Robust optimization applied to the dose calculation in radiation therapy for breast cancer. An introduction to the problem

Mónica Hernández Lordui

Advisors: María Eugenia Puerta Yepez, Dr. Mathematical Sciences
Gonzalo Cabal Arango, Dr. Medical Physics
Universidad EAFIT
Department of Mathematical Sciences
PhD in Mathematical Engineering
Seminario Doctoral 1

15 de junio de 2018
Introduce the problem of robust optimization applied to intensity modulated radiation therapy, the way in which its has been addressed, emphasizing the uncertainties modeling and optimization methods.
Overview

1 Introduction and motivation

2 IMRT
   - Basics
   - Inverse planning

3 Robust optimization
   - Uncertainties
   - Dose calculation

4 References
Estimated number of incident cases, females, worldwide (top 10 cancer sites) in 2012

Breast 1,671,149 (25.1%)
Colorectum 614,304 (9.2%)
Lung 583,100 (8.8%)
Cervix uteri 527,624 (7.9%)
Stomach 320,301 (4.8%)
Corpus uteri 319,605 (4.8%)
Ovary 238,719 (3.6%)
Thyroid 228,083 (3.5%)
Liver 228,082 (3.4%)
Others 1,756,613 (26.4%)

Total: 6,657,518

Data source: GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
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Estimated number of deaths, females, worldwide (top 10 cancer sites) in 2012

- Breast: 521,907 (14.7%)
- Lung: 491,223 (13.8%)
- Colorectum: 320,294 (9%)
- Cervix uteri: 265,672 (7.5%)
- Stomach: 254,103 (7.2%)
- Liver: 224,492 (6.3%)
- Pancreas: 156,564 (4.4%)
- Ovary: 151,917 (4.3%)
- Oesophagus: 118,952 (3.4%)
- Others: 928,916 (26.2%)

Total: 3,548,190

Data source: GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
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Figure: The organs at risk

Introduction and motivation

Figure: Skin Toxicities. Desquamation and hyper-pigmentation.

“3D conformal radiotherapy (CFRT) links 3D CT visualisation of the tumour with the capability of the linear accelerator to shape the beam both geometrically and by altering the fluence of the beam. This encloses the target volume as closely as possible while reducing dose to adjacent normal tissues” (Dobbs et al., 2009, p. 21).

**Figure:** Crossfire irradiation with five beams.

Problem

Tumor with concave regions

Tumor

Critical Structure
Uncertainties

Voxel

A voxel is the unit of minimum volume within (or into) a 3D or 4D image of the target volume.

Figure: A 3-D plot of the prescription dose (white wireframe) is superimposed on the target volume, with the bladder and rectum shown above.

Uncertainties: Respiratory dynamic

Figure: Voxel trajectory projected into the AP-CC plane and 4D-CT images, corresponding to dose calculation geometries: exhale, 20% inhalation, and 100% inhalation.

Uncertainties: Respiratory dynamic

Figure: Voxel trajectory projected into the AP-CC plane and 4D-CT images, corresponding to dose calculation geometries: exhale, 20% inhalation, and 100% inhalation.

Uncertainties: Variations in patient positioning

Uncertainties: Alignment of beams treatment

Uncertainties: Alignment of beams treatment

Effects of motion on the dose

Figure: Motion leads to a blurring of the dose distributions, which causes an increased beam penumbra.

Retrieved from: Worst case optimization: a method to account for uncertainties in the optimization of intensity modulated proton therapy. Department of Medical Physics in Radiation Oncology, German Cancer Research Center (DKFZ).
How do you make the modeling of respiratory motion uncertainties?

- Interval analysis
- Fuzzy theory
- Stochastic model:
  * Stationary or not
  * What is your probability distribution?

How do you make the modeling of positional uncertainty?
Uncertainties: Modeling of respiratory motion

Jiang, S. et al., 2003
Uncertainties: Modeling of respiratory motion

Jiang, S. et al., 2003

\( \Phi_i = \frac{i\pi}{4}, \; i = 1, 2, \ldots, 8 \)

\( d_i^j = d_i^j(\Phi_i) \)

\( j = 1, 2, \ldots, 5 \) (fields)
Uncertainties: Modeling of respiratory motion

Bortfeld, T. et al., 2004

Figure: Probability density function (PDF) non-Gaussian obtained from several cycles of breathing motion (recorded by tracking an internal marker in the lung).
Uncertainties: Modeling of respiratory motion


Probability distribution Gaussian for uncertain positioning:

\[ P(\Delta r) = \frac{1}{2\pi \sigma^2} \exp\left(-\frac{\Delta r^2}{2\sigma^2}\right) \]

\(r\): Vector coordinates to parametrize a point inside the geometry of the patient
Uncertainties: Modeling of respiratory motion

Cham et al., 2006. PDF from marker position.

$X$: Domain of the pmf.

$p$: Nominal pmf.

$U$: Part of the domain representing inhale, such that, $U \subset X$. 
Uncertainties: Modeling of respiratory motion

Heath et al, 2009. 4D CT was used.

Figure: Respiratory amplitude and baseline distributions (both normal, with standard deviation 5 mm, $P(A)$ and $P(b0)$.)
**Figure:** CTV is the center red square, PTV margin is the gray square

**Figure:** Potential scenarios (no shift, left, right, down, up, respectively). The CTV voxels are the center four-by-four square, surrounded by the healthy structure. Darker gray indicates higher dose delivered, lighter indicates lower.
Robust optimization refers to the modeling of optimization problems with data uncertainty.
Robust optimization applied to IMRT:

Ensure maximum coverage in diseased tissue with minimal dose exposure in healthy tissue under scenarios of uncertainty.
Robust optimization

Mathematical model for finding constraint-robust solutions. Consider an optimization problem of the form:

$$\min_x f(x, p)$$

subject to:

$$G(x, p) \in K, \quad p \in U \text{ and } x \in S(p) = \bigcap_p \{x : G(x, p) \in K\}$$

Where:
- $x$ are decision variables, $f$ is the objective function, $p$ uncertainties, $G_i(x, p) \in K$ are constrained set, $U$ uncertainty set
Dose calculation


\[
\begin{align*}
\text{minimize} & \quad \sum_{v \in V} \sum_{b \in B} \sum_{x \in X} \Delta_{v,x,b} p(x) w_b \\
\text{subject to} & \quad \sum_{b \in B} \sum_{x \in X} \Delta_{v,x,b} p(x) w_b \geq \theta_v, \\
w_b & \geq 0.
\end{align*}
\]

Where:

- $\Delta$ : Matrix
- $v$ : Voxel
- $x$ : Shift from nominal position
- $b$ : Per unit intensity of beamlet
- $p(x)$ : Probability mass function
- $\theta_v$ : Prescribe dose
- $w_b$ : Weight of beamlet $b$
Dose calculation

Jan Unkelbach and Thomas Bortfeld, 2008.

$$\min_{w} \langle (E) \rangle = \int \int E(w; \delta, \Delta s) P(\delta) P(\Delta s) d\delta d\Delta s$$

subject to $w_j \geq 0 \quad (j = 1, \ldots, N)$

$w$: Fluence map
$E$: Function of the dose distribution
$P(\delta)$ and $P(\Delta s)$: Gaussian distribution (range and rigid shift uncertainty, respectively).

With objective function:

$$E = \sum_n \frac{\alpha_n}{|V_n|} \sum_{i \in V_n} (D_i - D_i^{\text{pres}})^2$$

$|V_n|$: Is set of voxels belonging to the volume of interest with index $n$
$\alpha_n$: The penalty factors that weight the objectives for different organs are chosen.
Dose calculation

Jan Unkelbacha and Thomas Bortfeld, 2008.

“Hence, the objective is a weighted sum of objectives for the individual scenarios, where the weight of an objective is given by the probability that the corresponding scenario occurs. If we do not account for uncertainty, we assign a weight of one to the nominal scenario, and the weight zero to all other scenarios. If we include uncertainty, we trade-off objectives for different scenarios.”

\[
\min_{x \in X} (f_1(x), \ldots, f_p(x))
\]

$f_i(x)$: Criteria or objective function

$x$: Decision variables

$X$: Constrains set that define the possible solutions

\[
\min_{x \in X} \sum_{k=1}^{p} \lambda_k f_k(x)
\]

$\textbf{Weighted sum Method}$

$k$: Scenarios, $\lambda$: Vector of weights
Communities

1. Department of Mathematics, Optimization and Systems Theory, Royal Institute of Technology (KTH), Sweden and RaySearch Laboratories, Stockholm, Sweden.
2. Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.
3. Department of Medical Physics in Radiation Therapy, Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany.
Thanks!