}{8a_j} + \sqrt{\left(\frac{x_j - \lambda a_j D_p^j}{8a_j} \right)^2 + \left(\frac{\lambda}{12a_j} \right)^3} \right)^{\frac{1}{3}} + \left(\frac{x_j - \lambda a_j D_p^j}{8a_j} - \sqrt{\left(\frac{x_j - \lambda a_j D_p^j}{8a_j} \right)^2 + \left(\frac{\lambda}{12a_j} \right)^3} \right)^{\frac{1}{3}}$$

else

$$u_j = \phi_j = -\frac{\alpha n_f}{2\beta} + \left(\frac{n_f^2 \left(\alpha^2 \nabla^2 x_j + \frac{\alpha^3 \nabla^2 n_f \lambda}{2\beta} \right)}{8\beta^2 v_j} + \sqrt{\left(\frac{n_f^2 \left(\alpha^2 \nabla^2 x_j + \frac{\alpha^3 \nabla^2 n_f \lambda}{2\beta} \right)}{8\beta^2 v_j} \right)^2 + \left(\frac{n_f^2 \left(\alpha^2 \nabla^2 \lambda - \alpha^2 v_j \right)}{12\beta^2 v_j} \right)^3} \right)^{\frac{1}{3}} +$$

$$\left(\frac{n_f^2 \left(\alpha^2 \nabla^2 x_j + \frac{\alpha^3 \nabla^2 n_f \lambda}{2\beta} \right)}{8\beta^2 v_j} - \sqrt{\left(\frac{n_f^2 \left(\alpha^2 \nabla^2 x_j + \frac{\alpha^3 \nabla^2 n_f \lambda}{2\beta} \right)}{8\beta^2 v_j} \right)^2 + \left(\frac{n_f^2 \left(\alpha^2 \nabla^2 \lambda - \alpha^2 v_j \right)}{12\beta^2 v_j} \right)^3} \right)^{\frac{1}{3}}$$

Hence, $g_2(x) = S_2^{-1}(\lambda x)$

For Example 2, with $\kappa = 1$, $a = 2$, and $\alpha^2 n_f > 2\beta$
$S_2^{-1}(x) \approx u \in \mathbb{R}^N$ such that:

if $j \leq \mathbb{T}$:

$$\begin{cases} u_j = \varnothing_j, & \text{if } j \leq T \\ u_j = \phi_j, & \text{otherwise} \end{cases}$$

where $\varnothing_j$ satisfies $a_j \varnothing_j^3 + b_j \varnothing_j^2 + c_j \varnothing_j + d_j = 0$ with $d_j = -\left(N_0 \alpha v_j + x_j \right)$

$$a_j = \frac{-N_0 \beta \left(\alpha^2 - \frac{2\beta}{n_f} \right) v_j}{n_f}, \quad b_j = N_0 \alpha \left(\frac{3\beta}{n_f} - \frac{\alpha^2}{2} \right) v_j, \quad c_j = N_0 v_j \left(\alpha^2 - \frac{2\beta}{n_f} \right) + \lambda$$

Hence, $g_2(x) \approx S_2^{-1}(\lambda x)$

For other methods of approximation see [51–53].

5. Conclusions

We have introduced and discussed a nonlinear optimization formulation called the split common coincidence point problem (SCCPP). We showed that this formulation is applicable to inverse planning optimization with increased flexibility in accommodating several biological and/or physical criteria recommended for RTP optimization. Although the objective functions are required to be convex, equivalent convex reformulations of commonly used non-convex objective criteria in RTP exist in the literature. We developed and proved convergence of an iterative algorithm to a solution of the SCCPP, which in this particular application corresponds to an extremum of some (bio)physically-based inverse planning optimization problem. In addition, we provided useful insights toward the implementation of the algorithm in a clinical setting.

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