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Multi-objective fluence map optimisation for intensity-modulated radiotherapy

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Outline

- **Introduction to radiation therapy**
  - External radiation therapy with photon beams
  - Treatment planning optimisation problems
  - Fluence map optimisation for IMRT
- **Mathematical aspects of fluence map optimisation**
  - Definitions and terminology
  - Single *versus* multi-objective optimisation
  - Finding Pareto solutions → Pareto efficient frontier (PEF)
  - Sandwich algorithm to approximate a convex PEF

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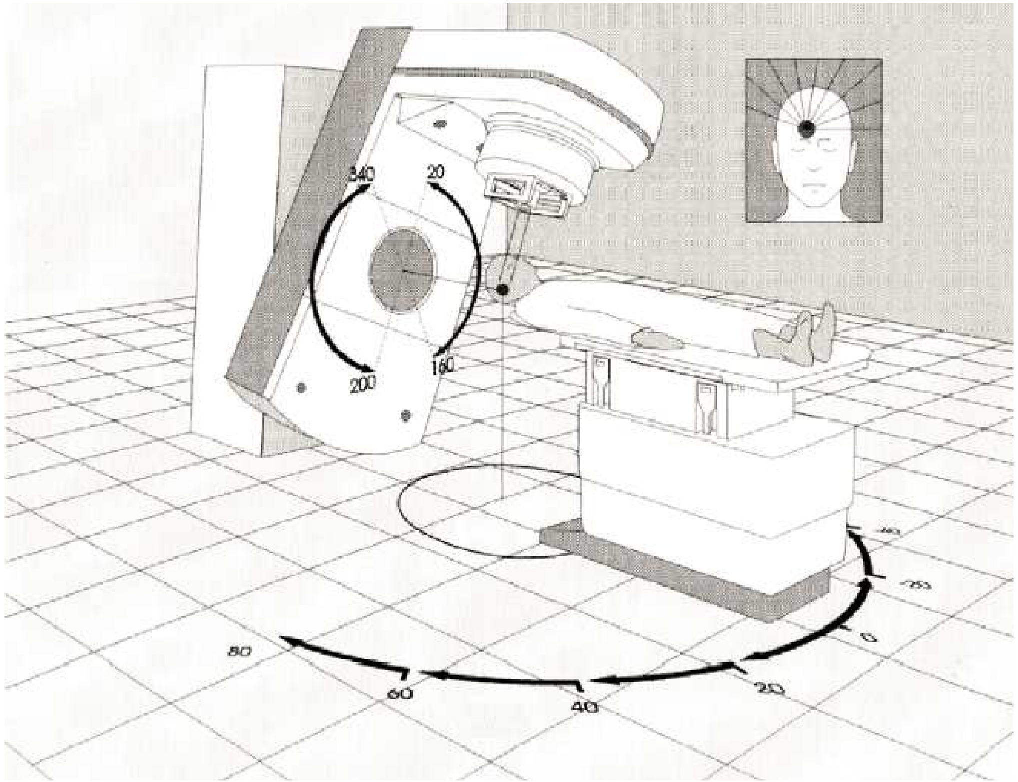
Radiation Therapy

- **Aim**
  - Eradicate all clonogenic tumour cells without damaging healthy normal tissues
- **Method**
  - Use ionising radiation to break DNA structures
- **Two types**
  - Brachytherapy : internal radioactive source irradiation
  - Teletherapy : external beam irradiation

External beam irradiation

- **Linear accelerator**
  - Photons
  - Electrons

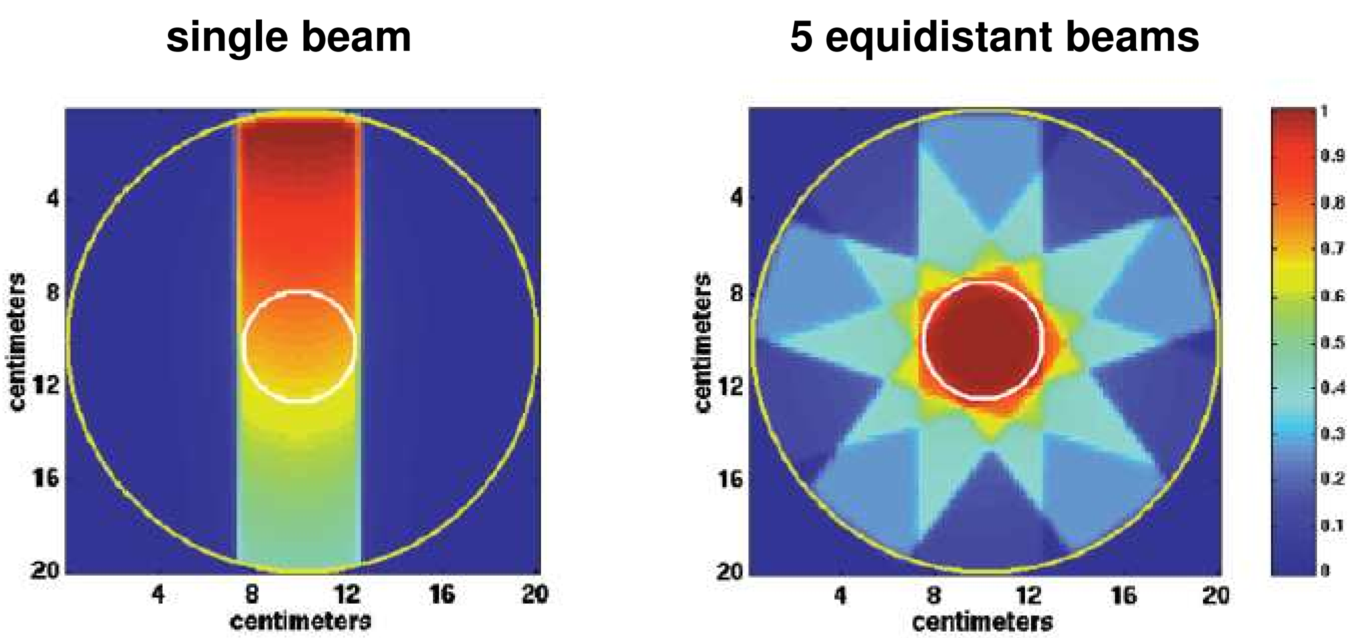


- **Degrees of freedom**
  - Gantry angle
  - Couch angle
  - Beam modality
  - Beam intensity
  - …

Treatment planning problem

- **Medical and biological parameters (*radiation oncologist*)**
  - Curative/palliative tumour dose
  - Tolerance dose for normal tissues
  - Fractionation scheme
- **Physics parameters (*clinical physicist*)**
  - Radiation geometry: beams numbers and angles
  - Beam shapes and intensity profiles

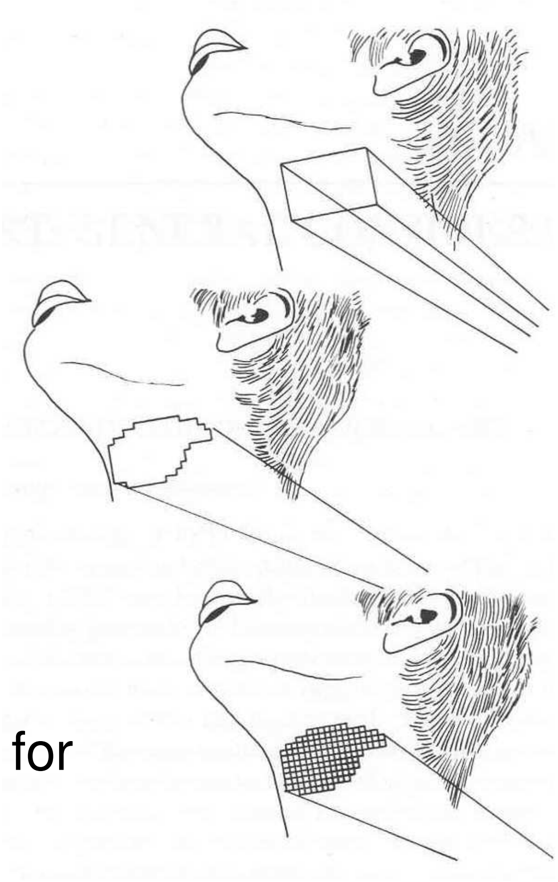
Beam numbers and angles



“Cross-firing beams” is basic principle to add up dose in tumour and keep dose in healthy tissue low

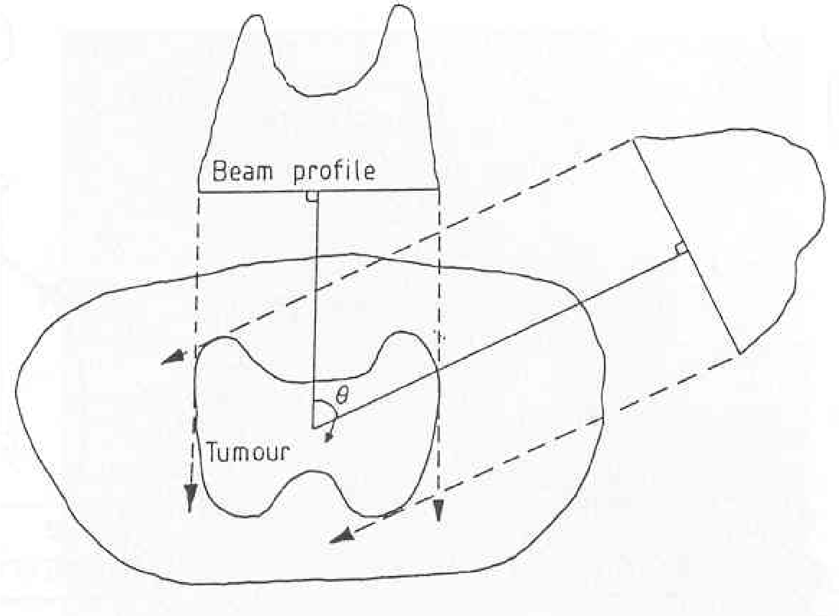
Beam shapes and intensity profiles

- Conventional RT
  - rectangular beam shape
  - uniform intensity distribution
- 3D-Conformation RT (3D-CRT)
  - MLC: irregular beam shape
  - uniform intensity distribution
- **Intensity-modulated RT (IMRT)**
  - non-uniform intensity distribution for tumour dose escalation and improved healthy tissue sparing



IMRT principle

- Intensity modulation of beam profiles
- Conformation of high-dose region to concave tumour anatomy



Optimisation problems in radiotherapy

- **Beam number problem:** How many beams should be used?
- **Beam direction problem:** What are optimal incidence angles?
- **Beam intensity problem:** How to find optimal beam profiles?
- **Beam aperture problem:** How to set MLC apertures?
- **Fractionation problem:** How to adapt to treatment response?

Optimisation problems in radiotherapy

- **Beam number problem:** How many beams should be used?
- **Beam direction problem:** What are optimal incidence angles?
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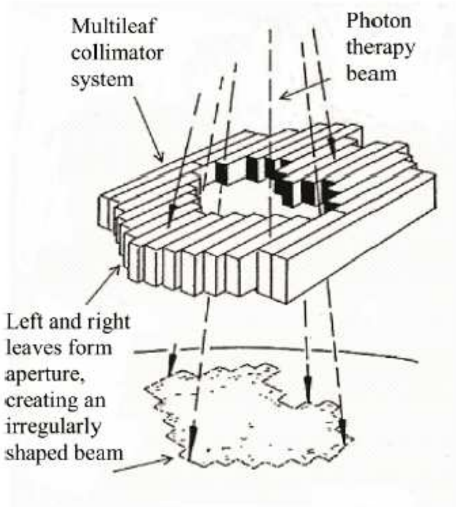
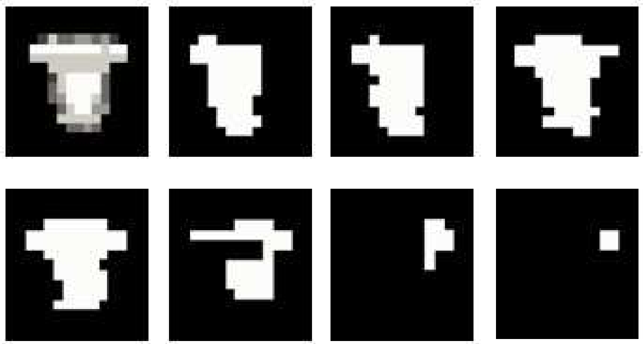
Beam shapes and intensity profiles

- **Beam shaping**
  - Multi leaf collimator (MLC) with tungsten leafs



- **Beam intensity modulation**
  - "Step-and-shoot" delivery
  - Fluence map



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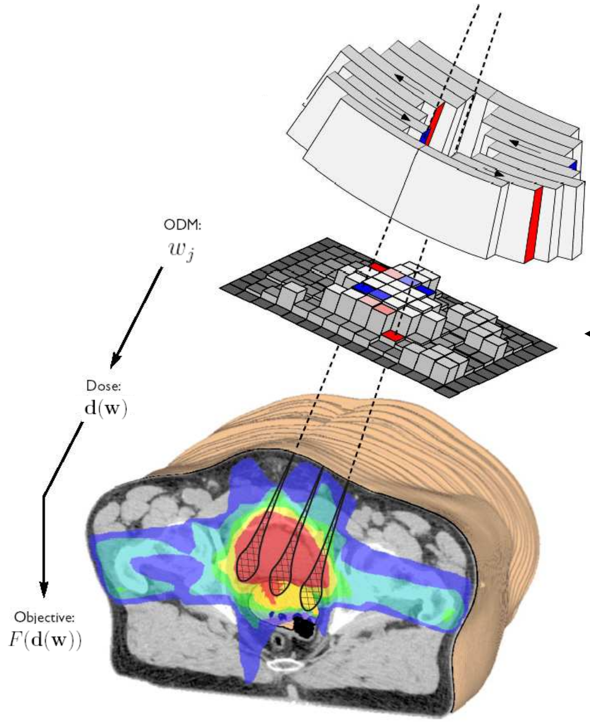
The "Fluence Map Optimisation" problem

- **Definitions and terminology**
  - pencil beams, bixel weights (w_j), dose distribution (d_i)



Fluence map

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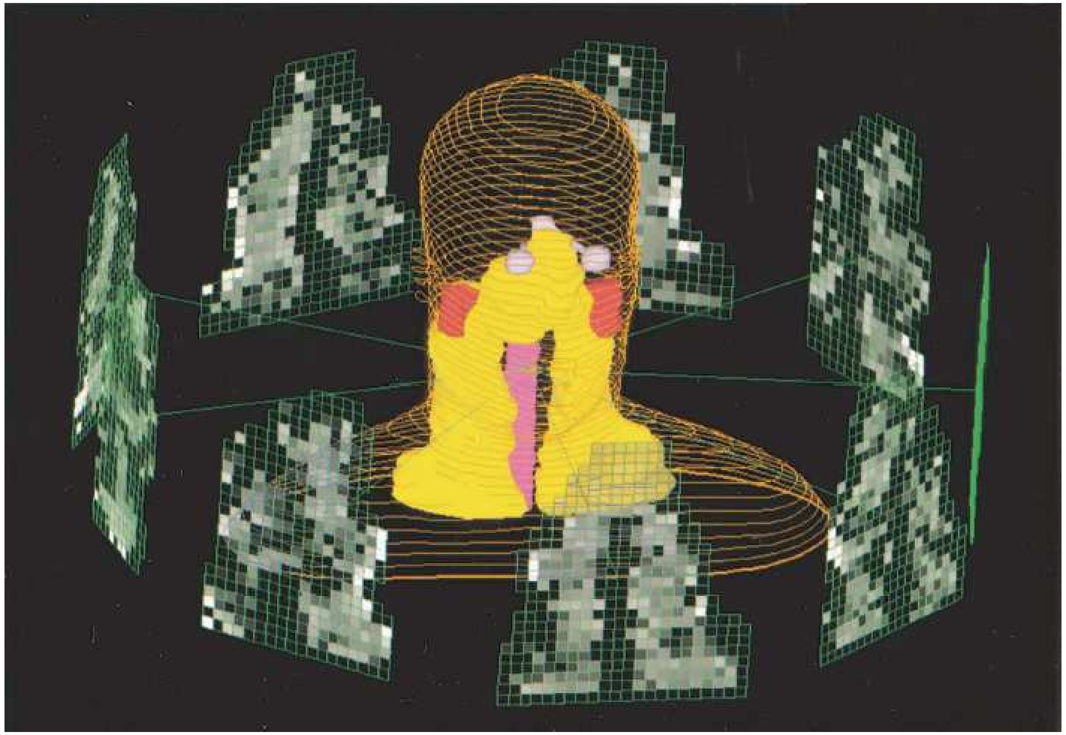
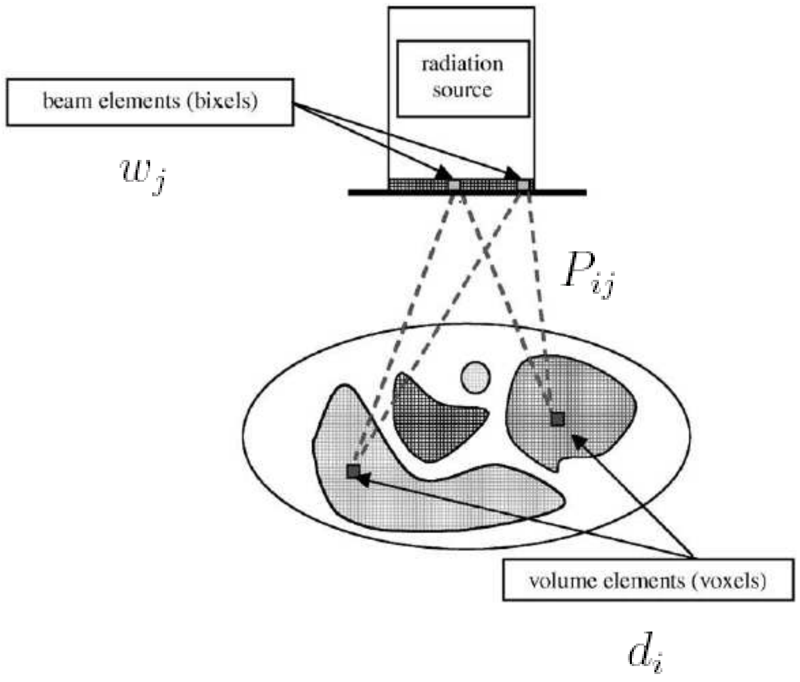
Clinical example: large-scale optimisation problem



- Head & neck tumour:
  - minimum tumour dose
  - uniform tumour dose
  - spare salivary glands
  - spare spinal cord
  - spare eye lenses
- 9 fixed coplanar beams
  - ~5000 bixel weights
- ~40000 dose voxels

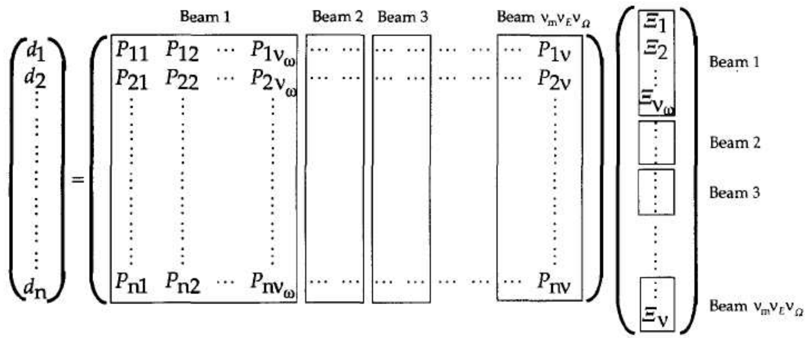
Mathematics of fluence map optimisation

- **Definitions and terminology**
  - pencil beam matrix / "influence matrix" (**P**)



$$d_i(\mathbf{w}) = \sum_{j=1}^{n} P_{ij} w_j$$

$$\mathbf{d}(\mathbf{w}) = \mathbf{P}\mathbf{w}$$



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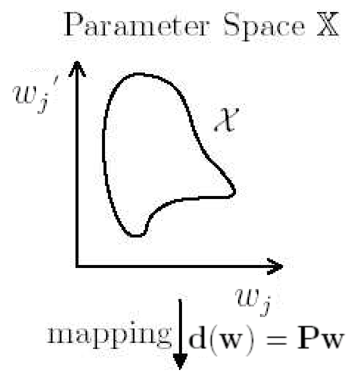
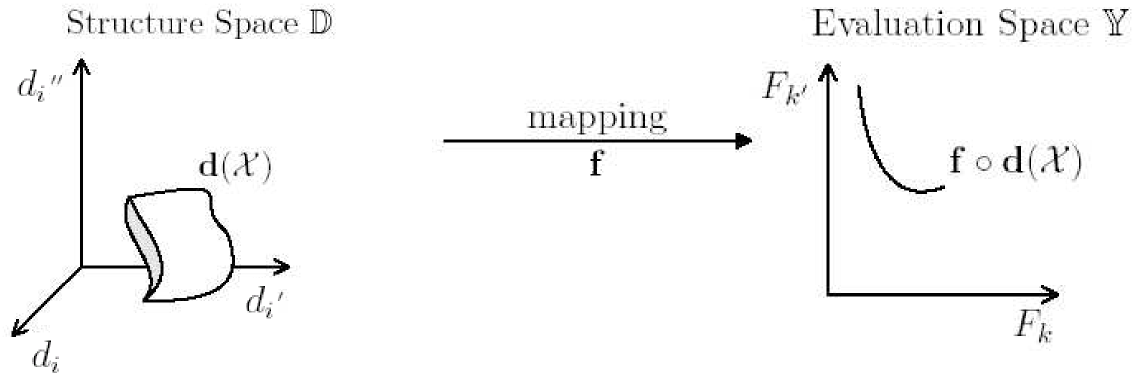
Mathematics of fluence map optimisation

- **Optimisation as *engineering design proces***



- **Design parameters: bixel weights**

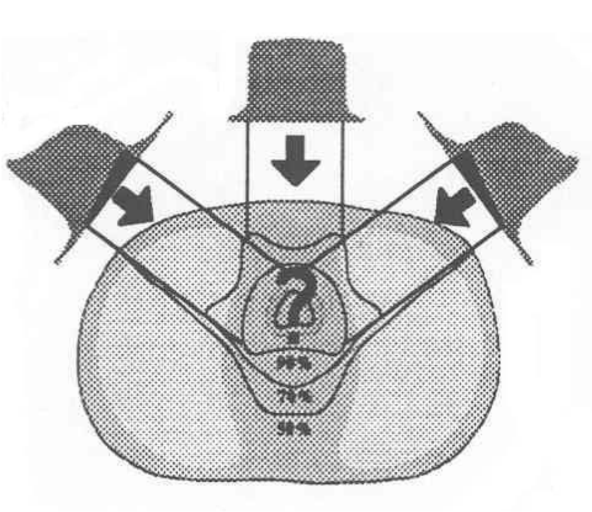
  constraints $\longrightarrow$ *feasible design space* $\mathcal{X}$



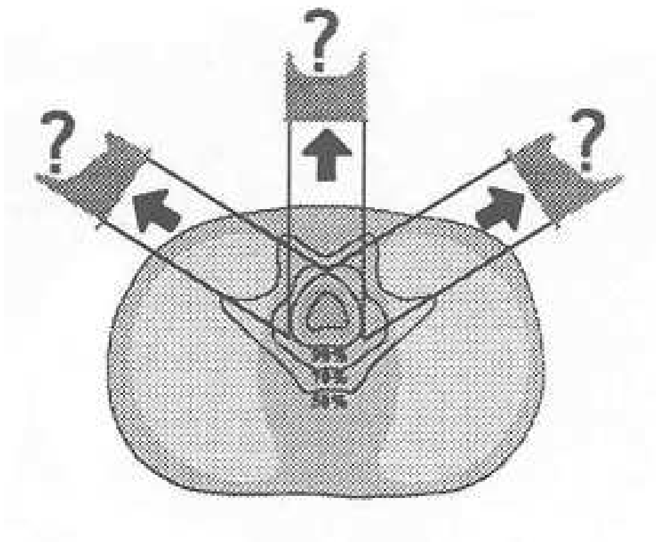
- **structure: dose distribution**
- **evaluation: cost functions**

Mathematics of fluence map optimisation

- **Cost functions**
  - <u>*forward*</u> *planning*: **evaluation** of resulting treatment plan
  - <u>*inverse*</u> *planning*: **steer mechanism** for optimisation



forward planning



inverse planning

Mathematics of fluence map optimisation

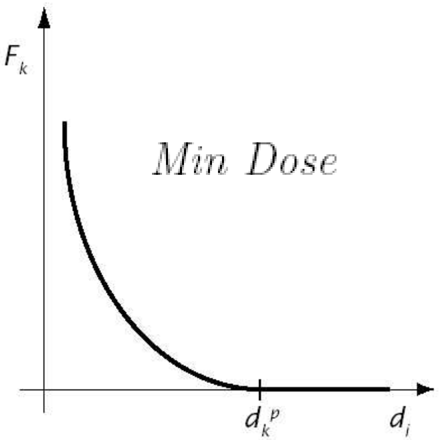
- **Objective functions:**
  - ***MinDose (MaxDose):*** ROI should receive at least (at most) a certain prescribed dose level
  - ***MinDVH (MaxDVH):*** certain <u>fraction</u> of ROI should receive at least (at most) a certain prescribed dose level
  - ***UniformDose:*** ROI should receive a dose as close as possible to a certain prescribed dose level

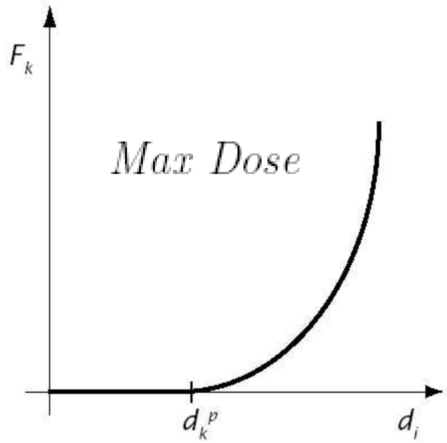
- **Constraint functions:**
  - Same as above
  - ***MaxUniformity:*** dose variation in ROI should be less than a prescribed percentage

Mathematics of fluence map optimisation

- **Least square based penalty functions**
  - *Min(Max) Dose:* $$F_k^r(\mathbf{d}) := \sum_{i \in V_j} \mu(d_i, d_k^p) \left(\frac{d_i - d_k^p}{d_k^p} \right)^2 \Delta v_i^j,$$

$$\mu(d_i, d_k^p) := \begin{cases} H(d_k^p - d_i) & : \ \textit{Min Dose} \text{ function} \\ H(d_i - d_k^p) & : \ \textit{Max Dose} \text{ function} \end{cases}$$





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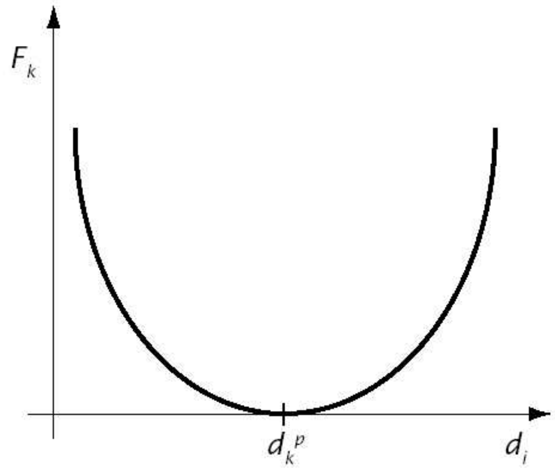
Mathematics of fluence map optimisation

- **Least square based penalty functions**

  - *Uniform Dose:* $$F_k^r(\mathrm{d}) := \sum_{i \in V_j} \mu(d_i, d_k^p) \left(\frac{d_i - d_k^p}{d_k^p} \right)^2 \Delta v_i^j,$$

$$\mu(d_i, d_k^p) = 1.$$



Single-objective optimisation model

- **Problem definition**

$$\begin{array}{ll} \min\limits_{\mathbf{w}} & F(\mathbf{d}(\mathbf{w})) \\ \text{s.t.} & \mathbf{w} \in [0,1]^n. \end{array}$$

- Weighting method: $$F(\mathbf{d}(\mathbf{w})) := \sum_{k=1}^{l} \lambda_k F_k(\mathbf{d}(\mathbf{w})).$$ $$\lambda_k \geq 0$$

$$F(\mathbf{d}(\mathbf{w})) = \lambda_1 F_1(\mathbf{d}(\mathbf{w})) + \lambda_2 F_2(\mathbf{d}(\mathbf{w})) + \ldots + \lambda_l F_l(\mathbf{d}(\mathbf{w}))$$

- Weighting factors express relative importance of conflicting objectives

Single-objective optimisation model

- **Weighting factors**
  - … have no direct clinical meaning
  - … must be determined empirically by a *trial-and-error* proces
  - … define an *a priori* choice for the trade-off between conflicting objectives

CollabORation: UvT and UMCN

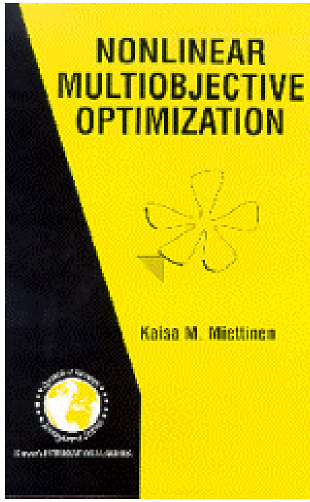
- **Interactive decision-support for treatment planning**
  - Handling of multiple objectives without artificial weighting factors
  - Sensitivity analysis of changes to objective functions
  - Develop tools for *a posteriori* decision-making

Multi-objective optimisation model

Problem definition

$$\min_{\mathbf{w}} \quad \mathbf{F}(\mathbf{d}(\mathbf{w})) = \begin{pmatrix} F_1(\mathbf{d}(\mathbf{w})) \\ F_2(\mathbf{d}(\mathbf{w})) \\ \vdots \\ F_l(\mathbf{d}(\mathbf{w})) \end{pmatrix}$$

$$\text{s.t.} \quad \mathbf{w} \in [0,1]^n.$$



- Pareto optimality:

Definition 2.1. An optimization (variable) vector $\mathbf{x}^* \in \mathcal{X}$ (in our case, $\mathbf{x}^* = \mathbf{d}(\mathbf{w}^*)$) is *Pareto optimal* (PO) for problem (5) if there does not exist another optimization vector $\mathbf{x} \in \mathcal{X}$ such that $F_i(\mathbf{x}) \le F_i(\mathbf{x}^*)$ for all $i = 1, \ldots, l$, and $F_j(\mathbf{x}) < F_j(\mathbf{x}^*)$ for at least one index j.

Multi-objective optimisation model

§ Pareto optimisation

- Set of all solutions for which no objective can be improved without deteriorating at least one of the other objectives

- There exists no single best solution, but instead there is a set of **best compromises**

- This set is called the "**Pareto efficient frontier**" **(PEF)**

Multi-objective optimisation model

§ **How to generate Pareto efficient solutions?**

§ Weighted Sum method:

$$\begin{aligned} \min_{\mathbf{x}} \quad & \sum_{k=1}^{l} \lambda_k F_k(\mathbf{x}) \\ \text{s.t.} \quad & \mathbf{x} \in \mathcal{X}. \end{aligned}$$

§ ε-constraint method:

$$\begin{aligned} \min_{\mathbf{x}} \quad & F_k(\mathbf{x}) \\ \text{s.t.} \quad & F_j(\mathbf{x}) \leq \varepsilon_j \qquad \text{for all } j = 1, \ldots, l, \quad j \neq l, \\ & \mathbf{x} \in \mathcal{X}, \end{aligned}$$

Generation of Pareto efficient frontier

- **Pros & Cons**

  - **Weighted Sum (WS) method:**

    + simple and computational efficient
    + does not change the constraint set of the problem
    – *a priori* unclear how to choose the weights
    – provides unique solution for convex problems only

  - **ε-constraint (EC) methode:**

    + *a priori* determine where to generate new Pareto point
    + gives unique solution for non-convex problems
    – changes the constraint set of the problem
    – slower than WS method

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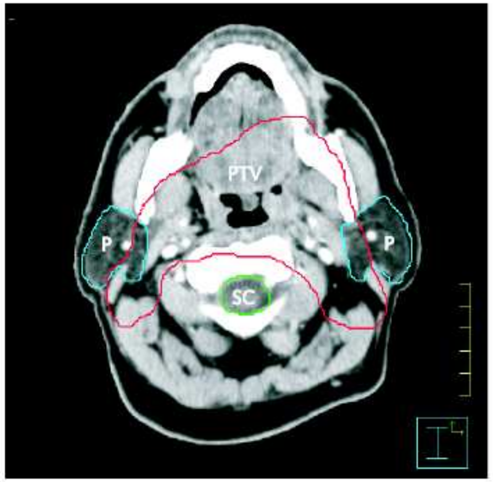
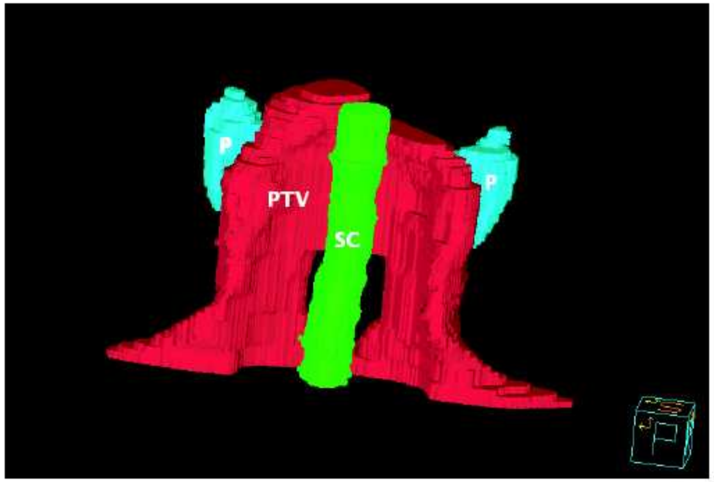
Generation of Pareto efficient frontier

§ **Clinical example**

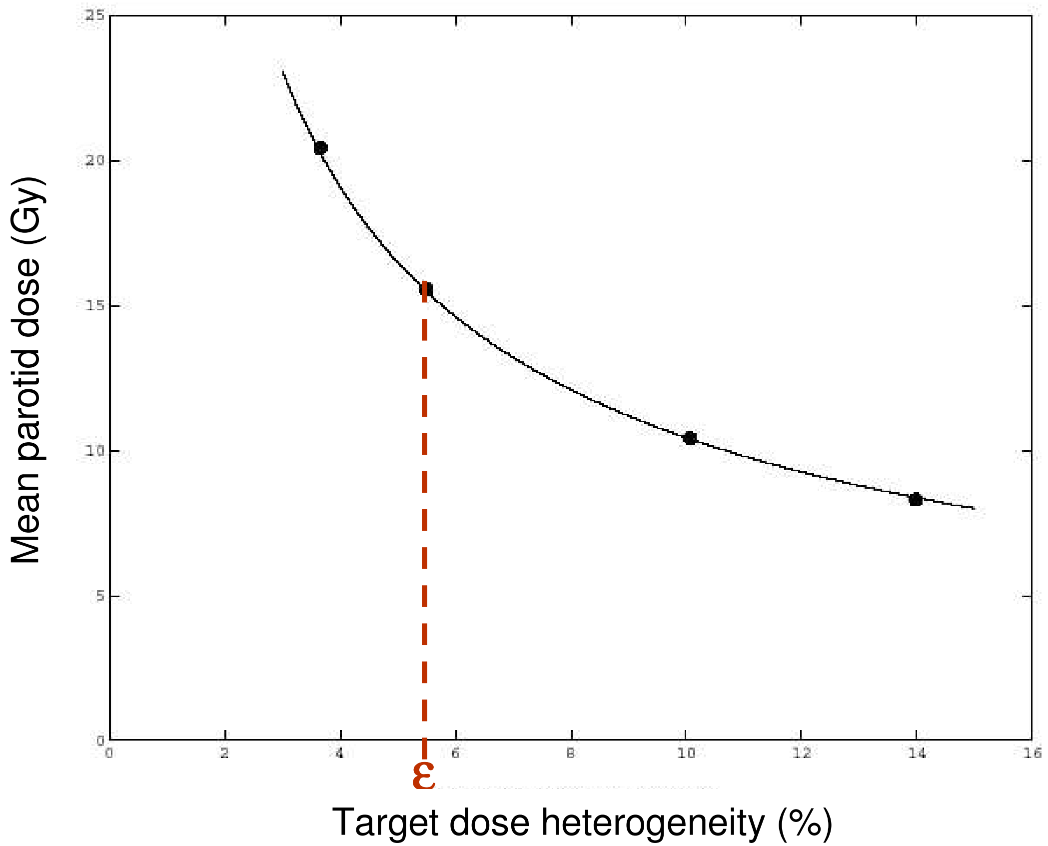




§ Aim: Quantify the trade-off between *target dose heterogeneity* (TDH) and *mean parotid dose* (MPD) for a fixed *mean target dose* (46 Gy)

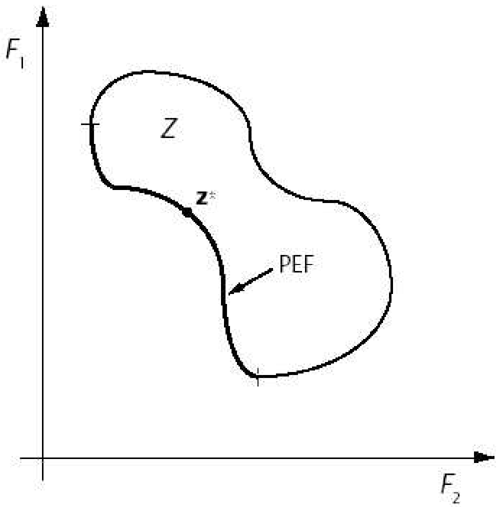
Generation of Pareto efficient frontier

- **Result for ε-constraint method**

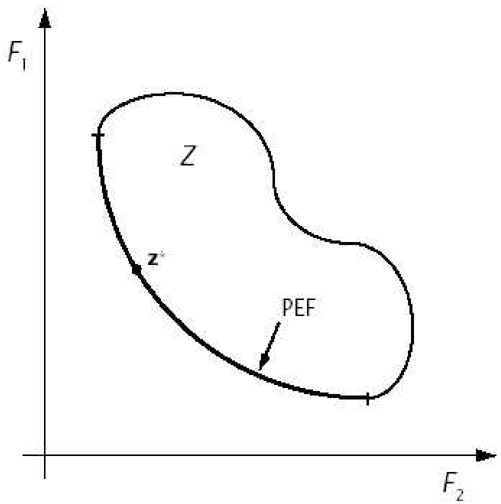


Generation of Pareto efficient frontier

- **Pareto Efficient Frontier (PEF)**
  - … is convex for a **convex optimisation problem**



non-convex PEF



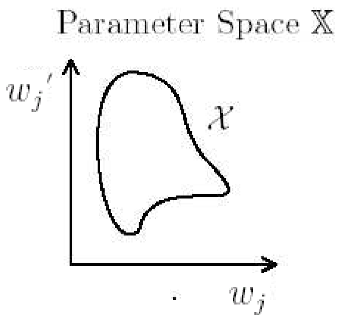
convex PEF

Generation of Pareto efficient frontier

§ **Convex optimisation problem:**

1. Feasible design space $\mathcal{X}$ is convex

   $\mathbf{w} \in [0,1]^n$ is *n*-dim hypercube



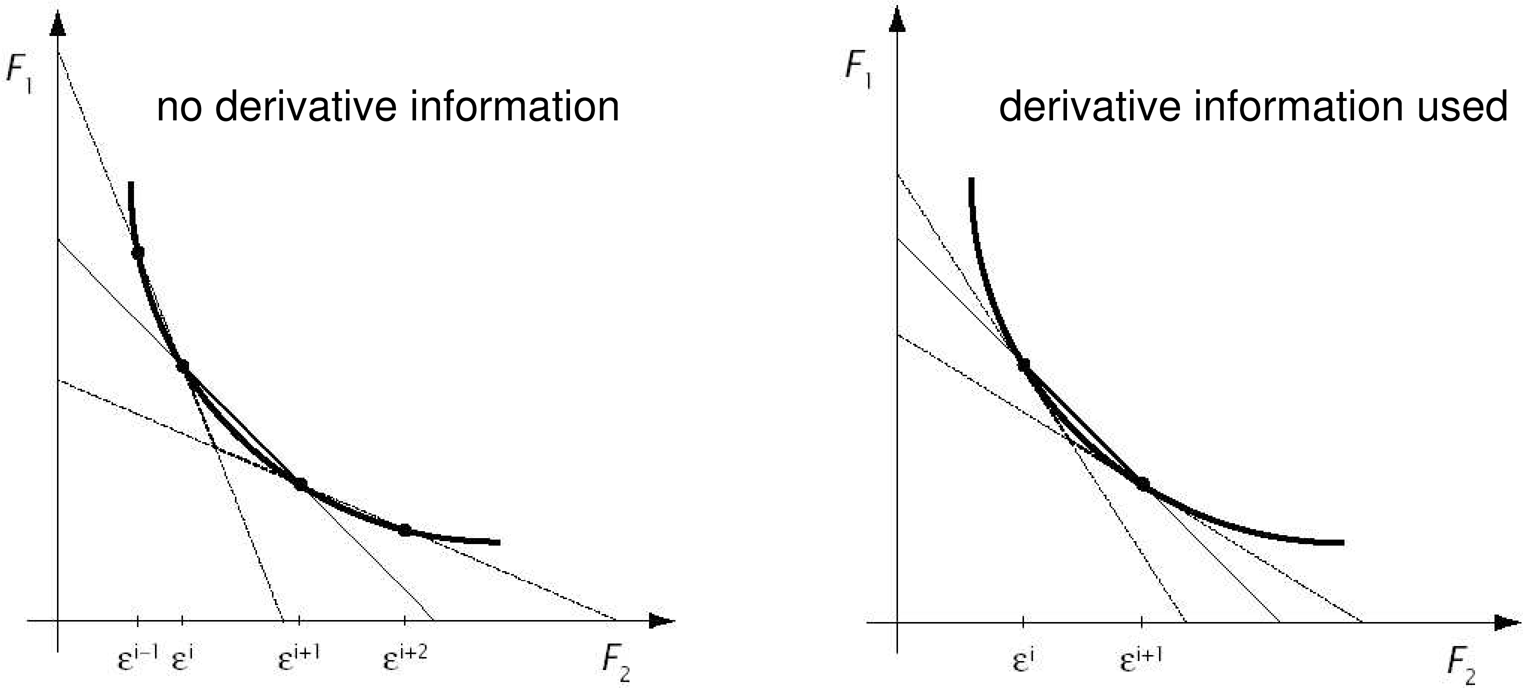
2. Objective functions are convex

Lemma 1. *A real-valued function f is convex (concave) if and only if its Hessian is positive (negative) semidefinite. It is strictly convex (concave) if and only if its Hessian is positive (negative) definite.*

Definition. *An $n \times n$ matrix P is called positive (negative) semidefinite if $x^T P x \geqslant (\leqslant)\, 0$ for all real vectors denoted by x, and positive (negative) definite if $x^T P x > (<)\, 0$ for $x \neq 0$.*

Generation of Pareto efficient frontier

- **Sandwich algorithm for convex objective functions**



Generation of Pareto efficient frontier

- **Iterative strategies to generate a new Pareto solution**

- Generate new solution where:

    - … difference between upper and lower bound is maximal (*MaxError*)

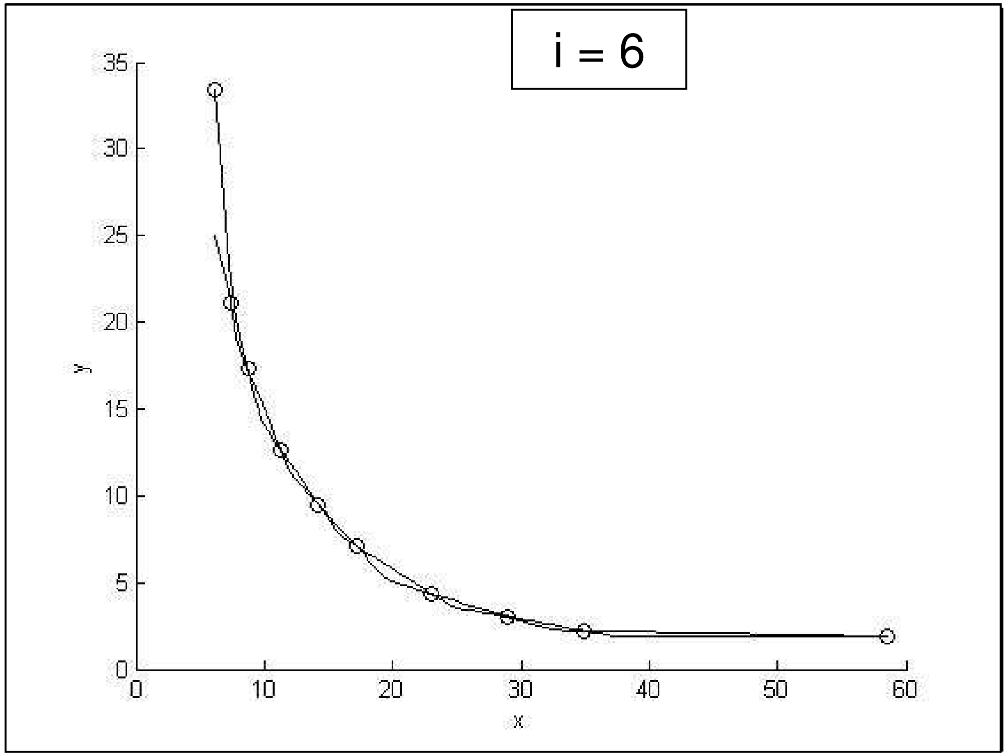
    - … area of uncertainty triangle is maximal (*MaxArea*)

    - … Hausdorff distance is maximal (*MaxHaus*)

      = maximum distance between shortest distances between upper and lower bounds

Generation of Pareto efficient frontier

§ **Iterative algorithm using the *MaxHaus* criterion**

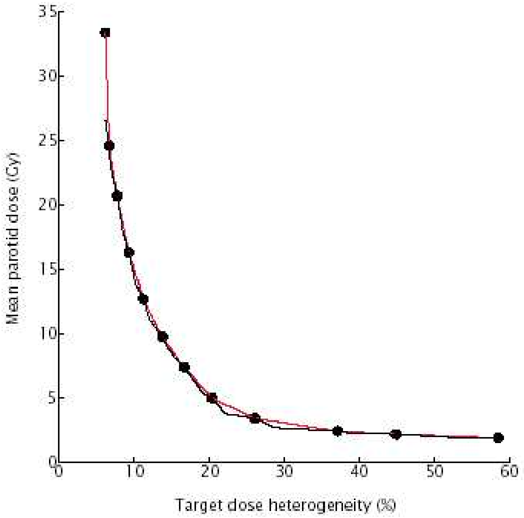


Generation of Pareto efficient frontier

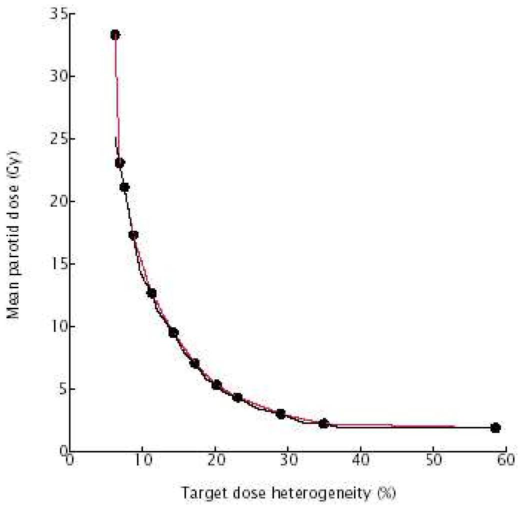
§ Comparison of iterative strategies

i = 6

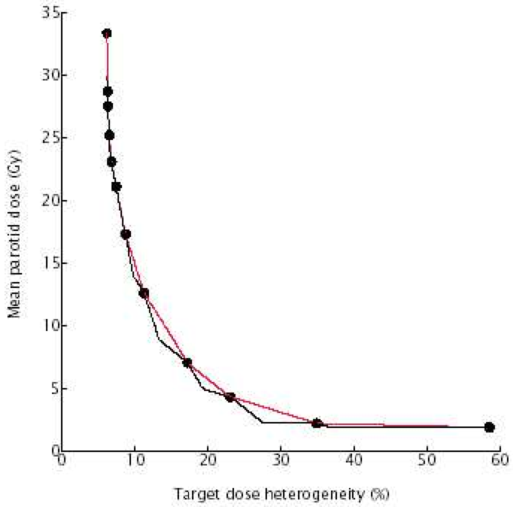
MaxHaus



MaxArea

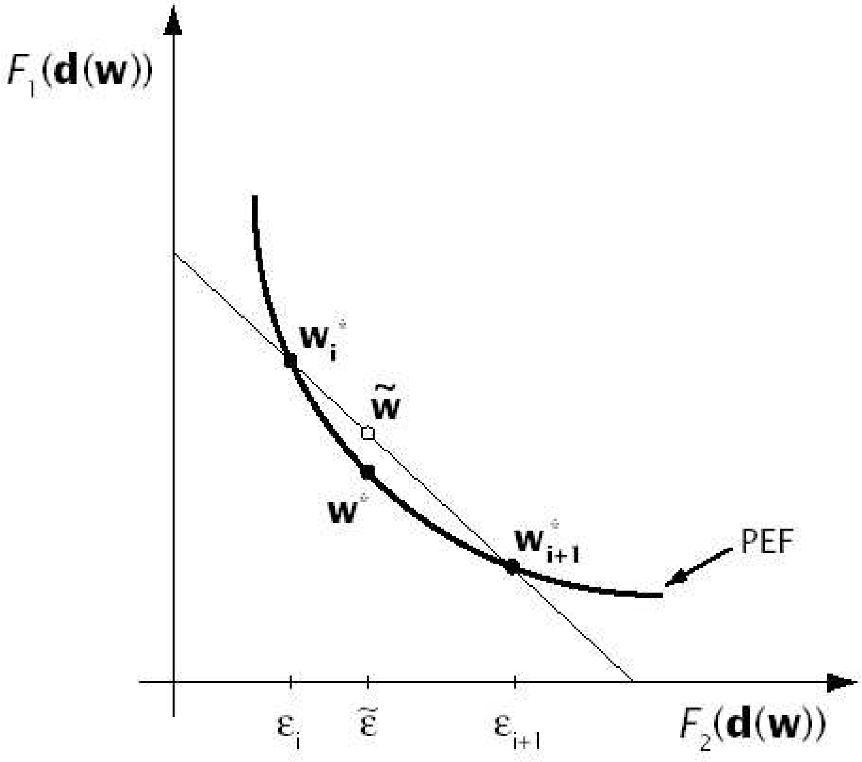


MaxError



Generation of Pareto efficient frontier

§ **Fluence Map Interpolation**



$$\tilde{\varepsilon} = \lambda\varepsilon_i + (1-\lambda)\varepsilon_{i+1}$$

$$\tilde{\mathbf{w}} := \lambda\mathbf{w}_\mathbf{i}^* + (1-\lambda)\mathbf{w}_\mathbf{i+1}^*$$

Conclusions

§ Radiotherapy & Operations Research

- Various optimisation problems occur in RT
- RT can benefit from OR optimisation techniques
- Other RT optimisation problems to be solved …
- OR meets RT: *2 RT OR ¬(2 RT)* ?

Acknowledgement

- Henk Huizenga
- Hans Kaanders

- Dick den Hertog
- Alex Siem
- Marianne van Lent