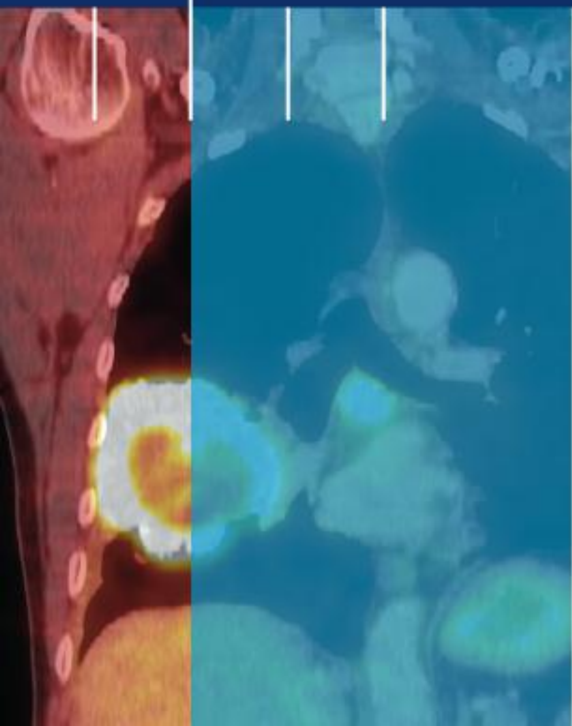
Peculiarities of the Radiation Treatment Planning Optimisation Problem: multiple objectives and user/algorithm interaction



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MAASTRO CLINIC (**MAAST**richt **R**adiation **O**ncology)

- Independent non-profit radiation oncology clinic
  - emphasis: academic cancer care and research
  - 20 radiation oncologists
  - 7 medical physicists
  - 5 biologists
  - >20 PhD students
  - 2 CT + 1 PET/CT scanners
  - 4 LINACs (+2 in satellite Venlo)
  - brachytherapy (^{125}I, ^{192}Ir)
  - >4000 new patients/year

Dutch radiotherapy centres

Oncology

- Main cancer treatment modalities:
  - surgery
  - chemotherapy (systemic/biological agents)
  - **radiotherapy** (ionising radiation)

- Radiotherapy:
  - treatment of choice in ~50% of the cases
  - **curative** intent : sterilise spread of tumour cells
  - **palliative** intent : alleviate pain symptoms to achieve highest quality of life

Radiotherapy

– Aim:

  • deliver therapeutic dose to tumour without damaging healthy normal tissues

– Radiation therapy modalities:

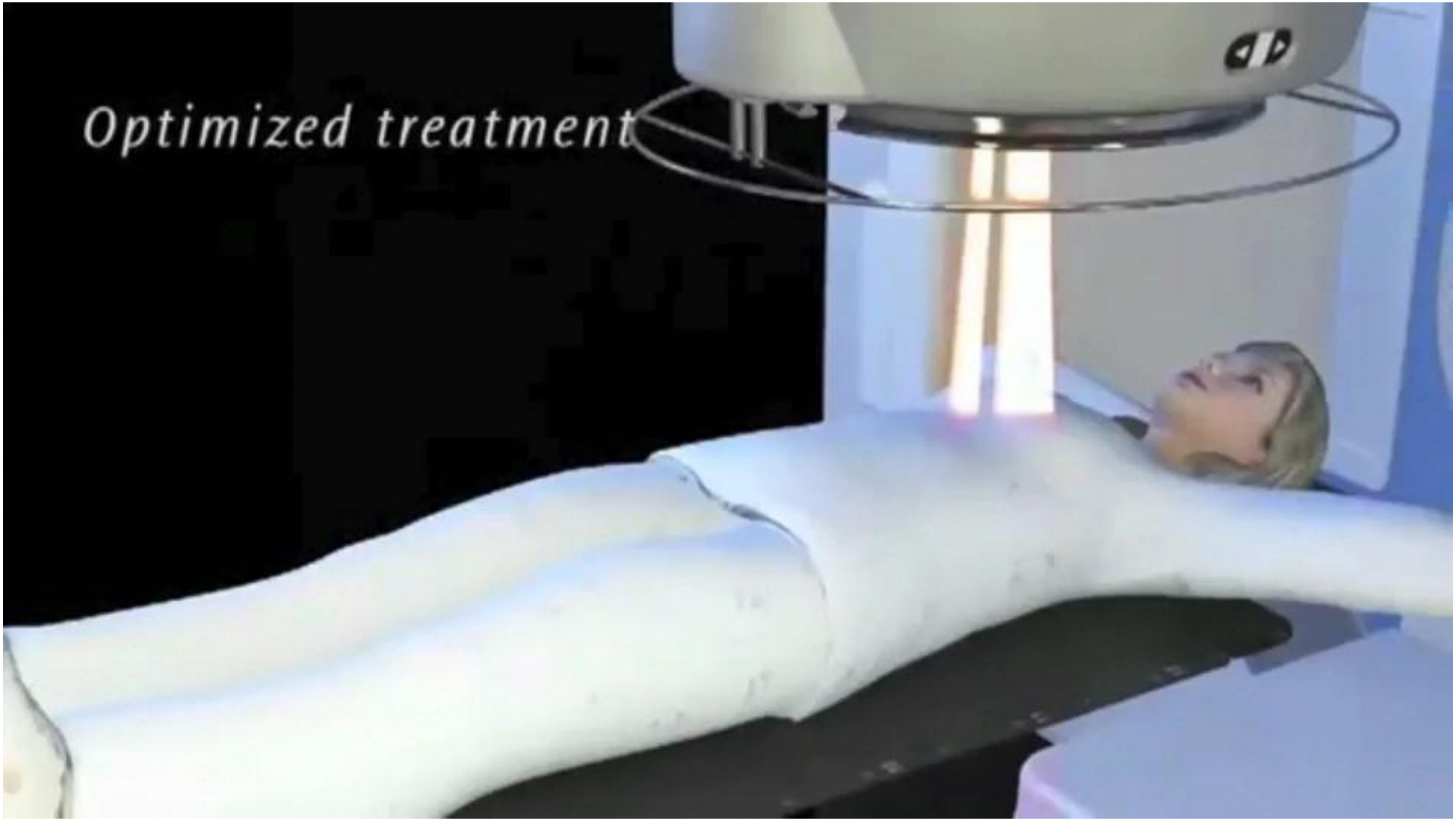
  • **internal** radioactive source (brachytherapy)
  • **external** particle beam accelerator (teletherapy)

External beam irradiation

- Particle accelerator generates high-energy rays of:
  - photons
  - electrons
  - protons
  - neutrons
  - …

- Energetic particles:
  - penetrate through the skin
  - interact with matter (*i.e.* tissues) by electrical forces
  - deposit dose (measured in J/kg) while losing kinetic energy

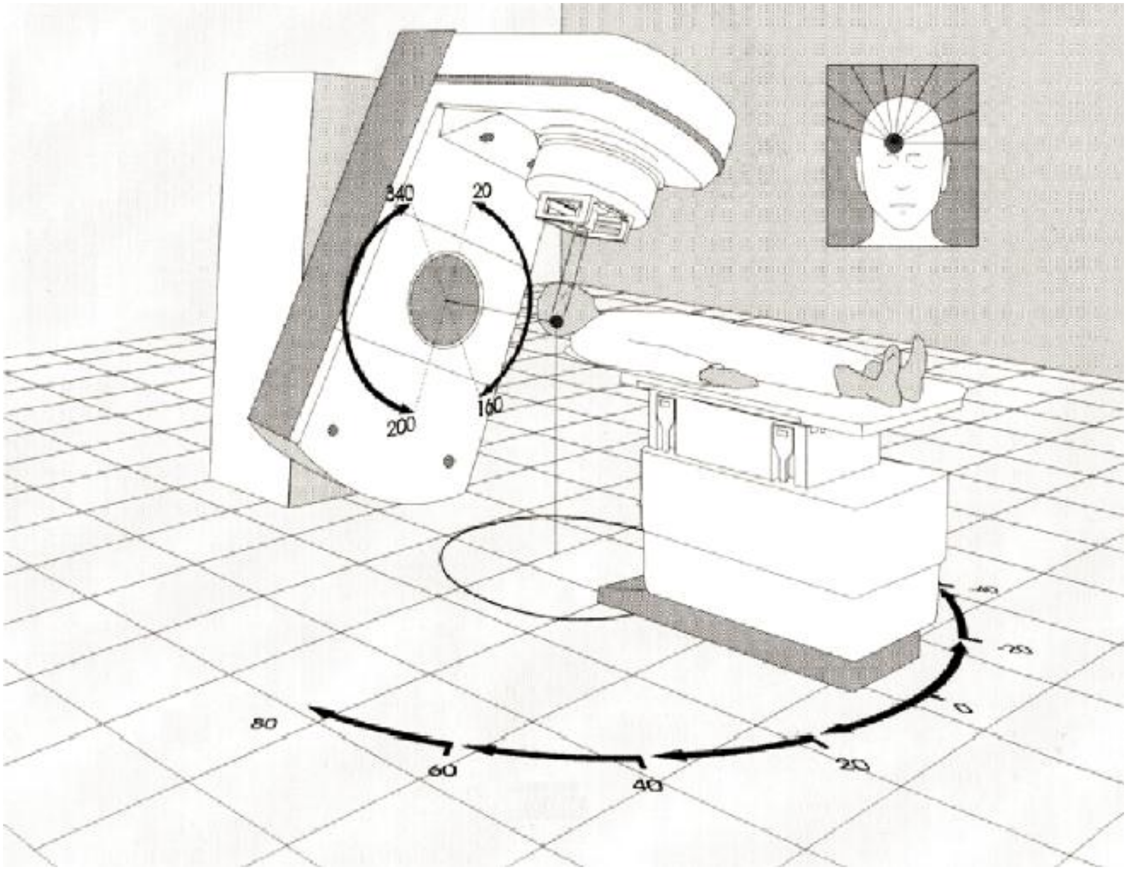
External beam photon therapy



External beam photon therapy: linear accelerator

– Degrees of freedom:

- gantry angle
- couch angle
- number of beams
- beam angles
- beam apertures
- beam intensities
- …



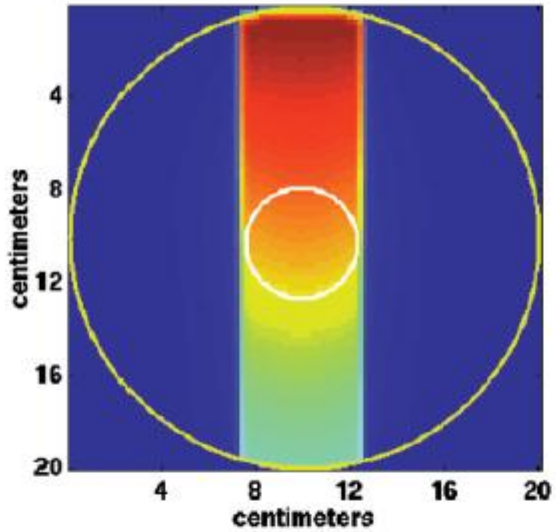
Treatment planning problem

- Medical and biological parameters: (*radiation oncologist*)
  - prescription dose level for tumour
  - tolerance dose levels for normal tissues
  - dose-time fractionation scheme

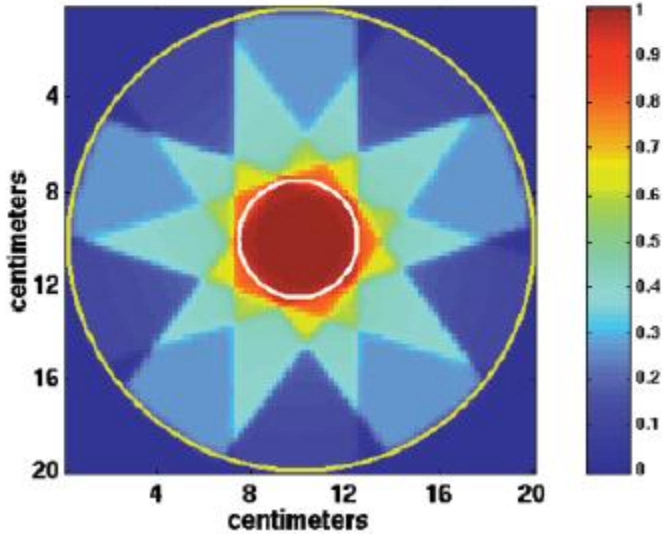
- Technical and physical parameters: (*medical physicist*)
  - treatment setup geometry: patient position relative to beam
  - beam arrangement: numbers, angles, …
  - beam settings: energy, shapes, intensity profiles, …

Beam number and angles

single beam



5 equidistant beams



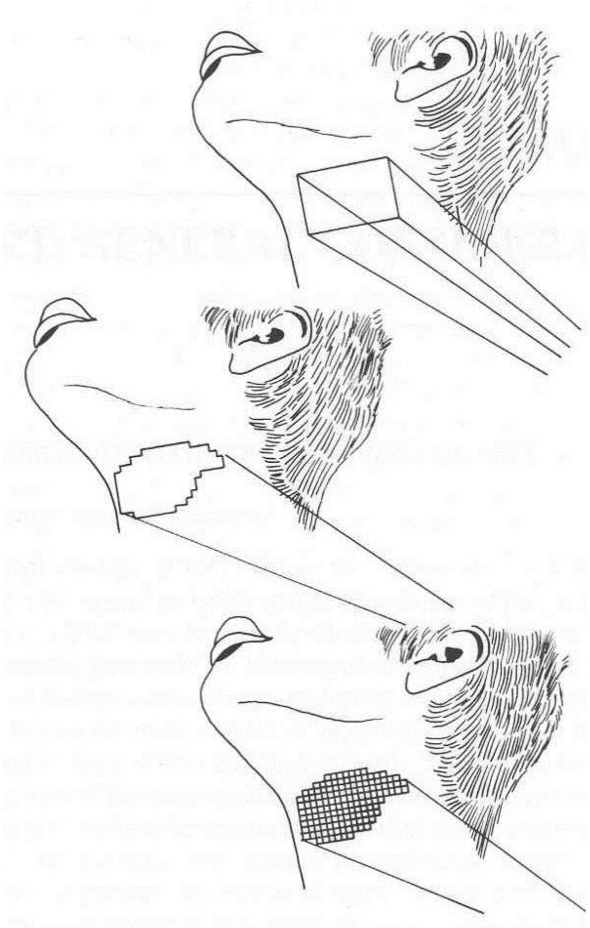
Cross-firing beams: basic principle to add up dose in tumour and keep dose in healthy tissues low

Beam shapes and intensities

- Conventional RT:
  - rectangular beam shape
  - uniform radiation intensity distribution

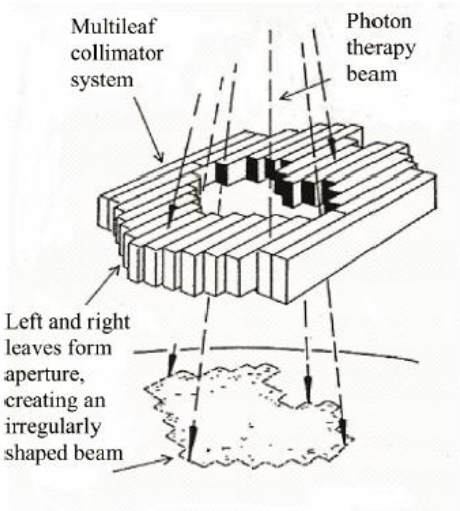
- 3D-Conformation RT (3D-CRT):
  - MLC: irregular beam shape
  - uniform radiation intensity distribution

- **Intensity-Modulated RT (IMRT):**
  - non-uniform intensity distribution

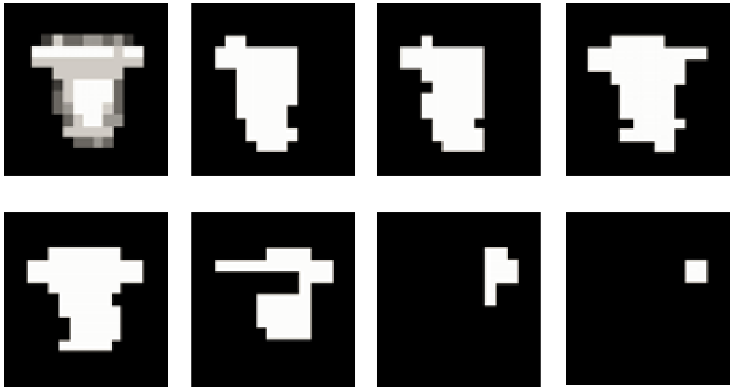


Beam shapes and intensities

– Beam shapes
  - multi-leaf collimator (MLC)
  - tungsten leafs



– Beam intensity modulation
  - different aperture shapes
  - same radiation intensity (fluence)
  - fluence map construction
  - beam intensity elements (bixels)



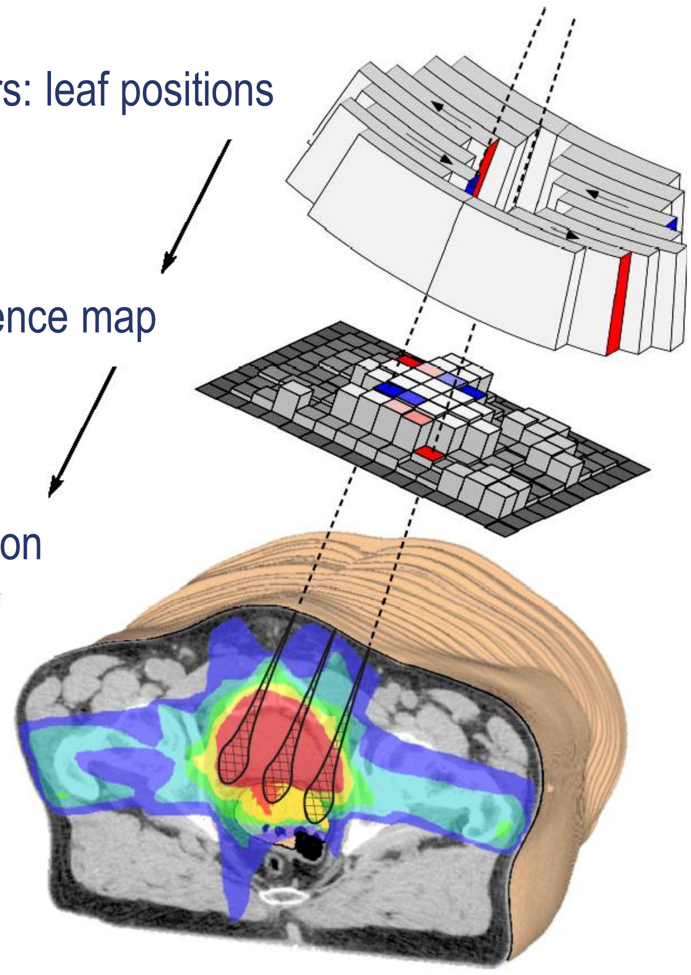
Forward problem: beam aperature optimisation

design parameters: leaf positions

fluence map

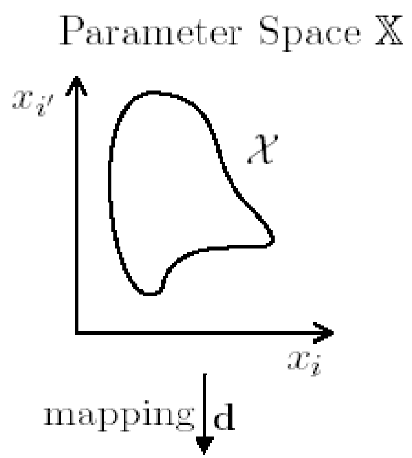
dose distribution

evaluation criteria: dosimetric quality



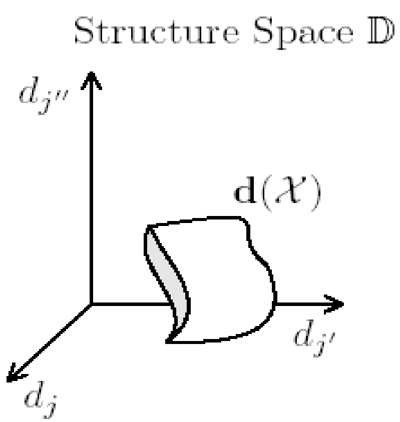
discretised set of pencil beams with tunable intensity levels

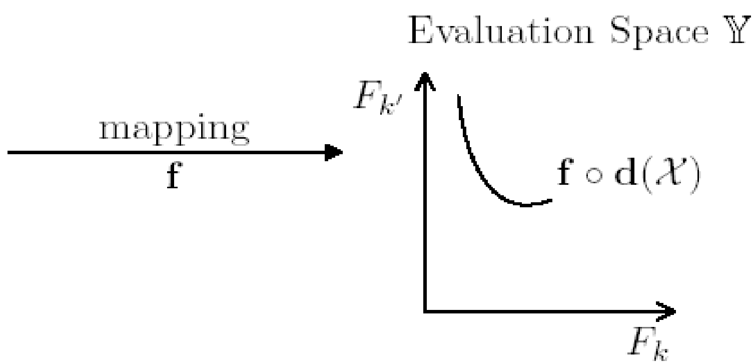
Mathematical model



design parameters: **leaf positions**

constraints $\rightarrow$ *feasible design space* $\mathcal{X}$

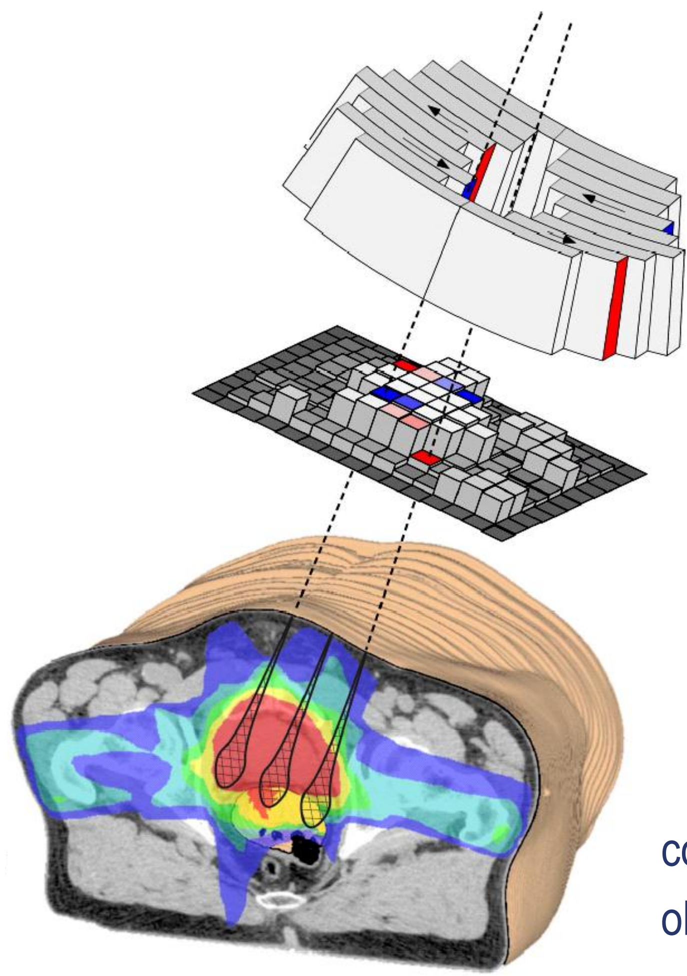




structure: **dose distribution**

evaluation: **cost functions**

Inverse problem: beam aperature optimisation



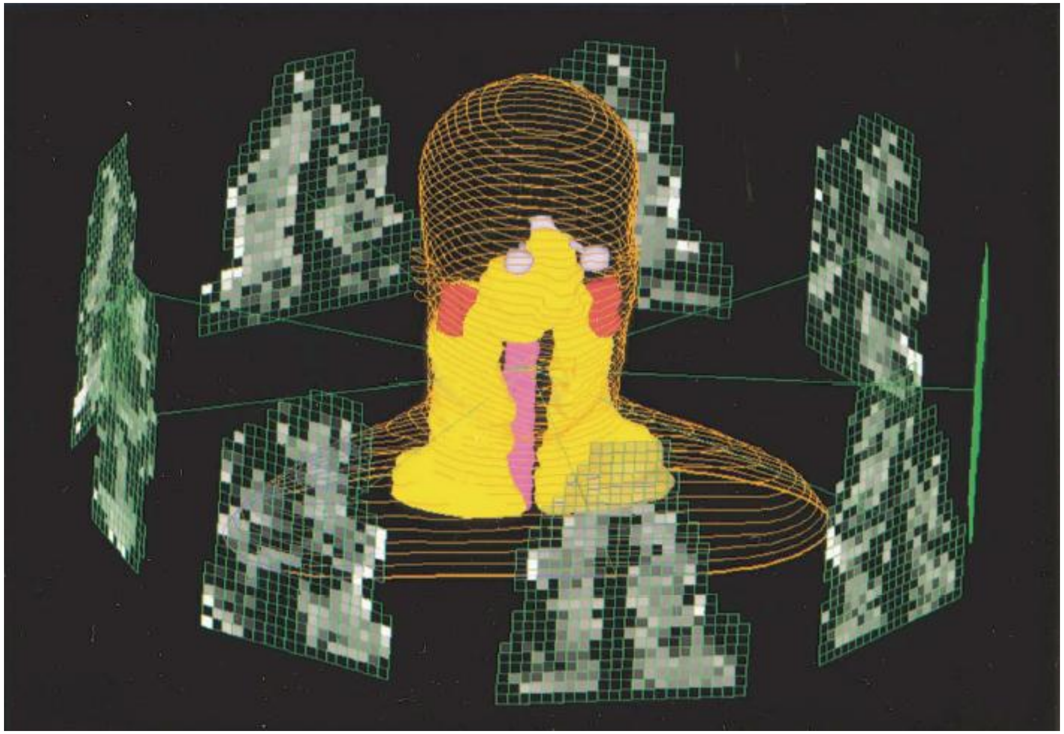
adjustment of design parameters

tunable intensity levels

cost functions define planning objectives and constraints

evaluation criteria: dosimetric quality

Large-scale optimisation problem: head & neck tumour

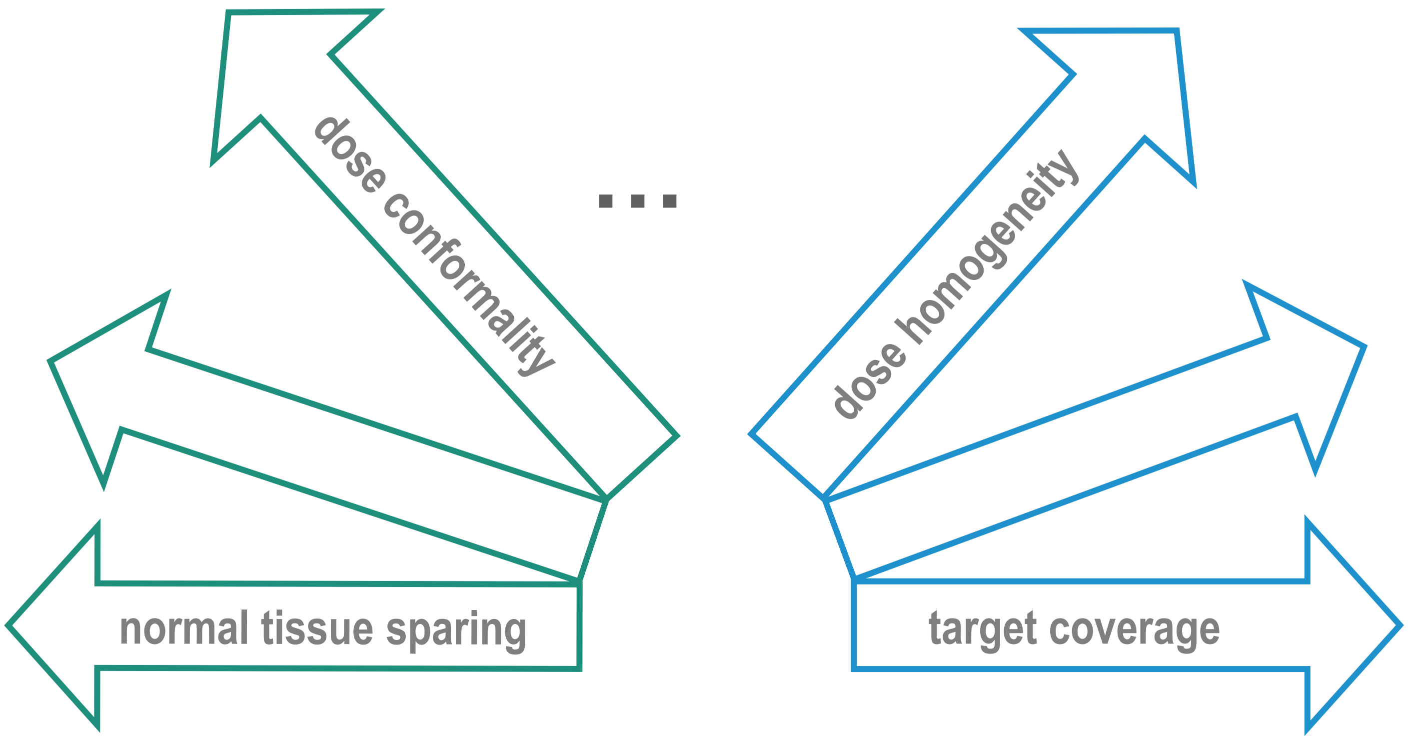


– Beam setup:
  - 9 fixed co-planar beams
  - 5000 bixels
  - 100000 voxels

– Clinical aims:
  - uniform tumour dose
  - spare salivary glands
  - spare optical system
  - spare spinal cord
  - …

Multi-criteria optimisation problem

– Define **objectives** and **constraints** to fulfill the **clinical aims**:



Cost functions

– Clinical aims require a **planning trade-off**:

- contradictory goals
- mutually dependent
- cannot be perfectly achieved
- subjective and highly case specific
- “best compromise” solution is unknown beforehand

Solving the optimisation problem

- Finding a "best compromise" solution requires:
  - decision-making strategy
  - user-algorithm interaction to guide the optimisation algorithm

- Use *a priori* information:
  - planner : preferences (*e.g.* ranking by importance)
  - algorithm : problem structure (*e.g.* convexity, curvature, …)

User-algorithm interaction

- ***A priori* preference methods:**
  - weighted-sum optimisation: weight factor tuning
  - constrained optimisation: priority level definition
    - pre-emptive goal programming
    - lexicographical ordering

- ***A posteriori* preference method:**
  - Pareto optimisation

Weighted-sum optimisation

– Should capture clinical judgement about **relative importance** of **target** (tumour) and **risk** (normal tissue) objectives

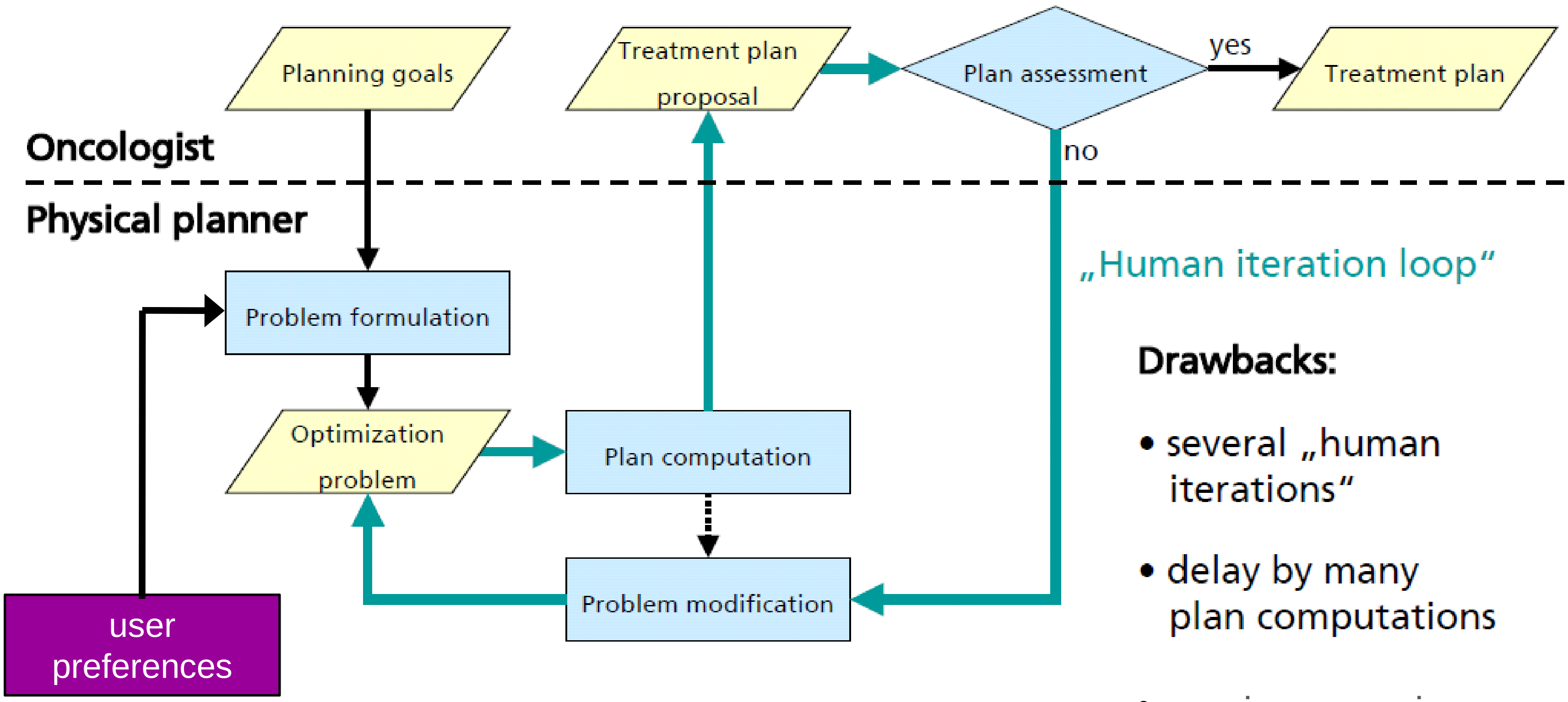
– Scalarisation approach: single-objective optimisation problem

weight factors

$$F = w_{\text{target}} \cdot F_{\text{target}} + w_{\text{risk1}} \cdot F_{\text{risk1}} + w_{\text{risk2}} \cdot F_{\text{risk2}} + \ldots$$

objective functions

Classical approach: treatment planning workflow



Drawbacks:

- several „human iterations“
- delay by many plan computations
- requires experience, expert knowledge

Weighting factors

– Disadvantages:

- require articulation of *a priori* preference information
- are often defined on arbitrary scales
- have no direct (clinical) meaning
- sensitivity of result to changes is unknown beforehand
- must be determined by **trial-and-error** process that involves multiple runs

User-algorithm interaction

- *A priori* **preference methods:**
  - weighted-sum optimisation: weight factor tuning
  - constrained optimisation: priority level definition
    - pre-emptive goal programming
    - lexicographical ordering
- *A posteriori* **preference method:**
  - Pareto optimisation

Constrained optimisation

- Objectives are handled one-by-one in a predefined order
- Solution should meet set of constraints while one objective is optimised
- Prioritised optimisation:
  - decision makers have hierarchical conception of planning goals
  - goals are addressed stepwise with highest order goals considered first
  - in subsequent steps:
    - achievements so far are turned into constraints
    - single new goal is incorporated into objective function

Constrained optimisation

- Advantages:
  - simple, straightforward
  - no tuning of weighting factors

- Disadvantages:
  - only one solution is generated
  - no trade-off information
  - no option to trade-off “small losses” for “large gains”

Limitations of *a priori* preference methods

- So far: *a priori* articulation of preference information required
  - weighting factors
  - priority levels
- Unclear in advance how (inter)dependent the objectives are
- User does not know whether optimal operating point is reached
  - "*what gain could be obtained if I was willing to accept a small loss?*"
- No trade-off information available

Let's try *a posteriori* preference methods

- Clinicians and treatment planners:
  - … have difficulty in defining complete representation of optimisation problem
  - … typically differ in how they define the problem
  - … are perfectly capable of ranking individual solutions (“IKIWISI approach”)

- Idea: decouple **optimisation** and **decision-making** process

- Provide framework for (interactive) *a posteriori* risk/benefit balancing

User-algorithm interaction

- *A priori* **preference methods:**
  - weighted-sum optimisation: weight factor tuning
  - constrained optimisation: priority level definition
    - pre-emptive goal programming
    - lexicographical ordering

- ***A posteriori*** **preference method:**
  - Pareto optimisation

Pareto optimisation

- All objective functions are considered **simultaneously**:

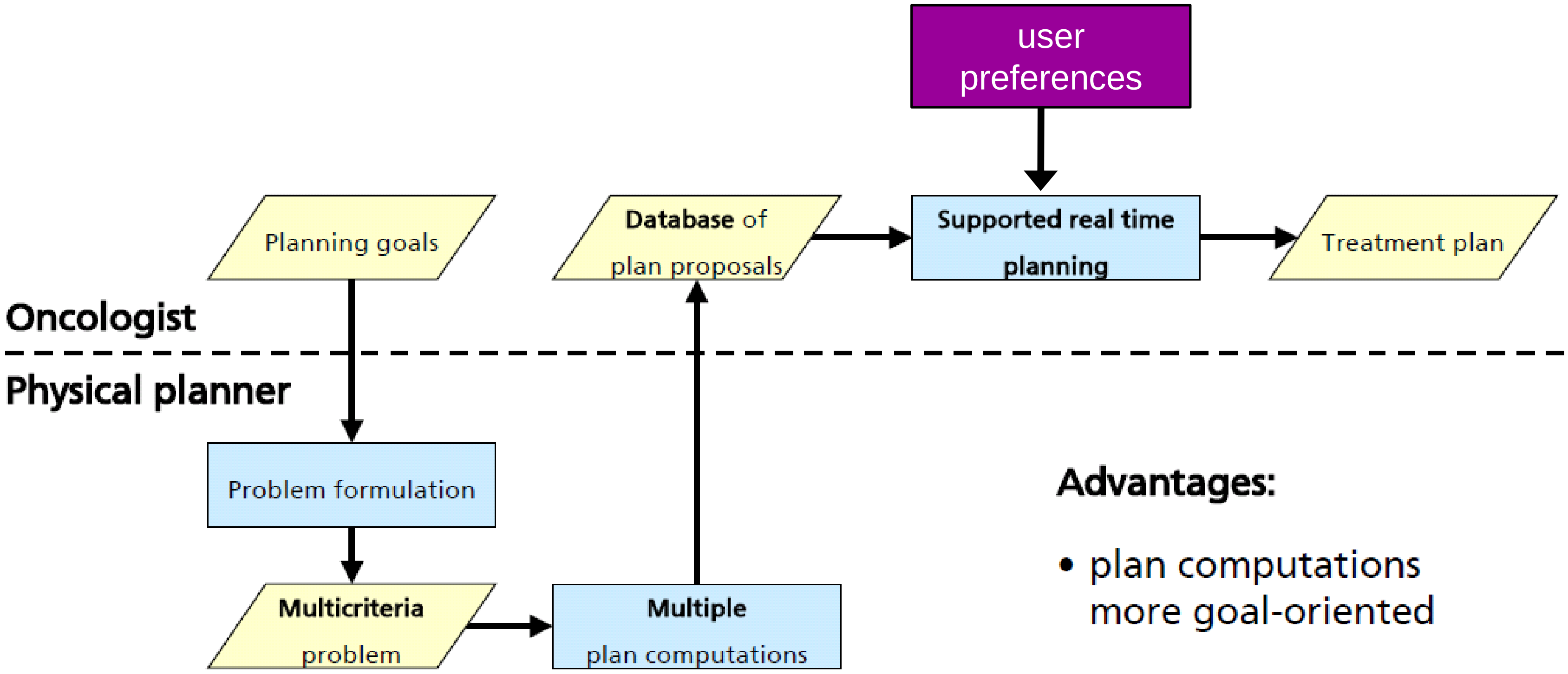
$$\min_{\mathbf{x}} \; \mathbf{F}(\mathbf{x}) = \left(F_1(\mathbf{x}), F_2(\mathbf{x}), \ldots, F_k(\mathbf{x}) \right)^{\mathrm{T}}$$

- No single best solution exists

- A set of "**best compromise**" solutions exists
  - no objective can be further improved without deteriorating at least one other

- In objective space: **Pareto efficient frontier**

Pareto approach



Advantages:

- plan computations more goal-oriented
- no delay in oncologist's (and planner's) workflow

Mathematical aspects

- How to generate a set of Pareto optimal treatment plans efficiently?
- Do different objective functions yield different Pareto efficient frontiers?
- How to navigate through Pareto optimal solutions?

Generation of Pareto efficient frontier

– Brute force strategy: generate-and-test method

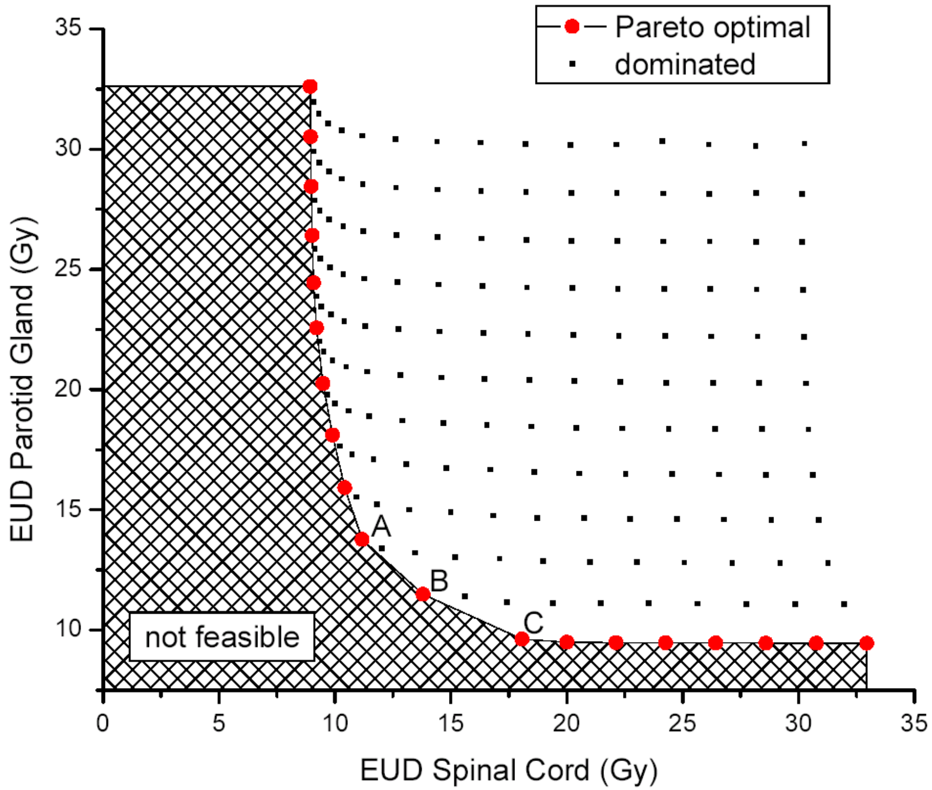
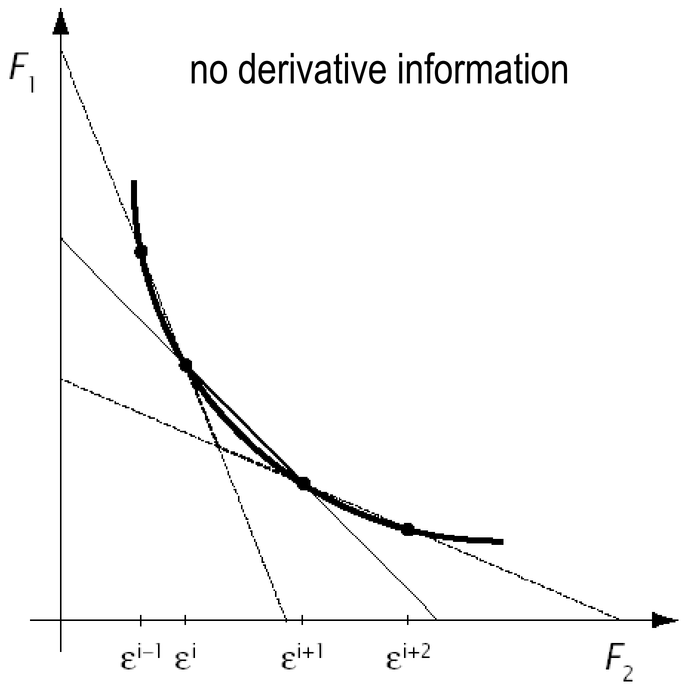
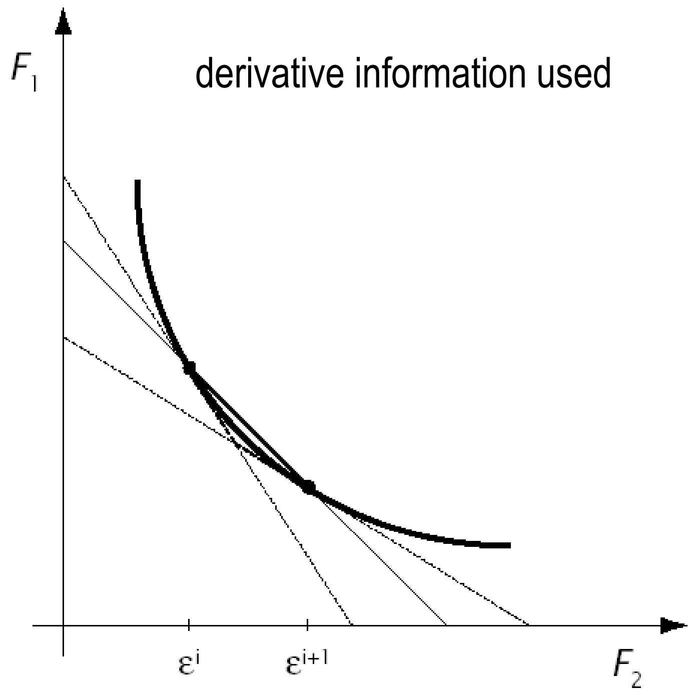


image courtesy: C. Thieke (2004)

Generation of Pareto efficient frontier

– Discrete approximation: use **sandwich algorithm** for convex problems



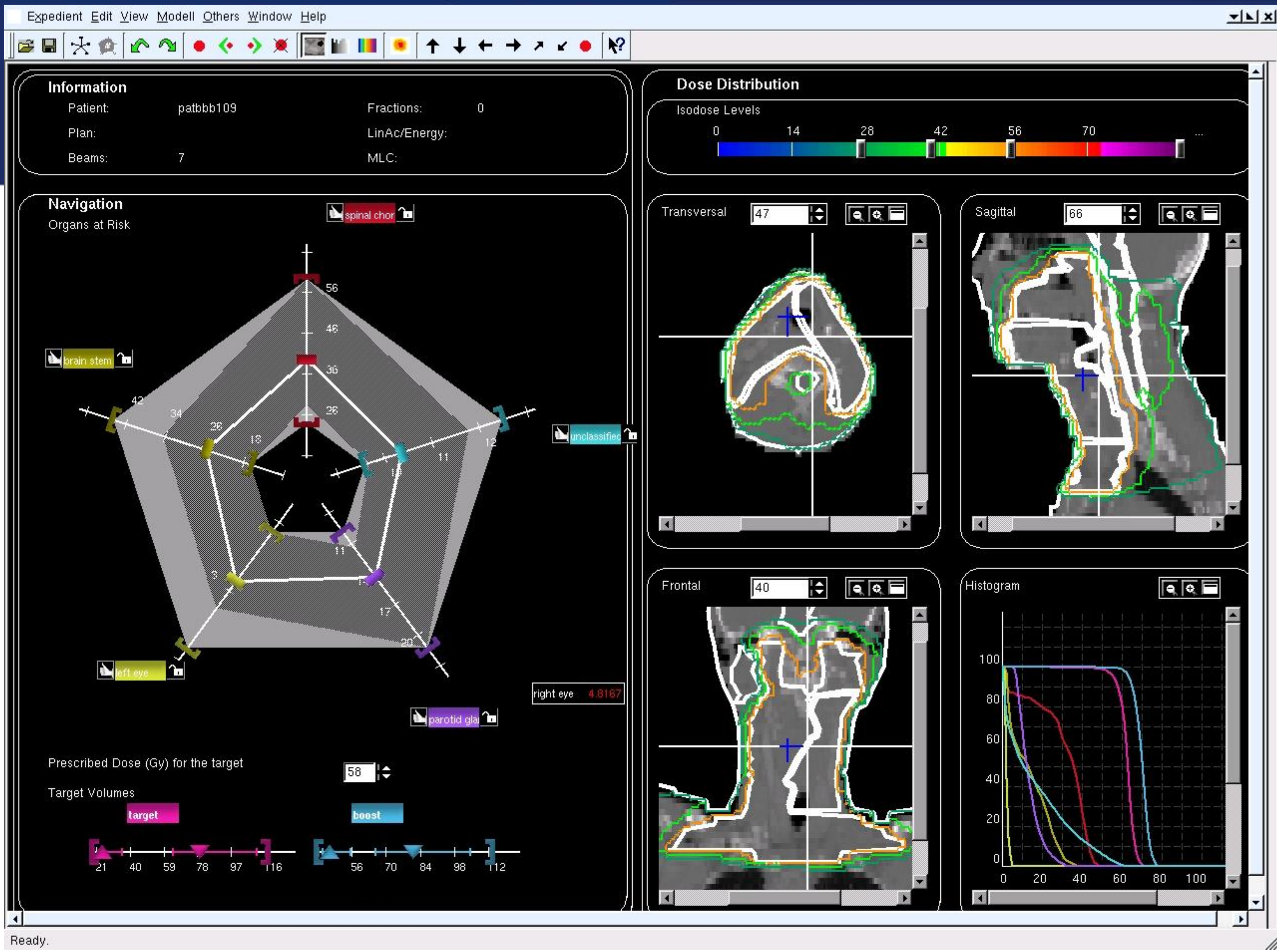


Hoffmann *et al*. Phys Med Biol (2006); Siem *et al*. INFORMS J Comput (2011)

Convexity analysis

- Sandwich algorithms rely on convex objective functions
- Convexity analysis conducted for different type of objective functions
- Results:
  - most functions are already convex
  - can be transformed into convex functions under Pareto invariance by applying strictly increasing transformations
  - transformation of different quality exist; some are ‘less convex’ than others
  - Pareto solutions can be approximated more efficiently by using transformations

Hoffmann *et al*. Phys Med Biol (2008); Siem *et al*. EJOR (2008)



Monz *et al.*, Phys Med Biol (2008)

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