

# Uncertainty-aware Multi-criteria Dose Optimization for Radiation Therapy

An overview of my bachelor thesis

Alexander Kaschta | November 6th, 2023

# Causes of Death

Table: Numbers of the most frequent causes of death in the year 2021 in Germany grouped according to their ICD-10-GM categories; Source: [1], [2]

<b>Cause</b>	<b>ICD-10-GM Code</b>	<b>Number of Deaths</b>
Diseases of the circulatory system	I00-I99	340 619
Malignant neoplasms (Cancer)	C00-C75	229 068
Mental and behavioral disorders	F00-F99	59 990
Diseases of the respiratory system	J00-J99	57 316
Other		336 694
<b>Total</b>		<b>1 023 687</b>

# Treatment Methods

- Goal: **best treatment for the patient**
- No cure
- Range of treatment options
  - Cure of all symptoms
  - Palliative care
- Three options, of a combination of those
- Depending on various properties like type, size, location, ...

## Surgery

- Requires solid, locally contained tumor
- Region must be accessible for surgery

## Chemotherapy

- Affects whole body
- Kills also healthy tissue

## Radiation Therapy

- Optimal for targeting small sections of tissue
- Affects all tissue along its path
- Complex beam calculations for optimal treatment

## How does it work?

- Ionizing radiation required
- Structural changes to the DNA of the cell
- Death of the cell
  
- Visible light can't transfer enough energy
- Suitable particles: photons, electrons, positrons, neutrons, protons and other charged ions
- Bragg peak crucial for precise targeting
- Uncertainty analysis only for protons and other charged ions

# Intensity Modulation

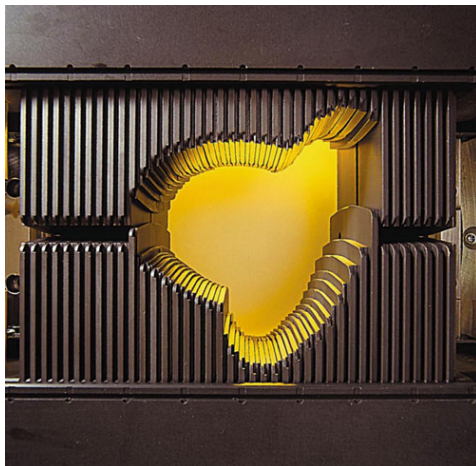


Figure: Example of a multileaf collimator used in clinics, like in [3]. For scale: each leaf is only a few millimeters thick.  
Source: [4]

# Treatment Planning

- Complex process
- Keeping track of all aspects

## 1. Scan of the patient

- MRI, CT, ...

## 2. Analysis of the data

- Identification of affected tissue, potential organs at risk (OAR) and constraints

## 3. Optimization

- Treatment plan optimization including all data and constraints

## 4. Review

- Selection of an optimal plan by experienced physicians and other medical staff

# Multi-Criteria Optimization

## Multi-Criteria Optimization

- Also known as Pareto Optimization
- Optimizing for multiple objectives simultaneously
- Considers trade-offs

## How it work?

- Solution  $A$  is dominated by solution  $B$  if  $A$  is worse in some criteria than  $B$  and doesn't improve in all other criteria over  $B$
- Optimal solution, if not dominated by any other solution
- Multiple optimal solutions possible
  
- Optimal treatment plans must be stable

# What is my part?



# Examples of Uncertainties

- Just a selection
- Position of the affected tissue
  - Tissue has grown
  - Filled stomach
- Physical uncertainties
  - Received dose by the patient
- Human error
  - Missed treatment appointment
  - Unreadable handwriting [5]
- Technical malfunction
  - Therac-25 [6]

# Approach

- matRad, developed by the German Cancer Research Center (DKFZ) [7], [8]
  - MATLAB based software
- Implementation of the *Rennen et al.* algorithm [9] by Tobias Becher into a fork of matRad [10]

## Evaluation of ideas on an example problem

- Change of Boundaries
  - Changing the Penalties
  - Modifications to the Cost Function
- 
- Example problem from *Rennen et al.* [9] and *Bokrantz and Forsgren* [11]
  - If successful, implementation on the treatment optimization

# Change of Boundaries

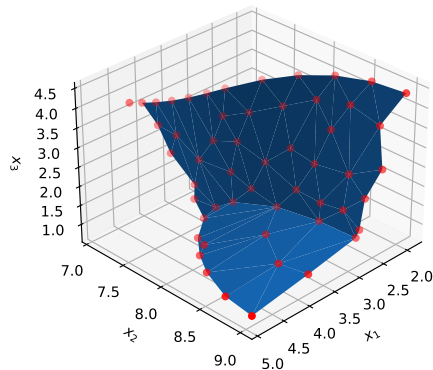


Figure: Pareto surface of the given example problem

# Changing the Penalties

- A weighted sum is used for all constraints
- Modification of the default weights  $w_i = 1$  for  $i \in \{1, 2, 3\}$

## Results

- Modified Pareto surface, when all weights very small  $w_i \ll 1$
- For all other cases: No visible modifications
  - Data analysis shows variations after the sixth decimal place
  - Variations constant in order of magnitude for all weight combinations
  - Very likely limits of numerical computations

# Modifications to the Cost Function

- Adding terms/expressions to the cost functions
- Newly added terms should represent uncertainties

## Results

- Visible changes to the Pareto surface
- Not all modifications deliver results

## New idea: Uncertainties Through Multiple Calculations

- Extract results from an optimal treatment plan
- Vary parameters using probability distributions and optimize again
- Methods is also successful

# Optimized Treatment Plan

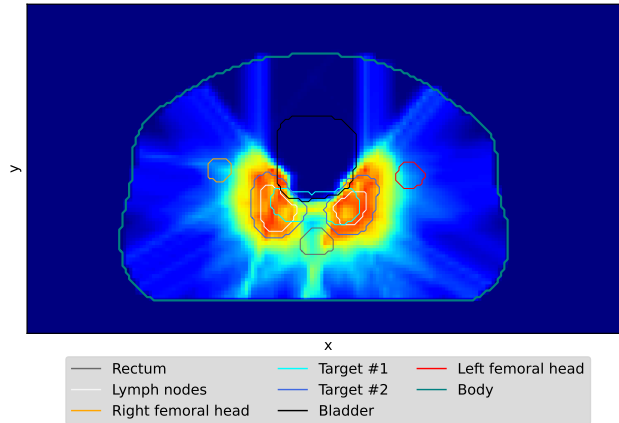


Figure: Pareto-optimal treatment plan for the treatment of prostate cancer, including the dose distribution and marked organs; CT scan from [12]

# Questions?

# Literature I

- [1] Statistisches Bundesamt (Destatis). *Gestorbene: Deutschland, Jahre, Todesursachen*. German. 2021. URL: <https://www-genesis.destatis.de/genesis//online?operation=table&code=23211-0001#astructure> (visited on July 2, 2023).
- [2] Statistisches Bundesamt (Destatis). *Anzahl der Gestorbenen nach Kapiteln der ICD-10 und nach Geschlecht für 2021*. Dec. 16, 2022. URL: [https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Gesundheit/Todesursachen/Tabellen/gestorbene\\_anzahl.html](https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Gesundheit/Todesursachen/Tabellen/gestorbene_anzahl.html).
- [3] Wolfgang Schlegel, Christian P. Karger, and Oliver Jäkel, eds. *Medizinische Physik*. Springer Berlin Heidelberg, 2018. DOI: 10.1007/978-3-662-54801-1.
- [4] Varian Newsroom. *Multileaf collimator*. Jan. 5, 2017. URL: <http://newsroom.varian.com/index.php> (visited on Jan. 5, 2017).



## Literature II

- [5] Daniel K Sokol and Samantha Hettige. “Poor Handwriting Remains a Significant Problem in Medicine”. In: *Journal of the Royal Society of Medicine* 99.12 (Dec. 2006), pp. 645–646. DOI: 10.1177/014107680609901219. URL: <https://journals.sagepub.com/doi/pdf/10.1177/014107680609901219> (visited on Aug. 15, 2023).
- [6] N.G. Leveson and C.S. Turner. “An investigation of the Therac-25 accidents”. In: *Computer* 26.7 (July 1993), pp. 18–41. DOI: 10.1109/mc.1993.274940.
- [7] Hans-Peter Wieser, Eduardo Cisternas, Niklas Wahl, Silke Ulrich, Alexander Stadler, Henning Mescher, Lucas-Raphael Müller, Thomas Klinge, Hubert Gabrys, Lucas Burigo, Andrea Mairani, Swantje Ecker, Benjamin Ackermann, Malte Ellerbrock, Katia Parodi, Oliver Jäkel, and Mark Bangert. “Development of the open-source dose calculation and optimization toolkit matRad”. In: *Medical Physics* 44.6 (May 2017), pp. 2556–2568. DOI: 10.1002/mp.12251.
- [8] Mark Bangert, Eduardo Cisternas, Hubert Gabryś, Thomas Klinge, Hennig Mescher, Lucas-Raphael Müller, Alexander Stadler, Niklas Wahl, and Hans-Peter Wieser. *e0404/matRad: Alan 2.1.0*. 2016. DOI: 10.5281/ZENODO.3879615.

## Literature III

- [9] Gijs Rennen, Edwin van Dam, and Dick den Hertog. “Enhancement of Sandwich Algorithms for Approximating Higher Dimensional Convex Pareto Sets”. In: *SSRN Electronic Journal* (2009). DOI: 10.2139/ssrn.1427721.
- [10] Tobias Becher. *matRad*. Version Pareto branch. DKFZ, Mar. 7, 2023. URL: <https://github.com/tobiasbecher/matRad>.
- [11] Rasmus Bokrantz and Anders Forsgren. “An Algorithm for Approximating Convex Pareto Surfaces Based on Dual Techniques”. In: *INFORMS Journal on Computing* 25.2 (May 2013), pp. 377–393. DOI: 10.1287/ijoc.1120.0508.
- [12] David Craft, Mark Bangert, Troy Long, Dávid Papp, and Jan Unkelbach. “Shared data for intensity modulated radiation therapy (IMRT) optimization research: the CORT dataset”. In: *GigaScience* 3.1 (Dec. 2014). DOI: 10.1186/2047-217x-3-37.

# Backup slides

# Constructed Phantom

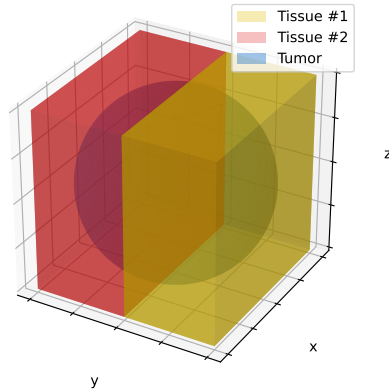


Figure: Visualization of a simple phantom consisting of a spherical tumor surrounded by two tissues with different sensitivity created using matplotlib

# Selection of Results

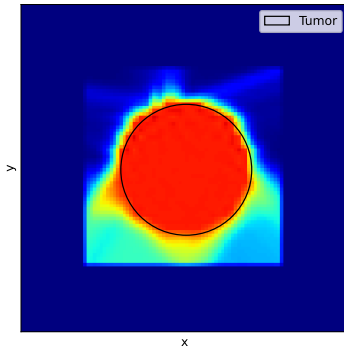


Figure: Uniformly irradiated tumor without uncertainties

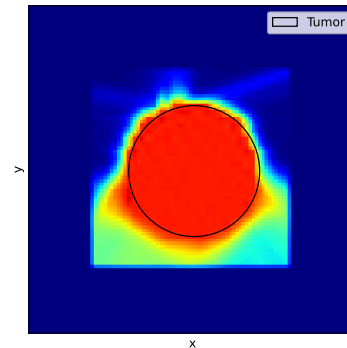


Figure: Uniformly irradiated tumor with added uncertainties

# Selection of Results

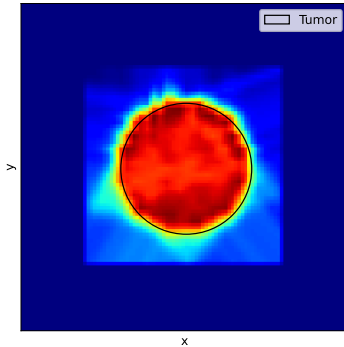


Figure: Unevenly irradiated tumor without uncertainties

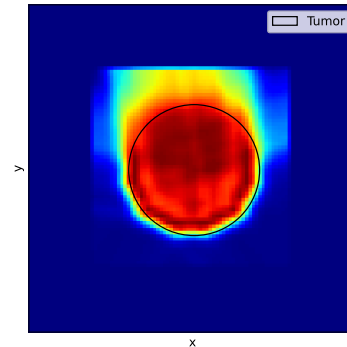


Figure: Unevenly irradiated tumor with added uncertainties

# Optimized treatment plan

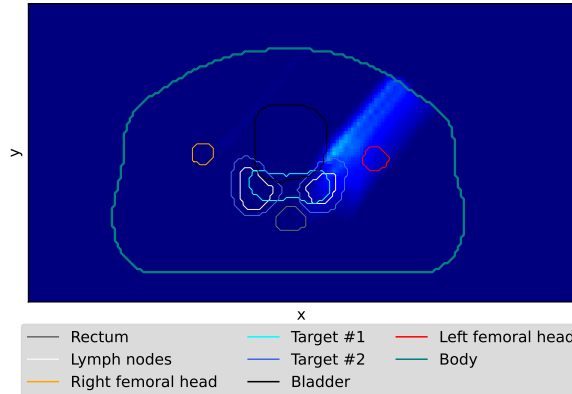


Figure: Single beam of a Pareto-optimal treatment plan for the treatment of prostate cancer, including the dose distribution and marked organs

## ICD-10

- 10th revision of International Statistical **C**lassification of **D**iseases and Related Health Problems
- Published 1994
- GM (German Modification)
  
- ICD-11 was released 2022