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Multiobjective approaches based on variable ordering structures for intensity problems in radiotherapy treatment

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Abstract

Recently, in many papers Intensity Modulated Radiotherapy Treatment problems are studied as multicriteria optimization problems with respect to a constant ordering cone. In these problems, the goal is to maximize the dose delivered to cancer tumor as well as to reduce side effects. However, from a practical perspective, it is more convenient to consider such problems with respect to a variable ordering structure. In this paper, we introduce a special cone-valued mapping based on the goal of cancer treatment. We consider a mathematical formulation of intensity problems equipped with this ordering structure. In addition, we derive necessary conditions for solutions of a vector-valued approximation problem with respect to a general ordering cone. Finally, we calculate in detail necessary conditions for minimal solutions of the intensity problem in radiotherapy treatment.

Key words: Variable ordering structure, intensity modulated radiotherapy treatment, dose response curve, threshold dose, vector-valued norm, coderivative, normal cone.

1 Motivation

Intensity Modulated Radiotherapy Treatment (IMRT) is an advancement in radiotherapy that allows modulating radiation intensity across a beam. Currently, it is being used to treat cancers of the prostate, head and neck, breast, lung as well as certain types of sarcomas. The basic idea of IMRT is to reduce the intensity of rays

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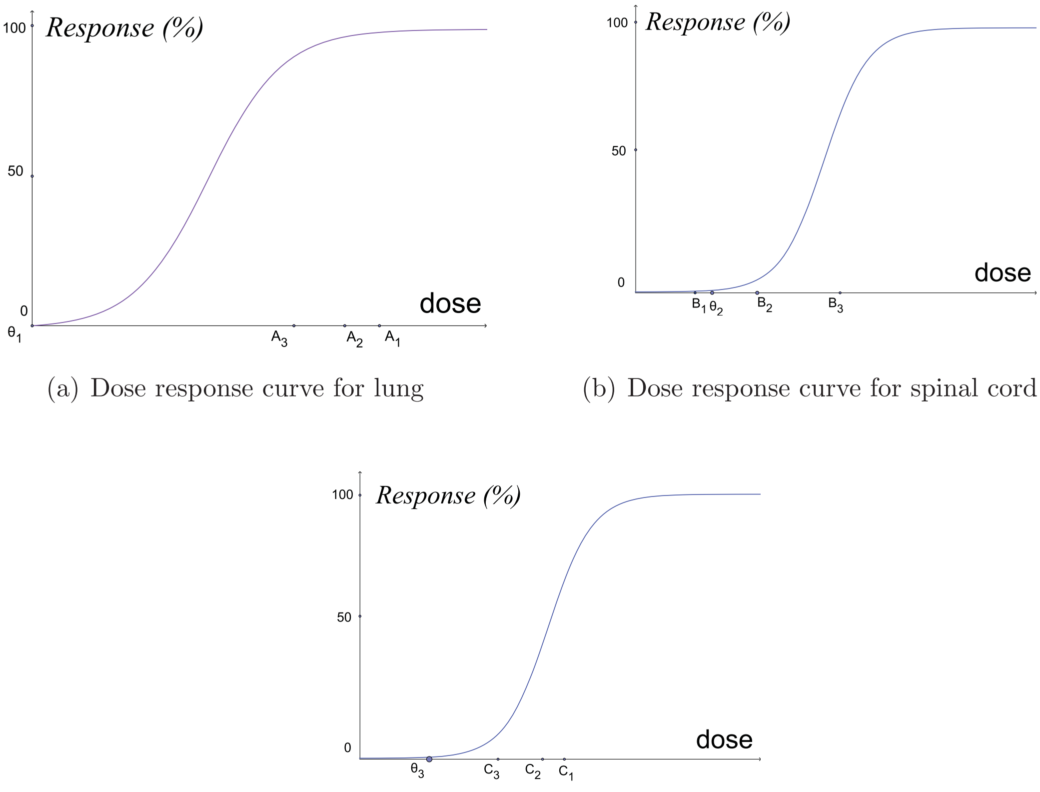
going through particularly sensitive critical structures and to increase the intensity of those rays seeing primarily the target volume.

The problem of calculating those intensities based on dose prescription in the target volume and the sorrounding critical structures is called inverse planning. This problem is modeled as a multicriteria optimization problem with an objective function depending on the specific goal that the treatment planner wants to achieve. In general, a level dose of radiation in the cancer organ should be closed to desired dose while it is absolutely necessary to avoid radiation in the organs out side the tumor (the critical organs) as much as possible. This inverse problem with respect to (w.r.t.) a constant cone is studied by several authors and can be divided into two categories, multiobjective nonlinear programming and multiobjective linear programming. For a general survey we refer the reader to [3]. However, from a practical perspective, it may seem more appropriate to concern this inverse problem as a multicriteria optimization problem w.r.t. a variable ordering structure, see [4]. This will be illustrated for a special problem in radiotherapy treatment in the following.

We consider the treatment of a lung cancer, lung is the most sensitive organ to radiotherapy damage. The dose delivered to lung is limited by spinal cord and heart (critical organs). Thus, to reduce side effects, the doses delivered to spinal cord and heart have to be minimized. A dose response curve describes the change in effect on an organ caused by differing levels of doses delivered to it. We suppose that the dose response curves for lung, spinal cord and heart in lung cancer treatment are illustrated in Fig1.



(a) Dose response curve for lung

(b) Dose response curve for spinal cord

(c) Dose response curve for heart

Figure 1: Dose response curves in lung cancer treatment

These curves can be used to estimate a threshold dose for each organ. The threshold dose is defined as the dose of radiation, below which the organism does not suffer from any effect. In mathematical point of view, it is the dose, below which the response is zero and above which it is nonzero ([7], [12]). In this case, we assume that θ_1, θ_2 and θ_3 are respectively the threshold doses of lung, spinal cord and heart. We now have a look at three treatment plans $(A_1, B_1, C_1), (A_2, B_2, C_2),$ and (A_3, B_3, C_3) where A_i, B_i, C_i are the doses delivered to lung, spinal cord and heart respectively, i=1,2,3. From a practical point of view, if the response of the organ on dose variations is relatively small, a rise of the dose delivered to that organ in favor of an improvement of the value for another organ is preferred ([4]). In more detail, we would not only prefer an improvement of the dose level in lung, spinal cord and heart but also to rise the dose delivered to spinal cord from B_1 to B_2 for reducing the dose amount in heart, for instance, from C_1 to C_2. The reason is that a large improvement in the effect on heart is reached by changing the dose to C_2 while the

effects on lung and spinal cord are reduced mildly.
We suppose that all treatment plans is a subset of $\mathbb{R}^3$ and consider a closed convex cone $\mathcal{C} \subset \mathbb{R}^3$. Suppose that we derive a mathematical model for this problem w.r.t $\mathcal{C}$. We denote $(A_2, B_2, C_2) \leq_{\mathcal{C}} (A_1, B_1, C_1)$ if $(A_1, B_1, C_1) - (A_2, B_2, C_2) \in \mathcal{C}$. We set $d := (A_1, B_1, C_1) - (A_2, B_2, C_2)$, it yields $d \in \mathcal{C}$. Since $\mathcal{C}$ is a cone, $\lambda d \in \mathcal{C}$ for all $\lambda > 0$ and therefore with (A_3, B_3, C_3) satisfies $(A_2, B_2, C_2) - (A_3, B_3, C_3) = \beta d$ with $\beta > 0$ we have $(A_3, B_3, C_3) \leq_{\mathcal{C}} (A_2, B_2, C_2)$ i.e (A_3, B_3, C_3) is 'better' than (A_2, B_2, C_2).
On the other hand, having a look at the dose response curve of spinal cord, the increase in the effect for spinal cord is large by changing the dose from B_2 to B_3. Therefore (A_3, B_3, C_3) might not be a preferred solution from a practical point of view. Thus, the choice of variable ordering cone depending on the actual doses in this circumstance seems to be more appropriate.
The rest of this paper is organized as follows. In Section 2, some preliminaries are given. In Section 3, we construct a variable ordering structure based on the goal of cancer treatment and formulate a mathematical problem for IMRT. In Section 4, a multiobjective approximation problem equipped with the proposed structure as well as a general cone-valued mapping is introduced. This section is also concerned with providing optimality conditions for nondominated solutions of this problem. In Section 5, we presents an application in radiotherapy treatment by giving specific conditions for minimal solutions of the mathematical formulation introduced in Section 3.

2 Preliminaries

2.1 Some notions related to variable ordering structures

Throughout this section, unless otherwise stated, X, Y and Z are taken as Banach spaces over the real field $\mathbb{R}$ with their dual X^*, Y^* and Z^* respectively. The closed unit ball in any space, say X, are denoted by $\mathbb{B}_X$, we obmit the subscript X when no confusion occurs. For a nonempty set $A \in X$ we define

$$\text{cone}\, A := \{ta : t \in \mathbb{R}_+, a \in A\} \text{ where } \mathbb{R}_+ = [0, \infty).$$

Recall that the affin hull of A is defined as

$$\text{aff}\, A := \{\sum_{i=1}^{l} \lambda_i x_i | x_i \in A, \lambda_i \in \mathbb{R}, \sum_{i=1}^{l} \lambda_i = 1, l \in \mathbb{N}\},$$

which is the smallest affine set containing A. The closure of aff A in X is called the closed affine hull of A and is denoted by $\overline{\text{aff}} A$. The relative interior rint A of A is

the interior of A with respect to $\overline{\text{aff}}A$.
A set $Q \subset Y$ is a cone if for every $q \in Q$ and for all $\lambda \geq 0, \lambda q \in Q$ holds true. A cone Q is called convex if $Q + Q \subseteq Q$. In addition, a cone Q is called pointed if $Q \cap (-Q) = \{0\}$ and Q is proper if $Q \neq Y$ and $Q \neq \{0\}$. For a cone $Q \subset Y$ we set $Q^+ := \{y^* \in Y^* |\ \forall\ y \in Q : y^*(y) \geq 0\}$ for the positive dual cone of Q. We say that a convex cone Q is well-based if there exists a bounded convex set B such that $Q = \mathbb{R}^+ B$ and $0 \notin \operatorname{cl} B$. So a cone Q having a convex weakly compact base is well-based.
We will give the definition of a normal cone which shows a connection between topology and order of the space Y. We say that a nonempty set U of the linear space Y is full with respect to the convex cone $Q \subset Y$ if $U = [U]_Q$, where

$$[U]_Q := (U + Q) \cap (U - Q);$$

note that $[U]_Q$ is full with respect to Q for every nonempty subset U of Y.

Definition 1 *(Normal cone, [1]) Let Q be a proper convex cone in a Banach space Y. Then Q is called normal if the origin $0 \in Y$ has a neighborhood base formed by full sets with respect to Q.*

Observe that the convex cone $C \subset \mathbb{R}^n$ is normal if and only if $\operatorname{cl} C$ is pointed, see [5, Corollary 2.2.11].

Although the definitions given below hold in arbitrary Banach spaces, we will apply a Theorem concerning to optimality conditions for vector problem w.r.t variable ordering structures which requires the Asplund property of the spaces in question. Thus, we recall that a Banach space X is Asplund if any convex continuous function $\varphi : U \to \mathbb{R}$ defined on an open convex subset U of X is Fréchet differentiable on a dense subset o U [13, Definition 1.22]. It is known that the reflexive Banach spaces and the Banach spaces with separable dual are Asplund spaces. Thus c_0 and l^p, $L^p[0,1]$ for $1 < p < \infty$ are Asplund spaces but l^1 is not an Asplund space.
Now we present the definition of variable ordering by Eichfelder [4].

Definition 2 *(Variable ordering structure, [4]) Let Y be Banach space and $\mathcal{K} : Y \rightrightarrows Y$ be a set-valued map such that for every $y \in Y, \mathcal{K}(y)$ is a proper convex cone. Then for every $y_1, y_2 \in Y$, we define*

$$y_1 \leq_{N,\mathcal{K}} y_2 \text{ if } y_2 \in y_1 + \mathcal{K}(y_1) \tag{1}$$
$$y_1 \leq_{P,\mathcal{K}} y_2 \text{ if } y_2 \in y_1 + \mathcal{K}(y_2). \tag{2}$$

If elements in the space Y are compared using the binary relation (1) or (2), then it is said that $\mathcal{K}$ defines a variable ordering structure on Y.

For convenience, from now on we write the notations $\leq_{N,\mathcal{K}}$, $\leq_{P,\mathcal{K}}$ by relaxed forms $\leq_N$ and $\leq_P$.
Before deriving the definitions for efficient solutions of a vector optimization problem w.r.t. a variable ordering structure, it is necessary to concern the definition of nondominated elements and minimal elements of sets w.r.t. variable ordering structures.

Definition 3 *Let A be a nonempty subset of Y, $\bar{a} \in A$, and $\mathcal{K} : Y \rightrightarrows Y$ be a cone-valued map. We say that:*

(i) $\bar{a}$ is a nondominated element of A w.r.t. $\mathcal{K}(\cdot)$ if there is no $a \in A \setminus \{\bar{a}\}$ such that $a \leq_N \bar{a}$,i.e., $\bar{a} \in a+\mathcal{K}(a)$ or equivalently $\bar{a} \notin \cup_{a\in A}(\{a\}+\mathcal{K}(a)\setminus\{0_Y\})$. The set of all nondominated elements of A w.r.t. $\mathcal{K}(\cdot)$ is denoted by $ND(A, \mathcal{K}(\cdot))$.

(ii) $\bar{a}$ is a minimal element of A w.r.t.$\mathcal{K}(\cdot)$ if there is no $a \in A \setminus \{\bar{a}\}$ such that $a \leq_P \bar{a}$, i.e., $\bar{a} \in a + \mathcal{K}(\bar{a})$, or equivalently $(\{\bar{a}\} - \mathcal{K}(\bar{a})) \cap A = \{\bar{a}\}$. The set of all minimal elements of A w.r.t. $\mathcal{K}(\cdot)$ is denoted by $Min(A, \mathcal{K}(\cdot))$.

Obviously, when $\mathcal{K}(\cdot) = \mathcal{C}$ where $\mathcal{C}$ is a pointed convex cone of Y, the concepts of nondominated elements and minimal elements are identical. In case $\mathcal{K}(\cdot)$ is a variable structure, the relationship between these efficient elements of a set is described by the following Proposition.

Proposition 1 *[2, Proposition 3.1] Let $\mathcal{K} : Y \rightrightarrows Y$ be an ordering map on Y, A be a nonempty subset of Y. Then we have:*

(i) If $\bar{y}$ is a minimal element of A w.r.t. $\mathcal{K}(\cdot)$, then it is a nondominated element of A w.r.t. the nonvariable ordering structure $\hat{\mathcal{K}}$ defined by $\hat{\mathcal{K}}(y) \equiv \mathcal{K}(\bar{y})$, $\forall\, y \in Y$.

(ii) Consider the ordering cone $\mathcal{C}_{\mathcal{K}} := \cap_{y\in A}\mathcal{K}(y)$ and assume that $\mathcal{C}_{\mathcal{K}} \neq \emptyset$. If $\bar{y}$ is a nondominated element of A w.r.t. $\mathcal{K}(\cdot)$, then it is a minimal element of A with respect to $\mathcal{C}_{\mathcal{K}}$.

We now consider a vector optimization problem w.r.t. a variable ordering structure and some concepts of its solution in the preimage space.
Given a continuous mapping $f : X \to Y$, a nonempty closed set $\Omega \subseteq X$ and a cone-valued ordering map $\mathcal{K} : Y \rightrightarrows Y$. We consider the $\mathcal{K}-$ the problem:

$$\mathcal{K} - \min_{x\in\Omega} f(x) \qquad (P_{\mathcal{K}})$$

Definition 4 *(Nondominated solutions and minimal solutions of a vector optimization problem w.r.t. a variable ordering structure)*
Consider the vector optimization problem $(P_{\mathcal{K}})$ *and* $\bar{x} \in \Omega$. *Then*

(i) $\bar{x} \in \Omega$ *is said to be a nondominated solution of problem* $(P_{\mathcal{K}})$ *if there is no* $x \in \Omega \setminus \bar{x}$ *such that*

$$f(x) \leq_N f(\bar{x}) \Leftrightarrow f(\bar{x}) \in f(x) + \mathcal{K}(f(x)).$$

(ii) A point $\bar{x} \in \Omega$ *is said to be a minimal solution of problem* $(P_{\mathcal{K}})$ *if there is no* $x \in \Omega \setminus \{\bar{x}\}$ *such that*

$$f(x) \leq_P f(\bar{x}) \Leftrightarrow f(\bar{x}) \in f(x) + \mathcal{K}(f(\bar{x})).$$

2.2 Normal cones and Coderivatives

In this section, we present some definitions of normal cones and coderivatives which are used to derive the optimal condition for vector optimization problem w.r.t. variable ordering structures. We begin with recalling notions of limits for set-valued mapping. Let X and Y be two Banach spaces, $F : X \rightrightarrows Y$ be a set-valued mapping with the domain and the graph are defined respectively by

$$\operatorname{dom} F := \{x \in X |\ F(x) \neq \emptyset\}$$

and

$$\operatorname{gph} F := \{(u, v) \in X \times Y |\ v \in F(u)\}.$$

We denote the upper limits and lower limits of F as $x \to \bar{x}$ by $\limsup_{x\to\bar{x}} F(x)$ and $\liminf_{x\to\bar{x}} F(x)$ which are defined respectively by:

$$\limsup_{x\to\bar{x}} F(x) := \{y \in Y |\ \exists \text{ sequences } x_k \to \bar{x} \text{ and } y_k \to y \text{ with } y_k \in F(x_k) \text{ for all } k \in \mathbb{N}\},$$

$$\liminf_{x\to\bar{x}} F(x) := \{y \in Y |\ \forall \text{ sequences } x_k \to \bar{x}\ , \exists\, y_k \in F(x_k) \text{ with } k \in \mathbb{N} \text{ such that } y_k \to y \text{ as } k \to \infty\}.$$

Definition 5 *(Normal cones, [11])*
Let X *be a Banach space,* S *be a nonempty subset of* X, *and let* $x \in S$. *We define the set of* $\varepsilon-$*normals to* S *at* x *as:*

$$\hat{N}_{\varepsilon}(S, x) := \{x^* \in X^* |\ \limsup_{v \xrightarrow{S} x} \frac{x^*(v - x)}{\|v - x\|} \leq \varepsilon\}. \tag{3}$$

When $\varepsilon = 0$, the elements in the right hand side of (3) are called Fréchet normals and their collection, denoted by $\hat{N}(S,x)$ is the Fréchet normal cone to S at x.
Let $\bar{x} \in S$. The (basic, limiting, Mordukhovich) normal cone to S at $\bar{x}$ is defined by

$$N(S,\bar{x}) := \{x^* \in X | \ \exists \ \varepsilon_k \downarrow 0, x_k \xrightarrow{S} \bar{x}, x_k^* \xrightarrow{w^*} x^*, x_k^* \in \hat{N}_{\varepsilon_k}(S,x_k), \ \forall k \in \mathbb{N}\}$$

When X is Asplund and S is closed around $\bar{x}$ the basic normal cone to S at $\bar{x}$ is:

$$N(S,\bar{x}) := \{x^* \in X | \ \exists \ x_k \xrightarrow{S} \bar{x}, x_k^* \xrightarrow{w^*} x^*, x_k^* \in \hat{N}(S,x_k), \ \forall k \in \mathbb{N}\}$$

Now we introduce the definition of Coderivative of a general set-valued mapping $F : X \rightrightarrows Y$. In the Section 4 following, this definition will be used for two special mappings: a vector-valued mapping $f : X \to Y$ and a cone-valued mapping $\mathcal{K} : Y \rightrightarrows Y$.

Definition 6 *(Fréchet coderivative and normal coderivative, [11])*
Let $F : X \rightrightarrows Y$ be a set-valued mapping and $(\bar{x},\bar{y}) \in \operatorname{gph} F$. The Fréchet coderivative of F at $(\bar{x},\bar{y})$ is the set-valued map $\hat{D}^*F(\bar{x},\bar{y}) : Y^* \rightrightarrows X^*$ defined by:

$$\hat{D}^*F(\bar{x},\bar{y})(y^*) := \{x^* \in X^* | \ (x^*,-y^*) \in \hat{N}(\operatorname{gph} F,(\bar{x},\bar{y}))\}.$$

The normal coderivative of F at $(\bar{x},\bar{y})$ is the set-valued map $D^*F(\bar{x},\bar{y}) : Y^* \rightrightarrows X^*$ given by:

$$D^*F(\bar{x},\bar{y})(y^*) := \{x^* \in X^* | \ (x^*,-y^*) \in N(\operatorname{gph} F,(\bar{x},\bar{y}))\}.$$

We recall in the following the definition of a sequentially normally compact set, a sequentially normally compact mapping as well as a partially sequentially normally compact mapping.

Definition 7 *[11, Definition 1.20 and 1.67] Let $F : X \rightrightarrows Y$ with $(\bar{x},\bar{y}) \in \operatorname{gph} F$, $S \subset Y$ be a closed set around $\bar{y} \in S$. Then*

(i) S is sequentially normally compact ((SNC), for short) at $\bar{y}$ if

$$y_n \xrightarrow{S} \bar{y}, y_n^* \xrightarrow{w^*} 0, y_n^* \in \hat{N}(S,y_n) \Longrightarrow y_n^* \xrightarrow{\|\cdot\|} 0.$$

(ii) F is sequentially normally compact ((SNC), for short) at $(\bar{x},\bar{y})$ if

$$(x_n,y_n) \xrightarrow{\operatorname{gph} F} (\bar{x},\bar{y}), (x_n^*,y_n^*) \xrightarrow{w^*} (0,0), (x_n^*,y_n^*) \in \hat{N}(\operatorname{gph} F,(x_n,y_n))$$
$$\Longrightarrow (x_n^*,y_n^*) \xrightarrow{\|\cdot\|} (0,0).$$

(iii) F is partially sequentially normally compact ((PSNC), for short) at $(\bar{x}, \bar{y})$ *if*

$$(x_n, y_n) \xrightarrow{\text{gph}\, F} (\bar{x}, \bar{y}), x_n^* \xrightarrow{w^*} 0, y_n^* \xrightarrow{\|\cdot\|} 0, (x_n^*, y_n^*) \in \hat{N}(\text{gph}\, F, (x_n, y_n))$$
$$\Longrightarrow x_n^* \xrightarrow{\|\cdot\|} 0.$$

Note that every nonempty set in a finite dimensional space is SNC at each of its points and a set-valued mapping F is SNC at $(\bar{x}, \bar{y})$ if its graph is SNC at $(\bar{x}, \bar{y})$. If F is single-valued, we may omit $\bar{y}$ in the Definition 7. It is shown in [11] that the PSNC property always holds when dim $X < \infty$ and there is no difference between definitions *(ii)* and *(iii)* in Definition 7 if $\dim Y < \infty$.

2.3 Normal cones calculus

In order to providing specific otimality conditions for solutions our problems, we recall some results of normal cone to some special sets in $\mathbb{R}^n$. These results are given and proven by Rockafelar and Wet in [15], so we omit their proofs in this paper.

Proposition 2 *(Normal cones to product sets, [15, Theorem 6.41])*
Let C_i *be closed subset of* $\mathbb{R}^{n_i}, i = 1, .., k$ *and* $\mathbb{R}^n = \mathbb{R}^{n_1} \times ... \times \mathbb{R}^{n_k}$. *If* $C = C_1 \times ... \times C_k$, *then at any* $\bar{x} = (\bar{x}_1, ..., \bar{x}_k) \in \mathbb{R}^n$ *it holds:*

$$N(C, \bar{x}) = N(C_1, \bar{x}_1) \times ... \times N(C_k, \bar{x}_k)$$

Proposition 3 *(Normal cones to boxes, [15, Example 6.10])*
Assume that $C = C_1 \times ... \times C_n$ *in which* C_i *is a closed interval in* $\mathbb{R}$. *Then at any* $\bar{x} = (\bar{x}_1, \bar{x}_2, .., \bar{x}_n) \in C$ *one has*

$$N(C, \bar{x}) = N(C_1, \bar{x}_1) \times ... \times N(C_n, \bar{x}_n), \text{ where}$$

$$N(C_i, \bar{x}_i) = \begin{cases} [0, \infty) & \text{if } \bar{x}_i \text{ is (only) the right end point of } C_i, \\ (-\infty, 0] & \text{if } \bar{x}_i \text{ is (only) the left end point of } C_i, \\ \{0\} & \text{if } \bar{x}_i \text{ is an interior point of } C_i, \\ (-\infty, \infty) & \text{if } C_i \text{ is a one-point interval.} \end{cases}$$

We now present a Theorem concerning nondomination conditions for vector optimization problem w.r.t. a cone-valued mapping. It will be adapted to provide necessary conditions for our problems in the next section.

Theorem 1 *[2, Theorem 4.12] Let* X, Y *be Asplund spaces,* $f : X \to Y$, $\mathcal{K} : Y \rightrightarrows Y$ *and a nonempty closed subset* $\Omega \subset X$. *Let* $\bar{x}$ *be a nondominated solution of problem* $(P_{\mathcal{K}})$. *Set* $\bar{y} := f(\bar{x})$ *and suppose that* $\mathcal{K}(\cdot)$ *satisfies the following conditions:*

(a) For all $y \in Y$, $\mathcal{K}(y)$ is a nonempty convex cone;

(b) There exists $e \in Y, e \neq 0$ such that $e \in \cap_{y \in Y} \mathcal{K}(y) \setminus (-\mathcal{K}(f(\bar{y}))$;

(c) There is a unique point y^* satisfying $-y^* \in D^*\mathcal{K}(\bar{y}, 0)(y^*)$.

Moreover, assume:

(i) $\mathcal{K}$ is SNC at $(\bar{y}, 0)$,

(ii) Either Ω is SNC at $\bar{x}$ or f is PSNC at $\bar{x}$,

(iii) $D^*f(\bar{x})(0) \cap (-N(\Omega, \bar{x})) = \{0\}$.

Then there is $y^* \in Y^* \setminus \{0\}$ such that

$$0 \in D^*f(\bar{x})(y^* + D^*\mathcal{K}(f(\bar{x}); 0)(y^*)) + N(\Omega, \bar{x}).$$

2.4 Vector-valued norm and its subdifferential

In this subsection, we assume that X and Y be Banach spaces, $C \subset Y$ be a proper closed convex cone. We denote the linear space of the continuous linear maps from X to Y by $L(X, Y)$. We consider the definition of the vectorial norm and the subdifferential of a vector-valued function.

Definition 8 *(Vectorial norm, [8]) A map $\| \cdot \| : X \to C$ is called vectorial norm if for all $x, x_1, x_2 \in X$ and $\lambda \in \mathbb{R}$ the following conditions hold:*

(1) $\|x\| = 0 \Leftrightarrow x = 0$;

(2) $\|\lambda x\| = |\lambda| \; \|x\|$;

(3) $\|x_1 + x_2\| \in \|x_1\| + \|x_2\| - C$.

Definition 9 *(Subdiferential of vector-valued function, [8]) Let X and Y be Banach spaces, $C \subset Y$ be a convex cone in Y, and $f : X \to Y$ be a given map. For an arbitrary $\bar{x} \in X$, the set*

$$\partial f(\bar{x}) := \{T \in L(X, Y) | \; \forall h \in X : f(\bar{x} + h) - f(\bar{x}) - T(h) \in C\}$$

is called the subdifferential of f at $\bar{x}$.

Remark 1 *We recall in the following the subdifferential of some special kinds of vector-valued function.*

(i) [8, Example 2.22] For the vector-valued norm function $\|\cdot\| : X \to Y$, $\bar{x} \in X$, *we have :*

$$\partial\|\bar{x}\| = \{T \in L(X,Y) |\ T(\bar{x}) = \|\bar{x}\| \text{ and for all } x \in X : T(x) \leq_C \|\bar{x}\|\}$$

where C *is a pointed convex cone in* Y.

(ii) [6, Theorem 4.1.12] Let $A \in L(X,Y)$ *and* A^* *denotes the adjoint operator to* A, $a \in Y$, $x^0 \in X$. *Then*

$$\partial\|A(\cdot)-a\|(x^0) = \{A^*T|\ T \in L(Y,\mathbb{R}),\ T(Ax^0-a) = \|Ax^0-a\| \text{ and } \|T\|_* \leq 1\}$$

where $\|\cdot\|$ *is a norm in* Y.

In order to derive the relationship between coderivative of a vector function and subdifferential of its scalarization, we need the Lipschitz property of a mapping which defined in the following.

Definition 10 *(Lipschitz and Strictly Lipschitzian mapping, [11]) Let* $f : X \to Y$ *be a vector mapping between Banach spaces.*

(i) f *is Lipschitz on* $U \subset X$ *if* $U \subset \operatorname{dom} F$, *and there exists* $l \geq 0$ *such that*

$$\|f(x) - f(x')\|_Y \leq l\|x - x'\|_X,\ \forall x, x' \in U.$$

(ii) f *is said to be Lipschitz around* $x \in X$ *if there is a neighbourhood* U_x *of* x *such that* f *is Lipschitz on* U_x.

(iii) f *is locally Lipschitz on a nonempty subset* D *of* X, *if* f *is Lipschitz around every point* $x \in D$.

(iv) Suppose that f *is Lipschitz continuous around* $\bar{x} \in X$, *then* f *is strictly Lipschitzian at* $\bar{x}$ *if there is a neighborhood* V *of the origin in* X *such that the sequence*

$$y_k := \frac{f(x_k + t_k v) - f(x_k)}{t_k}, k \in \mathbb{N},$$

contains a norm convergent subsequence whenever $v \in V, x_k \to \bar{x}$ *and* $t_k \to 0$.

(v) Suppose that f *is Lipschitz continuous around* $\bar{x}$, *then* f *is* f *is* ω^**-strictly Lipschitzian at* $\bar{x}$ *if there is a neighborhood* V *of the origin in* X *such that for any* $v \in X$ *and any sequences* $\{x_k\} \to \bar{x}$, $t_k \downarrow 0$, *and* $\{y_k^*\} \xrightarrow{w^*} 0$ *one has* $\langle y_k^*, y_k\rangle \to 0$ *as* $k \to \infty$, *where* $\{y_k\}$ *are defined in (iv).*

It is shown in [11] that when Y is finite-dimensional, both (iv) and (v) of the Definition 10 reduce to the class of locally Lipschitzian mapping $f : X \to \mathbb{R}^n$. It is known that in a finite dimensional normed linear space, every scalar, proper convex function is Lipschitz around any interior point of its domain [14, Theorem 10.4] . In addition, in [10] , the authors proved that a convex vector function from a convex subset D of $\mathbb{R}^m$ to $\mathbb{R}^n$ is locally Lipschitz on rint D. When a vector-valued mapping is ω^*-strictly Lipschitz, we have the following relationship between coderivative of it and the subdifferential of its scalarization.

Proposition 4 *[11, Theorem 3.28] Let f be a mapping $f : X \to Y$ between Asplund space X and a Banach space Y. Then for all $y^* \in Y^*$ it holds*

$$D^* f(\bar{x})(y^*) = \partial(y^* \circ f)(\bar{x}) \neq \emptyset$$

provided that f is ω^*-strictly Lipschitz at $\bar{x}$.

The following Proposition concerning the Lipschitz property of a norm-vector function.

Proposition 5 *[1, Lemma 5] We assume that C is a proper normal cone. If the vector-valued norm $\|\!| \cdot \|\!| : X \to C$ is continuous around a given point $x \in X$, then $\|\!| \cdot \|\!|$ is Lipschitz.*

Obviously $\mathbb{R}^n_+$ is a closed and pointed cone, then Proposition 5 holds true if $C = \mathbb{R}^n_+$.

3 Beam intensity problem with Variable ordering structures

3.1 A variable ordering cone relevant to radiotherapy treatment

As shown in [3], in order to derive a mathematical model for the beam intensity optimization problem, the beam is discretized into p bixels or beamlets. The 3D volume of patient is divided into l voxels which inclued l_T tumor voxels, l_C critical organ voxels ($l = l_T + l_C$) in which T represents the tumor, C represents critical organs. The dose deposited in voxel i at unit intensity for bixel j is denoted by $a_{ij} \in \mathbb{R}$. We assume that the dose deposition matrix $A = (a_{ij}) \in \mathbb{R}^{l \times p}$ is given. We denote the beam intensity by $x \in \mathbb{R}^p$. Then, beam intensity and dose have the following relationship

$$d = Ax$$

where $d \in \mathbb{R}^l$ is a dose vector and its element d_i correspond to the dose deposited in voxel i. We assume that A can be partioned and reordered into sub-matrices $A_T \in \mathbb{R}^{l_T \times p}$ and $A_C \in \mathbb{R}^{l_N \times p}$ whose rows corresponding to tumor and normal voxels.

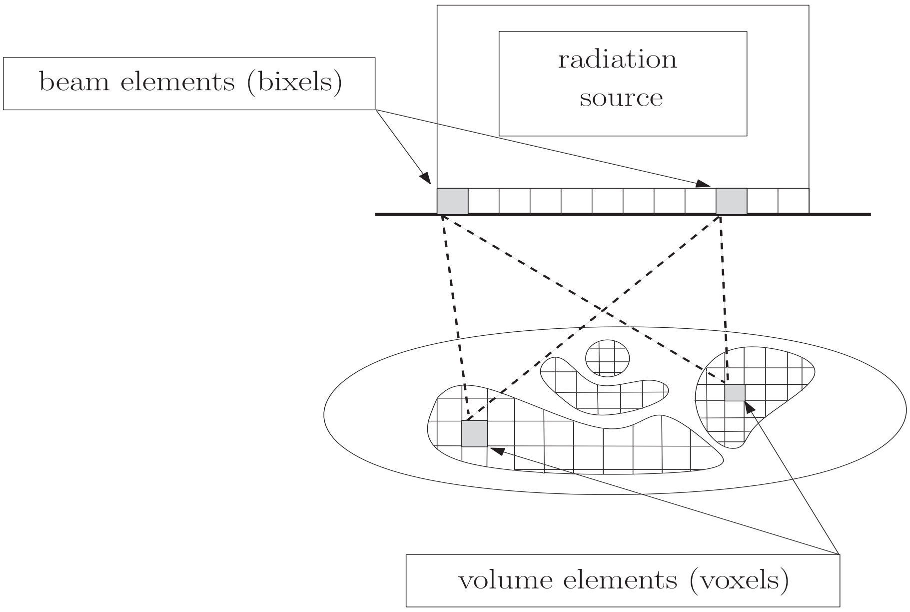


Figure 2: Discretization of patient into voxels and of beam into bixels ([3])

Obviously, the dose delivered to tumor and critical organ voxels are $A_T x$ and $A_C x$ respectively. $A_C x$ can be partioned into $A_{C_1}, ..., A_{C_k}$ according to the doses deposited in k different critical organs $C_1, ..., C_k$. Because different tissues can tolerate different amounts of radiation, the radiation oncologist need to determine a "prescription dose" which consists of the target dose for the tumor $TG \in \mathbb{R}^{l_T}$, the lower bounds and upper bounds on the dose to tumor voxels $TLB, TUB \in \mathbb{R}^{l_T}$, the upper bounds on the dose to normal voxels CUB. CUB can be divided into $C_1UB, C_2UB, ..., C_kUB$ according to the voxels corresponding to different critical organs. In radiation treatment, threshold dose is defined as the amount of radiation that is required to cause a specific tissue effect.

As has been outlined before, a vector optimization with respect to a variable ordering cone models for radiotherapy treatment is more appropriate than that one w.r.t. a constant cone. From a practical perspective, a dose delivered to a critical organ should be reduced when it exceeds the threshold dose of that organ. If not, we can increase this dose in favour of an improvement in the value of another critical organ. Therefore, we propose a variable ordering structure in the space $\mathbb{R}^n$ as follows. Given $\theta \in \mathbb{R}^n$, for every $y = (y_1, y_2, ..., y_n) \in \mathbb{R}^n$ we set:

$$I^{>}(y) := \{i \in \{1, 2, ..., n\} | \; y_i > \theta_i\}$$

and

$$I_{\leq}(y) := \{i \in \{1, 2, ..., n\} |\ y_i \leq \theta_i\}.$$

Obviously, for each $y \in \mathbb{R}^n$ it holds: $I^{>}(y) \cup I_{\leq}(y) = \{1, 2, ..., n\}$.
The variable ordering map $\mathcal{K}(\cdot)$ is defined by

$$\mathcal{K} : \mathbb{R}^n \rightrightarrows \mathbb{R}^n$$

where for each $y \in \mathbb{R}^n$ the image set $\mathcal{K}(y)$ is given by

$$\mathcal{K}(y) := \begin{cases} \{d \in \mathbb{R}^n |\ d_i \geq 0 \text{ for } i \in I^{>}(y) \text{ and } d_j \in \mathbb{R} \text{ for } j \notin I^{>}(y)\} & \text{if } I^{>}(y) \neq \emptyset, \\ \mathbb{R}^n & \text{if } I^{>}(y) = \emptyset. \end{cases} \tag{4}$$

This set-valued mapping will be used in the following subsection to construct an intensity problem in radiotherapy treatment when θ is chosen appropriately .

3.2 A beam intensity problem in radiotherapy treatment

Now we construct a mathematical formulation of the beam intensity problem.
Suppose that θ_{C_i} is given threshold dose of critical organ i, i=1,..,k. Since the deviation from the dose delivered to tumor organ to the target dose is always non-negative and should be minimized, we set $\theta := (0, \theta_{C_1}, ..., \theta_{C_k}) \in \mathbb{R}^{k+1}$. The set of bound conditions for beam intensity is given by

$$\Omega := \{x \in \mathbb{R}^p |\ 0 \leq x, TLB \leq A_T x \leq TUB, A_{C_i} x \leq C_i UB \text{ for } i = 1, .., k\}.$$

By using the variable ordering mapping $\mathcal{K}(\cdot)$ given by (4) with $n := k + 1$, the problem of finding beam intensity in radiotherapy treatment can now be formulated as a special case of $(P_{\mathcal{K}})$ introduced in Section 2.1

$$\text{Minimize } f(x) \text{ subject to } x \in \Omega \text{ with respect to } \mathcal{K}(\cdot) \tag{P_1}$$

where

$$f : \mathbb{R}^p \to \mathbb{R}^{k+1}$$

$$f(x) := \begin{pmatrix} \|A_T x - TG\|_\infty \\ \|A_{C_1} x\|_\infty \\ ... \\ \|A_{C_k} x\|_\infty \end{pmatrix},$$

The first criterion can be interpreted as the deviation from the prescribed dose to the tumor. $\|A_{C_i} x\|_\infty$ is the dose to the critical organ i (i=1,..,k). The objective function can be constructed by using Euclidean norm, see [9]. However, this norm allows the averaging out of large deviations on a small tissue by small or no deviation on a large tissue. Therefore it seems to be more reasonable to use the maximum norm.

In the following, we present some properties of the proposed variable ordering cone $\mathcal{K}(\cdot)$.

Proposition 6 *Consider the variable ordering structure given by (4) and let Ω be a subset of $\mathbb{R}^n$. Then, the following assertions hold:*

(i) For each $y \in \mathbb{R}^n$, $\mathcal{K}(y)$ is a closed and convex cone and $\mathbb{R}^n_+ \subseteq \mathcal{K}(y)$. In addition, $\mathcal{K}(y)$ is pointed if and only if $y_i > \theta_i,\ \forall\ i = 1, 2, .., n$.

(ii) For all $y^1, y^2 \in Y$, $y^1 - y^2 \in \mathbb{R}^n_+$ implies $\mathcal{K}(y^1) \subseteq \mathcal{K}(y^2)$.

(iii) If $\bar{y} \in \Omega$ satifies $I^>(\bar{y}) \neq \emptyset$, then there exists $e \neq 0$ such that

$$e \in \cap_{y\in\Omega}\mathcal{K}(y) \setminus (-\mathcal{K}(\bar{y})).$$

(iv) $\operatorname{gph}\mathcal{K}$ is a closed subset of $\mathbb{R}^n \times \mathbb{R}^n$.

Proof.

(i) Obviously, for all $y \in \mathbb{R}^n$ we have that $\mathcal{K}(y)$ is a closed and convex cone. $\mathcal{K}(y)$ is pointed if and only if $\mathcal{K}(y) \cap (-\mathcal{K}(y)) = \{0\}$. From the definition of $\mathcal{K}(\cdot)$, it holds

$$\mathcal{K}(y) \cap (-\mathcal{K}(y)) = \{d \in \mathbb{R}^n |\ d_i = 0 \text{ with } i \in I^>(y) \text{ and } d_i \in \mathbb{R}, \text{otherwise.}\}$$

Thus, $\mathcal{K}(y)$ is pointed if and only if $I^>(y) = \{1, 2, ..., n\}$, i.e., $y_i > \theta_i,\ \forall\ i = 1, 2, ..., n$.

(ii) It follows from $y^1 - y^2 \in \mathbb{R}^n_+$ that $y^1_i \geq y^2_i,\ \forall\ i = 1, 2, .., n$. Therefore, $\forall\ i \in I^>(y^2)$ we have $y^1_i \geq y^2_i > \theta_i$, i.e., $i \in I^>(y^1)$. Thus, $I^>(y^2) \subseteq I^>(y^1)$ and we obtain that $\mathcal{K}(y^1) \subseteq \mathcal{K}(y^2)$.

(iii) Assume that $i_0 \in I^>(\bar{y})$ i.e., $y_{i_0} > \theta_{i_0}$. It follows from the definition of $\mathcal{K}(\cdot)$ that if $d = (d_1, .., d_n) \in (-\mathcal{K}(\bar{y}))$ then $d_{i_0} \leq 0$. Taking $e := (e_1, ..., e_n)$ where $e_i > 0$ for all $i = 1, 2, .., n$, then $e \in \mathbb{R}^n_+$. Since $\mathbb{R}^n_+ \subseteq \cap_{y\in\Omega}\mathcal{K}(y)$, it yields $e \in \cap_{y\in\Omega}\mathcal{K}(y)$. Because $e_{i_0} > 0$, we have that $e \notin (-\mathcal{K}(\bar{y}))$.
Therefore, $e \in \cap_{y\in\Omega}\mathcal{K}(y) \setminus (-\mathcal{K}(\bar{y}))$.

(iv) Consider a consequence $\{(y^k, d^k)\} \subset \operatorname{gph}\mathcal{K}$ which convergences to (y, d) when $k \to \infty$. We need to show that $(y, d) \in \operatorname{gph}\mathcal{K}$. Suppose that

$$(y^k, d^k) = (y^k_1, y^k_2, ..., y^k_n, d^k_1, d^k_2, ..., d^k_n)$$

and

$$(y, d) = (y_1, y_2, ..., y_n, d_1, d_2, ..., d_n).$$

To proceed, we consider the following cases.
Case 1: $I^>(y) \neq \emptyset$. We will prove that $\forall\ i \in I^>(y) : d_i \geq 0$.
Because

$$y_i > \theta_i \text{ and } \{y_i^k\} \to y_i \text{ when } k \to \infty,$$

it holds

$$\exists\ k_0 \in \mathbb{N}^* \text{ such that } \forall\ k \geq k_0 : y_i^k > \theta_i.$$

Since

$$(y_1^k, y_2^k, ..., y_n^k, d_1^k, ..., d_n^k) \in gph\mathcal{K}, \text{ and } \forall\ k \geq k_0 : y_i^k > \theta_i,$$

we get

$$d_i^k \geq 0, \ \forall\ k \geq k_0.$$

Taking into account $d_i^k \to d_i$ when $k \to \infty$, it yields $d_i \geq 0, \ \forall\ i \in I^>(y)$.
Thus, $(y, d) \in \text{gph}\,\mathcal{K}$.
Case 2: $I^>(y) = \emptyset$, i.e., $y_i \leq 0, \ \forall\ i = 1, 2, ..., n$. It follows directly from the definition of $\mathcal{K}$ that $(y, d) \in \text{gph}\,\mathcal{K}$.

□

4 Optimality conditions for multiobjective approximation problems

4.1 Optimality conditions for nondominated solutions of approximation problems w.r.t. a general ordering structure

We begin this section by introducing in the following a vector approximation problem which is considered as a general problem of the beam intensity problem in radiotherapy treatment.
Let A_i be linear mappings from $\mathbb{R}^m$ to $\mathbb{R}^{m_i}$, $a_i \in \mathbb{R}^{m_i}, i = 1, 2, ...n$, $\| \cdot \|_i$ be norms in $\mathbb{R}^{m_i}$. Given a nonempty closed set $\Omega \subseteq \mathbb{R}^m$ and a set-valued map $\mathcal{K} : \mathbb{R}^n \rightrightarrows \mathbb{R}^n$ satisfying $\mathcal{K}(y)$ is a closed, convex cone for each $y \in \mathbb{R}^n$. We consider the following problem:

$$\text{Minimize } f(x) \text{ subject to } x \in \Omega \text{ with respect to } \mathcal{K}(\cdot), \qquad (P_2)$$

where

$$f : \mathbb{R}^m \to \mathbb{R}^n$$

$$f(x) := \begin{pmatrix} \|A_1x - a_1\|_1 \\ \|A_2x - a_2\|_2 \\ ... \\ \|A_nx - a_n\|_n \end{pmatrix},$$

In Section 4.2 we will discuss the problem (P_2) with a special ordering map given by (4). Now we present necessary conditions for nondominated solutions of the vector approximation problem (P_2).

Theorem 2 *We consider the problem (P_2) w.r.t. a cone-valued mapping $\mathcal{K} : \mathbb{R}^n \rightrightarrows \mathbb{R}^n$. Suppose that $\bar{x} \in \Omega$ is a nondominated solution of (P_2), $\bar{y} := f(\bar{x})$. We assume that the following conditions hold:*

(i) $\forall\ y \in \mathbb{R}^n$, $\mathcal{K}(y)$ is a nonempty convex cone.

(ii) There exists $e \in \mathbb{R}^n$, $e \neq 0$ with $e \in \cap_{y\in\mathbb{R}^n}\mathcal{K}(y) \setminus (-\mathcal{K}(\bar{y}))$.

(ii) There is a unique point y^* satisfying $-y^* \in D^*\mathcal{K}(\bar{y}, 0)(y^*)$.

Then there are $y^* \in \mathbb{R}^n \setminus \{0\}$ and corresponding $z^* \in (y^* + D^*\mathcal{K}(\bar{y}; 0)(y^*))$ and $T_i \in L(\mathbb{R}^{m_i}, \mathbb{R})$ satisfying $T_i(A_i(\bar{x}) - a^i) = \|A_i(\bar{x}) - a^i\|_i$ and $\|T_i\|_{i^*} \leq 1$ such that

$$0 \in \sum_{i=1}^{n} A_i^* z^* T_i + N(\Omega, \bar{x}).$$

Proof. We will prove that the condions (i), (ii) and (iii) in Theorem 1 are satisfied. Since both the objective function f and the ordering mapping $\mathcal{K}$ act between two finite dimensional spaces, $\mathcal{K}$ is SNC at $(\bar{y}, 0)$ and f is PSNC at $\bar{x}$.
Now we set

$$C := \mathbb{R}^n_+ = \{(c_1, c_2, .., c_n) \in \mathbb{R}^n | \ \forall\ i = 1, 2.., n : c_i \geq 0\}.$$

Obviously, f is a continuous convex mapping and C is a convex pointed cone we have that f is Lipschitz on Ω (Proposition 5). Therefore, taking into account the relationship between coderivative of a vector function with subdiferential of its scalarization (Proposition 4) it holds:

$$\forall\ y^* \in \mathbb{R}^n,\ \forall\ \bar{x} \in \Omega : D^*f(\bar{x})(y^*) = \partial(y^* \circ f)(\bar{x})$$

It yields $D^*f(\bar{x})(0) = \{0\}$ and $D^*f(\bar{x})(0) \cap (-N(\Omega, \bar{x})) = \{0\}$.
In view of Theorem 1, there exists $y^* \in Y^* \setminus \{0\}$ such that

$$0 \in D^*f(\bar{x})(y^* + D^*\mathcal{K}(\bar{y}, 0)(y^*)) + N(\Omega, \bar{x}).$$

This means, there is $z^* \in (y^* + D^*\mathcal{K}(\bar{y}, 0)(y^*))$ satisfying

$$\begin{aligned} &0 \in D^* f(\bar{x})(z^*) + N(\Omega, \bar{x}) \\ \Leftrightarrow &0 \in \partial(z^* \circ f)(\bar{x}) + N(\Omega, \bar{x}). \end{aligned}$$

Taking into account the formulation of coderivative of a vector-valued norm function in Remark 1 we have that

$$\exists\ T_i \in L(\mathbb{R}^{m_i}, \mathbb{R}), T_i(A_i(\bar{x}) - a^i) = \|A_i(\bar{x}) - a^i\|_i \text{ and } \|T_i\|_{i^*} \leq 1, (i = 1, ..., n)$$

such that

$$0 \in \sum_{i=1}^{n} A_i^* z^* T_i + N(\Omega, \bar{x}).$$

□

4.2 Optimality conditions for vector approximation problem w.r.t. the proposed ordering structure

This section is concerned with deriving optimality conditions for the following problem which is a special case of (P_2) when the ordering $\mathcal{K}(\cdot)$ is given by (4):

$$\text{Minimize } f(x) \text{ subject to } x \in \Omega \text{ with respect to } \mathcal{K}(\cdot) \qquad (P_3)$$

where

$$f : \mathbb{R}^m \to \mathbb{R}^n$$

$$f(x) := \begin{pmatrix} \|A_1 x - a_1\|_1 \\ \|A_2 x - a_2\|_2 \\ \cdots \\ \|A_n x - a_n\|_n \end{pmatrix},$$

and $\mathcal{K}(\cdot)$ is determined by (4).
Notice that (P_3) is our beam intensity problem (P_1) when we choose $\theta := (0, \theta_1, ..., \theta_k)$, $m := p, n := k + 1, A_1 := A_T, A_{j+1} := A_{C_j},\ j = 1, ..., k$ and $\| \cdot \|_i := \| \cdot \|_\infty,\ \forall\ i = 1, ..., n$.

It is necessary to determine $D^*\mathcal{K}(\bar{y}, 0)(y^*)$ in order to derive a specific optimality conditions for nondominated solutions as well as minimal solutions of the problem (P_3). In the following we will determine $D^*\mathcal{K}(\bar{y}, 0)(y^*)$ by calculating the normal cone $N(\operatorname{gph} \mathcal{K}, (\bar{y}, 0))$.

The theorem below describes the formulation of the basic normal cone to a subset $\Omega \subseteq \mathbb{R}^n$ being locally closed around $\bar{x} \in \Omega$.

Theorem 3 *[11, Theorem 1.6] Let $\Omega \in \mathbb{R}^n$ be locally closed around $\bar{x} \in \Omega$. Consider the associated distance function*

$$\operatorname{dist}(x, \Omega) := \inf_{u \in \Omega} \|x - u\|$$

and define the Euclidean projector of x to Ω by

$$P(x, \Omega) := \{\omega \in \Omega | \ \|x - \omega\| = \operatorname{dist}(x, \Omega)\} \tag{5}$$

where $\|\cdot\|$ is Euclide norm in $\mathbb{R}^n$. Then it holds:

$$N(\Omega, \bar{x}) = \limsup_{x \to \bar{x}} \hat{N}(\Omega, x)$$

$$N(\Omega, \bar{x}) = \limsup_{x \to \bar{x}} [\operatorname{cone}(x - P(x; \Omega))]$$

Now we rewrite the graph of mapping $\mathcal{K}(\cdot)$ as a union of product of subsets.
For each $I \subseteq \{1, 2, ..., n\}$ we set:

$$U_I := \{y \in \mathbb{R}^n | \ I^{>}(y) = I\}$$

and

$$\mathbb{R}^n_I := \{d \in \mathbb{R}^n | \ d_i \geq 0, \ \forall \ i \in I, d_i \in \mathbb{R} \text{ with } i \notin I\}.$$

Obviously, if $y \in U_I$ then $\mathcal{K}(y) = \mathbb{R}^n_I$. Therefore, we get

$$\operatorname{gph} \mathcal{K} = \cup_{I \subseteq \{1,2,...,n\}} U_I \times \mathbb{R}^n_I.$$

Since $\operatorname{gph} \mathcal{K}$ is closed (Proposition 6) and taking into account Theorem 3, we have

$$N(\operatorname{gph} \mathcal{K}, (\bar{y}, 0)) = \limsup_{(y,d) \to (\bar{y}, 0)} [\operatorname{cone}((y, d) - P((y, d); \cup_{I \subseteq \{1,2,...,n\}} U_I \times \mathbb{R}^n_I))].$$

This analysis leads to the question if we can provide the results of Euclidean projector to graph of $\mathcal{K}(\cdot)$ which gives the formulation of the normal cone to its graph by using Theorem 3. This is discussed in the theorem below.

Theorem 4 *Given a point $\theta = (\theta_1, ..., \theta_n) \in \mathbb{R}^n$ and a set-valued mapping $\mathcal{K} : \mathbb{R}^n \rightrightarrows \mathbb{R}^n$ determined by (4). For each element $(y, d) \in \mathbb{R}^n \times \mathbb{R}^n$ we set*

$$J^{\geq}(d) := \{i \in \{1, 2, ..., n\} | \ d_i \geq 0\}$$

and

$$I^{>}(y) := \{i \in \{1, 2, ..., n\} | \ y_i > \theta_i\}.$$

Then, it holds for the Euclidean projector given by (5) that *(i)* *If* $I \not\subseteq I^{>}(y)$ *then* $P((y,d);U_I \times \mathbb{R}^n_I) = \emptyset$.

(ii) *If* $I \subseteq I^{>}(y)$ *then*

(a)

$$P((y,d);U_I \times \mathbb{R}^n_I) = \{(y^I, d^I) \in U_I \times \mathbb{R}^n_I\},$$

where $(y^I, d^I) := (y^I_1, .., y^I_n, d^I_1, ..., d^I_n)$ *determined by:*

$$\begin{aligned} d^I_i =& d_i, \forall\ i \in (\{1,2,...,n\} \setminus I) \cup J^{\geq}(d); \\ d^I =& 0,\ \forall\ i \in I \setminus J^{\geq}(d); \\ y^I_i =& \theta_i,\ \forall\ i \in I^{>}(y) \setminus I; \\ y^I_i =& y_i,\ \forall\ i \in (\{1,2,...,n\} \setminus I^{>}(y)) \cup I. \end{aligned}$$

(b) $\operatorname{dist}((y,d), U_I \times \mathbb{R}^n_I) = \sqrt{\sum_{i \in I^{>}(y) \setminus I} (y_i - \theta_i)^2 + \sum_{i \in I \setminus J^{\geq}(d)} (d_i)^2}$;

(iii) $P((y,d); \operatorname{gph} \mathcal{K}) = \cup_I P((y,d);U_I \times \mathbb{R}^n_I)$
where $I = \operatorname{argmin}_{I \subseteq I^{>}(y)} dist((y,d), U_I \times \mathbb{R}^n_I)$.

Proof. Consider I and I' are two arbitrary subsets of $\{1,2,...,n\}$ we have that

$$(U_I \times \mathbb{R}^n_I) \cap (U_{I'} \times \mathbb{R}^n_{I'}) = \emptyset \text{ with } I \neq I',$$

therefore

$$P((y,d); \cup_{I \subseteq \{1,2,...,n\}} U_I \times \mathbb{R}^n_I) = \operatorname{argmin}_{(y^I,d^I) \in U_I \times \mathbb{R}^n_I} (\|(y,d) - (y^I, d^I)\|^2).$$

Thus, with each $I \subset \{1, 2..., n\}$, we need to find $P((y,d);U_I \times \mathbb{R}^n_I)$.

(i) $I \not\subseteq I^{>}(y)$ i.e., $\exists\ i_0 \in I$ but $i_0 \notin I^{>}(y)$, we will prove that

$$P((y,d);U_I \times \mathbb{R}^n_I) = \emptyset.$$

Indeed, suppose that there is an element $(y^I, d^I) \in U_I \times \mathbb{R}^n_I$ such that

$$\|(y^I, d^I) - (y,d)\|^2 = \inf_{(\omega,\gamma) \in U_I \times \mathbb{R}^n_I} \|(\omega, \gamma) - (y,d)\|^2.$$

We assume that $(y^I, d^I) = (y^I_1, y^I_2, ..., y^I_n, d^I_1, d^I_2, ..., d^I_n)$, and $y^I_{i_0} = \theta_{i_0} + \varepsilon$ with $\varepsilon > 0$ (because $y^I \in U_I$ and $i_0 \in I$).
We consider the point

$$(y^*, d^*) := (y^*_1, y^*_2, ..., y^*_n, d^*_1, d^*_2, ..., d^*_n)$$

determined by

$$y_{i_0}^* = \theta_{i_0} + \frac{\varepsilon}{2}, y_i^* = y_i^I \text{ for } i \in \{1, 2, ..., n\} \setminus \{i_0\}$$

and

$$d_k^* = d_k^I, k = 1, 2, ..., n.$$

Obviously, $(y^*, d^*) \in U_I \times \mathbb{R}_I^n$. Now we get

$$\begin{aligned}
\|(y^*, d^*) - (y, d)\|^2 &= \sum_{i=1}^{n} ((y_i^* - y_i)^2 + (d_i^* - d_i)^2) \\
&= \sum_{i \in \{1,2,..,n\} \setminus \{i_0\}} (y_i^* - y_i)^2 + (y_{i_0}^* - y_{i_0})^2 + \sum_{i=1}^{n} (d_i^* - d_i)^2 \\
&= \sum_{i \in \{1,2,..,n\} \setminus \{i_0\}} (y_i^I - y_i)^2 + (\theta_{i_0} + \frac{\varepsilon}{2} - y_{i_0})^2 + \sum_{i=1}^{n} (d_i^I - d_i)^2 \\
&< \sum_{i \in \{1,2,..,n\} \setminus \{i_0\}} (y_i^I - y_i)^2 + (\theta_{i_0} + \varepsilon - y_{i_0})^2 + \sum_{i=1}^{n} (d_i^I - d_i)^2 \\
&\quad \text{(because } y_{i_0} \le \theta_{i_0} \text{ since } i_0 \notin I^>(y)) \\
&= \sum_{i \in \{1,2,..,n\} \setminus \{i_0\}} (y_i^I - y_i)^2 + (y_{i_0}^I - y_{i_0})^2 + \sum_{i=1}^{n} (d_i^I - d_i)^2 \\
&= \sum_{i=1}^{n} ((y_i^I - y_i)^2 + (d_i^I - d_i)^2) \\
&= \|(y^I, d^I) - (y, d)\|^2
\end{aligned}$$

Thus, $(y^*, d^*) \in U_I \times \mathbb{R}_I^n$ and $\|(y^*, d^*) - (y, d)\|^2 < \|(y^I, d^I) - (y, d)\|^2$, this is a contradiction with the definition of (y^I, d^I):

$$\|(y^I, d^I) - (y, d)\|^2 = \inf_{(\omega,\gamma) \in U_I \times \mathbb{R}_I^n} \|(\omega, \gamma) - (y, d)\|^2.$$

(ii) (a) Let $I \subseteq I^>(y)$ and take an arbitrary element $(y^I, d^I) \in U_I \times \mathbb{R}_I^n$, we have that

$$\begin{aligned}
\|(y^I,d^I)-(y,d)\|^2 &= \sum_{i=1}^{n}(y_i^I-y_i)^2+\sum_{i=1}^{n}(d_i^I-d_i)^2\\
&= \sum_{i\in I}(y_i^I-y_i)^2+\sum_{i\in I^>(y)\setminus I}(y_i^I-y_i)^2+\sum_{i\in\{1,2,...,n\}\setminus I^>(y)}(y_i^I-y_i)^2\\
&+ \sum_{i\in(\{1,2,...,n\}\setminus\{I\cup J^{\geq}(d)\})}(d_i^I-d_i)^2+\sum_{i\in I\setminus J^{\geq}(d)}(d_i^I-d_i)^2\\
&+ \sum_{i\in J^{\geq}(d)\setminus I}(d_i^I-d_i)^2+\sum_{I\cap J^{\geq}(d)}(d_i^I-d_i)^2\\
&\geq \sum_{i\in I^>(y)\setminus I}(y_i^I-y_i)^2+\sum_{i\in I\setminus J^{\geq}(d)}(0-d_i)^2\\
&\geq \sum_{i\in I^>(y)\setminus I}(\theta_i-y_i)^2+\sum_{i\in I\setminus J^{\geq}(d)}(0-d_i)^2.
\end{aligned}$$

The last conclution is obtained since: $\begin{cases}\forall\ i\in I^>(y)\setminus I: y_i>\theta_i \text{ and } y_i^I\leq\theta_i,\\ \forall\ i\in I\setminus J^{\geq}(d): d_i^I\geq 0 \text{ and } d_i<0.\end{cases}$

Therefore, $\|(y^I,d^I)-(y,d)\|^2\geq\sum_{i\in I^>(y)\setminus I}(\theta_i-y_i)^2+\sum_{i\in I\setminus J^{\geq}(d)}(0-d_i)^2$, and the equation holds true if we choose

$$\begin{aligned}
d_i^I=&d_i,\ \forall\ i\in(\{1,2,...,n\}\setminus I)\cup J^{\geq}(d);\\
d^I=&0,\ \forall\ i\in I\setminus J^{\geq}(d);\\
y_i^I=&\theta_i,\ \forall\ i\in I^>(y)\setminus I;\\
y_i^I=&y_i,\ \forall\ i\in(\{1,2,...,n\}\setminus I^>(y))\cup I.
\end{aligned}$$

(b) It is obviously that if $I\subseteq I^>(y)$ then

$$\operatorname{dist}((y,d),U_I\times\mathbb{R}^n_I)=\sqrt{\sum_{i\in I^>(y)\setminus I}(y_i-\theta_i)^2+\sum_{i\in I\setminus J^{\geq}(d)}(d_i)^2}.$$

(iii) Now we prove that $P((y,d),\operatorname{gph}\mathcal{K})=\cup_I P((y,d);U_I\times\mathbb{R}^n_I)$ where

$$I=\operatorname{argmin}_{I\subseteq I^>(y)}\operatorname{dist}((y,d),U_I\times\mathbb{R}^n_I).$$

Since $\operatorname{gph}\mathcal{K}$ is a closed set, it holds $P((y,d),\operatorname{gph}\mathcal{K})\neq\emptyset$ [15, Example 1.20]. Suppose that

$$(\hat{y},\hat{d})\in P((y,d),\operatorname{gph}\mathcal{K}),$$

then

$$\exists\ J\subset\{1,2,...,n\}\text{ such that }(\hat{y},\hat{d})\in U_J\times\mathbb{R}^n_J.$$

It holds

$$\begin{aligned} d((y,d),(\hat{y},\hat{d}) &= d((y,d),\operatorname{gph}\mathcal{K}) \\ &\le d((y,d),U_J \times \mathbb{R}^n_J) \\ &\le d((y,d),(\hat{y},\hat{d})). \end{aligned}$$

The equation holds true if $(\hat{y},\hat{d}) = P((y,d),U_J \times \mathbb{R}^n_J)$. Taking into account (i) and (ii) we get $J \subseteq I^>(y)$. The proof is complete.

□

The following remark shows how one obtains the Euclidean projector of an arbitrary point in $\mathbb{R}^n \times \mathbb{R}^n$ to the graph of the mapping $\mathcal{K}(\cdot)$, the normal cone to its graph as well as its coderivative.

Remark 2 *(i) We can get the projection of (y,d) to $\operatorname{gph}\mathcal{K}$ through these following steps:*
Step 1: Determining $I^>(y)$.
Step 2: With each $I \subseteq I^>(y)$, we calculate $d((y,d),U_I \times \mathbb{R}^n_I) = \sigma_I$ and

$$P((y,d);U_I \times \mathbb{R}^n_I) = \{(y^I,d^I) \in U_I \times \mathbb{R}^I : d((y^I,d^I),U_I \times \mathbb{R}^n_I) = \sigma_I\}.$$

Step 3: Find $\sigma := min_{I\subseteq\{1,2,..,n\}}\{\sigma_I\}$ and

$$P((y,d),\operatorname{gph}\mathcal{K}) = \cup_I P((y,d);U_I \times \mathbb{R}^n_I)$$

where I satisfies $I \subseteq I^>(y)$ and $d((y,d),U_I \times \mathbb{R}^n_I) = \sigma$.

(ii) From the Theorem 4 above we obtain:

$$N(\operatorname{gph}\mathcal{K},(\bar{y},0)) = \limsup_{(y,d)\to(\bar{y},0)} \operatorname{cone}((y,d) - P((y,d),\operatorname{gph}\mathcal{K}) \tag{6}$$

where $P((y,d),\operatorname{gph}\mathcal{K})$ is determined in Theorem 4 (iv) and we get

$$D^*\mathcal{K}(\bar{y},0)(y^*) = \{x^* \in \mathbb{R}^n |\ (x^*,-y^*) \in N(\operatorname{gph}\mathcal{K},(\bar{y},0))\} \tag{7}$$

where $N(\operatorname{gph}\mathcal{K},(\bar{y},0))$ given by (6).

Now we derive the optimality condition for nondominated solutions of the problem (P_3).

Theorem 5 *Suppose that $\bar{x} \in \Omega$ is a nondomiated solution of the problem (P_3), $\bar{y} := f(\bar{x})$. We assume that* *(i)* $I^{>}(\bar{y}) \neq \emptyset$.

(ii) *There is a unique point* y^* *such that* $-y^* \in D^*\mathcal{K}(\bar{y}, 0)(y^*)$.

Then, there exists $y^* \in \mathbb{R}^n \setminus \{0\}$ *and corresponding* $z^* \in (y^* + D^*\mathcal{K}(\bar{y}; 0)(y^*))$ *and* $T_i \in L(\mathbb{R}^{m_i}, \mathbb{R})$ *satisfying*

$$T_i(A_i(\bar{x}) - a^i) = \|A_i(\bar{x}) - a^i\|_i \text{ and } \|T_i\|_{i^*} \leq 1 (i = 1, 2.., n) \text{ such that}$$

$$0 \in \sum_{i=1}^{n} A_i^* z^* T_i + N(\Omega, \bar{x}).$$

where $D^*\mathcal{K}(\bar{y}, 0)(y^*)$ *is determined by (6) and (7).*

Proof. For every $y \in \mathbb{R}^n$, $\mathcal{K}(y)$ is a closed convex cone (Proposition 6 (i)). Since $I^{>}(\bar{y}) \neq \emptyset$ and by using Proposition 6(iii) it holds

$$\exists\, e \in \mathbb{R}^n, e \neq 0 : e \in \cap_{y \in \mathbb{R}^n} \mathcal{K}(y) \setminus (-\mathcal{K}(\bar{y})).$$

Applying directly Theorem 2 and the formulation of $D^*\mathcal{K}(\bar{y}, 0)(y^*)$ given in Remark 2(ii) we obtain the desired conclusion. □

At this point it is interesting to investigate whether it is possible to provide a specific formulation of $D^*\mathcal{K}(\bar{y}, 0)(y^*)$ as well as the condition for y^* in Theorem 5 when $\bar{x}$ is a minimal solution of (P_3). We will see below that this is possible if we use some results given in Proposition 2 and Proposition 3.

Proposition 7 *Let* $\mathcal{K}(\cdot)$ *be a set-valued map given by (4). Suppose that* $\bar{x}$ *is a minimal solution of* (P_3) *and* $\bar{y} := f(\bar{x})$. *Then*

(i) *The normal cone to* $\mathcal{K}(\bar{y})$ *at 0 is given by:*

$$N(\mathcal{K}(\bar{y}), 0) = N_1 \times ... \times N_n$$

where for $i = 1, 2..., n$

$$\begin{cases} N_i := (-\infty, 0] & \text{with } i \in I^{>}(\bar{y}), \\ N_i := \{0\} & \text{with } i \notin I^{>}(\bar{y}). \end{cases} \tag{8}$$

(ii) *It holds* $D^*\mathcal{K}(\bar{y}, 0)(y^*) = \{0\}$ *and* $y^* \in \mathcal{K}(\bar{y})^+$.

Proof.

(i) Because $\bar{x}$ is a minimal solution of (P_3), it follows from Proposition 1 that it is also a nondominated solution of the problem (P_3) w.r.t. the nonvariable odering cone-valued $\mathcal{K}(\cdot) := \mathcal{K}(\bar{y})$.
From the definition of $\mathcal{K}(\cdot)$, we get $\mathcal{K}(\bar{y}) = K_1 \times ... \times K_n$ where for $i = 1, 2.., n$

$$\begin{cases} K_i := [0, +\infty) & \text{with } i \in I^>(\bar{y}), \\ K_i := \mathbb{R} & \text{with } i \notin I^>(\bar{y}). \end{cases} \tag{9}$$

Taking into account Proposition 3 and the formular of K_i in (9) it holds

$$N(\mathcal{K}(\bar{y}), 0) = N(K_1, 0) \times N(K_2, 0) \times ... \times N(K_n, 0) = N_1 \times ... \times N_n$$

where for i=1,2,..,n:

$$\begin{cases} N_i := (-\infty, 0] & \text{if } K_i = [0, +\infty), \\ N_i := \{0\} & \text{if } K_i = \mathbb{R}. \end{cases} \tag{10}$$

Thus, from (9) and (10) it yields:

$$N(\mathcal{K}(\bar{y}), 0) = N_1 \times ... \times N_n$$

where for i=1,2,..,n:

$$\begin{cases} N_i := (-\infty, 0] & \text{with } i \in I^>(\bar{y}), \\ N_i := \{0\} & \text{with } i \notin I^>(\bar{y}). \end{cases} \tag{11}$$

(ii) Since

$$N(\operatorname{gph} \mathcal{K}, (\bar{y}, 0)) = N(\mathbb{R}^n \times \mathcal{K}(\bar{y}), (\bar{y}, 0)) = \{0\} \times N(\mathcal{K}(\bar{y}), 0)$$

and

$$D^*\mathcal{K}(\bar{y}, 0)(y^*) = \{x^* \in \mathbb{R}^n | \ (x^*, -y^*) \in N(\operatorname{gph} \mathcal{K}, (\bar{y}, 0))\}$$

it holds $D^*\mathcal{K}(\bar{y}, 0)(y^*) = \{0\}$.
It remains to prove that $y^* \in \mathcal{K}(\bar{y})^+$. Indeed, taking $d \in \mathcal{K}(\bar{y})$, we have that

$$d_i \geq 0, \ \forall \ i \in I^>(\bar{y}) \text{ and } d_i \in \mathbb{R}, \ \forall \ i \notin I^>(\bar{y}). \tag{12}$$

In addition,

$$\mathcal{K}(\bar{y})^+ := \{y^* \in \mathbb{R}^n | \ y^*(d) \geq 0, \ \forall \ d \in \mathcal{K}(\bar{y})\}.$$

Since $y^* \in -N(\mathcal{K}(\bar{y}), 0)$ and taking into account (11) it yields for $i = 1, 2.., n$:

$$\begin{cases} y_i^* \geq 0, & \forall \ i \in I^>(\bar{y}) \\ y_i^* = 0, & \forall \ i \notin I^>(\bar{y}). \end{cases} \tag{13}$$

It implies from (12) and (13) that $y^* \in \mathcal{K}(\bar{y})^+$, which is the desired conclusion.

□

The following Theorem presents the optimality conditions for minimal solutions of (P_3).

Theorem 6 *Consider the problem (P_3) w.r.t. the ordering cone $\mathcal{K}(\cdot)$ given by (4). Assume that $\bar{x} \in \Omega$ is a minimal solution of it, $\bar{y} := f(\bar{x})$. Suppose that $I^{>}(\bar{y}) \neq \emptyset$, then there exists $y^* \in \mathcal{K}(\bar{y})^+ \setminus \{0\}$ and $T_i \in L(\mathbb{R}^{m_i}, \mathbb{R})$ satisfying*

$$T_i(A_i(\bar{x}) - a^i) = \|A_i(\bar{x}) - a^i\|_i \text{ and } \|T_i\|_{i^*} \leq 1 \text{ such that}$$

$$0 \in \sum_{i=1}^{n} A_i^* y^* T_i + N(\Omega, \bar{x}).$$

Proof. Because $\bar{x}$ is a minimal solution of (P_3), it is also a nondominated solution of (P_3) w.r.t. to a nonvariable cone $\mathcal{K}(\cdot) = \mathcal{K}(\bar{y})$ (Proposition 1). Taking into account Theorem 5 with the assertions $D^*\mathcal{K}(\bar{y}, 0)(y^*) = \{0\}$ and $y^* \in \mathcal{K}(\bar{y})^+$ of Proposition 7 it follows

$$\exists\ y^* \in \mathcal{K}(\bar{y})^+ \setminus \{0\} \text{ and } T_i \in L(\mathbb{R}^{m_i}, \mathbb{R}) \text{ satisfying}$$

$$T_i(A_i(\bar{x}) - a^i) = \|A_i(\bar{x}) - a^i\|_i \text{ and } \|T_i\|_{i^*} \leq 1 \text{ such that}$$

$$0 \in \sum_{i=1}^{n} A_i^* y^* T_i + N(\Omega, \bar{x}).$$

□

5 Application in radiotherapy treatment

Now we concern the problem (P_1) which is a mathematical model of beam intensity problem in radiotherapy treatment. Suppose that $\theta_T := 0$ and $\theta_{C_i} \geq 0$, $i = 1, ..., k$ are threshold doses of k critical organs. As we have illustrated, the beam intensity we need to find is a minimal solution $\bar{x} \in \mathbb{R}^p$ of (P_1). In the following, we will show that the assumption (b) of Theorem 1 is fullfied when we consider the problem (P_1).

Remark 3 *From the practical point of view, we can see that if $\bar{x}$ is a minimal solution of (P_1) and $\bar{y} := f(\bar{x})$ then $I^{>}(\bar{y}) \neq \emptyset$. Indeed, suppose that $I^{>}(\bar{y}) = \emptyset$, i.e., $\bar{y}_1 \leq 0$ and $\bar{y}_i \leq \theta_{C_i}$, $\forall\ i = 1, 2, .., k$. Since $\bar{y}_1 = \|A_T\bar{x} - TG\| \geq 0$, it yields $\bar{y}_1 = 0$. This condition means that the dose $A_T\bar{x}$ delivered to the tumor is equal to the desired dose TG. Because of this large dose, some other critical organs will suffer from some effects. From this circumstance, there exists $i \in \{1, 2, .., k\}$ such that $\bar{y}_i > \theta_{C_i}$. Thus,*

we arrive at a contradiction to $I^>(\bar{y}) = \emptyset$.
Because of $I^>(\bar{y}) \neq \emptyset$, taking into account assertion (ii) of Proposition 6, there exists $e \neq 0$ and $e \in \cap_{y\in\Omega}\mathcal{K}(y) \setminus (-\mathcal{K}(\bar{y}))$, i.e., the condition (b) of Theorem 1 satisfies.

To this end, we present the following Corollary about the conditions for the beam intensity which we search when dealing with the inverse problem in IMRT. It is concerned as a direct consequence of Theorem 6. Since the proof is mostly similar to that of Theorem 6 with the only exception being the condition $I^>(\bar{y}) \neq \emptyset$ is relaxed, the proof is omitted.

Corollary 1 *Let $\theta = (0, \theta_{C_1}, ..., \theta_{C_k}) \in \mathbb{R}^{k+1}$ is given and suppose that $\bar{x} \in \Omega$ is a minimal solution of the beam intensity problem (P_1) w.r.t. the ordering cone $\mathcal{K}(\cdot)$ determined by (4). Let $\bar{y} := f(\bar{x})$, then there exists $y^* \in \mathcal{K}(\bar{y})^+ \setminus \{0\}$ and $T_1 \in L(\mathbb{R}^{l_T}, \mathbb{R})$, $T_i \in L(\mathbb{R}^{l_{C_{i-1}}}, \mathbb{R})$, $i = 2, .., k+1$ satisfying*

$$T_1(A_T\bar{x} - TG) = \|A_T\bar{x} - TG\|_\infty, T_i(A_{C_{i-1}}\bar{x}) = \|A_{C_{i-1}}\bar{x}\|_\infty, i = 2, ..., k+1$$

and

$$\|T_j\|_\infty \leq 1 \text{ for all } j = 1, .., k+1$$

such that

$$0 \in \sum_{j=1}^{k+1} A_j^* y^* T_j + N(\Omega, \bar{x}).$$

6 Conclusion

This paper concerns a beam intensity problem in IMRT and introduces a special variable order depending on the value of the objective function which relates to the doses delivered to the tumor organ as well as the critical organs. A vector approximation problem is also considered as a generation for a formulation for inverse beam intensity problem. We derive the optimal conditions for solutions of the vector approximation problem w.r.t. a general cone-valued mapping as well as the proposed variable order. The beam intensity we look for in IMRT is concerned as a minimal solution of this problem equipped with our ordering structure. In this paper, we calculate and obtain a specific formulation of optimality conditions for this minimal solution.

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