Erasmus MC
University Medical Center Rotterdam

3TU.AMI
MATHEMATICS FOR INNOVATION

Daniel den Hoed
Cancer Center

Optimization in cancer treatment: indefinitely a problem?

--- an application ---

Sebastiaan Breedveld

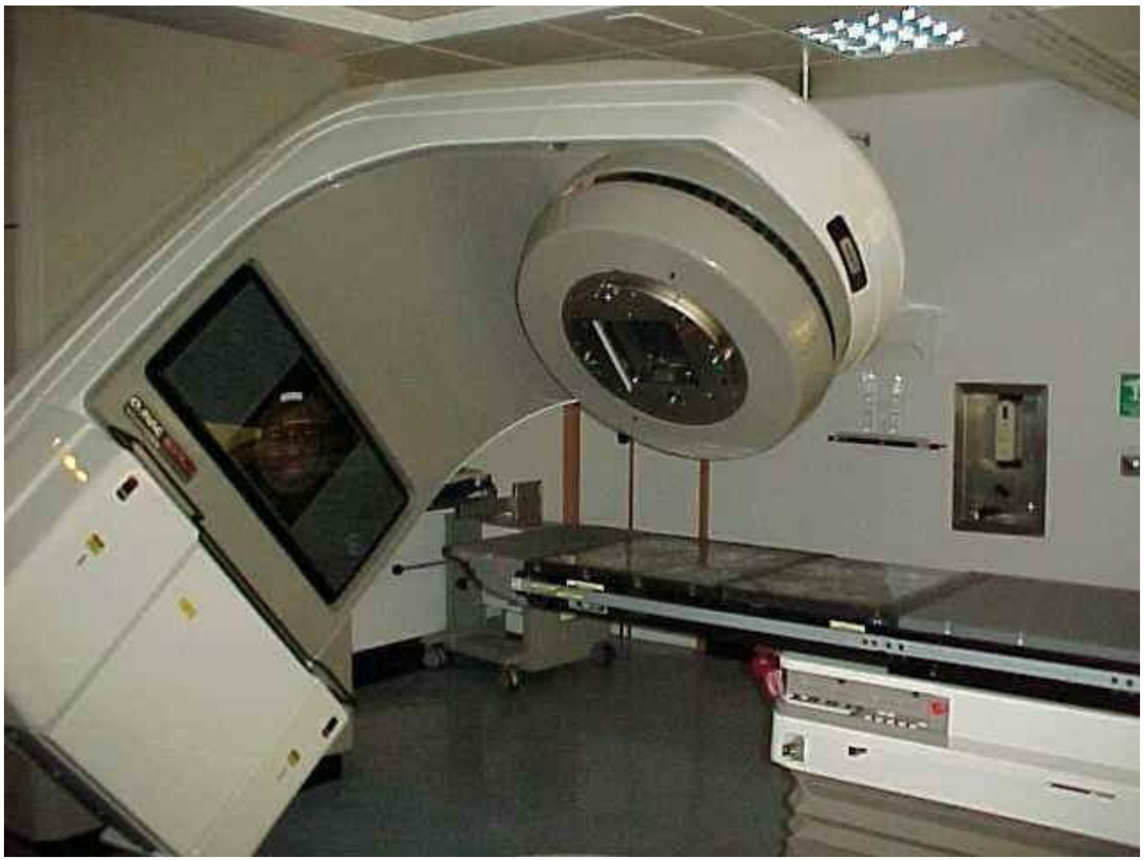
Indefinite Systems Workshop

TU Eindhoven, April 17th 2012

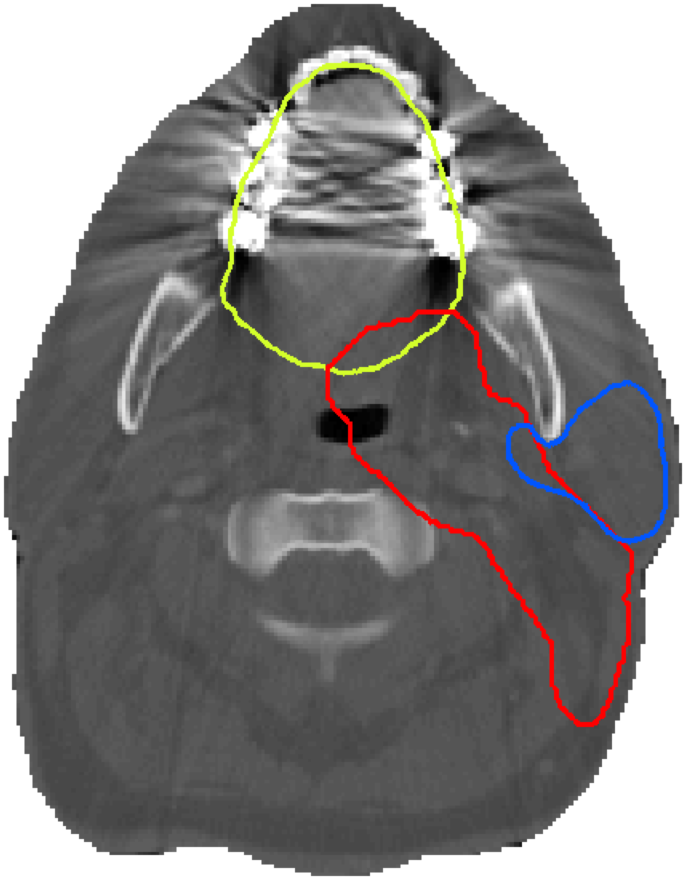
Erasmus MC

Radiation therapy (radiotherapy)

- Treatment of cancer by irradiating the tumour with ionising beams
- Treatment device can rotate around the patient
- Beam can be modulated

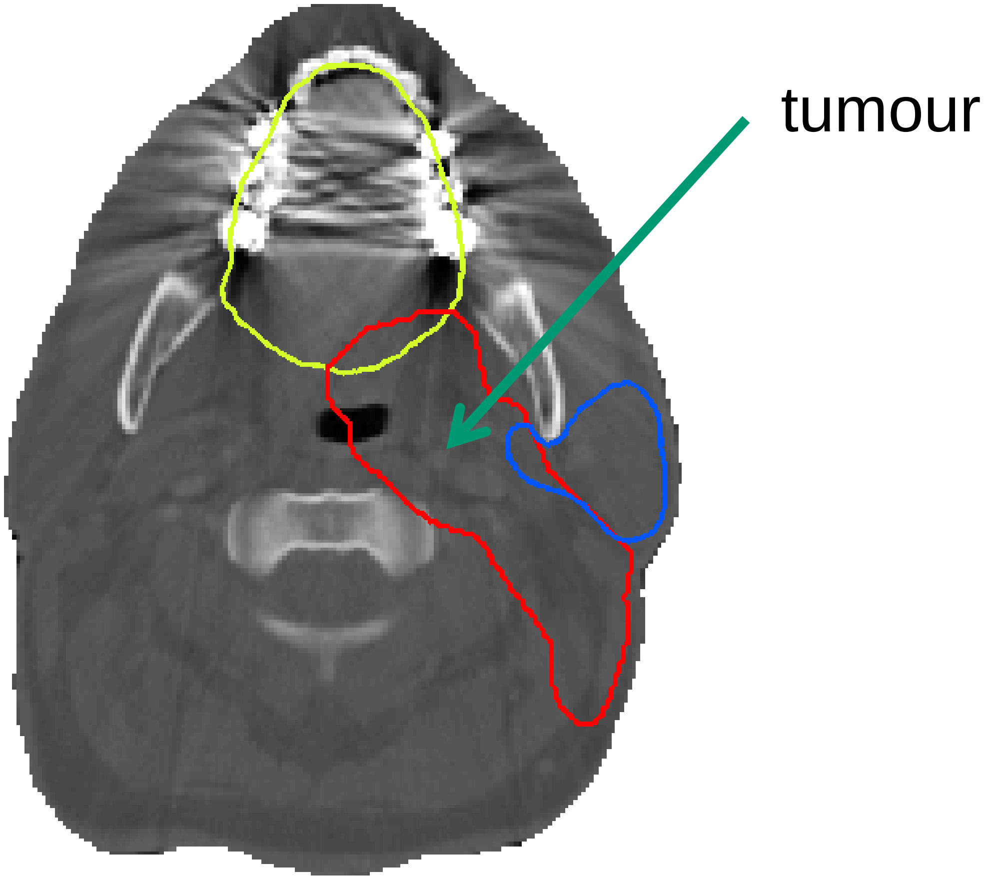


Radiotherapy treatment



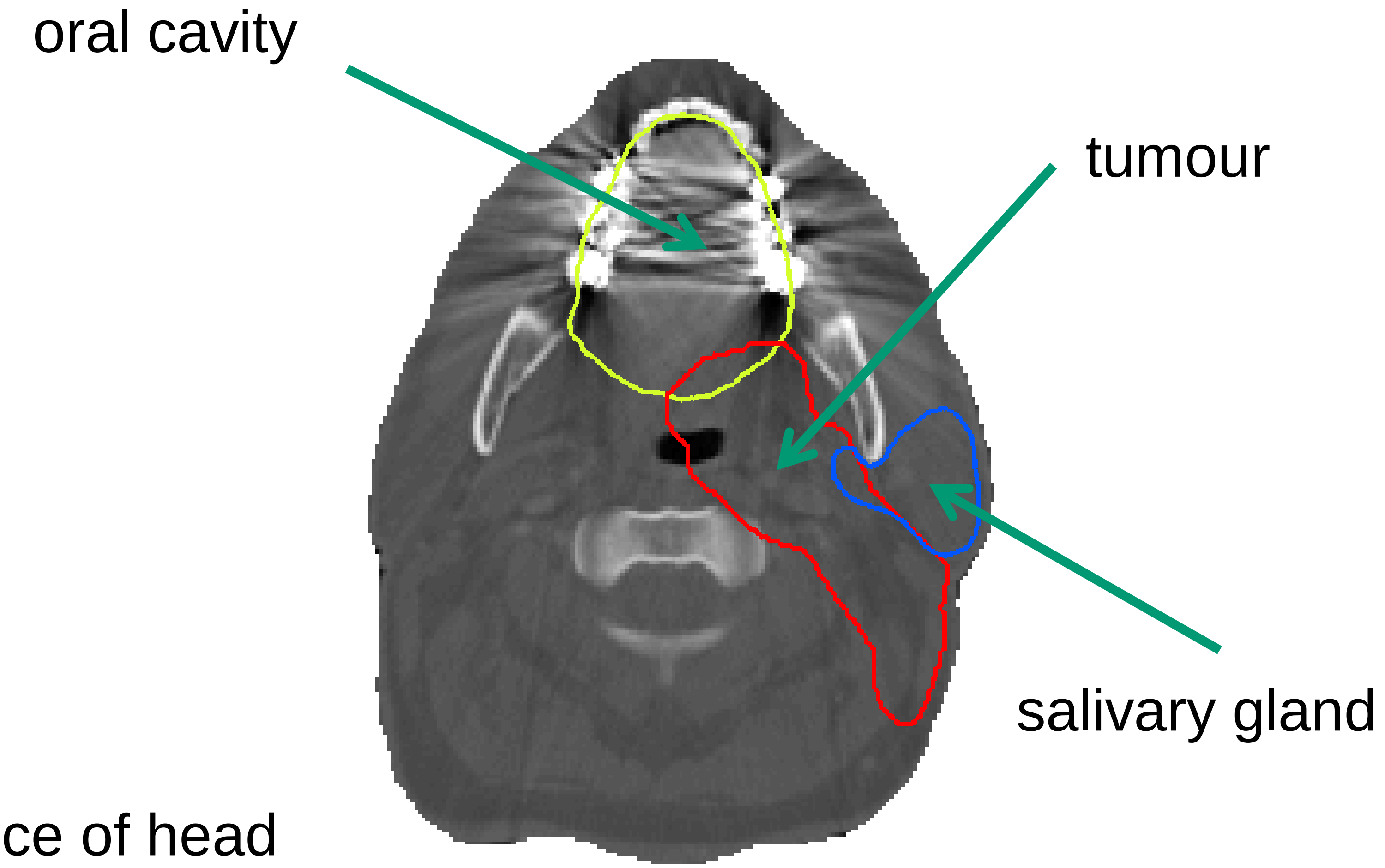
CT slice of head

Radiotherapy treatment



CT slice of head

Radiotherapy treatment



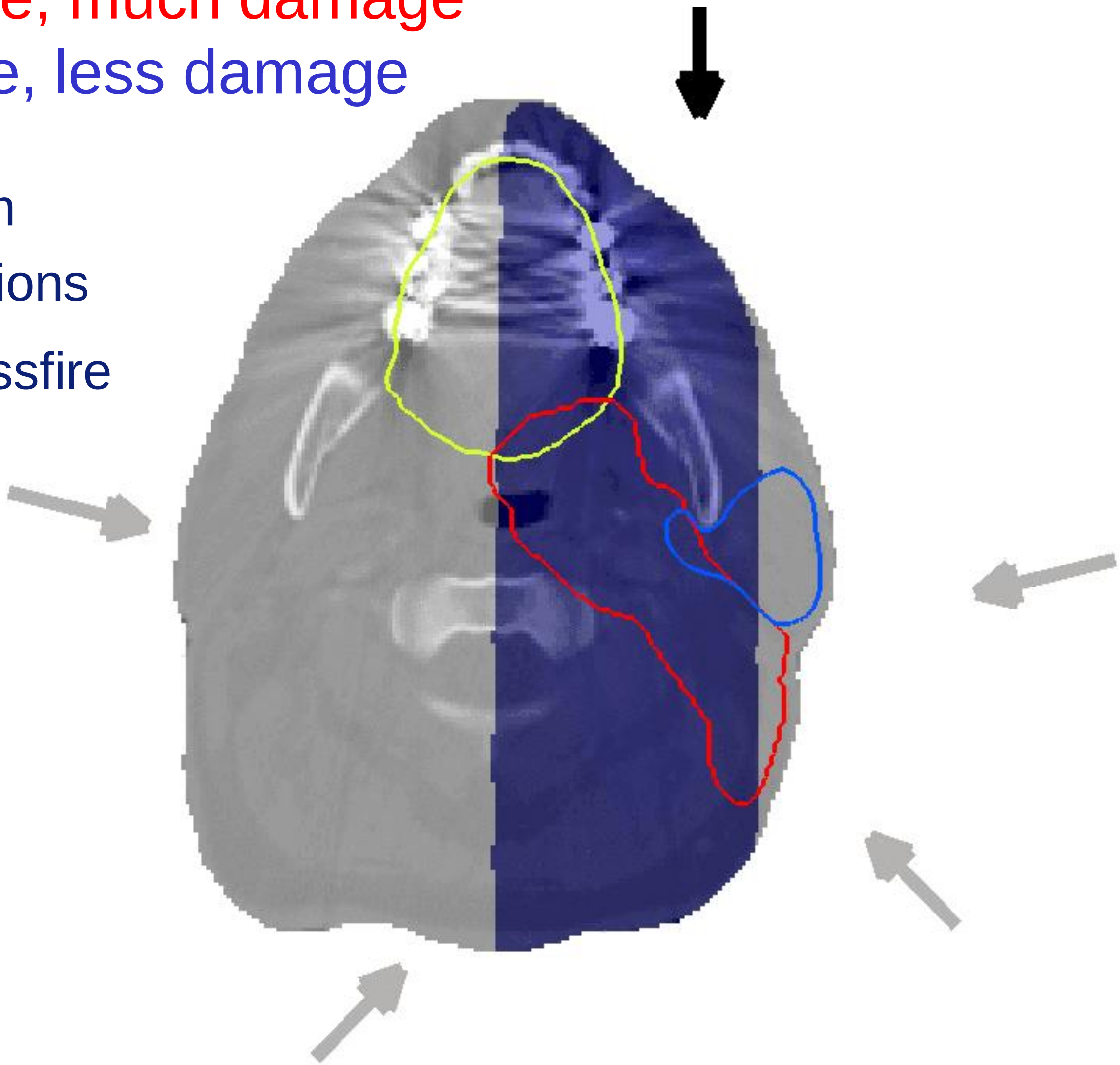
CT slice of head

Radiotherapy treatment

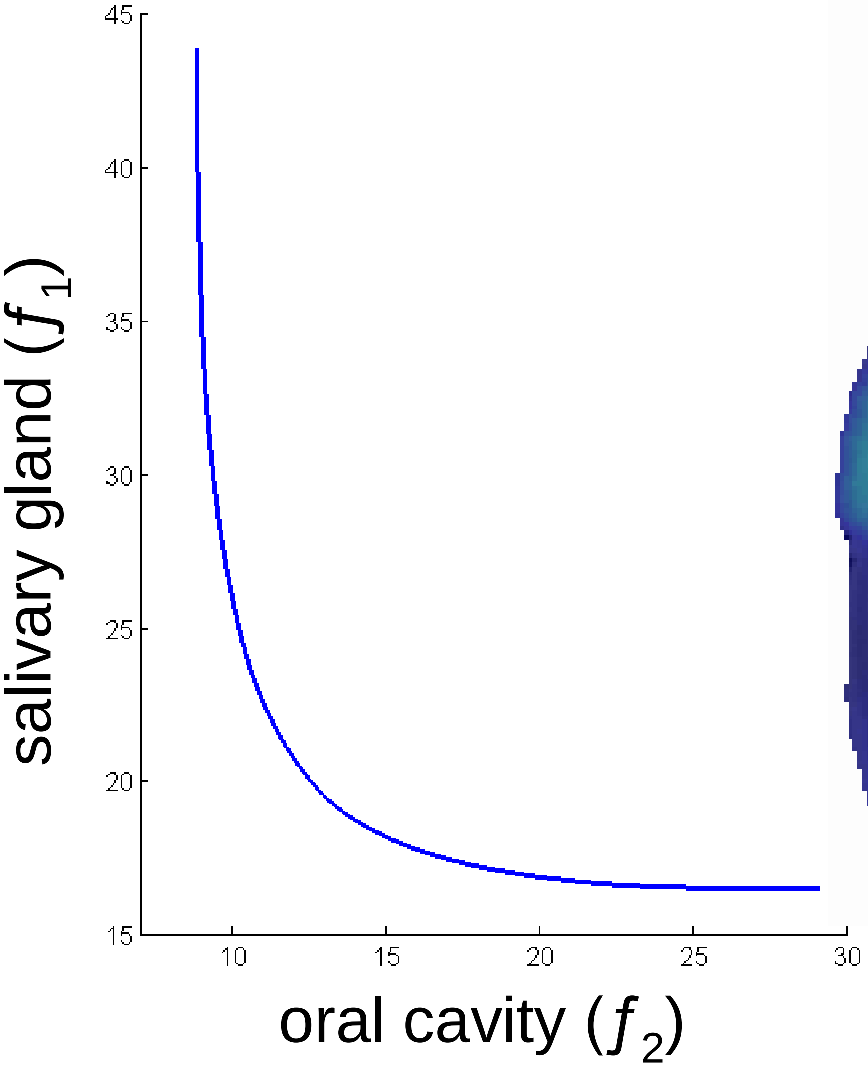
Red: high dose, much damage

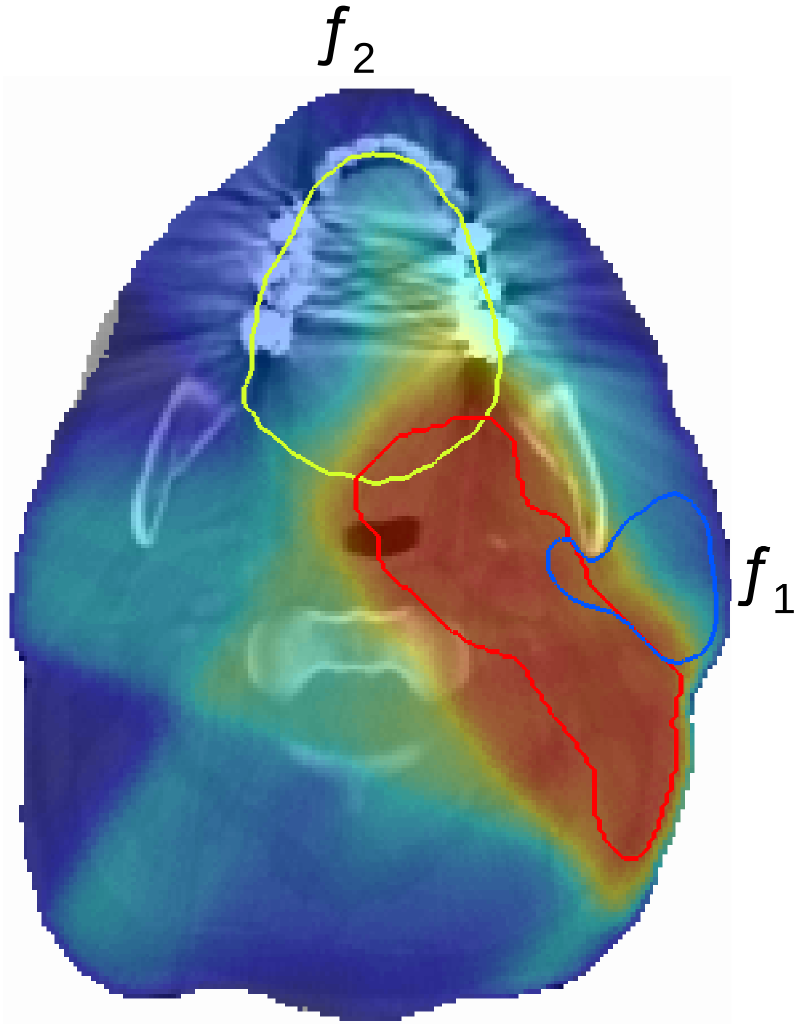
Blue: low dose, less damage

- Irradiation from different directions
- Tumour in crossfire

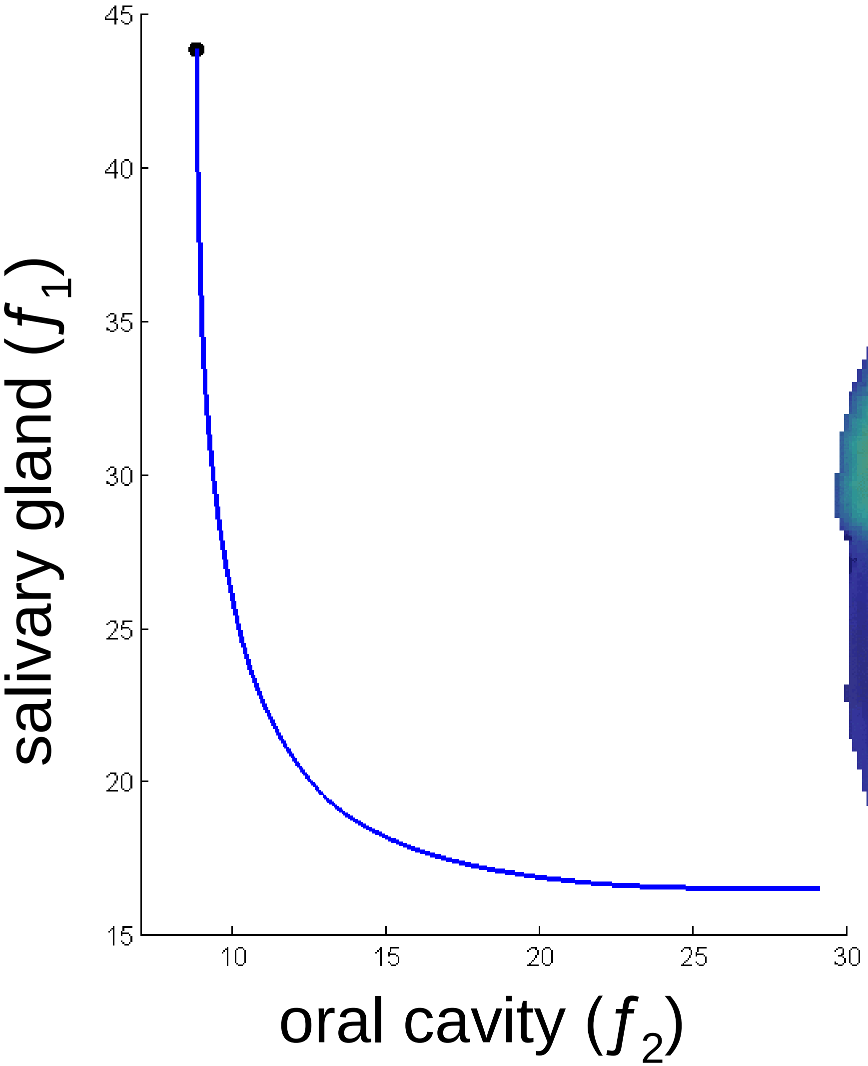


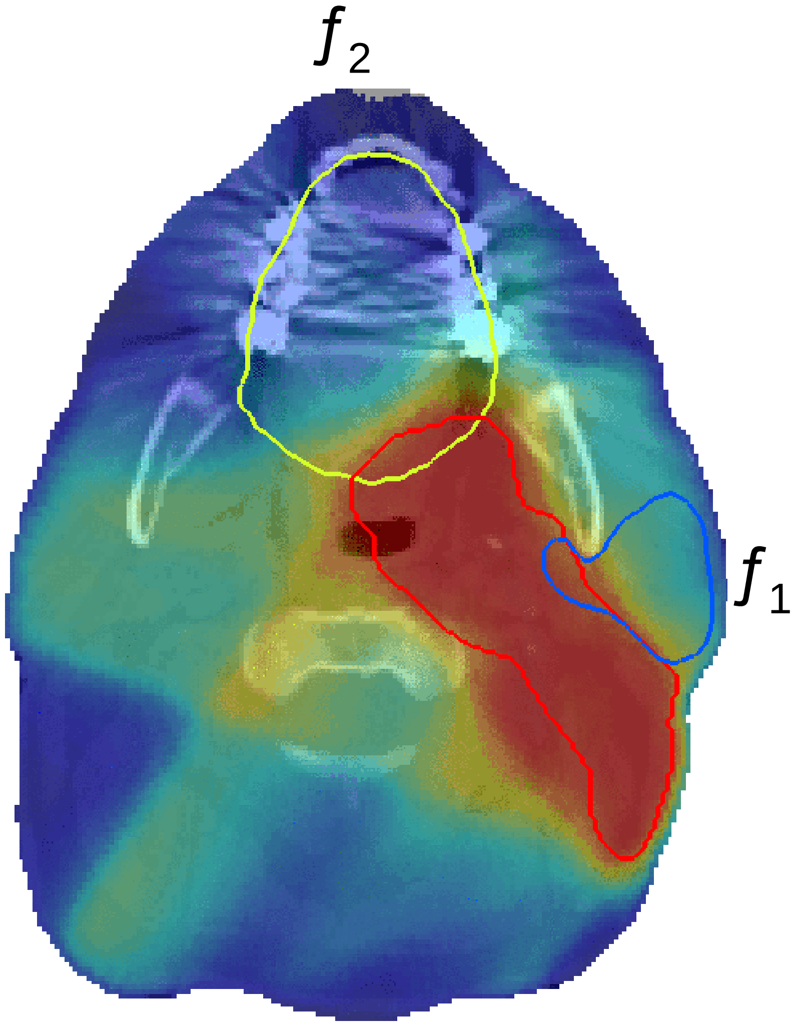
Treatment plan optimization: trade-offs





Treatment plan optimization: trade-offs





Treatment planning

- Objective: eliminate tumour and maximize functionality of organs
- Planning is multi-criterial, non-convex (broader scale: combinatorial)
- Many optimizations have to be performed
- Time to finish: 1 work-day maximum

At ErasmusMC – Daniel den Hoed, Rotterdam:

- 15 treatment devices
- 5500 patients per year
- ~20 new patients (thus plans) per day

  → each patient has an individual plan

Treatment planning

- Reduced to general optimization problem

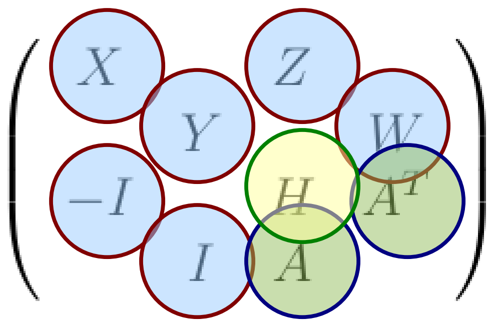
$$\begin{array}{rl} \text{minimize} & f(x) \\ \text{subject to} & h(x) \leq b \\ & x \geq 0 \end{array}$$

- n: represents discretisation x of fluence (modulation).
  - Dimension: ~ 500-5000, or ~15.000 for other treatment modalities
- m: constraints: discretisation of organs in the patient
  - Dimension: > 50.000

Interior-point optimization: a short HOWTO

System size 2m+2n

$$
\begin{aligned}
\text{minimize} \quad & f(x) \\
\text{subject to} \quad & h(x) \leq b \\
& x \geq 0
\end{aligned}
$$



$$
\begin{pmatrix} \Delta z \\ \Delta w \\ \Delta x \\ \Delta y \end{pmatrix} = \begin{pmatrix} \mu e - XZe \\ \mu e - WYe \\ -\nabla f - A^T y + z \\ b - h(x) - w \end{pmatrix}
$$

Diagonal matrices

Hessian / second derivatives

Matrix of derivatives

Interior-point optimization: a short HOWTO

- Symbolic elimination to reduced Karush-Kuhn-Tucker, size m+n

$$\begin{pmatrix} H + ZX^{-1} & A^T \\ A & -WY^{-1} \end{pmatrix}$$

- Indefinite system!

Solve this system!

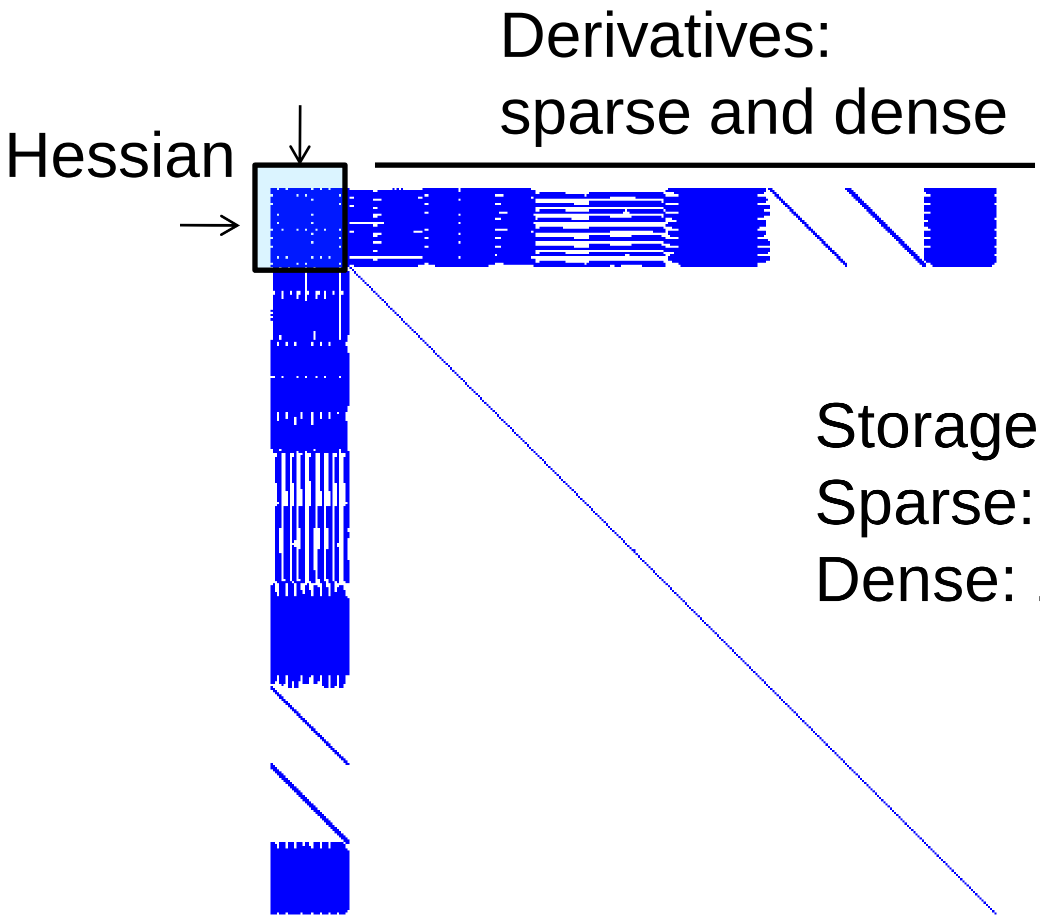
(one way or another)

Problems with radiotherapy:

- Matrix of derivatives A is not sparse
- Hessian H is not sparse

→System cannot be constructed

Sparsity pattern of indefinite system



Storage requirements:
Sparse: 750MiB
Dense: 17 GiB

Approaches: from optimization

- Further reduce system to dimension n (current approach):

$$N = H + X^{-1}Z + A^T(W^{-1}Y)A$$

  - Pros: small symmetric, dense system; Hessian for free (smart implementation); improves condition; mostly positive definite for non-convex problems
  - Cons: requires O(m*n^2) matrix-matrix multiplications

- Quasi-Newton approaches:
  - BFGS: only for Hessian, was already for free
  - L-BFGS: for indefinite system, but cannot handle bounds/constraints
  - L-BFGS-B: can handle bounds (TODO)

Approaches: direct indefinite systems

- Because of the size and non-sparsity, construction of system is not efficient.
- LDL^T results in large, dense L
- Classic methods (GMRES, CG, etc) do not work well
- IDRs (Induced Dimension Reduction, Sonneveld and van Gijzen, 2008) works best

- General problem: to work for interior-point optimization, solve system within machine precision?