

Nordic cooperation and clinical trials in proton therapy

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Why proton therapy?

- Long-term survival after cancer treatment 50% → 75% the last 30 years
- Approximately 50% of cancer patients receive radiotherapy
- In Norway 10.000-15.000 survivors with significant late side effects
- Proton therapy allows for a more precise and gentler radiotherapy

- Another option: Increase the dose to the tumor aiming at curing more patients while accepting that the side effects are not reduced

Some numbers and facts

- Norway: Around 14.000 patients treated with standard RT (photons) per year
- 39 linacs in Norway -> 330 patients per room
- Protons: 200-300 patients per room per year -> capacity 600-900 patients per year -> 4-7% of all treatments
- Proton therapy 3 times more expensive than photons
- Proton therapy is given in the same way as standard RT (target volume, total dose, number of fractions, treatment time (typically 5-6 weeks))
- Before 2025, around 50 patients were sent abroad for proton therapy – children and young adults, brain tumors - 100-150 patients standard indication?
- Aim: 75-80% in clinical trials

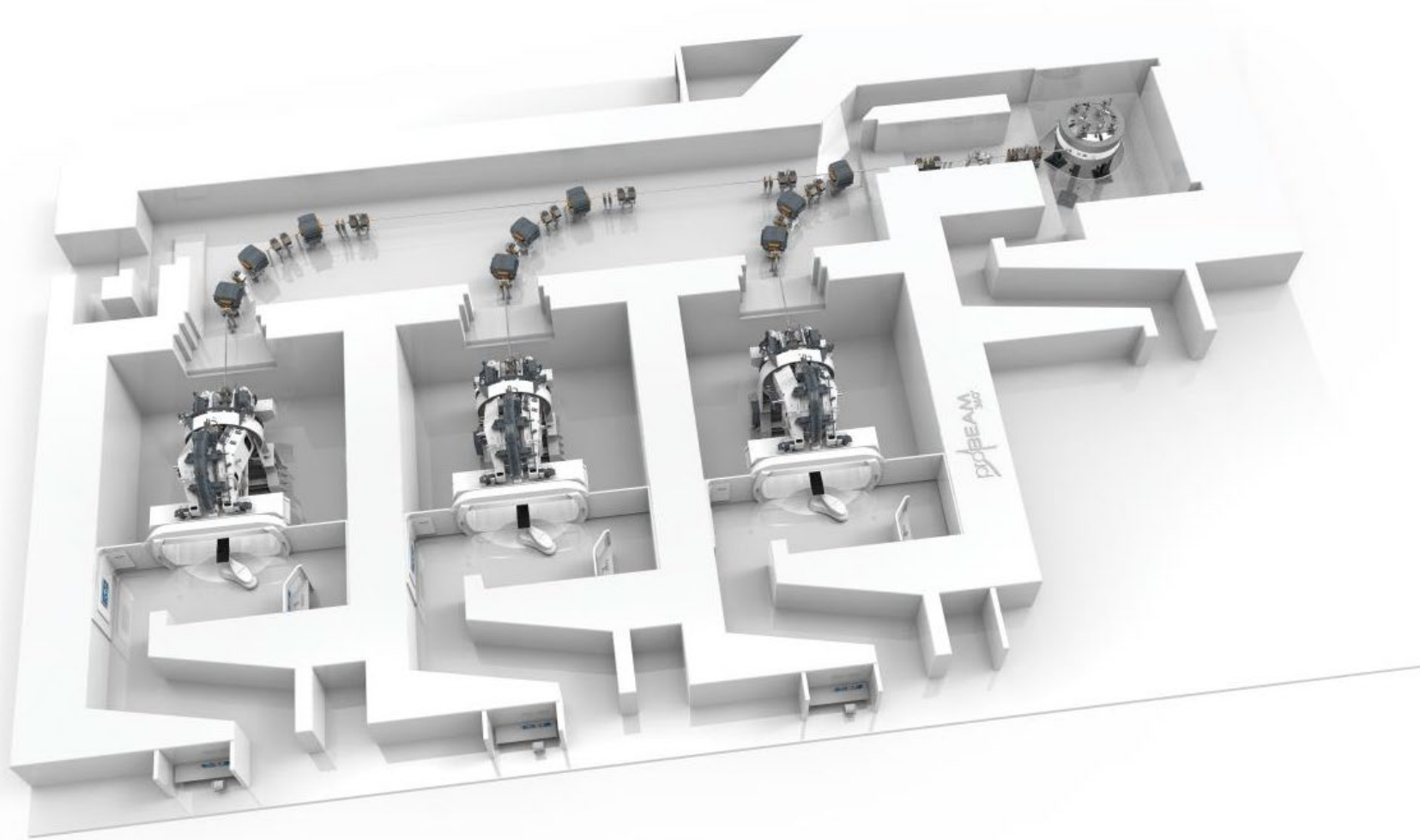


Oslo University Hospital – Radium Hospital
2 treatment rooms and 1 research room
Started March 17 2025



Haukeland University Hospital
1 treatment room and 1 research room
Started May 7 2025

Proton therapy system - Varian ProBeam360



Proton treatment room



Skandion, Uppsala, Sweden

- Started 2015
- 2 treatment rooms



Aarhus, Denmark

- Started 2019
- 3 treatment rooms + research room

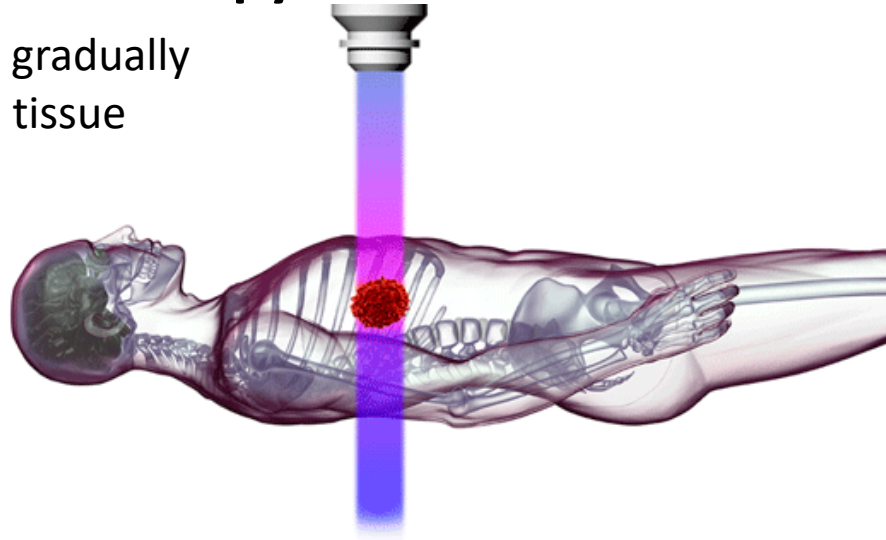


Nordic cooperation

- Patients have been sent from Norway for proton therapy at Skandion and Aarhus
- Proton facilities in Oslo and Bergen inspired by especially Aarhus
Procedure documents
Competency plans
- Proton therapy course in Denmark – Plans for expanding to a Nordic course
- Conferences – “Nordic Proton Symposium” Oslo, May 22, 2025
- Cooperation through the European Particle Therapy Network (EPTN) network
Workpackages (Clinical, QA and Dosimetry, Image-Guided Particle Therapy, Treatment Planning, Radiobiology, Health Economics, Data Registry)

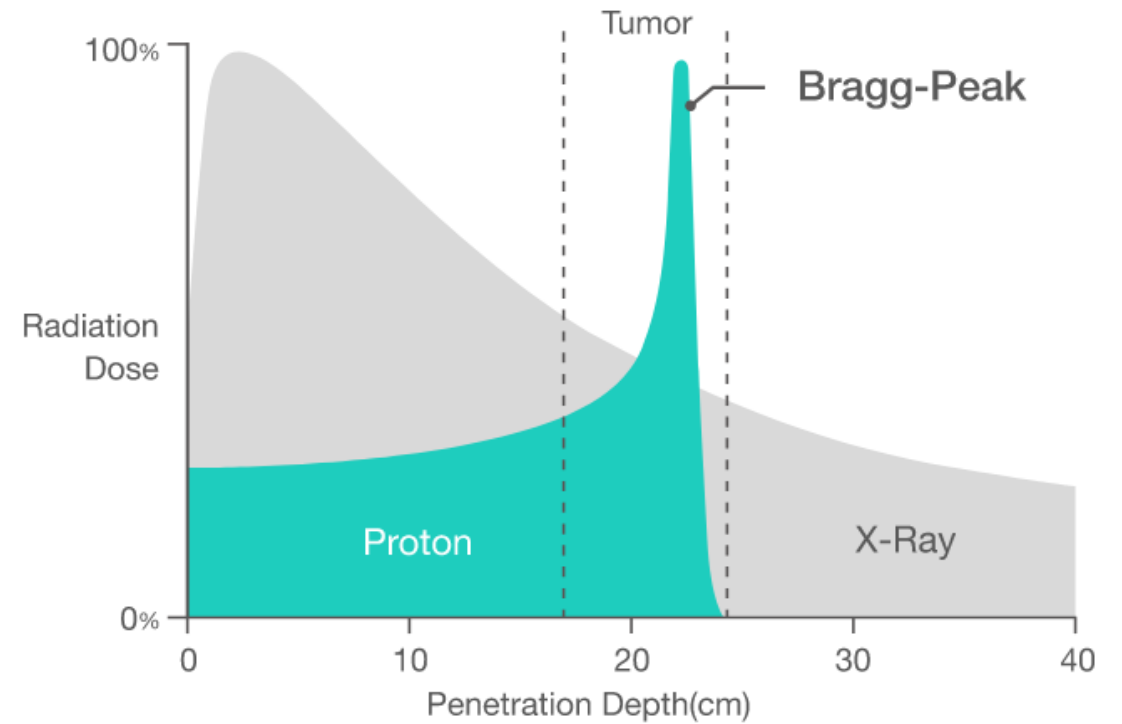
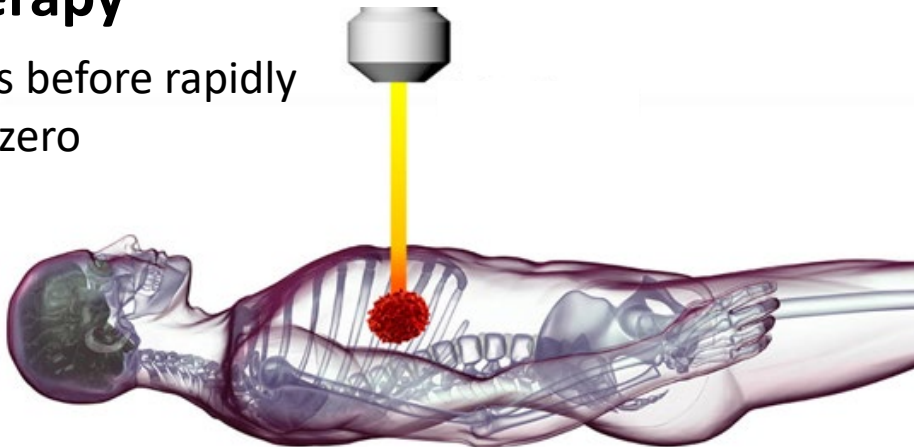
Standard radiotherapy

Dose decreases gradually deeper into the tissue

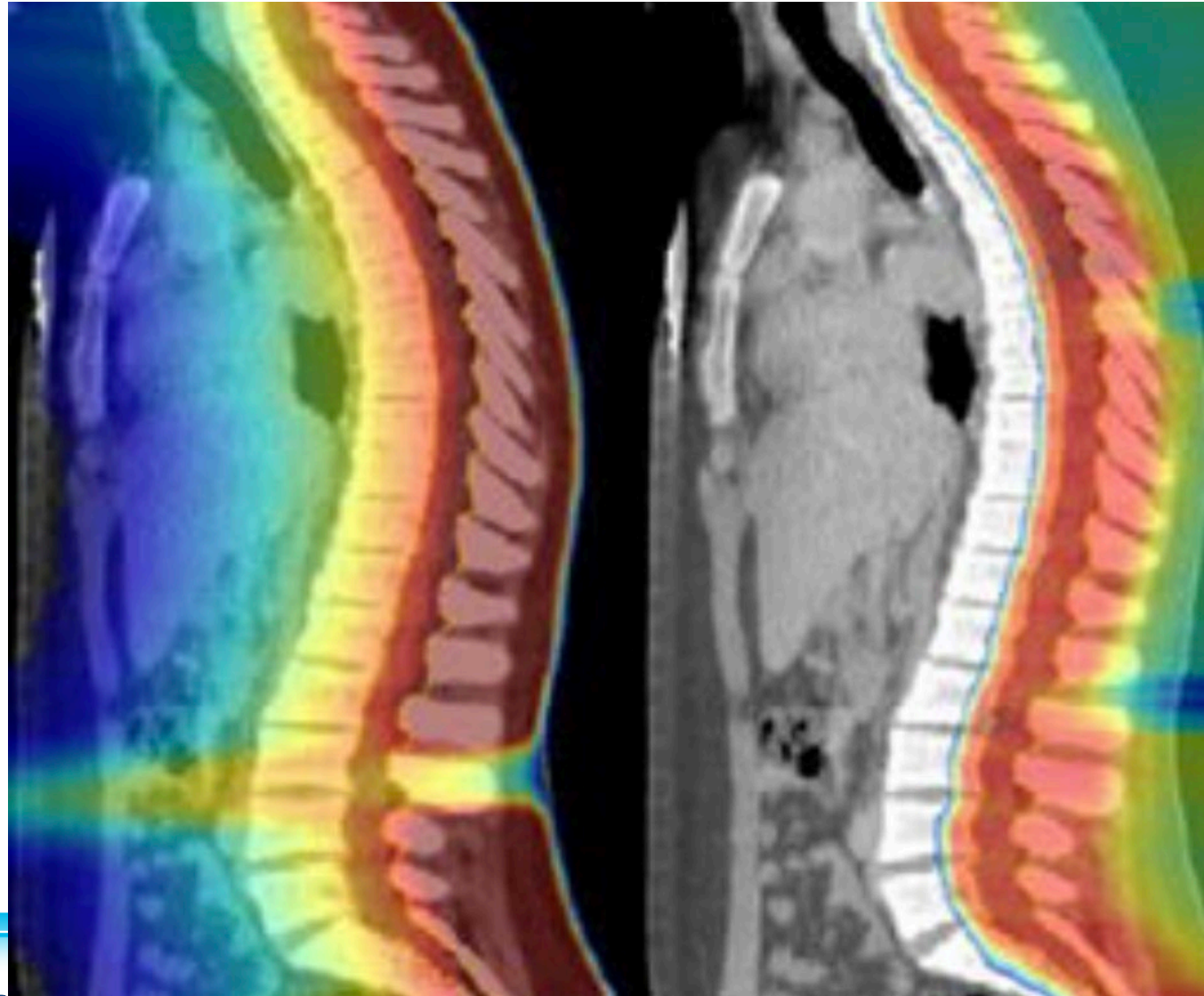


Proton therapy

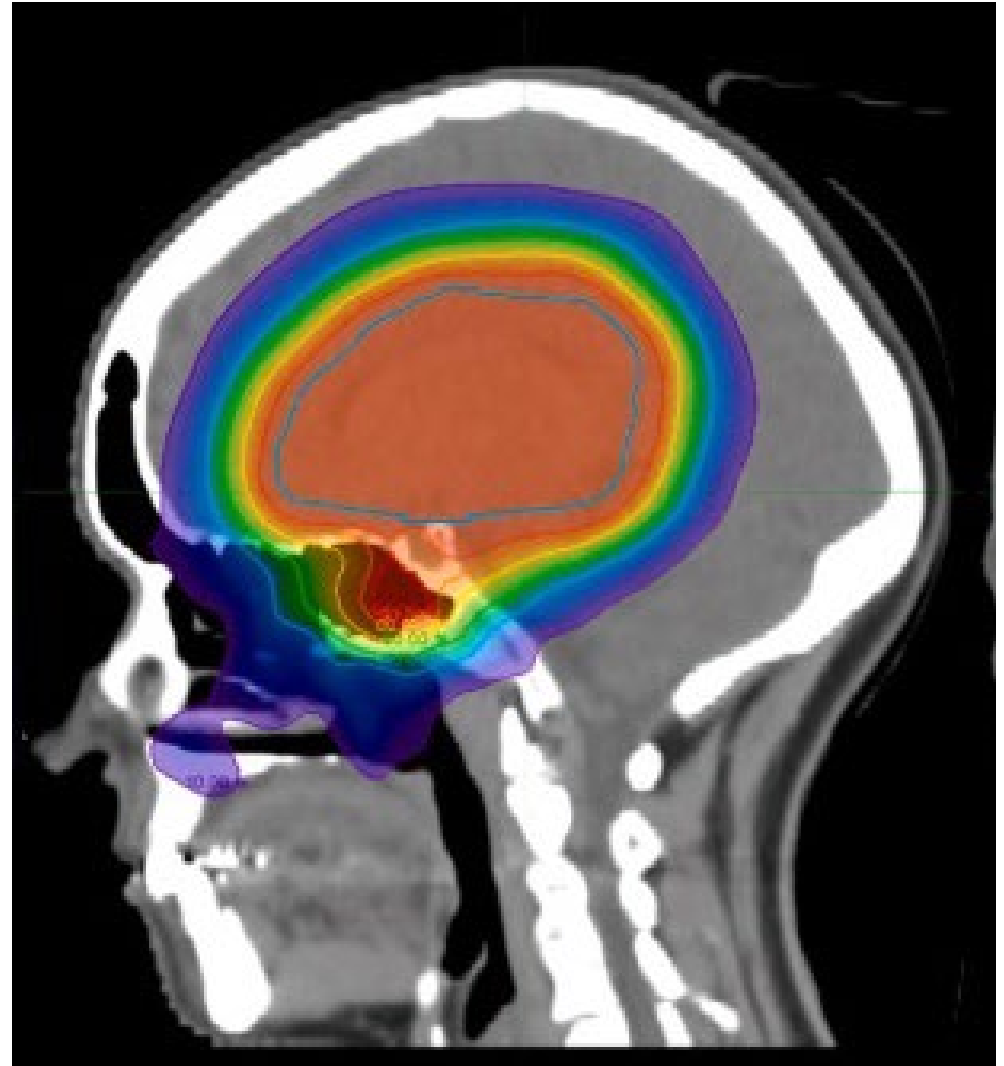
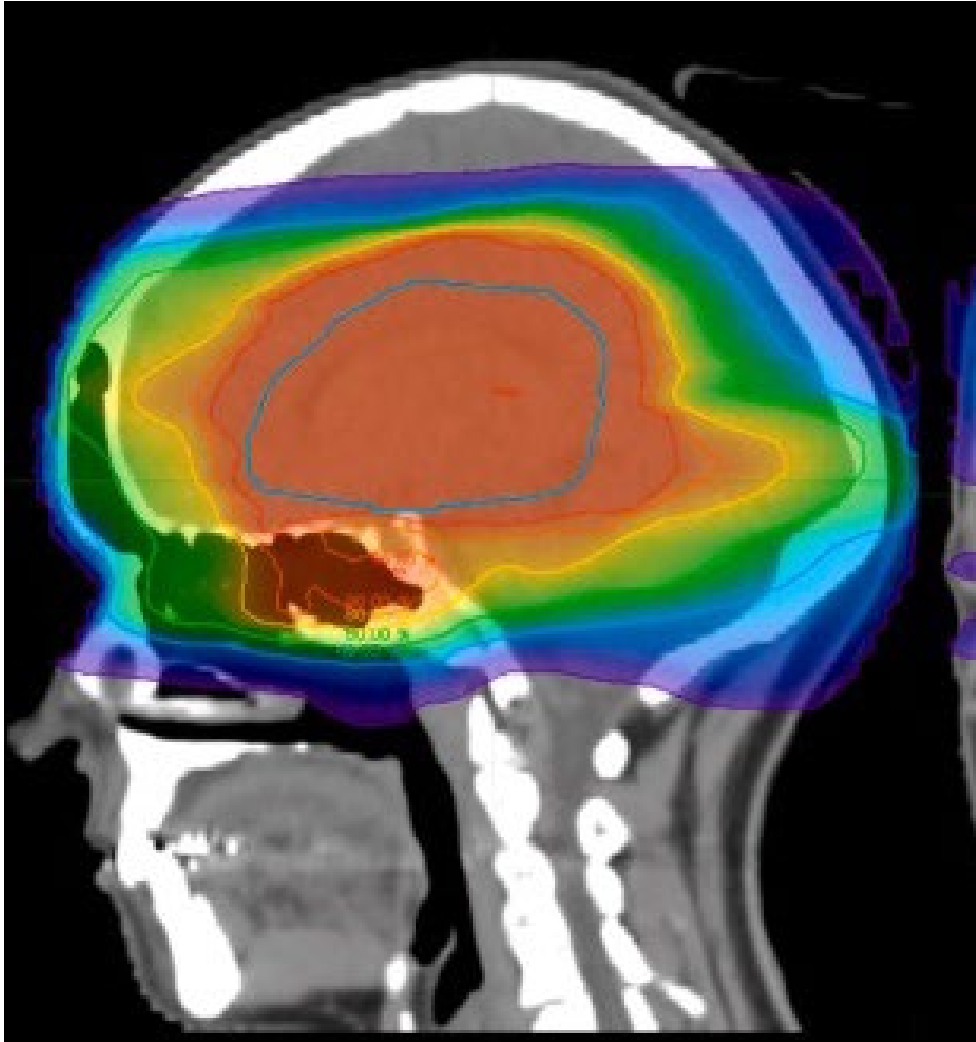
Dose increases before rapidly decreasing to zero



Radiotherapy of whole central nervous system



Radiotherapy of brain tumor



Special for proton therapy - uncertainties

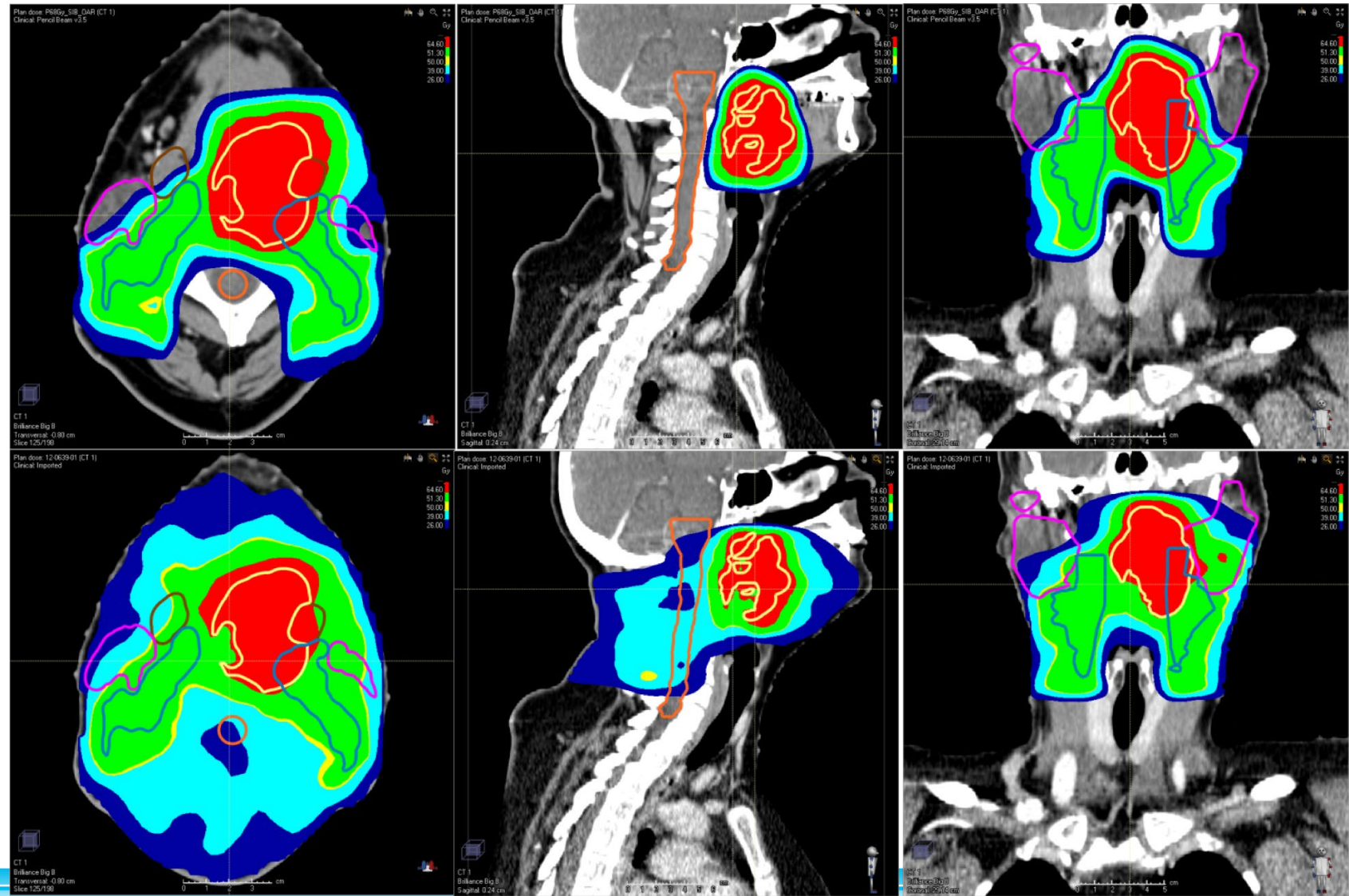
1. Uncertainty in the biological effect of the proton dose
2. Direction-dependent uncertainties
 - 1) Patient movements
 - 2) Calculation of proton dose from CT images
3. Changes inside the patient → require re-planning of treatment (resource-demanding)

Uncertainty in the biological effect of proton dose

What do we know?

- Children: Evidence that proton therapy reduces
 - Impairments in brain function
 - Hormonal disturbances
 - Hearing loss
 - Damage to blood vessels (e.g., heart and brain)
- Lung cancer: Randomized trial showed similar level of side effects
- Esophageal cancer: Randomized trial ↓ side effects
- Head and neck cancer: Randomized trial ↓ side effects (need of feeding tube, weight loss)
- Prostate cancer: Randomized trial showed similar level of side effects
- Radiation-induced cancer: Registry studies: ↓

Double planning



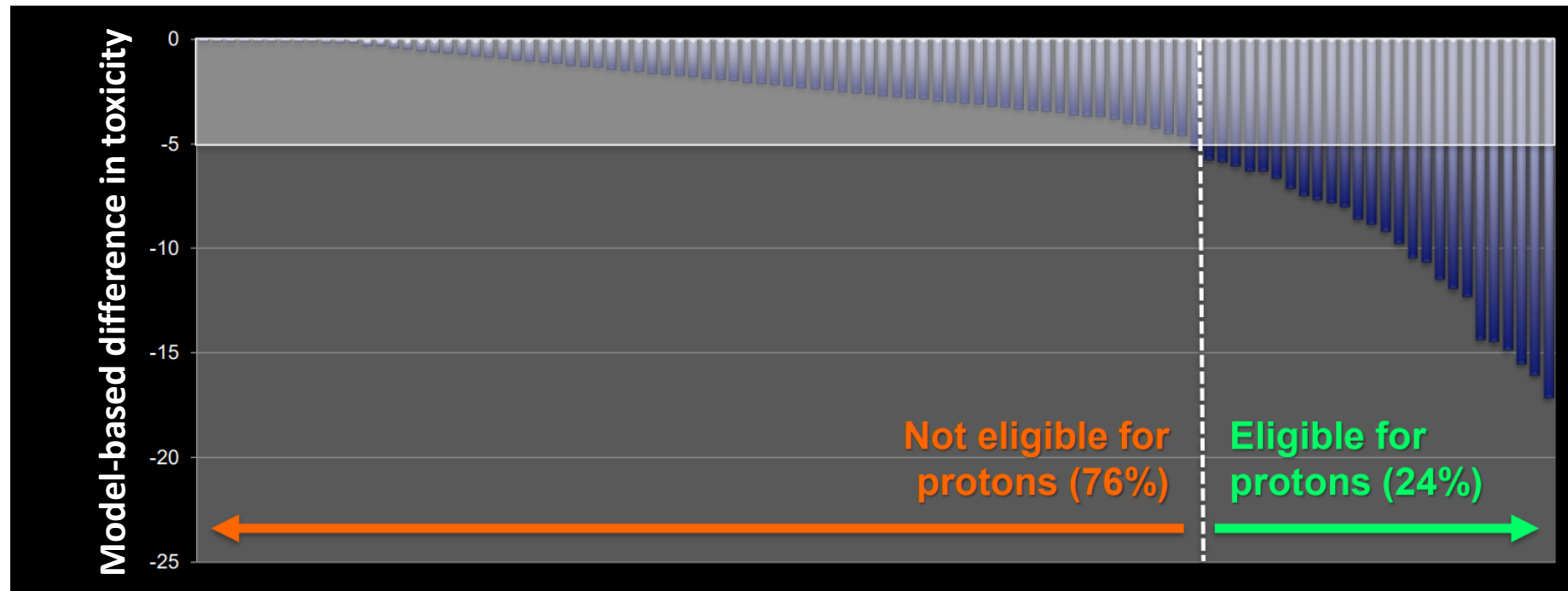
Model-based selection

Endpoint: tube feeding dependence, head and neck cancer



umcg

Hans Langendijk *et al*

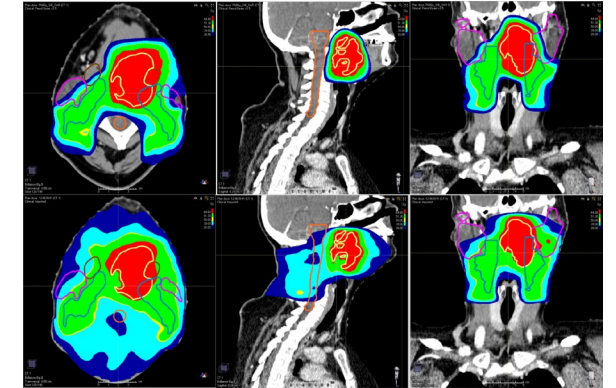
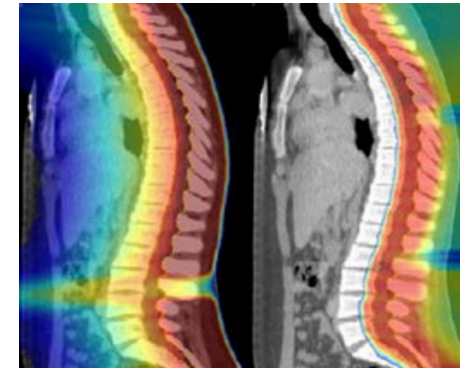


→ Not all patients need proton therapy

How to decide?

- Double planning – strict model (dosimetric) criteria

- Standard indications
Not necessary
with double planning



- Clinical trials

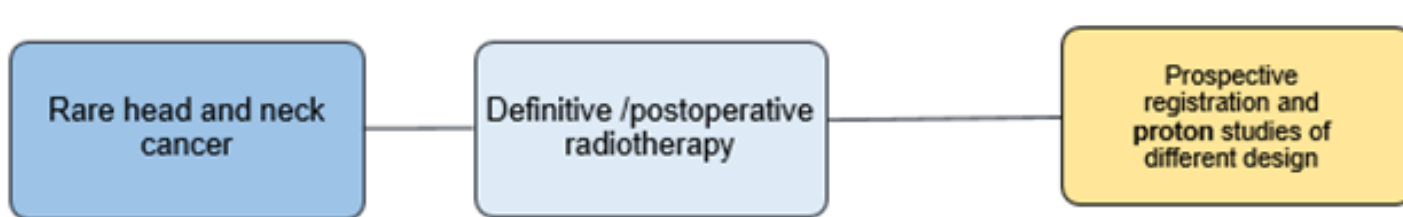
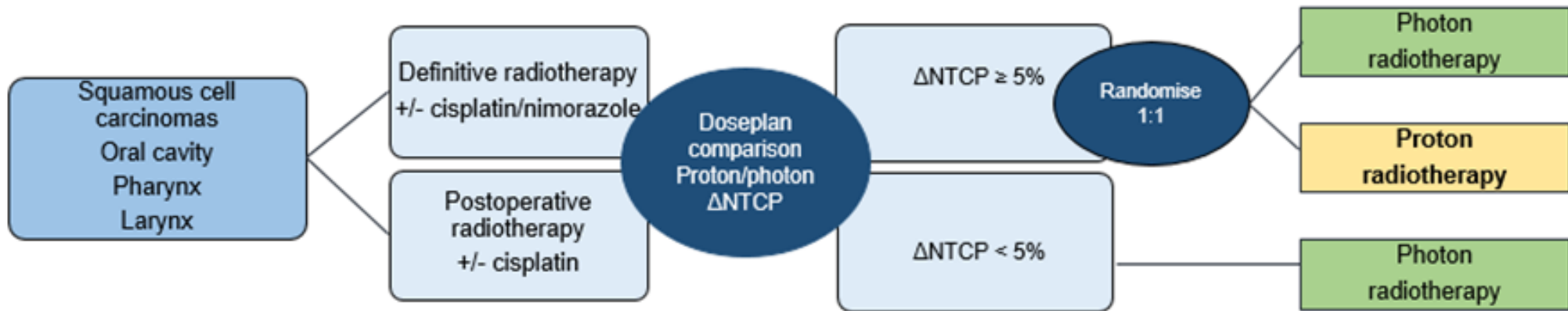


Current clinical trials plans

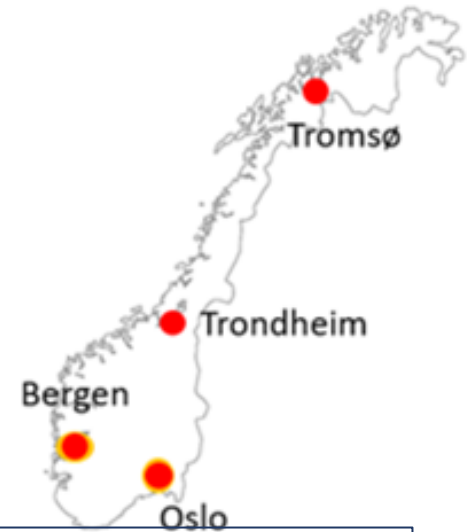
- PRO-GLIO – CNS - RCT
- SACRO, Fa-RMS – sarcomas
- Pediatric cancer trials – pediatric cancer trials
- RADPAINT – head and neck cancer - dosepainting - RCT
- PROTECT – oesophageal cancer - RCT
- PRORADNOR – head and neck cancer - RCT
- Sarcoma trial – soft tissue sarcoma
- PRORECT - rectal cancer - RCT
- PRO-Hodgkin - Hodgkin's lymphoma



PRORADNOR



Translational studies
Biomarkers for personalised cancer treatment.



PI Hanne Eide, Oslo University Hospital

Conclusions

- Proton therapy is a more resource-demanding form of radiotherapy.
- It spares low to moderate doses – differences in side effects are difficult to measure – but it probably reduces the risk of radiation-induced cancer.
- Patient selection:
 - Standard indications: Children and young adults with tumors in or near the central nervous system
 - Double planning – photon vs proton
 - Nordic clinical studies are important to gain more knowledge about which patients benefit most from proton therapy