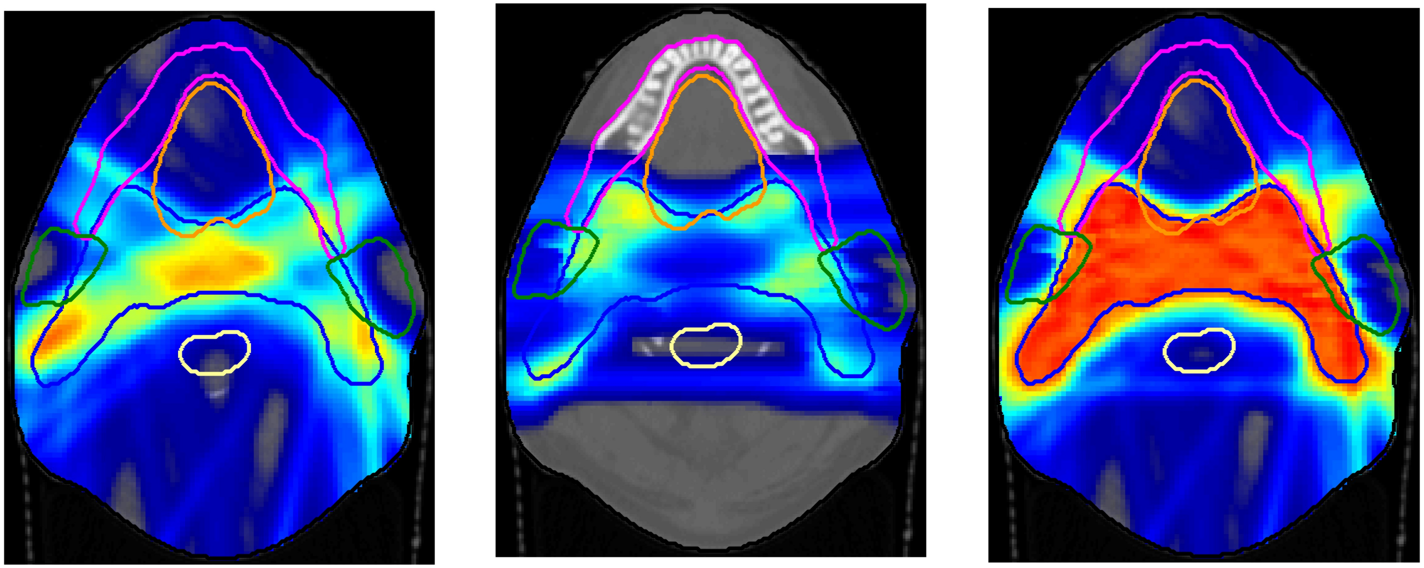

Combined proton-photon treatments

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M. Bangert, N. Wahl (DKFZ)
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Why combined proton-photon treatments?

Photons better in some aspect

- Penumbra (e.g. range shifter)
- RBE issues (OARs in the CTV)
- Robustness (e.g. lung, breast)
- Fixed beam line (limited angles)

1. **Combining a fixed proton beam line with photons**

Protons are a limited resource

- Not all patients who may benefit from protons have access to protons
  - ~100 centers
  - >10’000 Linacs

2. **Can we increase the overall benefit of proton therapy by delivering a subset of fractions with protons?**

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Big Gantries

Accelerators are quite compact

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Combined treatments with a fixed proton beam line

Consider the following treatment room:

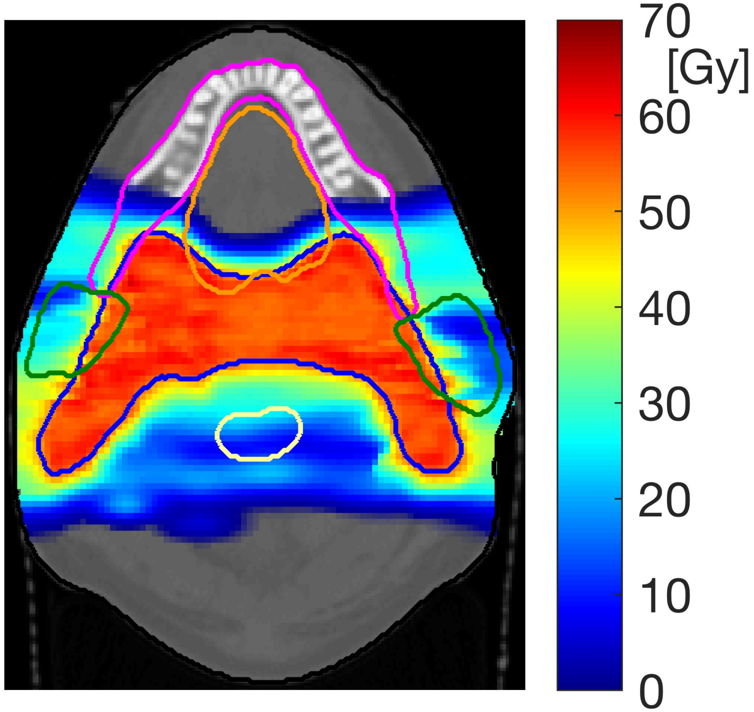
- Robotic couch to treat in lying position
- Standard linac or Cyber knife
- Fixed proton beam line with pencil beam scanning

Rationale:

- Can fit into a bunker designed for a standard linac
- Lower cost
- If protons alone are suboptimal, photon beams can compensate
- Treatment performed with standard immobilization devices

Potential application: head & neck cancer

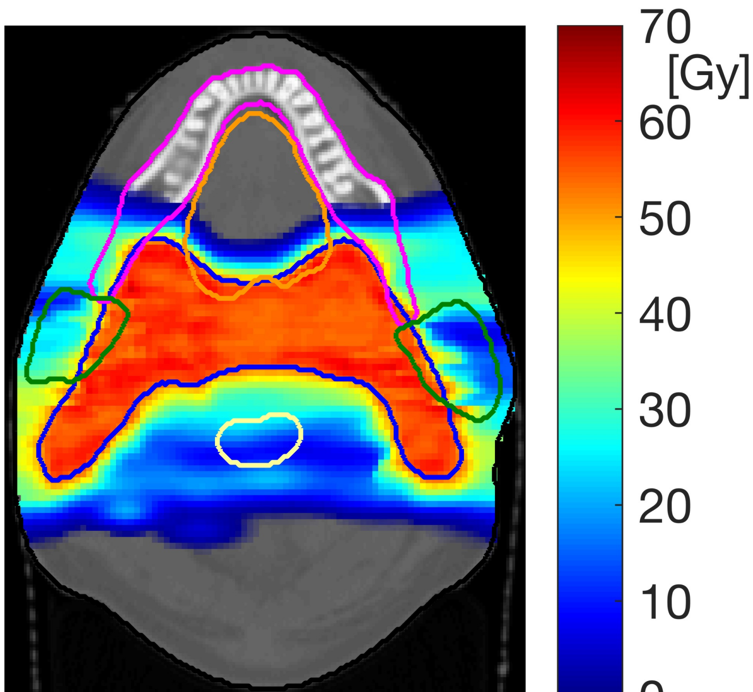
Proton beams only in a
coronal plane are suboptimal



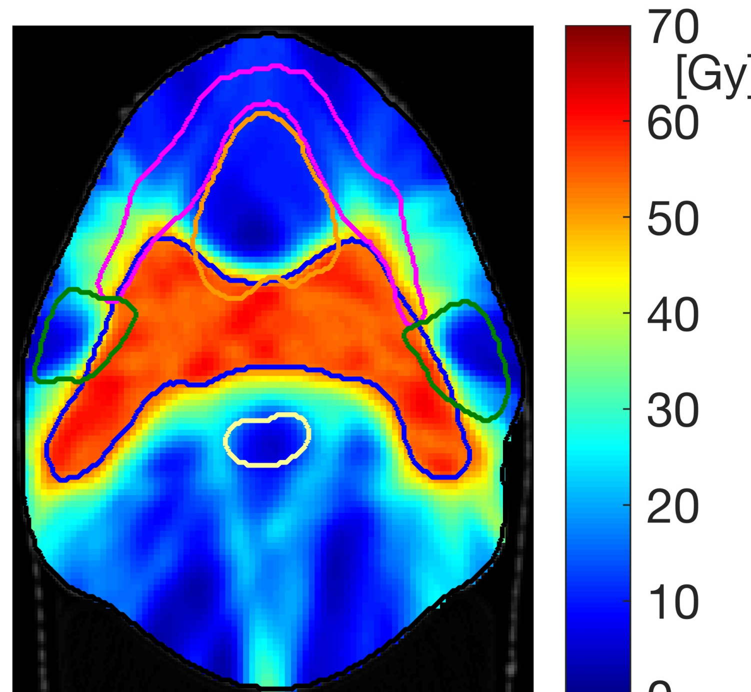
Potential application: head & neck cancer

Horizontal proton beams suboptimal for the parotid

VMAT delivers a dose bath to the oral cavity



Protons



VMAT

Planning method

Simultaneous optimization of proton and photon beams

minimize $f(d)$ Objective function for cumulative dose

subject to
$$d_i = \underbrace{\sum_k D_{ik}^p x_k^p}_{\text{proton dose}} + \underbrace{\sum_j D_{ij}^\gamma x_j^\gamma}_{\text{xray dose}}$$

$x_k^p \geq 0 \quad x_j^\gamma \geq 0$ non-negative fluence

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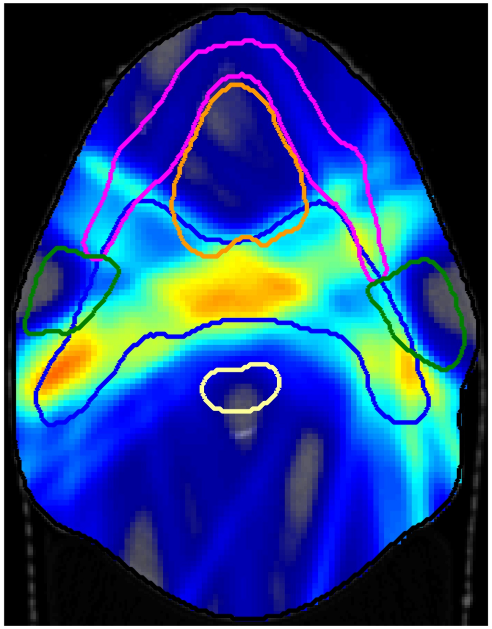
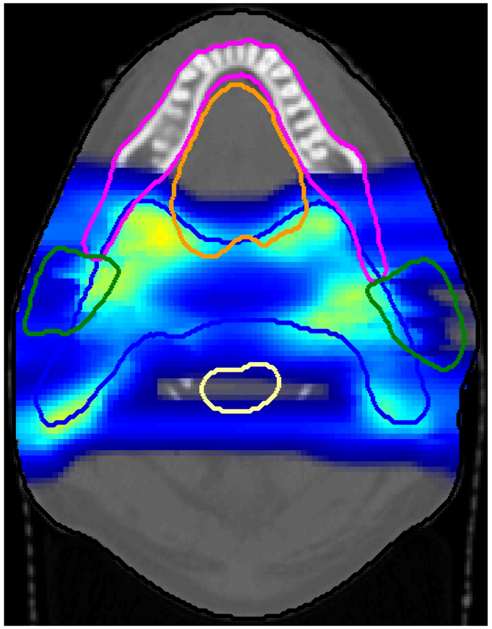
Optimal combination

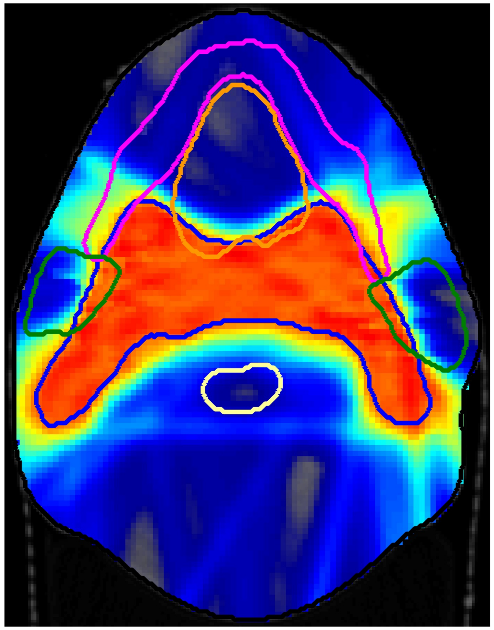
Both modalities used



VMAT contribution



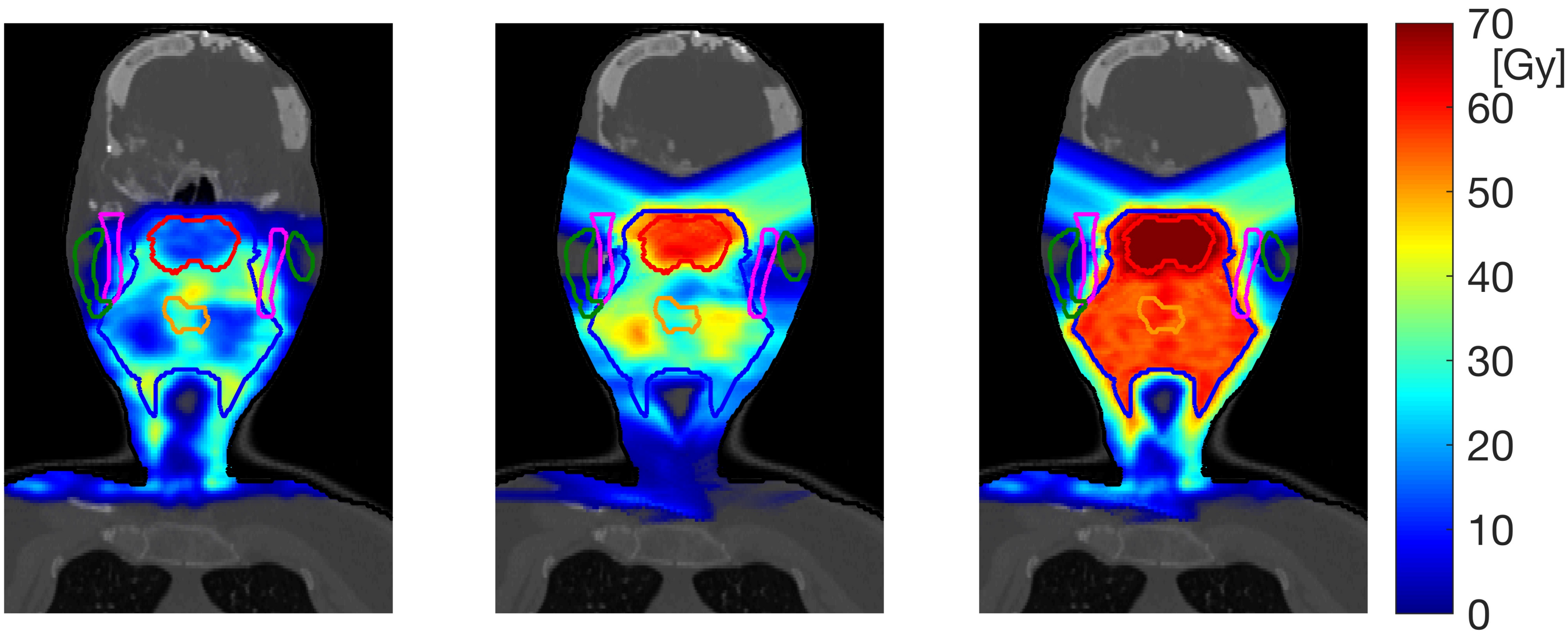
Proton contribution



Cumulative dose

Optimal combination

Protons deliver most of the dose

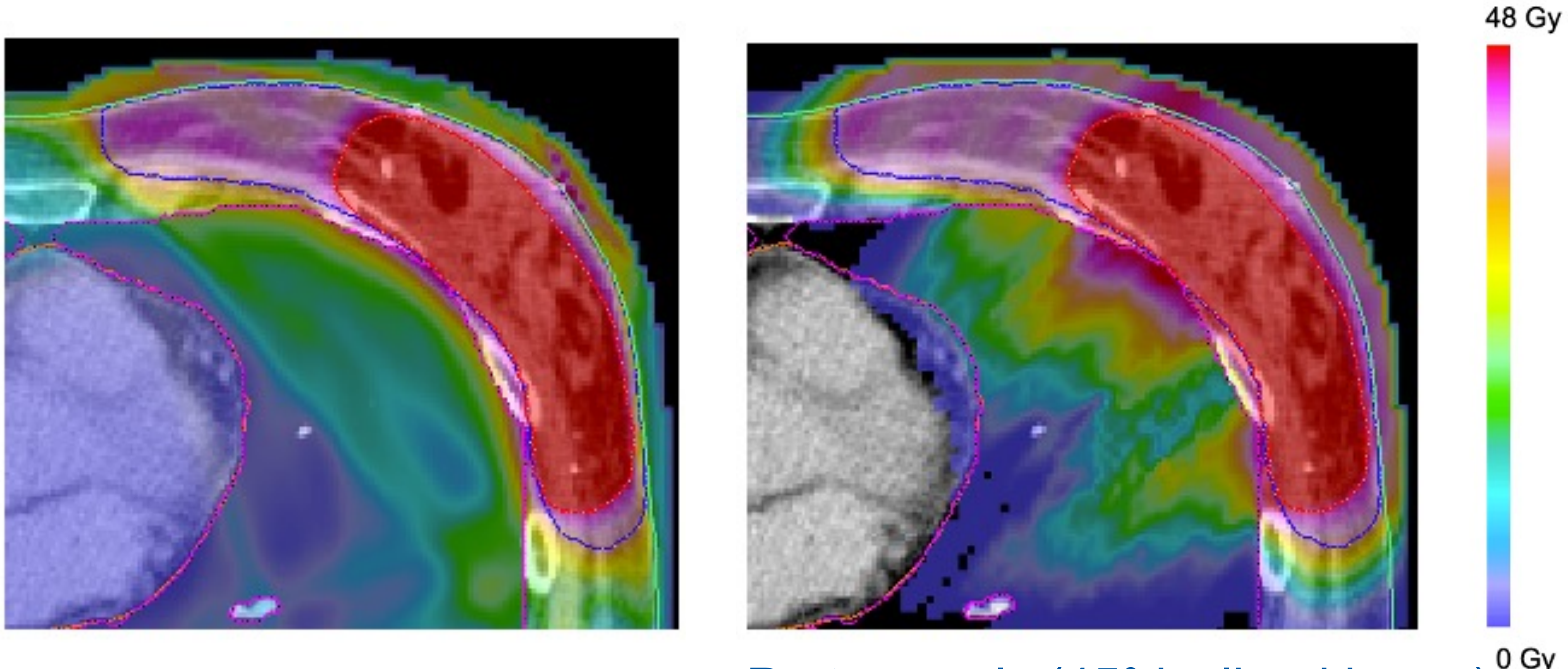


VMAT contribution

Proton contribution

Cumulative dose

Application to breast cancer



IMRT only

- increased lung/heart dose for concave targets

Protons only (45° inclined beam)

- overshoot into the lung

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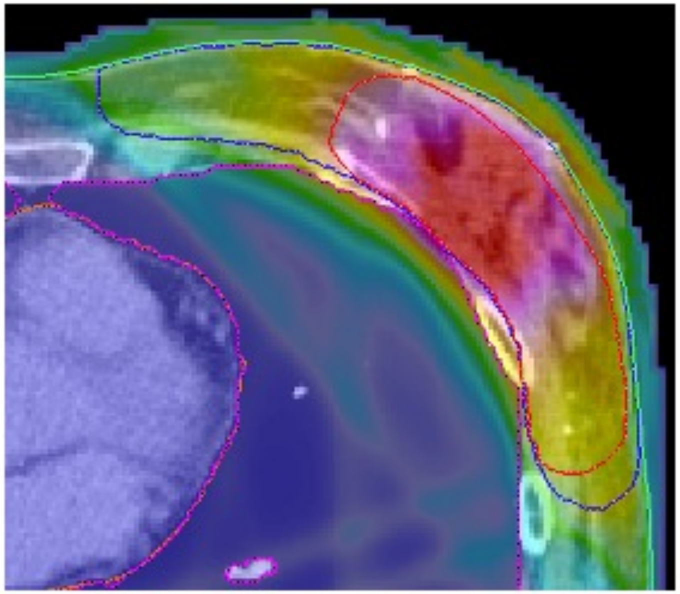
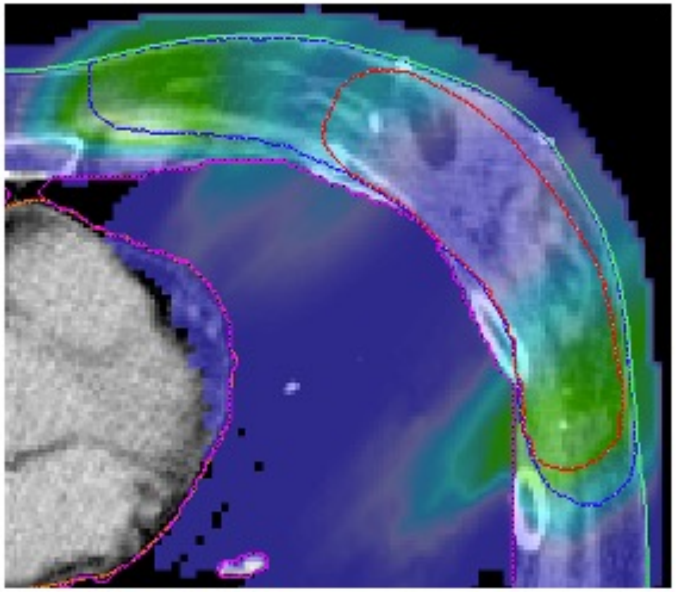
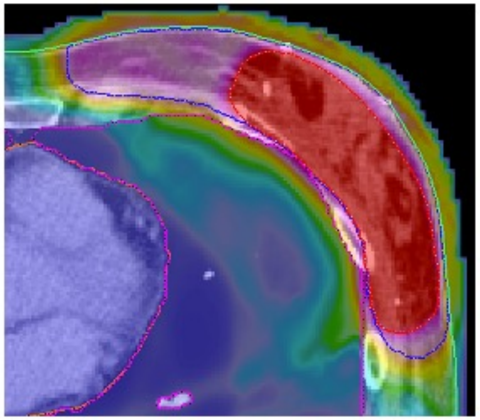
Application to breast cancer





IMRT contribution

tangential beams can treat most of the target and improve robustness



cumulative dose

Proton contribution

can deliver dose to lymph nodes and parts of the breast

Combined treatments with a fixed proton beam line

Fixed proton beamlines can more easily be installed in existing hospitals

- Potential for wide-spread implementation of protons at lower cost

Main approach to using fixed beamlines: treatment on rotating chair

Here: consider combined proton-photon RT as alternative approach

- Photons improve conformity if protons alone are suboptimal
- A photons component may improve robustness

Here: Demonstrated for head & neck and breast

Ongoing: Evaluate potential across treatment sites

Lit: Fabiano 2020, green J

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1. **Combining a fixed proton beam line with photons**

Protons are a limited resource

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  - ~100 centers
  - >10’000 Linacs

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Content

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a) **What is the optimal allocation of proton fractions over the patient cohort?**

b) **How can a limited number of proton fractions be used optimally**

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Proton slot allocation

Consider NTCP model-based approach to proton patient selection

- Dutch system, Langendijk et al
- Patients get either protons or photons
- Decide based on NTCP difference

Can we better utilize proton resources through combined treatments?

(deliver some fractions with protons and some with photons)

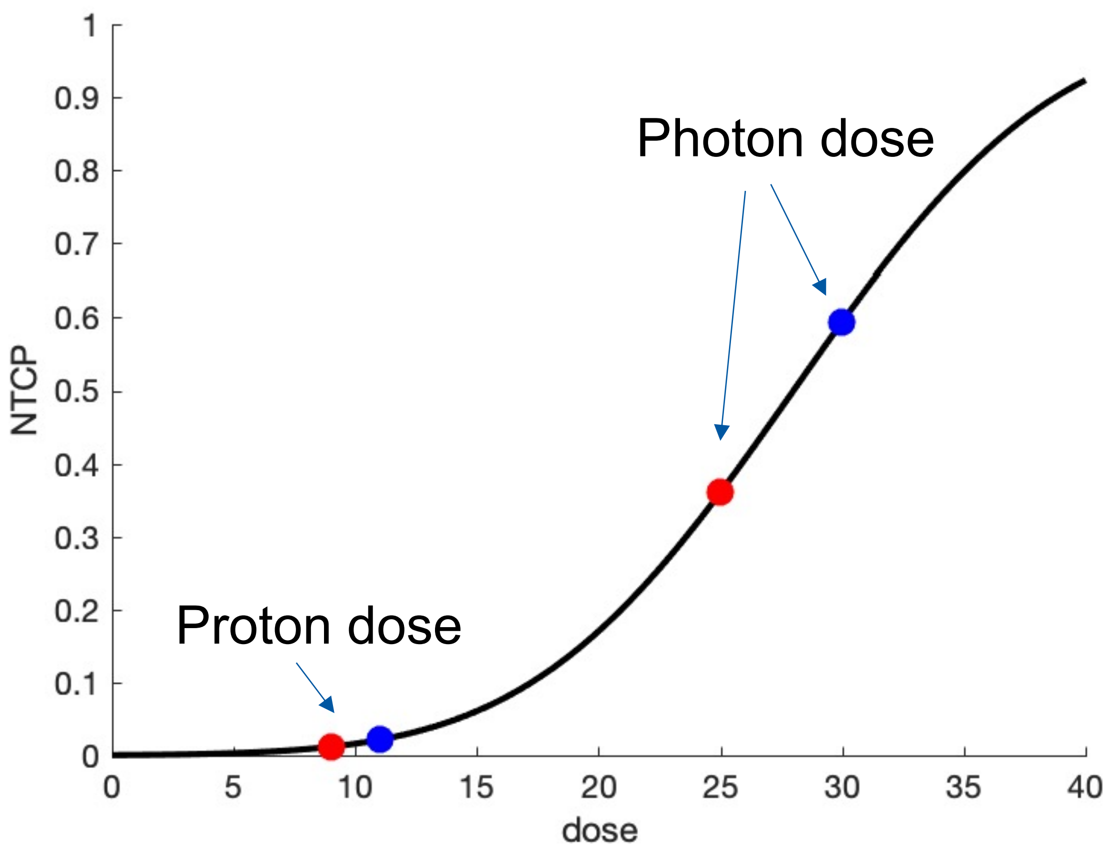
We ask: **How many proton fractions should each patient receive?**

Rather than: **Who should receive protons and who not?**

Proton slot allocation

Two-fold rationale

1. Diminishing return on the flat part of the NTCP curve



Proton slot allocation

Two-fold rationale

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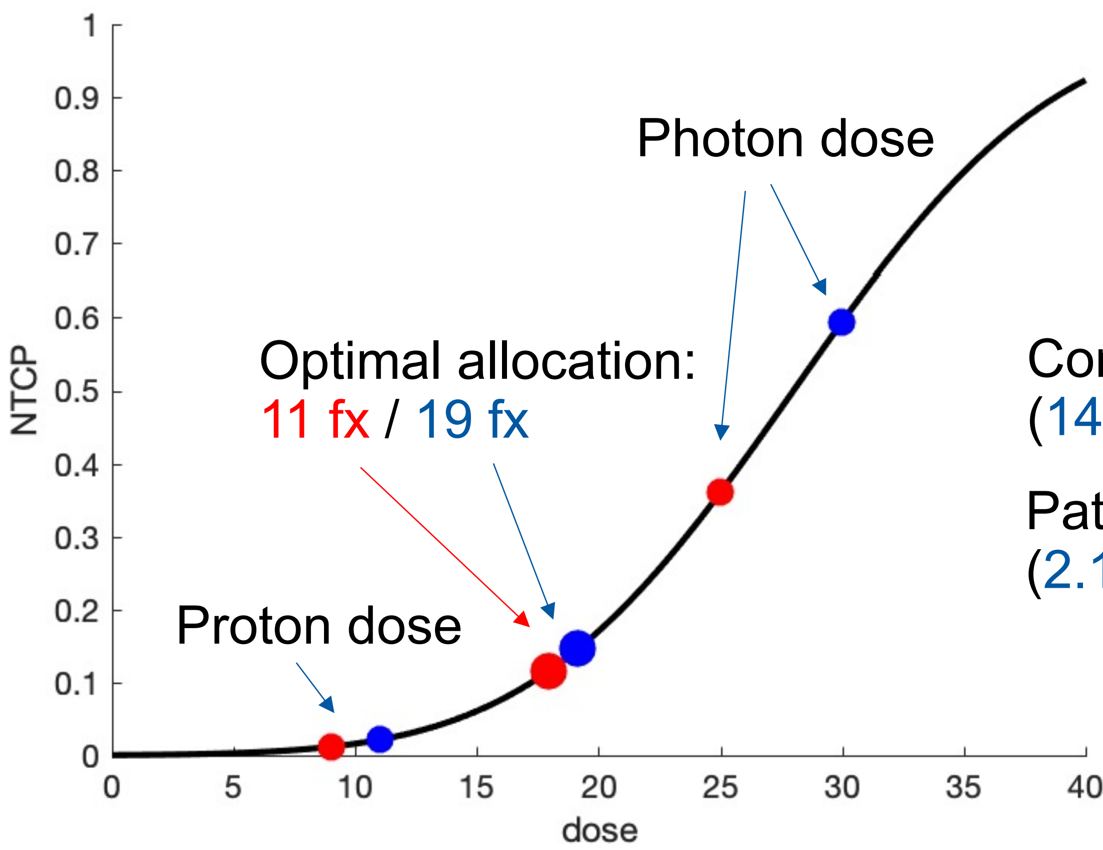

Combined treatment:
(14.6 + 11.6)/2 = 13.1

Patient selection:
(2.1 + 36.1)/2 = 19.1

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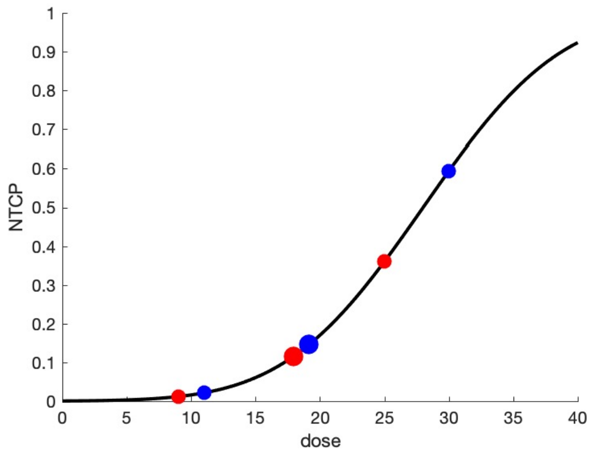
Proton slot allocation

Two-fold rationale

1. Diminishing return on the flat part of the NTCP curve



2. Patient selection schemes face a tradeoff between

   a) making use of all proton slots, and
   b) keeping slots available for patient with large benefit

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Proton slot allocation

Consider a clinic with

- single room proton machine
- 30-fraction H&N cancer treatments
- 100 patients per year
    - 2 new patients per week, 12 patients under treatment
- Assume 3 proton slots available each day for H&N patients

Goal:

Optimally assign proton fractions to minimize the total number of complications over all H&N patients treated at the department

Proton slot allocation

Idea: Daily proton slot re-assignment

- On each treatment day, consider all patients under treatment
- For each patient, calculate the incremental NTCP reduction for delivering today's fraction with protons instead of photons

➢ Give today's proton fractions to those patients who benefit the most from one additional proton fraction

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Proton slot allocation

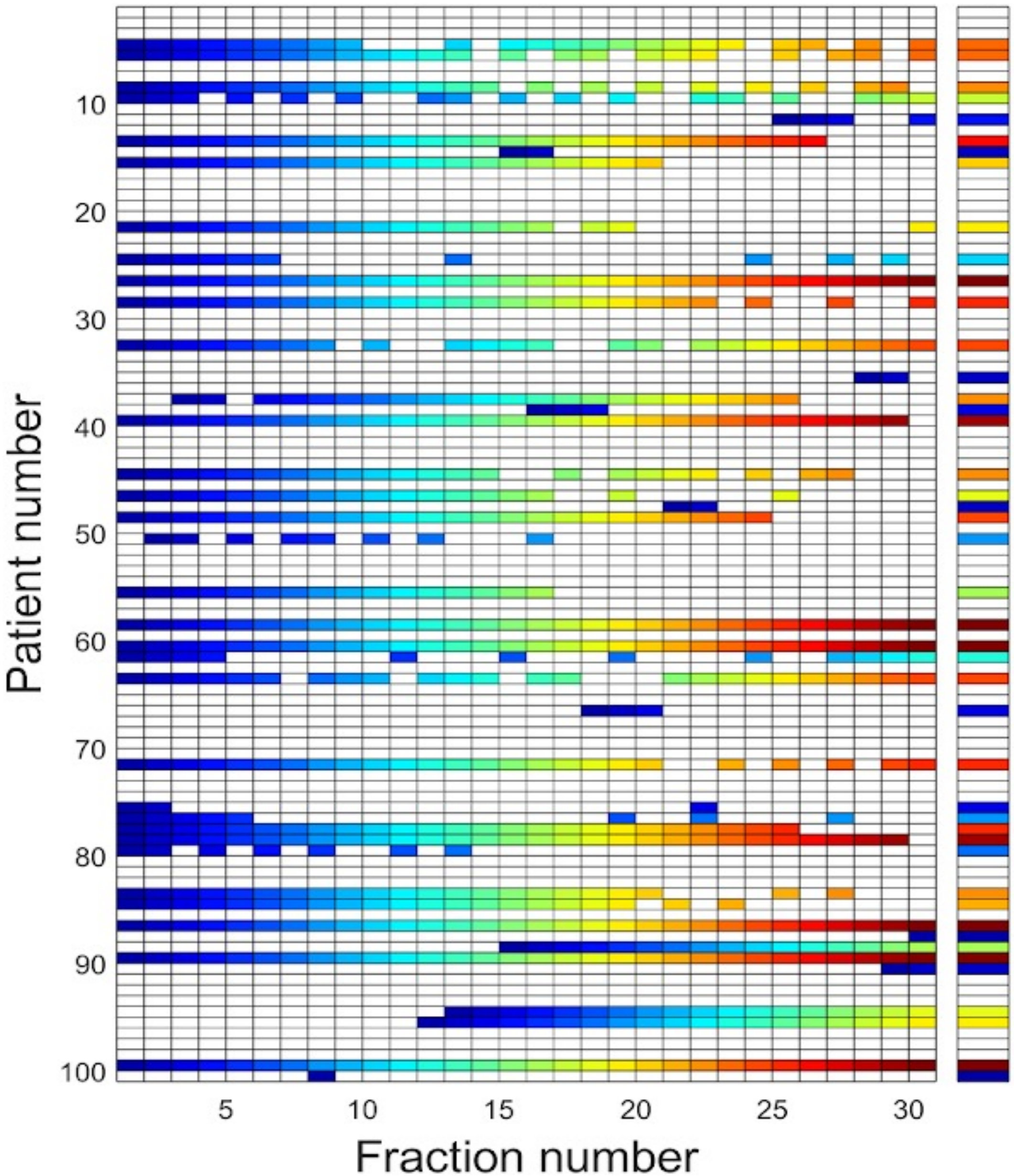
We simulate this process:

- Each day, there is a 40% chance a new patients starts
- Sample IMRT and IMPT mean doses for
  - contralateral parotid
  - oral cavity
  - PCM

  from a 6D Gaussian (derived from a plan comparison study)

- Sum of NTCP for xerostomia and dysphagia is calculated

  (using Dutch models)



100 consecutive patients

(about 1 year)

few patients receive only protons

some start with protons and switch to xrays when patients with larger benefit start treatment

some start with xrays and switch to protons once patients with larger benefit finish treatment

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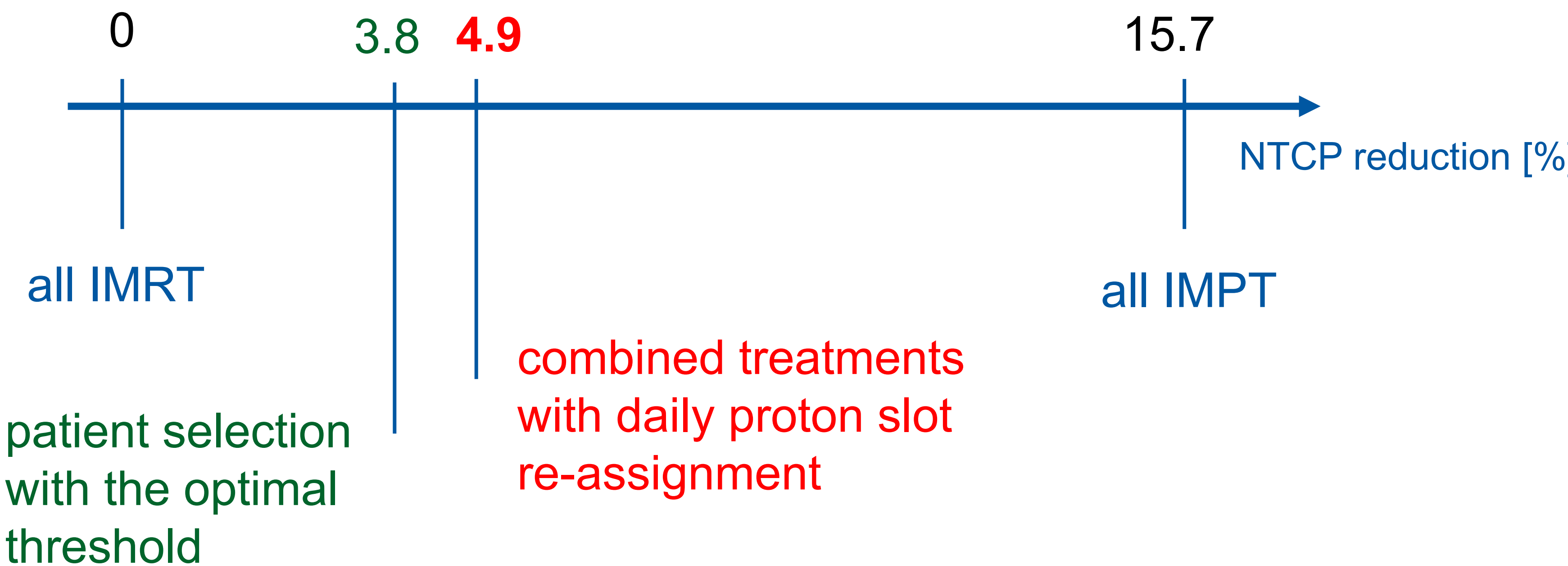
Optimally make use of limited proton fractions



Lit: Loizeau 2021, red J

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Optimally make use of limited proton fractions

For H&N cancer we stay with standard fractionation

- Proton and Photon plans deliver 2 Gy per fraction
- The benefit of combined treatments is not huge

Can we better exploit the proton fractions?

Yes, for tumors eligible for hypofractionation

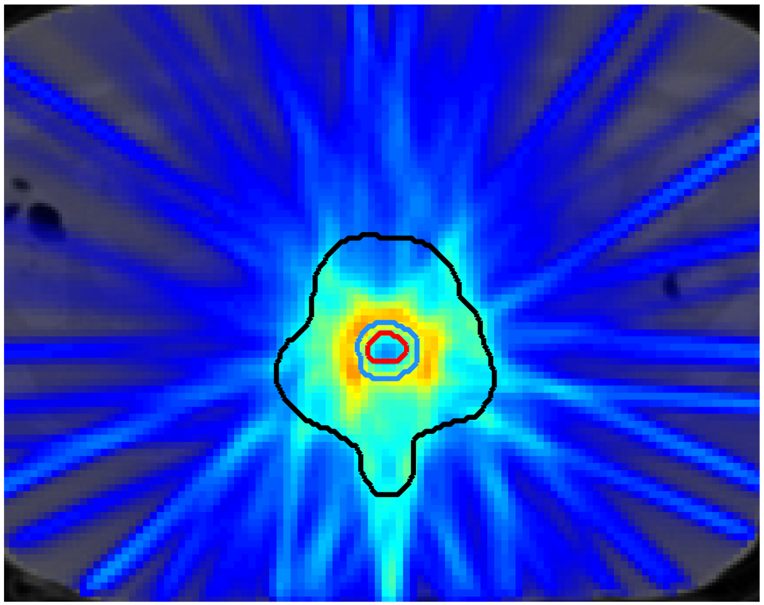
E.g. in liver SBRT we may increase the dose for a proton fraction

But, what if parts of the target volume overlays OARs

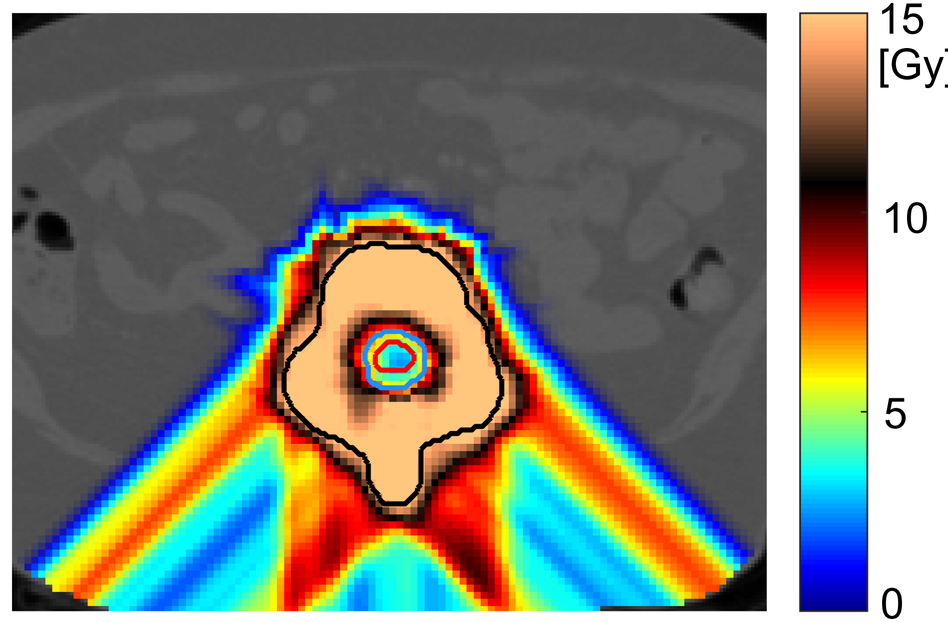
Protons may deliver an overproportionate dose to parts of the target

Lit: Unkelbach 2018, green J; Fabiano 2020, red J

Example: Spinal metastasis with epidural involvement

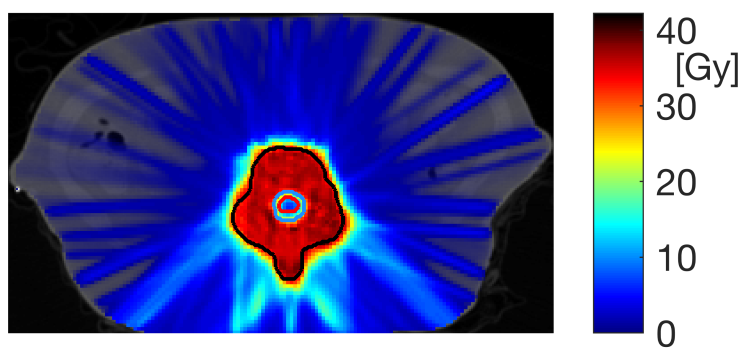


4 VMAT fractions



1 IMPT fraction

achieve uniform fractionation near the cauda



cumulative biological dose

over-proportionate dose contribution to the remaining target volume

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Conclusions

1. Combined proton-photon radiotherapy with a fixed beam line may be a concept for cost-effective proton therapy

   - Protons and photons delivered in the same fraction
   - Photon improve the dose distribution for a given patient

2. Combined proton-photon treatments allow for better utilization of limited proton resources

   - Protons and photons delivered in separate fractions
   - Maximize the benefit of protons for the population

Literature

Fixed proton beamline
+ IMRT/VMAT
Fabiano 2020, green J

Triple modality
IMRT/IMPT/MERT
optimization
Kueng 2021, PMB

Joint IMRT/IMPT
optimization with
homogeneity objectives
Gao 2019, PMB

Proton slot allocation
for a H&N cohort
Loizeau 2021, red J

BED-based optimal
fractionation in proton-
photon liver SBRT
ten Eikelder 2019, PMB

Joint BED-based
optimization of proton
and photon fractions
Unkelbach 2018, green J
Fabiano 2020, red J