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

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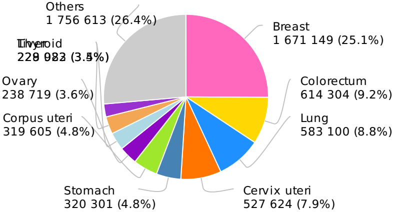
Objective

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

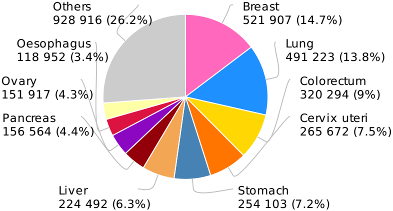
Estimated number of incident cases, females, worldwide (top 10 cancer sites) in 2012



Total : 6 657 518

Data source:GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

Estimated number of deaths, females, worldwide (top 10 cancer sites) in 2012



Total : 3 548 190

Data source:GLOBOCAN 2012
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)

International Agency for Research on Cancer
World Health Organization

Introduction and motivation

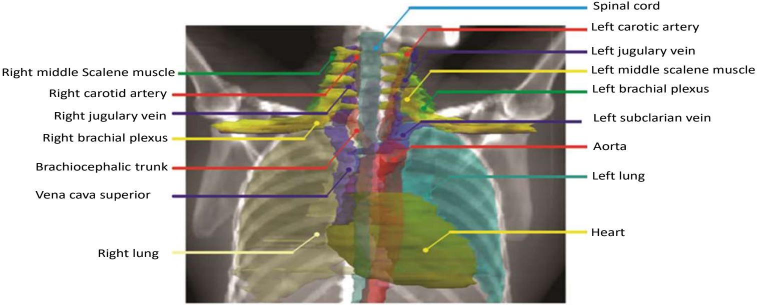


Figure: The organs at risk

Retrieved from: Principles and practice of modern radiotherapy techniques in breast cancer. New York: Springer.

Introduction and motivation

Figure: Skin Toxicities. Desquamation and hyper-pigmentation.

Retrieved from: Principles and practice of modern radiotherapy techniques in breast cancer. New York: Springer.

IMRT

"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).

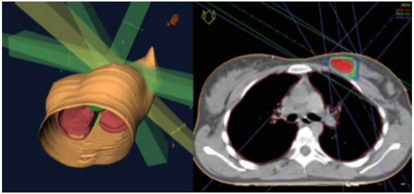
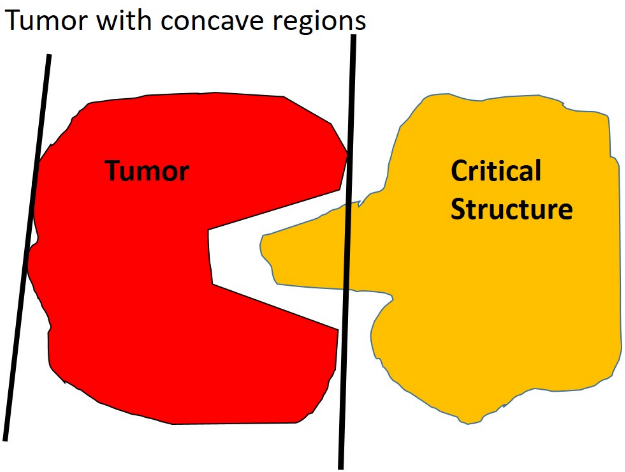


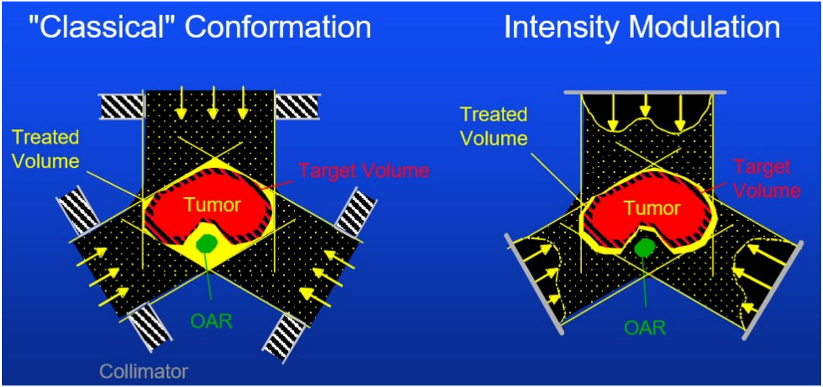
Figure: Crossfire irradiation with five beams.

Retrievered from: Principles and practice of modern radiotherapy techniques in breast cancer. New York: Springer.

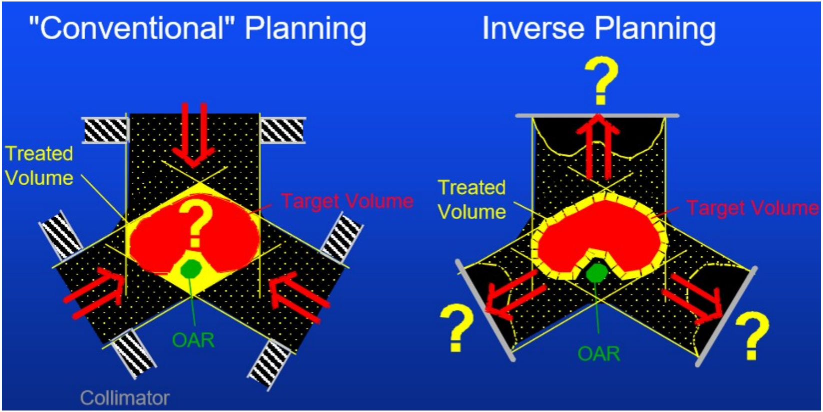
Problem



Solution with IMRT



Bortfeld, T. et al. Current IMRT Optimization Algorithms: Principles, Potencial and Limitations.[Figura]. Retrieved from: Lecture Notes.



Bortfeld, T. et al. Current IMRT Optimization Algorithms: Principles, Potencial and Limitations.[Figura]. Retrieved from: Lecture notes.

Voxel

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

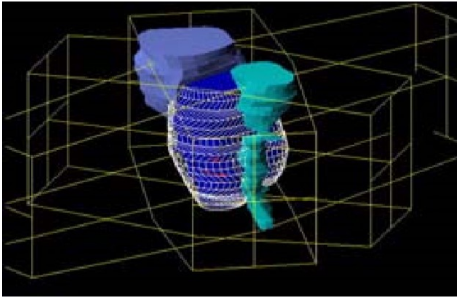


Figure: A 3-D plot of the prescription dose (white wireframe) is superimposed on the target volume, with the bladder and rectum shown above.

Retrieved from: Radiation Oncology Physics: A Handbook for Teachers and Students. International Atomic Energy Agency.

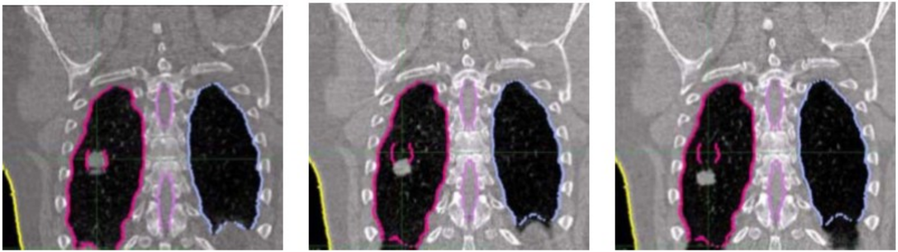
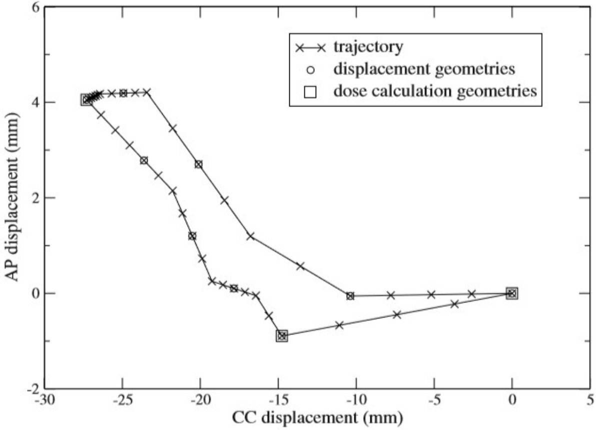


Figure: Voxel trajectory projected into the AP-CC plane and 4D-CT images, corresponding to dose calculation geometries: exhale, 20% inhalation, and 100% inhalation.

Retrieved from: Incorporating uncertainties in respiratory motion into 4D treatment plan optimization. Med. Phys.

Uncertainties: Respiratory dynamic



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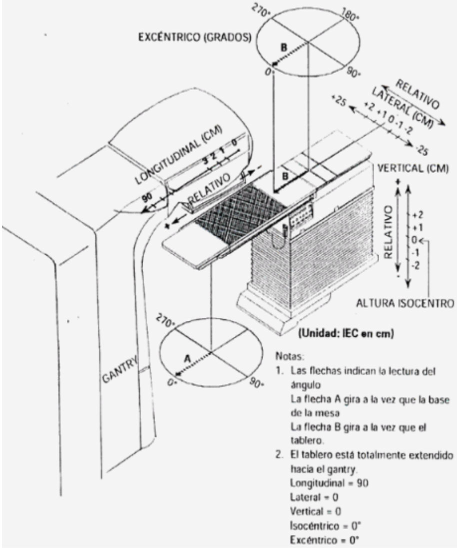
Retrieved from: Incorporating uncertainties in respiratory motion into 4D treatment plan optimization. Med. Phys.

Uncertainties: Variations in patient positioning

Retrieved from: Practical Radiotherapy Planning. London: Hodder Arnold.

Uncertainties: Alignment of beams treatment

Retrieved from: http://www.elcomercio.es/20130216/asturias/nuevo-huca-contara-tres-201302161719.html



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Effects of motion on the dose

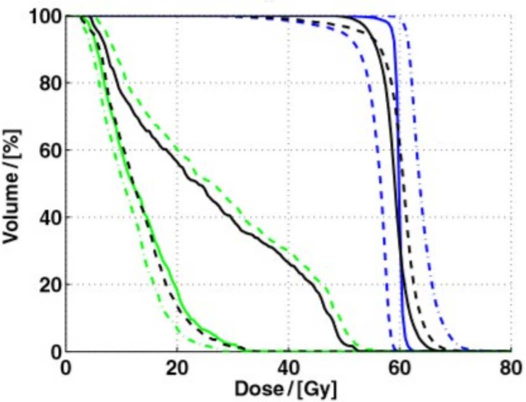


Figure: Motion leads to a blurring of the dose distributions, which causes an increased beam penumbra.

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).

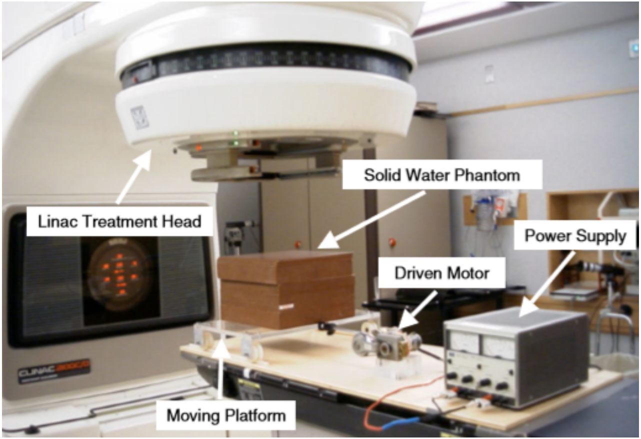
Uncertainties in radiotherapy: Modeling

How do you make the modeling of respiratory motion uncertainties?

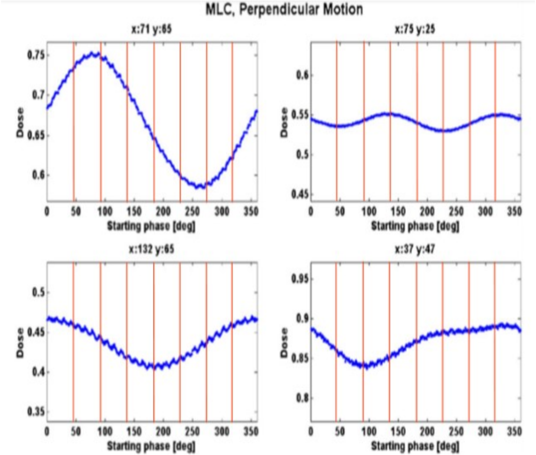
- Interval analysis
- Fuzzy theory
- Stochastic model:
  - * Stationary or not
  - * What is your probability distribution?

How do you make the modeling of positional uncertainty?

Jiang, S. et al., 2003



Jiang, S. et al., 2003



Phi: motion phase

d : dose

$$\Phi_i = i\pi/4, \; i = 1, 2, ..., 8$$

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

$$j = 1, 2, ..., 5 \; (\textit{fields})$$

Bortfeld, T. et al., 2004

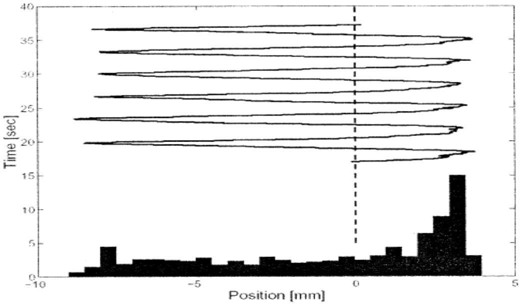


Figure: Probability density function (PDF) non-Gaussian obtained from several cycles of breathing motion (recorded by tracking an internal marker in the lung).

Unkelback, J. and Oelfke, 2004.

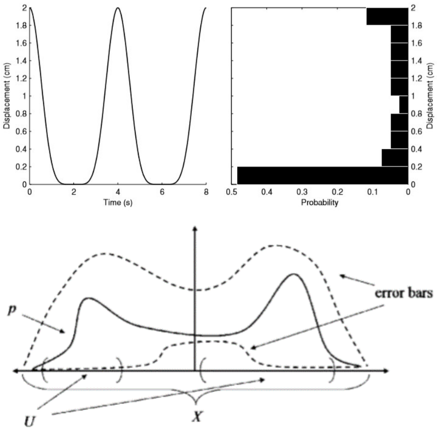
Probability distribution Gaussian for uncertain positioning:

$$P(\triangle r) = \frac{1}{2\pi\sigma^2} exp(-\frac{\triangle r^2}{2\sigma^2})$$

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, $U \subset X$.

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

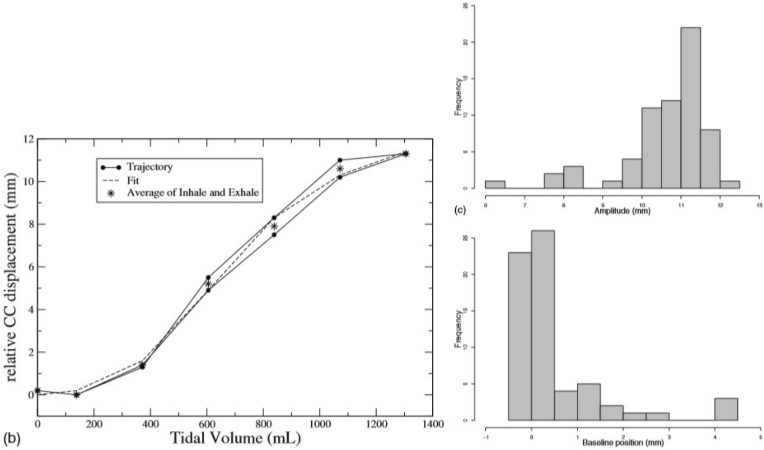


Figure: Respiratory amplitude and baseline distributions (both normal, with standard deviation 5 mm, P(A) and P(b0).

Dose calculation

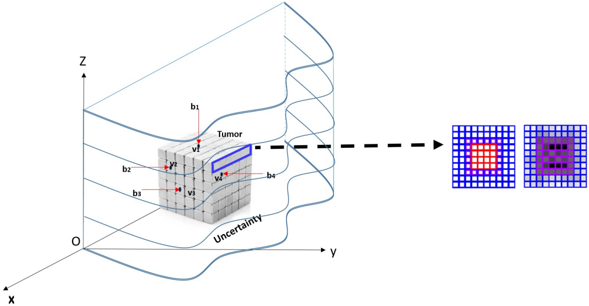


Figure: CTV is the center red square, PTV margin is the gray square

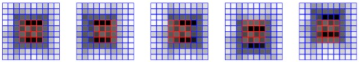


Figure: Potential scenarios (no shift, left, right, down, up, respectively). The CTV voxels are the center four-by-four square, surrounded by the healthy structure. Darker gray indicates higher dose delivered, lighter indicates lower.

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:

$$\min_{x} \quad f(x,p)$$

subject to:

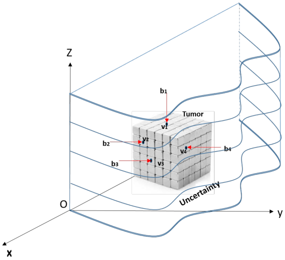
$$G(x,p) \in K, \quad p \in U \; and \; x \in S(p) = \bigcap_{p} \{x : G(x,p) \in K\}$$

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

Timothy Chan, Thomas Bortfeld and John N. Tsitsiklis (2006).
Fredriksson, A., 2012



$$\begin{aligned} \underset{w}{\text{minimize}} \quad & \sum_{v\in V}\sum_{b\in B}\sum_{x\in X} \triangle_{v,x,b}\, p(x) w_b \\ \text{subject to} \quad & \sum_{b\in B}\sum_{x\in X} \triangle_{v,x,b}\, p(x) w_b \geq \theta_v, \\ & w_b \geq 0. \end{aligned}$$

Where :

$\triangle$	:	Matrix
v	:	Voxel
x	:	Shift from nominal positi
b	:	Per unit intensity of beam
$p(x)$	:	Probability mass function
θ_v	:	Prescribe dose
w_b	:	Weight of beamlet b

Dose calculation

Jan Unkelbach and Thomas Bortfeld, 2008.

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

$$\text{subject to} \ \ w_j \geq 0 \quad (j = 1, ..., N)$$

w: Fluence map
E: Function of the dose distribution
P(δ) and P(Δs): Gaussian distribution (range and rigid shift uncertainty, respectively).
With objective function:

$$E = \sum_{n} \frac{\alpha_n}{\mid V_n \mid} \sum_{i \in V_n} (D_i - D_i^{pres})^2$$

$\mid V_n \mid$: Is set of voxels belonging to the volume of interest with index n
α_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."

$$\min_{x \in X} (f_1(x), ..., f_p(x))$$

$f_i(x)$: Criteria or objective function

x: Decision variables

X: Constrains set that define the possible solutions

$$\min_{x \in X} \sum_{k=1}^{p} \lambda_k f_k(x) \quad \textit{Weighted sum Method}$$

k: Scenarios, λ: 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.

References

[1] Barrett, A., Dobbs, J., Morris, S., Roques, T. (2009). Practical Radiotherapy Planning. London: Hodder Arnold.

[2] Haydaroglu, A., Ozyigit, G. (2013). Principles and practice of modern radiotherapy techniques in breast cancer. New York: Springer.

[3] Bortfeld, T., Jiang, S. B., Rietzel, E. (January de 2004). Effects of motion on the total dose distribution. Seminars in Radiation Oncology, 14(1), 41-51.

[4] Chan, T., Bortfeld, T., Tsitsiklis, J. (2006). A robust approach to IMRT optimization. Physics in Medicine and Biology, 2567-2583.

[5] Heath, E., Unkelbach, J. and Oelfke, U. (2009). Incorporating uncertainties in respiratory motion into 4D treatment plan optimization. Med. Phys.

[6] Chu, M., Zinchenko, Y., Henderson, S. G., and Sharpe, M. B. (2005). Robust optimization for intensity modulated radiation therapy treatment planning under uncertainty. Physics in Medicine and Biology, 50(23), 5463.
[7] Pugfelder, D., Wilkens, J. and U Oelfke. (2008). 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), Im Neuenheimer Feld 280, 69120 Heidelberg, Germany.
[8] Jan Unkelbach and Thomas Bortfeldb. (2009). Reducing the sensitivity of IMPT treatment plans to setup errors and range uncertainties via probabilistic treatment planning. Medical Physics 36, 149.
[9] OMS. (2017). Cancer. Centro de prensa: datos y cifras.
[10] Ervin B. Podgorak. (2005). Radiation Oncology Physics: A Handbook for Teachers and Students. International Atomic Energy Agency.

Thanks!