Selection of candidates for proton therapy in a national multidisciplinary setting - the Danish experience

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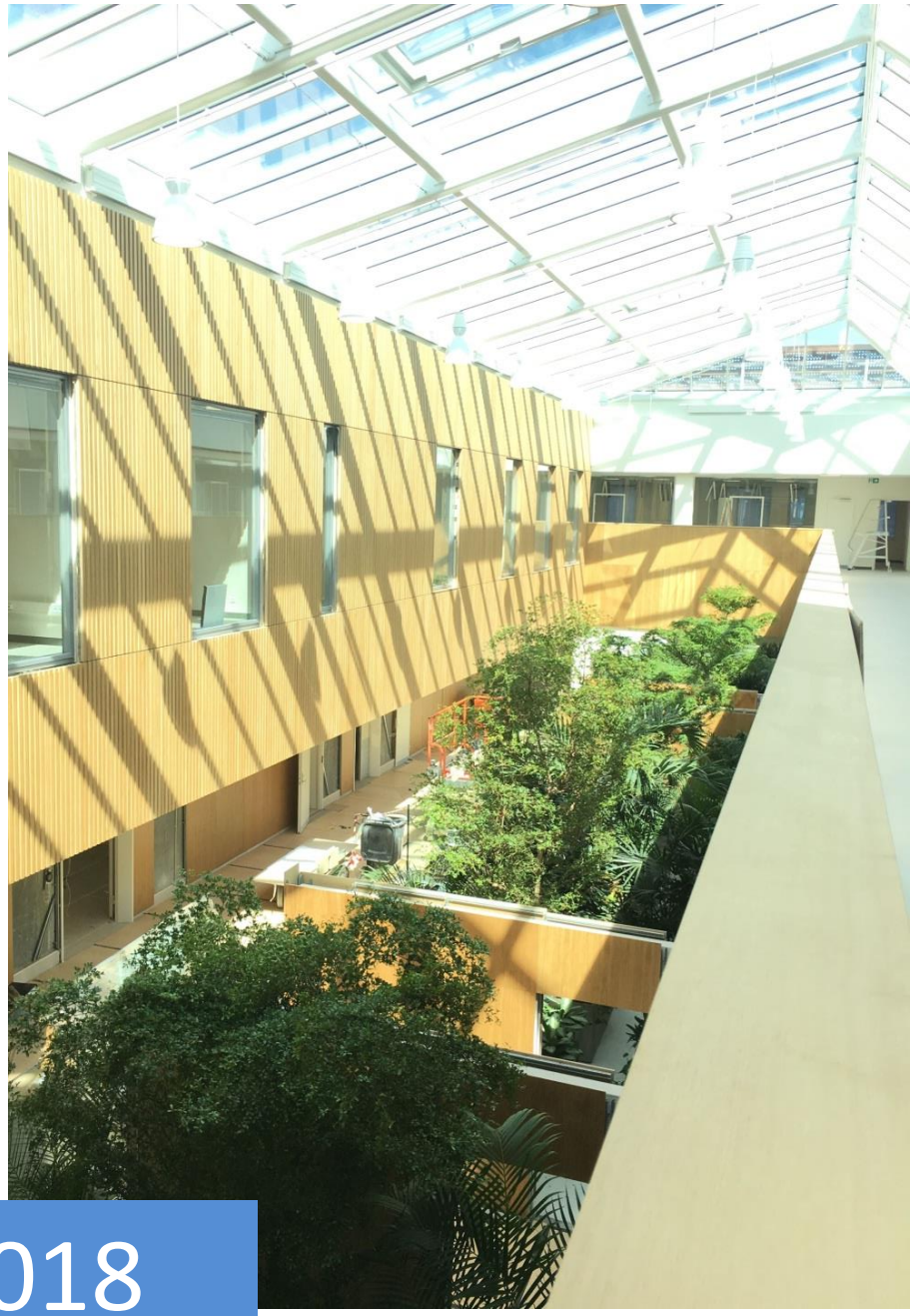
ENLIGHT

2017 Aarhus

The Danish Centre for Particle Therapy - A national proton therapy facility

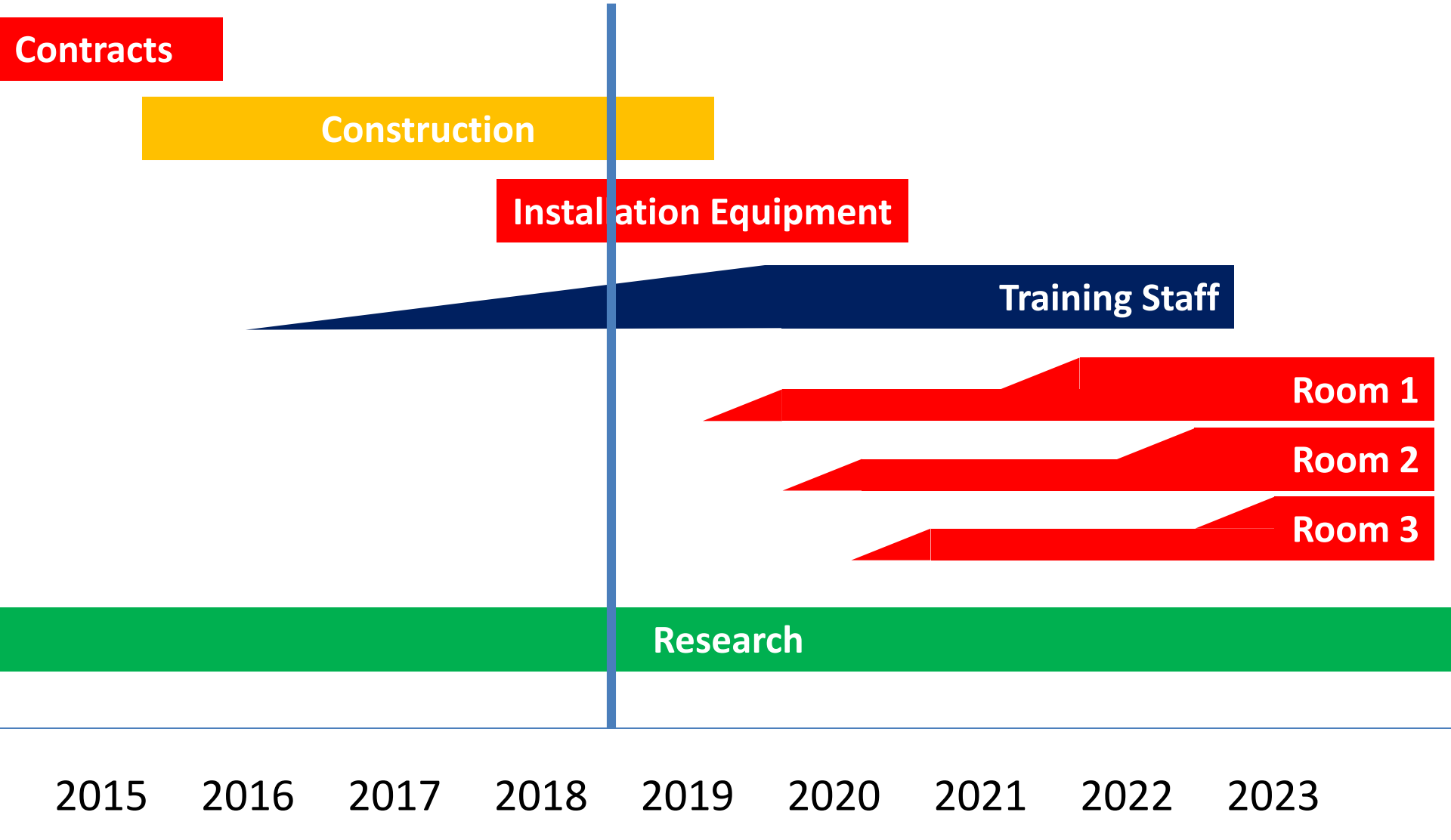
- Cyclotron, 3 gantries, PBS, Varian Probeam
- 1 research room w/ horizontal beam, PBS
- PET/CT, MRI, CT
- Initial costs covered by donation and Danish government
- Running costs part of public health care service
- Clinical start Jan 2019 (CNS, HN, PED)
- Ramp up >1000 patients/year by 2024, 85% in clinical trials


June 10, 2017



June 2018

Timeline


Contracts
Construction
Installation Equipment
Training Staff
Room 1
Room 2
Room 3
Research
2015
2016
2017
2018
2019
2020
2021
2022
2023

Treatment planning workshop Dec 4, 2017

DCPT proton therapy @DCPTprotons · 3 t
National #ProtonTherapy treatment planning workshop with speakers Håkan Nyström and @mschwarz. Participant from 6 Danish centres and #DCPT.

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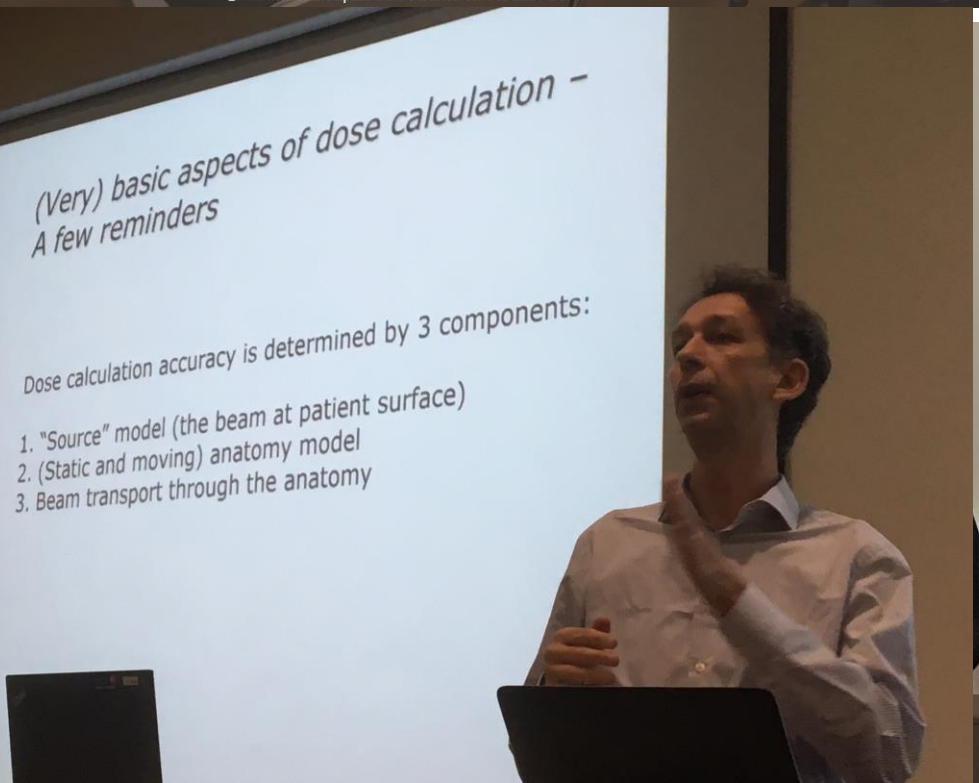

DCPT proton therapy @DCPTprotons · 3 t
National #ProtonTherapy treatment planning workshop with speakers Håkan Nyström and @mschwarz. Participant from 6 Danish centres and #DCPT.

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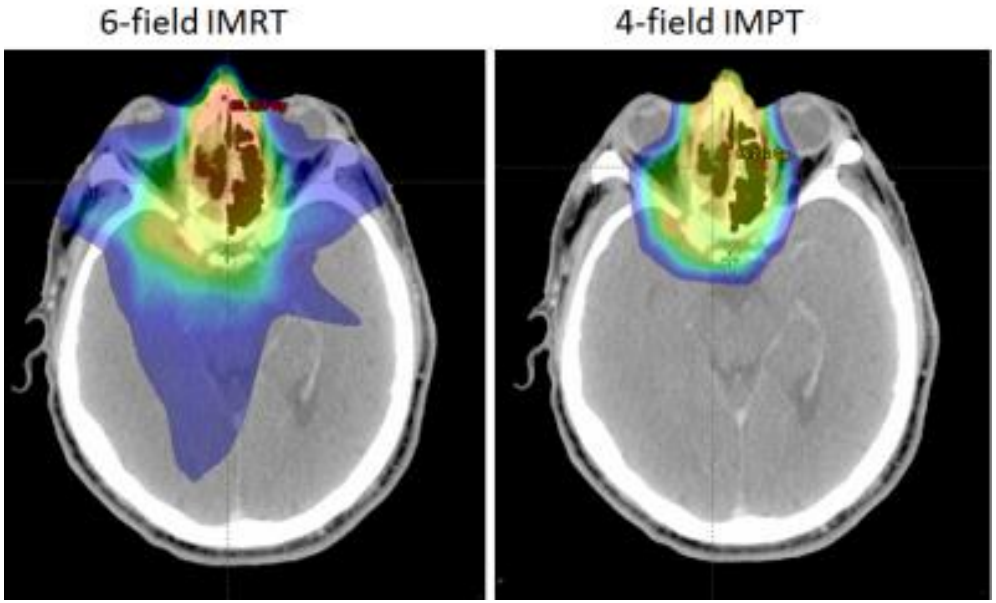
Indications for particle therapy

1. Reduce serious complications
    1. *especially relevant for tumours near the CNS*
    2. *reduce secondary cancer risk, especially in children and adolescents*
2. Dose escalation and increased tumor control

Comparison of dose distribution



Examples of ”established” indications

Pediatric and adolescent

CNS: medulloblastoma, arteriovenous malformations, ependymomas, craniopharyngiomas, CNS germ cell tumours, primitive neuroectodermal tumours, and low grade gliomas

Non-CNS: sarcomas including chordoma and chondrosarcoma, rhabdomyosarcoma, Ewing’s sarcoma, pineal tumours, and lymphoma.

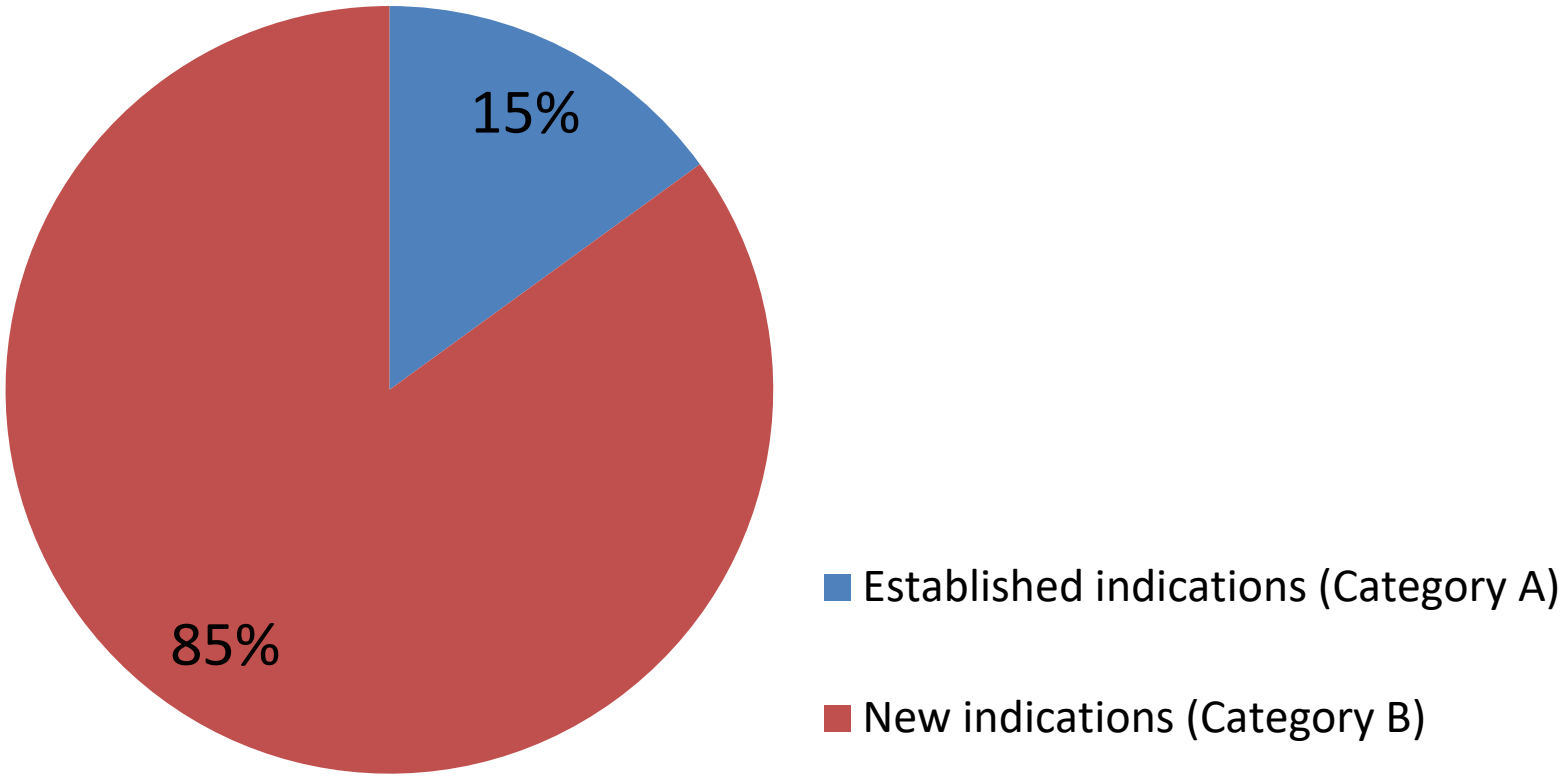
Adults

CNS: arteriovenous malformations, benign meningioma, neuromas, craniopharyngioma, CNS germ cell tumours, and low grade gliomas

Non-CNS: sarcoma including chordoma and chondrosarcoma, lymphoma in patients under the age of 30 years, and paranasal sinus and nasal cavity tumours.

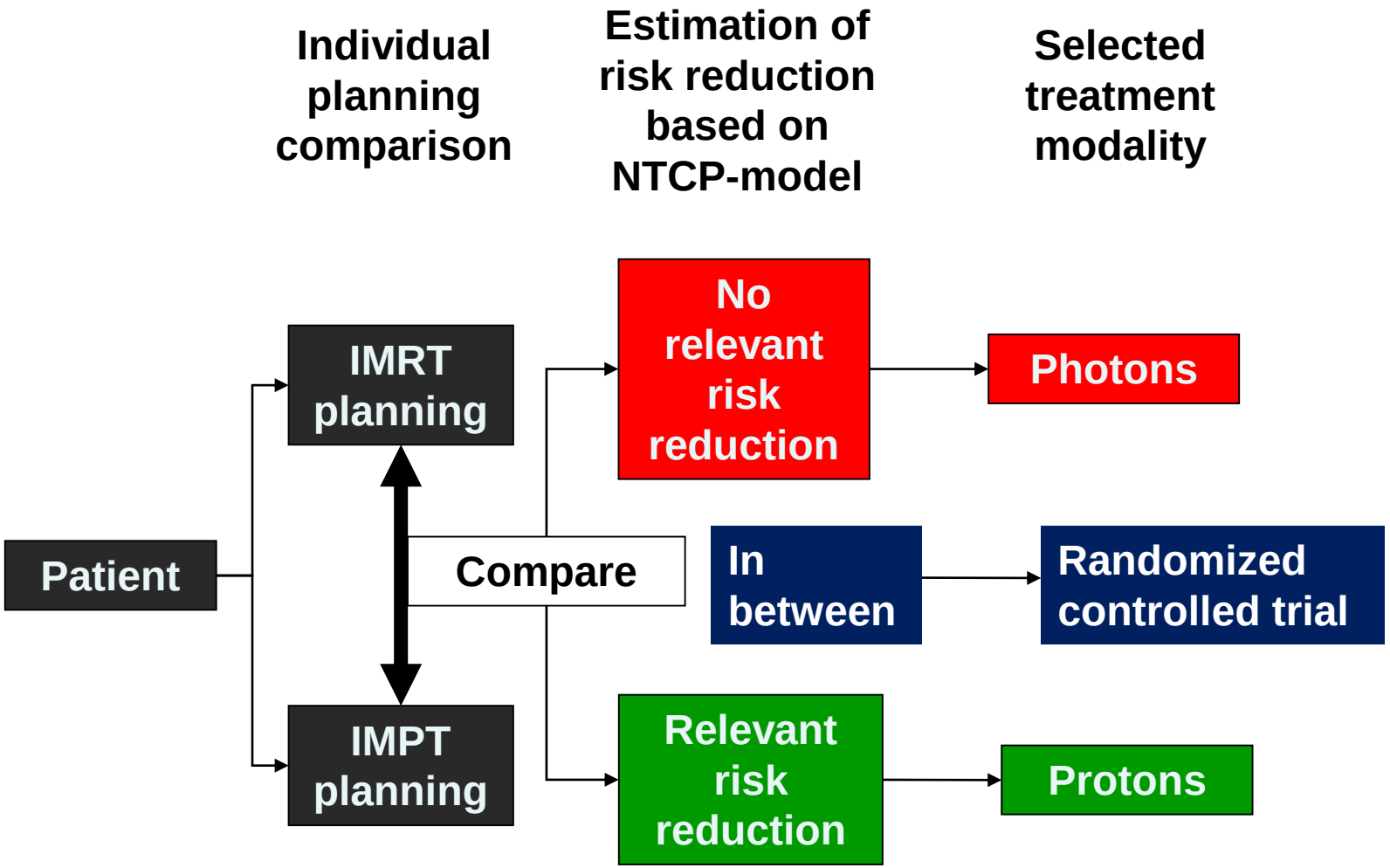
Capacity >1000 patients per year

Aim is to have 85% of all patients included in clinical trials



Model-based selection of patients

using ΔNTCP as a "predictive biomaker"



Langendijk et al, Radiother Oncol 2013

Unsolved issues in the model based approach for selection of patients

- A proper morbidity (NTCP) model requires good knowledge of morbidity dose-volume effects, and a number of clinical co-factors (age, chemo, PS, co-morbidities etc) - for many potential indications such data do not exist (yet)
- Definition of 'clinically significant morbidity' is not simple – needs to be validated and quality assured
- Requires well-functioning national / international collaborations with databases and treatment plan bank
- Method must be validated across centers and countries

Grau, Radiother Oncol 2013

Danish Multidisciplinary Cancer Groups (DMCGs)

AKUT LEUKÆMIGRUPPEN (ALG)

DANISH BREAST CANCER COOPERATIVE GROUP (DBCG)

DANISH COLORECTAL CANCER GROUP (DCCG)

DANISH HEAD AND NECK CANCER GROUP (DAHANCA)

DANSK OKULÆR ONKOLOGI GRUPPE (DOOG)

DANSK ANAL CANCER GRUPPE
Pt. ingen hjemmeside - nærmere følger

DANSK GYNÆKOLOGISK CANCER GRUPPE OG DATABASE (DGCG & DGCD)

DANSK LUNGE CANCER GRUPPE (DLCG)

DANSK LYMFOM GRUPPE (DLG)

DANSK MELANOM GRUPPE (DMG)

DANSK MYELOMATOSE STUDIEGRUPPE

DANSK NEUROONKOLOGISK GRUPPE (DNOG)

DANSK PANCREAS CANCER GRUPPE (DPCG)

DANSK PÆDIATRISK HÆMATOLOGI OG ONKOLOGI (DAPHO)

DANSK SARKOM GRUPPE

DANSK STUDIEGRUPPE FOR KRONISKE MYELOIDE SYGDOMME

DANSK UROLOGISK CANCER GRUPPE (DUCG)

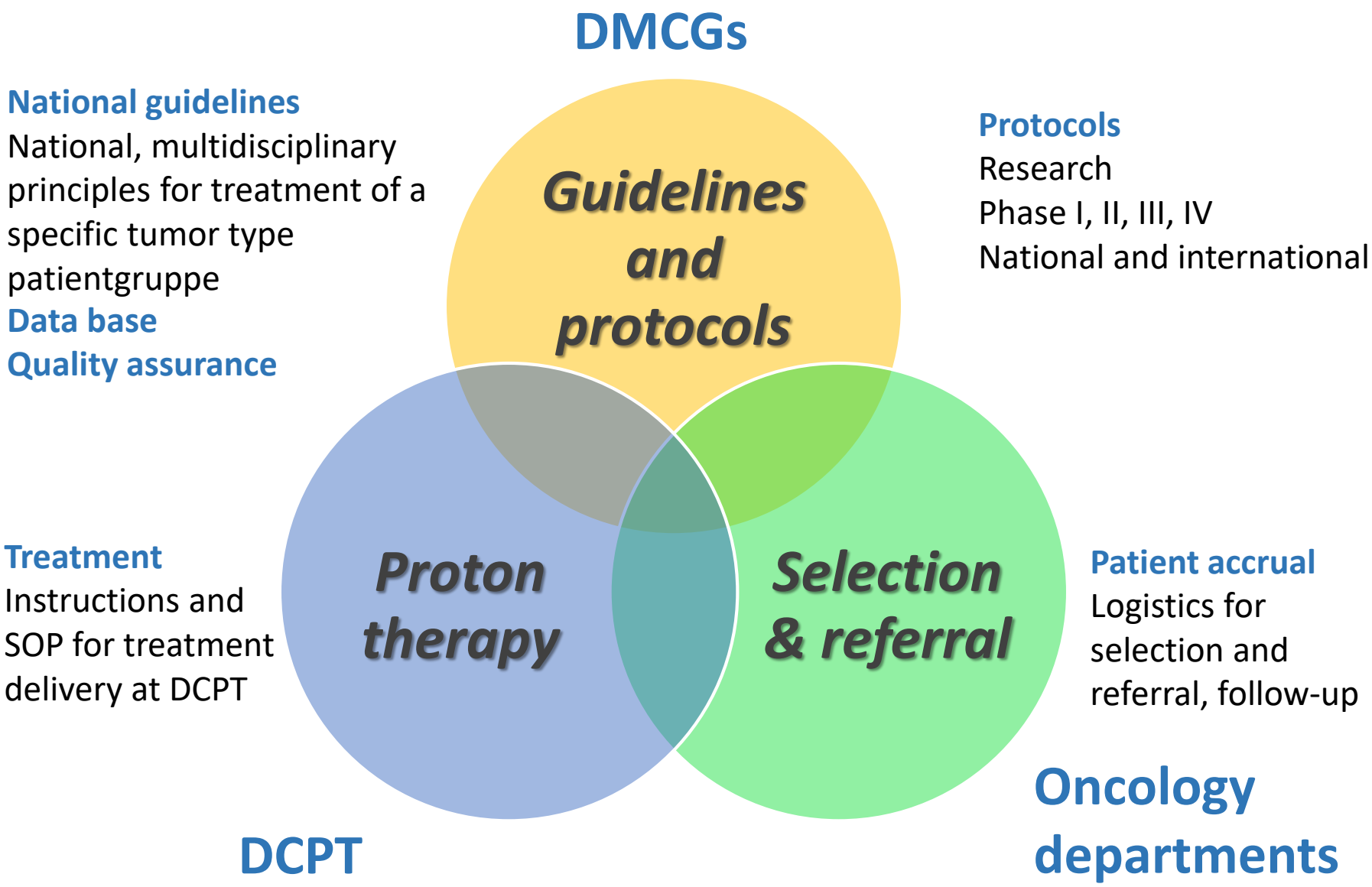
ØVRE GASTROINTESTINAL CANCER (ØGC)

DMCG-PAL

- Clinical guidelines
- Databases
- Biobanks
- Early warnings
- Research protocols
- International collaboration
- Quality assurance

Tasks for the DMCGs

- Morbidity recording inkl. PROM
- Define ”clinically relevant morbidity”
- Databases
- Dose plan bank
- NTCP modelling of existing data
- Comparative dose planning studies (IMRT – IMPT)
- Validation – national and international
- Protocol writing (non-inferiority, case control, RCT mv.)
- Conduct proton studies
- Follow-up collection
- Reporting, papers, etc.


DMCGs
National guidelines
National, multidisciplinary principles for treatment of a specific tumor type patientgruppe
Data base
Quality assurance
Guidelines and protocols
Protocols
Research
Phase I, II, III, IV
National and international
Treatment
Instructions and SOP for treatment delivery at DCPT
Proton therapy
Selection & referral
Patient accrual
Logistics for selection and referral, follow-up
DCPT
Oncology departments

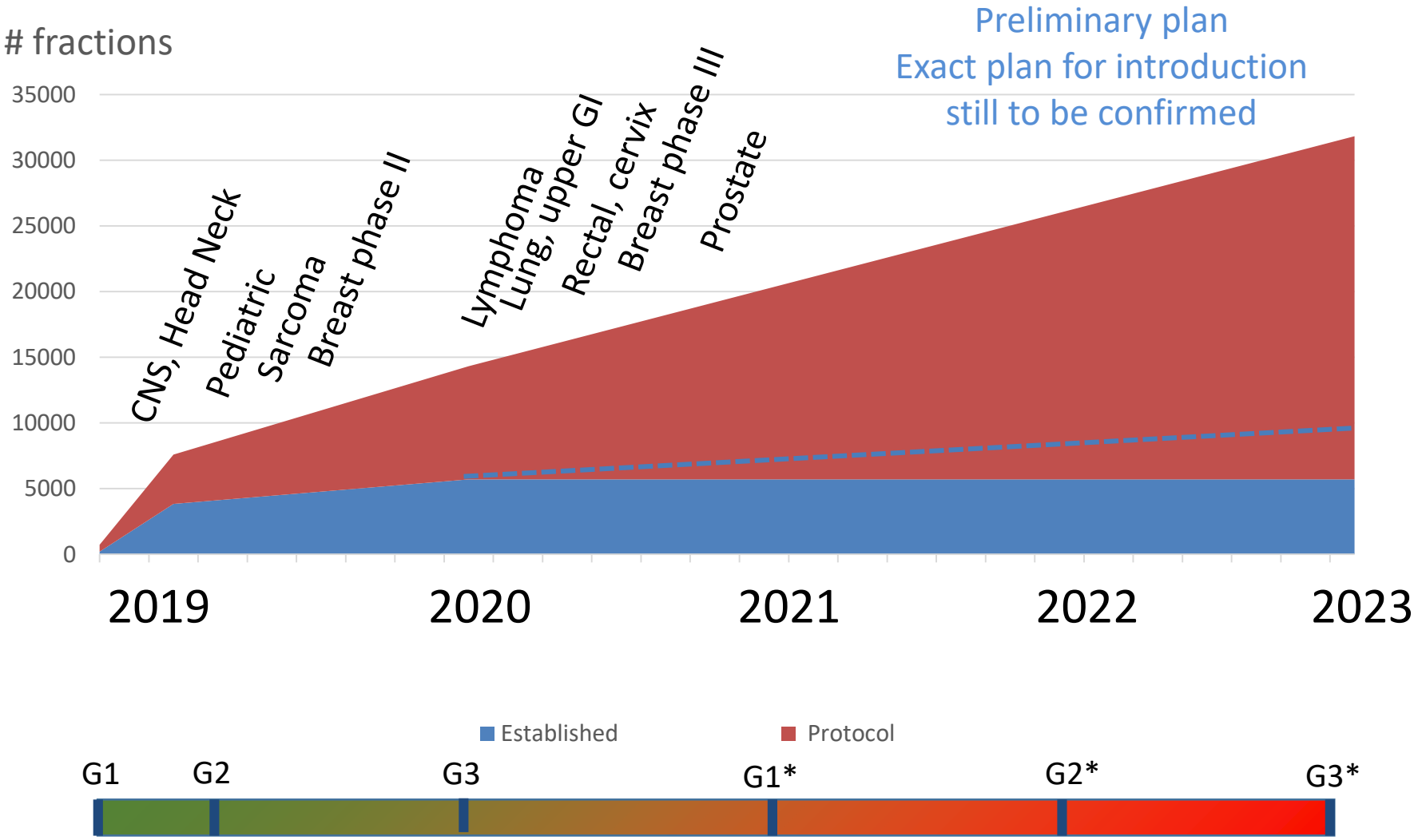
Clinical protocols developed with DMCGs




Children – DAPHO
Brain – DNOG
Eye – DOOG
Head and neck – DAHANCA
Lung – DOLG
Breast – DBCG
Upper gastrointestinal – DECV
Liver – gall bladder – DLGCG
Pancreas – DPG
Rectal – DCCG
Anal canal – DACG
Cervix – DGCG
Prostate – DAPROCA
Sarcoma – DSG




Capacity ramp-up



The European Particle Therapy Network (EPTN)

Vision and scope for clinical trials in the EPTN - ESTRO Task Force

- **Emphasis should be on performing high quality trials with properly selected candidates and using relevant, validated clinical endpoints**

- A number of **pivotal RCTs** are urgently needed, but most patients will enter **other types of controlled trials,** and we need to develop, test and validate the methodologies (e.g. “cohort multiple RCT”)
- **Model-based selection** as predictive biomarker is a useful concept for NTCP based studies, and this concept should later be extended to incorporate also TCP
- Trials involving **photons** are welcome, as particle therapy should be seen as an integral component of radiation oncology
- Prospective **data collection** also for patients treated outside of clinical trials will be promoted
- The infrastructure for particle therapy trials and prospective databases is being developed in a collaboration between EPTN and **EORTC**

Conclusions

- The Danish Centre for proton Therapy will have large capacity for clinical trials; the plan is to have 85% of patients in trials
- The clinical trials with proton therapy will be developed though a close collaboration with the Danish Multidiciplinary Cancer Groups (DMCG)
- In most cases particle therapy will be applied to prevent radiation-induced side effects and/or induction of secondary tumours
- For the validation of these types of applications, the model-based approach with comparative dose planning will be used, to select patients for protocols (randomized or non-randomized)
- Collaboration on trials and uniform prospective data registration is essential. We will collaborate through the European Particle Therapy Network (EPTN) and other channels