PROGRAMME
DCCC Radiotherapy Annual Meeting 2024

Monday November 18

09:30-15:00 DESIRE national user meeting (plenary)
14:00-15:00 Open session in reirradiation workshop (meeting rooms, first floor)

16:00-16:10 Welcome to DCCC RT Annual Meeting

16:10-17:45 Advances in adaptive radiotherapy
Moderators: WP4 chairs Laura Patricia Kaplan, Næstved, Thomas Ravkilde, Aarhus, Mette van Overeem Felter, Herlev

- Status from the WP4 Group by WP chairs
- The clinical rational for adaptive radiotherapy – Mette van Overeem Felter, Herlev
- Offline adaptive radiotherapy
    - Adaptive proton therapy – Ulrik Elstrøm, Aarhus
    - Lung cancer – Hella Sand, Aalborg
- Online adaptive radiotherapy
    - Development and implementation of online adaptation using ETHOS
        - Daily IGRT versus daily online ART for patients with prostate cancer – Kirsten Jakobsen, Næstved
        - Anal cancer/bladder cancer – Patrik Sibolt, Herlev
    - Development and implementation of online adaptation using MR-linac
        - Pancreas/cervix cancer – Anders Bertelsen, Odense
        - Lung Cancer – Kristian Boye, Copenhagen
    - Development and implementation of online adaptation using other software
        - Rapid-Care: A phase II trial for fast track palliative radiotherapy for bone metastases – Rune Thing, Vejle
        - Dose tracking/motion management – Thomas Ravkilde, Aarhus

17:50-18:30 Flash talks session #1
Moderators: Faisal Mahmood, Odense & Martin Berg, Vejle

- Setup repeatability with cone-beam CT is similar for radiotherapy in deep-inspirational breath-hold and free-breathing in paediatric patients: results of the TEDDI trial – Daniella Østergaard, Copenhagen
- Simulation-free online adaptive radiotherapy for patients with metastatic spinal cord compression – a feasibility study – Lisette Sandt, Herlev
- Drift motion and setup errors of mediastinal lymph nodes during DIBH radiotherapy of lung cancer – Sara Shahzadeh, Aarhus
- First clinical online real-time motion-including prostate and bladder dose reconstruction during prostate SBRT delivery – Per Poulsen, Aarhus
- Predicting Outcomes in Head and Neck Cancer: The Role of Technological Advancements in Radiotherapy – Sarah Stougaard, Odense
- Time-dependent diffusion MRI as a potential quantitative imaging biomarker for radiotherapy – Minea Jokivuolle, Odense

- Systematic differences in derived diffusion MRI parameters in pancreatic cancer across centers – Anne L. H. Bisgaard, Odense

19:00 Networking dinner

Tuesday November 19

08:20-08:25 Welcome & introduction to programme

08:25-09:05 Presentation of new workgroups
Moderators: Jesper Eriksen, Aarhus & Stine Korreman, Aarhus
- Reirradiation – Lone Hoffmann, Aarhus & Heidi S. Rønde, Aarhus
- Palliative RT – Lars Fokdal, Vejle & Gitte Persson, Herlev
- Recurrence mapping – Jasper Nijkamp, Aarhus & Ivan Vogelius, Copenhagen
- NIMBUS national MR development – Faisal Mahmood, Odense & Jesper Kallehauge, Aarhus

09:05-09:50 Flash talks session #2
Moderators: Claus Andersen, Risø & Ivan Vogelius, Copenhagen
- Skin sparing of fractionated FLASH in a murine model – Line Kristensen, Aarhus
- Experimental evaluation of the Effects of Hypoxia on FLASH – Anna Holtz Hansen, Aarhus
- Spectral CT in radiotherapy – Jens Edmund, Herlev
- An interactive deep-learning workflow for head and neck gross tumor volume segmentation – Jasper Nijkamp, Aarhus
- Sharing AI delineation functions using a national data infrastructure – Simon Long Krogh, Odense
- Attitudes towards AI-generated risk prediction in patients with early breast cancer: a multi-center survey – Frederik Voigt Carstensen, Copenhagen
- Development of national AI models for automated target delineation in breast cancer radiotherapy for the 'DBCG DL Nation' prospective randomized trial – Emma Skarsø Buhl, Aarhus
- AI-based dose prediction to identify suboptimal radiotherapy treatment plans – Camilla Panduro Nielsen, Odense

09:50-10:15 Coffee

10.15-10:35 NARLAL 2 setup and outcome – Tine Schytte, Odense
Moderator: Mette van Overeem Felter, Herlev

10:35-12:00 Re-think interactive session: Design and conduct of national radiotherapy trials
Moderators: Mette van Overeem Felter, Herlev, Sidsel Højklint Poulsen, Copenhagen, Anne Bisgaard, Odense & Camilla Panduro Nielsen, Odense

12:00-12:50 Lunch

12:50-13:45 Flash talks session #3
Moderators: Claus Behrens, Herlev & Cai Grau, Aarhus
- Internal mammary node irradiation in node-positive breast cancer patients treated 2007-2014: The DBCG IMN2 study – Anders W. Mølby Nielsen, Aarhus
- Validating the ESTRO target consensus: pattern of breast cancer failures in the DBCG Skagen trial 1 – Kristine Høgsbjerg, Aarhus

- Quality assurance of internal mammary node irradiation in the DBCG IMN2 study 2007-2014 – Lasse Refsgaard, Aarhus
- Whole brain radiation therapy for patients with brain metastases: Are we able to select the right patients for treatment? – Lars Fokdal, Vejle
- Pre-trial quality assurance in the Nordic small cell lung cancer trial – Sara Linde, Aarhus
- Exploring alternative endpoints after local therapy in patients with EGFR or ALK mutated non-small cell lung cancer – Michael Ruben Teindl Laursen, Herlev
- Heart and Lung Dose as Predictors of Overall Survival in Patients with Locally Advanced Lung Cancer. A Danish National Multicenter Study – Agon Olloni, Odense
- Impact of elective target and nodal boost on acute gastrointestinal toxicity in cervix cancer: EMBRACE-II findings – Mayuri Charnalia, Aarhus
- Assessing treatment plan quality in DAHANCA 35: A comparative analysis of photon and proton radiotherapy – Camilla Panduro Nielsen, Odense
- Proton therapy for second primary breast cancer – first experience and presentation of a new DBCG prospective cohort study – Stine Elleberg Petersen, Aarhus

13:45-14:05 Coffee

14:05-14:45 Emerging national trials and initiatives
Moderators: Morten Høyer, Aarhus & Jimmi Søndergaard, Aalborg

- Breast cancer: DBCG DL Nation – Stine Korreman, Aarhus & Maja Maraldo, Copenhagen
- Head and neck cancer: DAHANCA 41 – Ruta Zukauskaite, Odense
- Prostate cancer: Randomized trial of focal boost and hypofractionation – Simon Buus, Aarhus
- Rectal cancer: PRORECT II – Camilla Kronborg, Aarhus

14:45-15:45 Closing session/debate: How do we improve inclusion in clinical trials?
Moderators: Birgitte Offersen, Aarhus & Gitte Persson, Herlev

Introductory talks

- Perspectives on accrual of patients in DBCG RT trials – Kristine Høgsbjerg, Aarhus
- Patterns of participation of head and neck cancer patients in DAHANCA clinical trials – Jesper Grau Eriksen, Aarhus
- Recruitment experience from ESO-SPARE – palliative radiotherapy for spinal cord compression – Gitte Persson, Herlev (tbc)
- Patient perspectives on participation in clinical trials – Anne Wilhøft Kristensen, Aarhus

General debate: How do we design trials so patients want to participate?

15:45-16:00 Closing remarks

ABSTRACTS

Flash talks session #1

- Setup repeatability with cone-beam CT is similar for radiotherapy in deep-inspirational breath-hold and free-breathing in paediatric patients: results of the TEDDI trial – Daniella Østergaard, Copenhagen
- Simulation-free online adaptive radiotherapy for patients with metastatic spinal cord compression – a feasibility study – Lisette Sandt, Herlev
- Drift motion and setup errors of mediastinal lymph nodes during DIBH radiotherapy of lung cancer – Sara Shahzadeh, Aarhus
- First clinical online real-time motion-including prostate and bladder dose reconstruction during prostate SBRT delivery – Karolina Klucznik, Aarhus
- Predicting Outcomes in Head and Neck Cancer: The Role of Technological Advancements in Radiotherapy – Sarah Stougaard, Odense
- Time-dependent diffusion MRI as a potential quantitative imaging biomarker for radiotherapy – Minea Jokivuolle, Odense
- Systematic differences in derived diffusion MRI parameters in pancreatic cancer across centers – Anne L. H. Bisgaard, Odense

Setup repeatability with cone-beam CT is similar for radiotherapy in deep-inspirational breath-hold and free-breathing in paediatric patients: results of the TEDDI trial

Daniella Elisabet Østergaard (1+6), Laura Rechner (2),Anni Young Lundgaard (3), Hanne Krogh Rose (4), Jolanta Hansen (4), Ivan Richter Vogelius (1+6), Lisa Lyngsie Hjalgrim (5), and Maja Vestmø Maraldo (1+6)

(1) Section of Radiotherapy, Department of Oncology, Rigshospitalet, Copenhagen, Denmark
(2) Department of Oncology, Herlev and Gentofte Hospital, Herlev, Denmark
(3) Department of Oncology, Odense University Hospital, Odense, Denmark
(4) Department of Oncology, Aarhus University Hospital, Aarhus, Denmark
(5) Department of Pediatric Haematology and Oncology, Rigshospitalet, Copenhagen, Denmark
(6) Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark

Intro:
Deep inspirational breath-hold (DIBH) is a standard motion management strategy for adults, but it is not used as a standard for children. DIBH has been proven feasible for children as young as five years old, hence the TEDDI trial introduces radiotherapy (RT) delivery in DIBH to children. In this context, evaluation of setup position uncertainties is needed. Here, we report the setup repeatability for children treated with RT in either DIBH or FB using daily cone-beam CT (CBCT).

Method:
Seven patients were included, and they all had treatment plans in both DIBH and FB made. Daily CBCT imaging was used for setup verification. Setup repeatability was assessed with offline registration of CBCTs to the planning-CT. A delta-value for offline-online registration for the translations (Vrt, Lng, Lat), and length of the delta-vector was calculated. Levene's test was used to test for homogeneity of variance. Anterior-posterior distance (APD) on CBCTs was measured to assess the quality of the breath-holds (BH). Motion uncertainty for FB and DIBH was calculated using the van Herk recipe.

Results:
Four patients were treated in DIBH, and three patients were treated in FB. The two groups were comparable in age (14-16y) and height (162-185cm). The clinical tumour volume varied from 29 ml to 570 ml for both groups. All fractions (F) was evaluated for DIBH and FB, 84F and 43F, respectively. The absolute delta for corrections demonstrated no differences in the size and distribution of corrections. This was confirmed by Levene's test which showed no significant difference for the two groups (p-value = 0,45). APD indicated consistent quality of the BH. Motion uncertainties for DIBH and FB were similar (∑ DIBH/FB: Vrt 0,05/0,03, Lng 0,14/0,12, Lat 0,05/0,05, σ DIBH/FB: Vrt 0,10/0,10; Lng 0,14/0,14; Lat 0,09/0,08).

Conclusion:
In the TEDDI trial there was no difference in setup repeatability with CBCT for DIBH or FB. Thus, DIBH should be considered as an option for children.

Simulation-free online adaptive radiotherapy for patients with metastatic spinal cord compression – a feasibility study

Sandt LJ (1), Åström LM (1), Nielsen AM (1), Persson GF (1,2)

(1) Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte, Copenhagen, Denmark.
(2) Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark

Introduction:
Metastatic spinal cord compression (MSCC) affects one in five patients with advanced cancer and requires urgent treatment. Obtaining a planning CT for target contouring and dose planning often involves lengthy stays and return visits, which can be exhausting for frail patients. A simulation-free approach, using the patient's diagnostic CT for treatment planning, eliminates the need for a separate planning CT. Combined with CBCT-guided online adaptive radiotherapy (oART), this allows real-time adjustment of the treatment plan by accounting for daily changes in position and anatomy.

The study aimed to evaluate the feasibility and time consumption of different simulation-free oART workflows for patients with MSCC to identify the best option for clinical use.

Materials and Methods:
Diagnostic CTs from patients previously treated for MSCC were used for treatment planning, while CBCT scans from their first treatment sessions served for simulation. Three simulation-free workflows were assessed: rigid contour propagation (RCP), deformable contour propagation (DCP), and an unsupervised workflow (deformable propagation without manual corrections). Time consumption, contours, and dose plans were evaluated for feasibility.

Results:
A total of 90 simulation-free treatments were simulated (based on 25 patients with 30 target sites). Median time consumption was 7.49 min. for RCP, 6.57 min. for DCP, and 3.27 min. for the unsupervised workflows. Contours from the adaptive plans closely matched those from the diagnostic CTs. All adaptive plans met all clinical goals for dose coverage.

Conclusion:
The unsupervised workflow was the fastest, but its full potential needs further study. The DCP workflow showed the greatest contouring accuracy and comparable dose coverage to the diagnostic CT, making it the preferred approach for future oART treatments.

Drift motion and setup errors of mediastinal lymph nodes during DIBH radiotherapy of lung cancer

Shahzadeh S (1), Poulsen P (1,2), Hoffmann L (2), Ehmsen ML (1), Knap MM (2), Worm E (2), Møller DS (2)

(1) Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
(2) Department of Oncology, Aarhus University Hospital, Aarhus, Denmark

Introduction:
Deep-inspiration breath-hold (DIBH) during lung radiotherapy can potentially reduce lung and heart dose compared to free breathing treatments. However, breath-hold variations may impact the treatment accuracy. We investigated the 3D geometrical errors and intrafraction drift motion of mediastinal lymph node (LN) targets during DIBH lung cancer treatments.

Methods:
This study includes three locally-advanced lung cancer patients treated with 5-6 field IGRT for primary tumors and involved mediastinal LNs. Each field was delivered in DIBH guided by an external gating block with 2mm external gating window. The mediastinal LN targets were marked with implanted fiducial markers. All fields had durations shorter than 20s and were delivered in a single breath-hold. For 6-9 fractions per patient, 5Hz fluoroscopic kV x-ray images were acquired during treatment delivery perpendicular to the treatment beam. Post-treatment, the marker positions in each kV image were used to determine the 3D marker motion in patient coordinates during treatment by a probability-based method. For all monitored fields, the mean LN position error relative to the planned position as well as the intra-field drift motion from the first 3s to the last 3s of the field delivery were determined.

Results:
The mean setup error during field delivery was -2.25±4.5mm (LR), 3.5±4.8mm (CC), and 2.8±3.0mm (AP). The three patients had systematic cranial drift motion during field delivery of 1.9mm, 5.5mm, and 5.1mm, respectively. Averaged over all three patients the intra-field drift motion was 0.4±0.9mm (LR), 3.8±2.1mm (CC), and 0.1±2.0mm (AP).

Conclusion:
A relatively large systematic cranial drift motion of 1.9-5.5mm occurred during DIBH field delivery despite a small external gating window of 2mm. Future analysis (performed before the DCCC-RT Annual Meeting) will include more patients as well as motion-including dose reconstruction for the LN targets.

First clinical online real-time motion-including prostate and bladder dose reconstruction during prostate SBRT delivery

Karolina A Klucznik(1), Thomas Ravkilde(2), Simon Skouboe(1), Paul Keall(3) ,Laura Happersett(4), Hai Pham(4), Brian Leong(4), Pengpeng Zhang(4), Grace Tang(4), Per R Poulsen(1,2)

(1)Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark(1)
(2)Department of Oncology, Aarhus University Hospital, Aarhus, Denmark
(3)Image X Institute, Sydney Medical School, University of Sydney, Australia
(4)Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, US

Introduction
Organ motion during prostate radiotherapy can cause dose distortions. Prostate motion monitoring to guide positioning corrections during treatment is currently possible on a conventional linear accelerator using research software. However, treatment outcome is more closely linked to the delivered dose, which is not yet available during treatment. The aim of this study was to perform the first online real-time motion-including dose reconstruction during stereotactic prostate radiotherapy (SBRT).

Methods
During prostate SBRT at the Memorial Sloan Kettering Cancer Center, the prostate motion is routinely monitored using MV-kV image pairs, and the patient's position is adjusted if the prostate position error exceeds 1.5mm (MV-kV guidance). The in-house developed software DoseTracker was integrated into this prostate SBRT workflow and utilized the prostate motion monitoring online for real-time motion-including prostate and bladder dose reconstruction during treatment for 20 patients. Motion-induced dose distortions were quantified by the differences in prostate CTV D95% and bladder V36Gy. Treatments without MV-kV guidance were simulated to assess the effect of the intrafractional patient repositioning. DoseTracker was validated against treatment planning system (TPS) dose calculations, where motion was emulated as multiple isocenter shifts.

Results
The mean(standard deviation, range) motion-induced difference in prostate CTV D95% and bladder V36Gy was -0.6%(1.1%, [-5.6,+1.6]%) and +0.1% (0.5%, [-1.0,+1.3]%) under MV-kV guidance and increased to -2.0% (6.6%, [-42.5,+1.8]%) and +4.1% (2.0%, [-5.8,+10.1]%) without MV-kV guidance. The root-mean-square error between DoseTracker and TPS doses was 0.8% (prostate CTV D95%) and 0.3% (bladder V36Gy).

Conclusion
We successfully performed world's first real-time motion including prostate and bladder dose reconstruction during prostate SBRT. MV-kV guidance accounted reliably for severe motion-induced dose distortions.

Predicting Outcomes in Head and Neck Cancer: The Role of Technological Advancements in Radiotherapy

Stougaard SW (1,2), Zukauskaite R (1), Röttger R (3), Lorenzen EB (1), Maximilian LK (1,2), Nielsen CP (1,2), Krogh SL (1), Brink C (1), Sommer JFA (1), Sarup N (1), Johansen J (1,4), Eriksen JG (5,6), Lønkvist CK (7), Friborg J (8), Hansen CR (1,2,4)

1: Department of Oncology, Odense University Hospital, Odense, Denmark
2: Department of Clinical Research, University of Southern Denmark, Odense, Denmark
3: Department of Mathematics and Computer Science, University of Southern Denmark, Odense, Denmark
4: Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
5: Department of Oncology, Aarhus University Hospital, Aarhus, Denmark
6: Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark
7: Department of Oncology, Copenhagen University Hospital Herlev, Herlev, Denmark
8: Department of Clinical Oncology, Rigshospitalet, Copenhagen, Denmark

Introduction
Over the past three decades, significant technological advancements have been made in radiotherapy (RT), yet the relationship between these developments and patient outcomes remains underexplored. This study aims to determine the impact of RT developments in head and neck (HN) cancer on survival and dysphagia and develop predictive outcome models.

Materials & Methods
Between January 2010 and December 2015, 1,948 HN cancer patients with pharyngeal and laryngeal squamous cell carcinomas were treated with definitive IMRT-based treatment at three Danish hospitals. Data on dysphagia, survival, and patient, tumour-, and RT characteristics were collected. An artificial intelligence (AI) model, validated and implemented in 2023, was applied on the CT-scans for robust and consistent segmentation of organs at risk (OAR). Initially, OAR segmentations of 150 patient CT-scans were processed by the AI model to identify potential technical issues. HN experts manually validated 15 scans to ensure accuracy before applying the model to the entire cohort. Secondly, outlier detection based on principal component analysis will be used on the OAR segmentations to identify potential abnormalities based on region of interest (ROI) features (e.g., volume, center of mass, area). Next, predictive models will be developed to determine key factors influencing survival and dysphagia, identifying significant patterns within the patient cohort. Mixed models will be used to account for repeated treatments, enhancing the reliability of the predictions while adjusting for potential confounders e.g. age, comorbidities, and tumour size. The models are expected to be generalisable and used for other side effects like xerostomia and mucositis.

Conclusion
Ultimately, this study aims to provide a comprehensive understanding of the relationship between advancements in RT and patient outcomes, offering valuable insights to improve predictions of survival and side effects in future patients.

Time-dependent diffusion MRI as a potential quantitative imaging biomarker for radiotherapy

Jokivuolle M (1,2), Mahmood F (1,2), Madsen KH (3,4), Lundell H (3,5)

(1) Laboratory of Radiation Physics, Department of Oncology, Odense University Hospital, Odense, Denmark; (2) University of Southern Denmark, Department of Clinical Research, Odense, Denmark; (3) Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital - Amager and Hvidovre, Copenhagen, Denmark; (4) Technical University of Denmark, Department of Applied Mathematics and Computer Science, Kongens Lyngby, Denmark; (5) Technical University of Denmark, Department of Health Technology, Kongens Lyngby, Denmark

Introduction

Non-invasive methods for tumor characterization are required to improve individualization of radiotherapy. Time-dependent diffusion MRI (TDD-MRI) utilizes diffusion time (td) -dependent differences in the apparent diffusion coefficient (ADC) to estimate tumor microstructure. [1] Clinical translation of TDD-MRI requires investigation of the method on clinically available systems. This study explored the ability of TDD-MRI to assess tumor heterogeneity in brain lesions on a clinical 1.5 T MRI system with moderate gradient strength (Gmax = 45 mT/m).

Materials and methods

Ten patients with brain lesions were imaged with TDD-MRI on a 1.5 T MRI scanner (Ingenia, Philips HealthCare). TDD-MRI was implemented as two standard diffusion MRI acquisitions (b-values = 0, 1250, 2500 s/mm2) with different diffusion times (td, short = 26 ms, td, long = 44 ms). The ADC maps were calculated separately for the two diffusion times, and the time-dependency (ΔADC = ADC(td, long) – ADC (td, short)) was investigated. The sign of the ΔADC reflects the dominating diffusion effect (ΔADC < 0: restricted diffusion; ΔADC > 0: diffusional exchange).

Results

The ΔADC maps indicated dominating restricted diffusion (ΔADC < 0) in contrast enhancing tumor regions, which supports the assumption of viable tumor with densely packed cells in these regions. [2] In the tumor cores, the ΔADC maps indicated dominating diffusional exchange (ΔADC > 0), which could mark disruptions of cell membranes due to necrosis. [3]

Conclusions

TDD-MRI on clinical 1.5 T MRI system showed time-dependent changes in ADC indicating areas of dominating restricted diffusion and dominating diffusional exchange. The results show promise for characterizing tumor sub-regions based on tumor microstructure for individualized radiotherapy.

References

[1] Reynaud, O. Frontiers in Physics. 2017.
[2] Eidel O et al. PLoS One. 2017.
[3] Grooten J et al. Cytokine. 1993.

Systematic differences in derived diffusion MRI parameters in pancreatic cancer across centers

Bisgaard ALH (1), Pfeiffer P (2,3), Schytte T(2,3), Bertelsen AS (1,2), Bernchou U (1,2), Mahmood F (1,2)

1: Laboratory of Radiation Physics, Odense University Hospital, Odense, Denmark
2: Department of Clinical Research, University of Southern Denmark, Odense, Denmark
3: Department of Oncology, Odense University Hospital, Odense, Denmark

Introduction
Biomarkers for prediction of outcome in patients with pancreatic cancer (PC) are warranted in order to personalize radiotherapy (RT). A single-centre pilot-study has indicated prognostic value of longitudinal diffusion-weighted magnetic resonance imaging (DWI) in PC, however, validation is required through multi-center studies. One potential challenge is that differences in patient cohorts and image acquisition techniques across centers may cause unwanted variation in quantitative DWI parameters. As a starting point for future multi-center studies, this study aims to explore for this variation in a multi-center PC patient cohort treated with RT on a 1.5T MRI-linac.

Materials and methods
This retrospective study included 167 patients with PC who were prospectively enrolled in the MOMENTUM trial (clinicaltrials.gov, NCT04075305)) at three centers. Data requests were approved by the involved centers and the MOMENTUM Data Management Task Force. Image data included pre-beam T2-weighted MRI and DWI from each RT fraction. The apparent diffusion coefficient (ADC) was extracted within clinically delineated gross tumour volumes.

Results
ADCs systematically differed between centres (median (10th and 90th percentiles) were 1.02 (0.66, 1.41), 1.13 (0.82, 1.60) and 1.15 (0.82, 1.75) mm/s2 for the three centers, respectively). DWI acquisition parameters, tumour types (primary/local recurrence/distant metastasis) and treatments (short course RT/long course RT/chemotherapy) varied across centers, factors, which may influence the ADC. Longitudinal ADC trends were observed at patient-level.

Conclusion
We have mapped the heterogeneity of a multi-center patient cohort, and detected systematic differences in derived DWI parameters across centers. These findings have broad implications on designing multi-center studies of DWI as a biomarker for prediction of outcome in patients with PC.

Flash talks session #2

- Skin sparing of fractionated FLASH in a murine model – Line Kristensen, Aarhus
- Experimental evaluation of the Effects of Hypoxia on FLASH – Anna Holtz Hansen, Aarhus
- Spectral CT in radiotherapy – Jens Edmund, Herlev
- An interactive deep-learning workflow for head and neck gross tumor volume segmentation – Zixiang (Alan) Wei, Aarhus
- Sharing AI delineation functions using a national data infrastructure – Simon Long Krogh, Odense
- Attitudes towards AI-generated risk prediction in patients with early breast cancer: a multi-center survey – Frederik Voigt Carstensen, Copenhagen
- Development of national AI models for automated target delineation in breast cancer radiotherapy for the 'DBCG DL Nation' prospective randomized trial – Emma Skarsø Buhl, Aarhus
- AI-based dose prediction to identify suboptimal radiotherapy treatment plans – Camilla Panduro Nielsen, Odense

Skin sparing of fractionated FLASH in a murine model

Kristensen L (1,2,3,4), Rohrer S (1,3), Hoffmann L (3,4), Præstegaard LH (4), Johansen JG (1,3), Grau C (1), Poulsen P (1,3), Sørensen BS (1,2,3,4)

1 Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
2 Department of Experimental Clinical Oncology, Aarhus University Hospital
3 Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
4 Department of Oncology, Aarhus University Hospital, Aarhus, Denmark

Background:
FLASH protects normal tissue from damage while effectively maintaining tumour control. This tissue-sparing effect has been demonstrated across various tissues and radiation methods. Up to 55% higher doses are required for FLASH to cause the same acute skin toxicity in mice as for conventional low-dose rates. Despite a decade of research, few have explored clinically relevant irradiation settings like fractionation. Those who have investigated fractionated FLASH have not enabled a quantitative evaluation. This study quantified the FLASH effect on acute skin toxicity using fractionated electron irradiation in a murine model.

Method:
In a water bath, the right hind leg of unanaesthetised female CDF1 mice was irradiated with a 16 MeV electron beam. The mice were randomised into groups of conventional (CONV, 0.188 Gy/s) or FLASH (228 Gy/s) dose rates. The dose was delivered in four fractions with one daily dose on four consecutive days (4 x 8.4-21.5 Gy). The radiation-induced skin toxicity on the foot was assessed daily, and the maximally reached score was used to generate dose-response curves. The protection ratio was calculated as the ratio between TD50 (dose giving 50% toxicity risk) for FLASH relative to CONV.

Results:
Fractionated electron FLASH irradiation required a 20% higher dose to cause the same skin toxicity as conventional low dose rates. The data included 4-8 mice per dose group. The worst toxicity presented itself around 13 days after first treatment.

Conclusion:
The study quantified the effect of electron FLASH, with a protection ratio of 20% for four-fraction irradiation. Compared to 46% protection with single-fraction electron FLASH, the fractionated FLASH protection is more than halved. Therefore, introducing FLASH irradiation to a fractionated scheme will aid in tissue protection for acute skin damage, but more fractions might reduce the tissue-sparing effect.

Experimental evaluation of the Effects of Hypoxia on FLASH

Anna Holtz Hansen, Line Kristensen, Lone Hoffmann, Lars Hjorth Præstegaard, Jens Overgaard, Jacob Graversen Johansen, Michael Robert Horsman, Per Rugaard Poulsen, Brita Singers Sørensen

Experimental Clinical Oncology, Department of Oncology, Research 1, Aarhus University Hospital ▪ Entrance C, Level 1, C106, Palle Juul-Jensens Boulevard 99, DK-8200 Aarhus N, Denmark

Background:
In recent years, FLASH-Radiotherapy (FLASH-RT) attracted growing interest for its ability to minimize toxicity to normal tissues while maintaining tumor control efficacy comparable to conventional (CONV) radiotherapy. However, the FLASH mechanism remains to be solved. A prominent assumption for the effectiveness of FLASH-RT suggests, that the induction of radiolytic oxygen depletion (ROD), is the main cause of radiation protection of normal tissues. This is based on the established understanding that hypoxic tissues exhibit increased radio resistance. The aim of this study is to supply experimental data on the validity of the ROD hypothesis, as an explanation for the FLASH sparing effect, by using an established radiobiological setup for in vivo irradiation of mice legs.

Methods:
The experimental setup involves four treatment groups of female C3HHeNRj mice, exposed to either CONV or FLASH electron radiation under aerobic or hypoxic conditions. Hypoxia will be induced by clamping the right hindleg with tourniquets to restrict blood supply prior to and during irradiation. The acute biological response to radiation will be measured using an acute skin toxicity assay, with skin damage scored on a scale from mild to severe. Late radiation damage will be assessed based on leg flexibility compared to the non-irradiated left leg.

Results:
The first data on clamped mouse legs with CONV confirm increased radio resistance due to the induced hypoxia. The first experiments with FLASH are planned for mid-September 2024 and the first preliminary data will be ready to present to the meeting.

Perspective:
If the protective effects of FLASH-RT are solely due to ROD, we would expect no difference between FLASH and CONV in acute or late damage grades when hypoxia is present during irradiation. This study aims to clarify the role of ROD in FLASH-RT by evaluating biological damage and considering oxygen levels during irradiation.

Spectral CT in radiotherapy

Edmund JM (1), Taasti VT (2), Sand HMB (3), Petersen SE (2), Rechner LA (1), Nielsen MS (3), Behrens C (1), Muren LP (2), Poulsen LØ (3), Persson G (1)

(1) Department of Oncology, Herlev and Gentofte University Hospital, Herlev, Demark.
(2) Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark.
(3) Department of Oncology, Aalborg University Hospital, Aalborg, Demark.

Dual-energy and photon-counting CT (DECT, PCCT) can produce novel post-processed image sets, which can provide additional quantitative and functional information. These image sets include high contrast and artifact reducing virtual monoenergetic images, blood perfusion (iodine) and non-contrast (water) maps, electron density and effective atomic number images, and visualization of different materials such as calcium plagues. These features are currently being heavily exploited in diagnostic radiology but their clinical implementation in radiotherapy (RT), where improved precision and biological information is highly warranted, is still scarce. A number of multi-disciplinary PhD studies at three hospitals (Herlev, DCPT, and Aalborg) have recently started investigating the potential RT specific benefits of DECT and PCCT.

The study aims include investigating how DECT and PCCT can improve dose calculation accuracy, including the reduction of beam hardening, improve the image quality for better delineation accuracy of both tumor and organs-at-risk, provide imaging biomarkers and recurrence classification for multiple treatment sites such as prostate and lung, and simulation free RT.

Although the studies have been initiated independently, cooperation including data sharing and co-supervision between the involved institutions are being established, and a national network within spectral CT in RT is emerging. An open discussion whether these projects could be enrolled in the existing structure or potentially a new work package of DCCC-RT is warranted.

An interactive deep-learning workflow for head and neck gross tumor volume segmentation

Wei Z (1,2), Ren J (1,2), Grau Eriksen J (3,4), Jensen K (2), Rahbek Mortensen H (2), Korreman S (1,2), Nijkamp J (1,2)

1 Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.
2 Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark.
3 Department of Oncology, Aarhus University Hospital, Aarhus, Denmark.
4 Department of Experimental Oncology, Aarhus University Hospital, Denmark.

Introduction:
We present an interactive deep learning (iDL) workflow, combining minimal input from physicians with DL to obtain clinically acceptable head and neck GTV segmentations. We illustrate performance using two datasets, and evaluate the tool with 3 observers.

M&M:
For tumor (GTVt), the starting point was a fully trained CNN, using CT, PET, MR-T1, MR-T2 as input. In the workflow, the clinician clicked in the center of the tumor, followed by outlining the tumor in three orthogonal planes. These delineations were used as label map for re-training the CNN for 20 iterations, with 4 augmentations per iteration.
For nodes (GTVn), clinicians were asked to provide clicks in suspect lymph nodes that needed to be included. The GTVn iDL method was based on using the clicks as an extra channel in the CNN, where only inference was need, no retraining.
Data1, 153 HNC patients from our clinic for training/validation, and a test set of 51 patients. Data2 (HECKTOR challenge), consisted of PET and CT data of 450 patients for training/validation, and 74 for testing.
For the observer study, 3 clinicians delineated 10 patients, where 3 patients were used as learning curve, and the rest for performance evaluation.

Results:
In simulation, the GTVt mean results were DSC 0.85, HD95 5.5 mm, and MSD 1.3 mm for Data1, and DSC 0.84, HD95 3.11 mm, and MSD 1.1 mm for Data2. For GTVn numbers were DSC 0.80, HD95 3.5 mm, and MSD 1.3 mm for Data1, and DSC 0.82, HD95 2.9 mm, and MSD 1.1 mm for Data2.
The observers needed on average 18 minutes per case. The added path length (APL, % of the contour adjusted to make it clinically acceptable) for GTVt was on average 19%, 42%, and 55% for the 3 observers. For GTVn only minor edits were needed (mean APL 10%, 12% and 15%).

Conclusion:
With iDL, high segmentation accuracies can be achieved. Especially for GTVn, the workflow was effective and highly appreciated by the clinicians. For GTVt, there is room for improvement in speed and accuracy.

Sharing AI delineation functions using a national data infrastructure

Krogh SL (1)
Samsøe E (2)
Mohammad Farhadi (2)
Thomas Hinz-Berg Johansen (2)
Nis Sarup (1)
Ebbe Lorenzen (1)
Janne Nørlykke Drudgaard (1)
Mette Klüver-Kristensen (1)
Ruta Zukauskaite (3)
Carsten Brink (1)
Christian Rønn Hansen (1,4,5)

1: Laboratory of Radiation Physics, Odense University Hospital, Odense, Denmark
2: Department of Oncology, Zealand University Hospital, Næstved, Denmark
3: Department of Oncology, Odense University Hospital, Odense Denmark
4: Danish Centre for Particle Therapy, Aarhus, Denmark
5: Department of Clinical Research, University of Southern Denmark, Odense, Denmark

Great leaps have been made in developing artificial intelligence (AI) solutions to time-consuming processes in radiation therapy (RT). Several clinically viable solutions have emerged, however, implementing such solutions in a clinical setting may require resources, which are not always available.
This work proposes a method to share data processing solutions using an existing data infrastructure.

The DcmCollab infrastructure connects all Danish RT centres to a central database, and has been in use since 2009.

The proposed solution extends the functionality of the DcmCollab system to trigger an automatic flow of forwarding data, and returning the results to the submitting centre.
To evaluate the effect of the solution, a test flow providing an AI delineation service was implemented. Medical doctors at a collaborating centre estimated the time saved using the provided solution.

The total processing time from submitting an image set to receiving an AI-generated structure set is 10-15 min. Since the image set can be sent directly from the scanner, the conventional treatment planning process is not delayed, while the contouring process is sped up.
After evaluating the delineations provided, the clinicians in the participating centre evaluated a time saving of 30%-40% compared to the manual workflow.

The proposed solution is built using the pre-existing Danish DcmCollab infrastructure and an nnUnet delineation service. Upon clinical implementation adherence to the EU Medical Device Regulative, and strict version logging is necessary. Furthermore, the surrounding infrastructure should be tested and security evaluated.

The possibility to share cutting-edge automation tools beyond the most privileged centres has the potential to increase quality of care, and to release human resources across all participating RT centres. Therefore, we consider the implementation costs of the solution worth the investment.

Attitudes towards AI-generated risk prediction in patients with early breast cancer: a multi-center survey

Carstensen FV (1), Matthiessen LW (2), Al-Rawi SAJ (3), Mogensen MB (4), Petersen J (5), Vogelius IR (6), Maraldo MV (7)

(1) Dept. of Oncology, Copenhagen University Hospital Rigshospitalet, Denmark
(2) Dept. of Oncology, Copenhagen University Hospital Herlev and Gentofte, Denmark
(3) Dept. of Oncology, Zealand University Hospital Næstved, Denmark
(4) ARTILLERY-consortium funded by the European Union, coordinated by Division of Imaging and Oncology, University Medical Center Utrecht, Utrecht, The Netherlands

Introduction:
In general, patients with early breast cancer (eBC) have a good prognosis with a long life-expectancy. Consequently, they are at risk of developing late side-effects of treatment as well as common chronic diseases, which may impact their quality of life. Most eBC patients receive radiotherapy as part of their adjuvant treatment. The ARTILLERY-consortium aims to develop reliable AI-models to predict the risk of developing cardiovascular disease (CVD), osteoporosis (OP), chronic obstructive pulmonary disease (COPD), and unfavorable body composition (UFB) based on the planning CT-scan used in radiotherapy of eBC. The objective of this survey is to clarify the patients' attitude towards such risk prediction in practice.

Materials and Methods:
The survey consisted of 2 questions on patient characteristics (age and current smoking status) and 4 questions on the interest of knowing the output of an AI-generated risk prediction of developing CVD, OP, COPD, and UFB. Patients were recruited from the three radiotherapy departments in eastern Denmark, either prior to or immediately after the planning CT-scan.

Results:
From Feb. 2024 to Jul. 2024 a total om 120 patients answered the survey (40 from each institution). Median age was 62 years (range 28 to 89 years). 12% (CI95% 6,5-18,8%) were active smokers. Most patients wanted a risk prediction, if possible, 93,3% (CI95% 87,3-97,1%), 95,8% (CI95% 90,5-98,6%), 92,5% (CI95% 86,2-96,5%), and 93,3% (CI95% 87,3-97,1%), respectively, for CVD, OP, COPD, and UFB.

Conclusions: In an unselected cohort of eBC patients in eastern Denmark planned for adjuvant radiotherapy, we found a highly positive attitude towards the use of an AI-generated risk prediction of developing common chronic diseases. A large, international survey is ongoing to elucidate possible differences in patient attitudes throughout Europe.

Development of national AI models for automated target delineation in breast cancer radiotherapy for the 'DBCG DL Nation' prospective randomized trial

Buhl E.S. (1,2), Lorenzen E.L. (3,4), Refsgaard L. (1), Nielsen A.W.M. (2,5), Brixen A.T.L. (6), Maae E (7), Holm H.S. (7), Schøler J. (7), Thai L.M.H. (1), Matthiessen L.W. (6), Maraldo M.V. (8,9), Nielsen M.M. (1), Johansen M.B. (10), Milo M.L. (11), Mogensen M. (8), Nielsen M.H. (12), Møller M. (11), Sand M. (10), Schultz P. (10), Al-Rawi S.A.J. (13), Esser-Naumann S. (13), Yammeni S. (11), Petersen S.E. (1), Offersen B.V. (2,5), Korreman S.S. (1,2)

1: Danish Center for Particle Therapy, Aarhus University Hospital
2: Department of Clinical Medicine, Aarhus University
3: Laboratory of Radiation Physics, Department of Oncology, Odense University Hospital
4: Department of Clinical Research, University of Southern Denmark
5: Department of Experimental Clinical Oncology, Aarhus University Hospital
6: Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte
7: Department of Oncology, Vejle Hospital, University hospital of Southern Denmark
8: Department of Oncology, Copenhagen University Hospital – Rigshospitalet
9: Department of Clinical Medicine, University of Copenhagen
10: Department of Oncology, Aarhus University Hospital
11: Department of Oncology, Aalborg University Hospital
12: Department of Oncology, Odense University Hospital
13: Department of Clinical Oncology and Palliative Care Zealand University Hospital

Introduction:
In breast cancer (BC) radiotherapy (RT), delineation of the target structures for irradiation, i.e. breast and regional nodes, is performed manually in CT scans. The delineation task is both time consuming and prone to variations among clinicians. Artificial intelligence(AI) is well suited as an aid for delineation tasks. The Danish Breast Cancer Group (DBCG) will investigate the clinical impact of AI-assisted delineation in a national prospective randomized trial. This study aimed to develop the AI models to be used in the trial.

Materials and methods:
In a national DBCG delineation workshop, 21 experts from all seven Danish RT centers spent more than 300 workhours to create a high-quality ground truth data set for 315 BC patients.
The generated data were used to train and test AI models to predict internal mammary nodes (IMN) and axillary nodal levels (LN). AI model predictions were quantitatively compared with ground truth (expert) delineations using the Dice Similarity Coefficient (DSC, ranging from 0~no overlap to 1~perfect match). In a qualitative evaluation, 14 experts assessed AI model predictions and expert delineations in a blinded comparison. The assessment ranked clinical usability on a scale from 1 to 4 (1:No corrections needed, 4:Easier to start from scratch).

Results:
The AI models achieved a median DSC=0.7 for IMN and DSC=0.8 for LN.
In the qualitative evaluation, AI model predictions achieved high scores comparable with expert delineations, with 36% of AI model predictions scoring 1 compared to 34% of expert delineations. The AI model predictions had fewer low scores, with 14% scoring 3 or 4, compared to 25% for expert delineations.

Conclusion:
AI models for automated target delineation in BC RT were developed, performing on par with expert delineators and in some cases exceeding. The models will be implemented nationally in a first-of-its-kind prospective randomized trial (DBCG DL Nation) comparing AI assisted with manual delineation.

AI-based dose prediction to identify suboptimal radiotherapy treatment plans

Nielsen C.P. (1,2), Huet-Dastarac M. (3), Zukauskaite R. (1,2), Johansen J. (1), Lee J.A. (3), Sterpin E. (3,4), Jensen K. (5), Friborg J. (6), Sommer J.F.A (1), Stougaard S. (1,2), Lorenzen E.L. (1,2), Brink C. (1,2), Barragán-Montero A.M. (3), Hansen C.R. (1,2,5)

1 Department of Oncology, Odense University Hospital, Denmark;
2 Institute of Clinical Research, University of Southern Denmark, Denmark;
3 Molecular Imaging, Radiotherapy and Oncology, Institut de Recherche Expérimentale et Clinique, UCLouvain, Belgium;
4 Department of Oncology, Laboratory of Experimental Radiotherapy, KU Leuven, Belgium;
5 Danish Centre for Particle Therapy, Aarhus University Hospital, Denmark;
6 Department of Oncology, Rigshospitalet, University Hospital of Copenhagen, Denmark

Introduction
Identifying and improving suboptimal radiotherapy plans can be vital for patients' chances of survival and risk of side effects. AI-based dose prediction algorithms have shown promising abilities to produce clinically acceptable dose distributions and could potentially be used to automatically identify suboptimal plans for further investigation.

Materials and methods
Photon radiotherapy plans were collected from 430 oropharynx cancer patients treated with 66 Gy in 33 fractions or 68 Gy in 34 fractions at Odense University Hospital between 2020 and 2023. All included plans adhered to the DAHANCA guidelines.
A Hierarchically Densely Connected U-net was developed for dose prediction, taking CT scans, target and OAR structures, prescription doses, and dose distributions as input. 90% of the data was used for 10-fold cross-validation, with 90% for training and 10% for validation. 10% was set aside for subsequent testing. The model was evaluated on the test data set by comparing the predicted and clinically applied dose distributions for each patient in the test set.

Results
The median difference between the predicted and clinically applied mean dose to PTV1 was 0.1% of the prescription dose (interquartile range [-0.3, 0.6]), -0.2% [-0.5, 0.6] to PTV2, and 0.1% [-0.3, 0.5] to PTV3. For the oral cavity, the median difference was 0.1 Gy [-1.3, 1.3]. It was 0.4 Gy [-0.9, 2.8] for the upper pharyngeal constrictor muscle, and -0.3 Gy [-1.6, 1.8] and 0.4 Gy [-0.8, 1.5] for left and right parotids, respectively.
The target coverage adhered to the DAHANCA guidelines for 81% of the predictions.

Conclusion
These results demonstrate the model's accuracy in predicting dose distributions, closely aligning with clinically applied ones. If a dose prediction algorithm can produce a high-quality dose distribution, it can be used for continuous quality assurance. In clinical trials, suboptimal dose distributions could be identified to ensure a consistently high plan quality.

Flash talks session #3

- Internal mammary node irradiation in node-positive breast cancer patients treated 2007-2014: The DBCG IMN2 study – Anders W. Mølby Nielsen, Aarhus
- Validating the ESTRO target consensus: pattern of breast cancer failures in the DBCG Skagen trial 1 – Kristine Høgsbjerg, Aarhus
- Quality assurance of internal mammary node irradiation in the DBCG IMN2 study 2007-2014 – Lasse Refsgaard, Aarhus
- Whole brain radiation therapy for patients with brain metastases: Are we able to select the right patients for treatment? – Lars Fokdal, Vejle
- Pre-trial quality assurance in the Nordic small cell lung cancer trial – Sara Linde, Aarhus
- Exploring alternative endpoints after local therapy in patients with EGFR or ALK mutated non-small cell lung cancer – Michael Ruben Teindl Laursen, Herlev
- Heart and Lung Dose as Predictors of Overall Survival in Patients with Locally Advanced Lung Cancer. A Danish National Multicenter Study – Agon Olloni, Odense
- Impact of elective target and nodal boost on acute gastrointestinal toxicity in cervix cancer: EMBRACE-II findings – Mayuri Charnalia, Aarhus
- Assessing treatment plan quality in DAHANCA 35: A comparative analysis of photon and proton radiotherapy – Camilla Panduro Nielsen, Odense
- Proton therapy for second primary breast cancer – first experience and presentation of a new DBCG prospective cohort study – Stine Elleberg Petersen, Aarhus

Internal mammary node irradiation in node-positive breast cancer patients treated 2007-2014: The DBCG IMN2 study

Nielsen, A.W.M. (1,2), Thorsen L.B.J. (1,2,3), Özcan D (1,4), Matthiessen LW (5), Maae E (6), Milo MLH (7), Nielsen MH (8), Tramm T (1,4), Overgaard J.(1,2), Offersen B.V.(1,2,3,8)

1: Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark.
2: Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
3: Department of Oncology, Aarhus University Hospital, Aarhus Denmark.
4: Department of Pathology, Aarhus University Hospital, Aarhus, Denmark.
5: Department of Oncology, Copenhagen University Hospital - Herlev and Gentofte, Copenhagen, Denmark.
6: Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
7: Department of Oncology, Aalborg University Hospital, Aalborg, Denmark.
8: Department of Oncology, Odense University Hospital, Odense, Denmark.
9: Danish Center for Particle Therapy, Aarhus University Hospital, Aarhus Denmark

Introduction
Internal mammary node irradiation (IMNI) improves overall survival (OS) in node-positive breast cancer (BC) patients. However, international controversy exists whether the effect remains in the landscape of modern adjuvant therapies. Therefore, the Danish Breast Cancer Group (DBCG) IMN2 study aimed to investigate the effect of IMNI in the era of modern adjuvant therapies.

Material and Methods
A nationwide prospective cohort study in node-positive BC patients treated with loco-regional radiotherapy (RT). Exclusion criteria were prior malignancies, bilateral BC, primary systemic therapy, recurrence before RT, and non-standard RT.
IMNI was indicated in right-sided patients but not in left-sided patients. IMNI was 3D-based RT. Systemic adjuvant treatment was taxan-based chemotherapy, tamoxifen/letrozole for endocrine therapy, and trastuzumab for HER2-positive patients. Data were collected from the DBCG database and the Danish Pathology Data Bank. Missing values and inconsistencies were handled with chart reviews. The primary end-point was OS. Secondary endpoints were BC mortality and distant recurrence. Cox regression analyses were used for adjusted hazard ratios (HR).

Results
Between January 2007 and May 2014, a total of 4,541 patients were included. Patient characteristics were distributed evenly between right- and left-sided patients.
Median follow-up was 13.7 years for OS. Survival rates at 15 years were 65.0% in patients with IMNI and 60.8% without leading to an adjusted HR of 0.85 (95%CI, 0.76-0.94; p=0.002). Corresponding HRs were 0.84 (95%CI, 0.74-0.95; p=0.008) for BC mortality and HR 0.87 (95%CI, 0.78-0.98; p=0.025) for distant recurrence. The 15-year cumulative incidence of death from ischemic or valvular heart disease was 0.2% in right-sided patients and 0.7% in left-sided.

Conclusions
IMNI reduced distant recurrences and BC mortality leading to an improved overall survival in node-positive BC patients treated with modern adjuvant therapies.

Validating the ESTRO target consensus: pattern of breast cancer failures in the DBCG Skagen trial 1

Høgsbjerg KW (1,2), Thomsen MS (3), Maae E (4), Berg M (5), Nielsen MH (6), Lorenzen EL (7), Maraldo M (8), Boye K (8), Stenbygaard L(9), Jensen I (10), Al-Rawi SA-J (11), Jacobsen KL (11), Matthiessen LW (12), Andersen K (12), Offersen BV (1,2,13)

1) Department of Experimental Clinical Oncology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark.
2) Department of Oncology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark.
3) Department of Medical Physics, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark.
4) Department of Oncology, Vejle Hospital, University of Southern Denmark, Beriderbakken 4, 7100 Vejle, Denmark.
5) Department of Medical Physics, Vejle Hospital, University of Southern Denmark, Beriderbakken 4, 7100 Vejle, Denmark.
6) Department of Oncology, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark.
7) Laboratory of Radiation Physics, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark.
8) Department of Clinical Oncology, Center for Cancer and Organ Diseases, Copenhagen University Hospital - Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark.
9) Department of Oncology, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark.
10) Department of Medical Physics, Aalborg University Hospital, Hobrovej 18-22, 9100 Aalborg, Denmark
11) Department of Oncology, Zealand University Hospital, Ringstedgade 61A, 4700 Næstved
12) Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte, Borgmester Ib Juuls Vej 1, 2730 Herlev
13) Danish Centre for Particle Therapy, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark.

Purpose/Objective: The phase III randomized clinical DBCG Skagen trial 1 (NCT02384733) randomized 2080 node-positive Danish breast cancer patients (pt) 50Gy/25fr versus 40Gy/15fr for loco-regional radiotherapy (RT) during 2015-2021. All target volume delineation had to follow the ESTRO consensus guideline for target volume delineation in early breast cancer and a report of loco-regional pattern of failure according to ESTRO guideline was pre-specified in the trial protocol to validate the clinical feasibility of the ESTRO guideline in high-risk breast cancer pt. Here we present the first analysis of the pattern of failure in pt from the DBCG Skagen trial 1.

Material/Methods: Loco-regional failure with or without distant failure as the first event was defined from all available imaging and matched with the planning CT scan, and classified as inside the CTV, inside the high-dose volume, as marginal misses, or outside.
Results: At a median follow-up of 4.5 years, locoregional recurrence was present in 53 pt; 29 pt with isolated locoregional failure and 24 with locoregional failure concurrent with distant failure. All pt except two had the loco-regional failure in the high-dose volume. Of the 29 pt with isolated loco-regional failure, all failures were in the high-dose volume. Of the 24 pt with loco-regional failure with concurrent distant failure, two had nodal failure at the edge of the high-dose volume.

Conclusion: The majority of loco-regional failures in high-risk breast cancer patients treated with adjuvant radiotherapy according to the ESTRO guideline and diagnosed with loco-regional failure were detected inside the high-dose volume of radiation. This pattern of failure strongly supports the feasibility of the ESTRO consensus guideline, indicating that there appears no need to expand the size of the nodal targets. As pre-specified, the loco-regional pattern of failure for the entire cohort in the DBCG Skagen trial 1 will be performed.

Quality assurance of internal mammary node irradiation in the DBCG IMN2 study 2007-2014

Refsgaard L. (1,2), Buhl E. S. (1,2) *, Nielsen A. W. M.* (2,3), Thomsen M. S. (4), Andersen K. (5), Jensen I. (6), Berg M. (7), Lorenzen E. L. (7), Thorsen L.B.J. (2,3,4), Overgaard J. (2,3), Korreman S.S. (1,2), Offersen B.V. (1,2,3,4)*
**Shared co-first authors*

1: Danish Center for Particle Therapy, Aarhus University Hospital, Aarhus Denmark.
2: Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
3: Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark.
4: Department of Oncology, Aarhus University Hospital, Aarhus Denmark
5: Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte, Copenhagen, Denmark.
6: Department of Medical Physics, Aalborg University Hospital, Aalborg, Denmark.
7: Department of Medical Physics, Vejle Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
8: Laboratory of Radiation Physics, Department of Oncology, Odense University Hospital, Odense, Denmark.
9: Department of Clinical Research, University of Southern Denmark, Odense, Denmark.

Introduction
The Danish Breast Cancer Group (DBCG) IMN2 study investigated the gain from internal mammary node irradiation (IMNI) in node-positive breast cancer (BC) patients. IMNI was indicated in right-sided patients, but not in left-sided. Target volume delineations were based mostly on bony landmarks in contrast to the contemporary vessel-based ESTRO consensus guideline. Our objective was to compare IMNI doses in right-sided versus left-sided BC patients.

Material and methods
Treatment plans and delineated structures including CTVn_IMN (IMN_old) for BC patients treated in 2008-14 were collected from the DBCG RT Nation study. During the study period, IMN_old was only delineated in right-sided patients. Right and left-sided CTVn_IMN structures were auto-segmented following the ESTRO guidelines (IMN_ESTRO). Due to cranial discordance between IMN_old and IMN_ESTRO, the IMN_ESTRO was separated into IMN_ESTRO_cranial and IMN_ESTRO_caudal.

Results
Treatment plans for 2,893 patients were available (63.7% of patients in the IMN2 study). In right-sided patients, the median IMN_old dose coverage (91.5%) was higher than IMN_ESTRO (70.0%), $p<0.001$. Dose coverage in IMN_ESTRO_caudal was comparable to IMN_old. Comparing IMN_ESTRO_caudal in all patients by laterality, the median V90% was 94.0% in right-sided patients and 20.1% in left-sided patients, $p<0.001$. Median mean heart doses were lower in right-sided patients (1.2Gy) than in left-sided patients (2.8Gy), $p<0.001$. Median mean lung doses were higher in right-sided patients (15.9Gy) than in left-sided patients (12.8Gy), $p<0.001$.

Conclusions
For IMN_ESTRO_caudal, we found a significantly higher IMN dose coverage in right-sided patients than in left-sided patients supporting patients were treated per protocol in the DBCG IMN2 study."

Whole brain radiation therapy for patients with brain metastases: Are we able to select the right patients for treatment?

Fokdal L (1,3), Stougaard J (1), Timm S (1,3), Thing RS (2), Nissen HD (2), Berg M (2), Madsen CV (1), Kristiansen C (1)

1. Department of Oncology Vejle Hospital, University Hospital of Southern Denmark, Denmark
2. Department of Medical Physics Vejle Hospital, University Hospital of Southern Denmark, Denmark.
3. Department of Regional Health Research, University of Southern Denmark, Odense, Denmark

Introduction:
Brain metastases (BM) have significant impact on morbidity and mortality in cancer patients. Treatment includes stereotactic radiotherapy or surgery in selected patients, the remaining patients may be treated with whole brain radiotherapy (WBRT) and/or prednisolone.
The life expectancy in patient treated with WBRT is generally short. This study investigates outcome and prognostic factors for OS after WBRT to be used for selection of patients for WBRT.

Material and methods:
Consecutive patients treated with WBRT in the Department of Oncology, Vejle Hospital from 2018-2023 were included. WBRT was delivered with 3D-technique. Patient demographics (gender, age, ECOG performance status (PS)), disease variables (diagnosis, number of brain metastases, meningeal carcinomatosis, extent of systemic disease) and treatment variables (systemic treatments, dose, fractionation) were analyzed with survival statistics, Cox regression analysis and ROC analyses. Different cut-off values for PS as predictor for 6-week survival were investigated.

Results:
A total of 392 patients (lung cancer n=240, breast cancer n=103, other cancers n=49) were evaluated. Radiotherapy schedule was 30 Gy/10 in 266 (67.9%) patients and 20 Gy/4-5 fractions in 126 patients (32.1%). Median follow-up was 3 (0-65) months. One month, 3 months and 6 months survival were 85.5%, 52.8%, and 30.7%, respectively. In the multivariate analysis, diagnosis (HR: 1.519 (95% CI: 1.039-2.221)), PS (HR: 8.346 (95% CI: 5.023-13.876)), and systemic disease (HR: 1.730 (95% CI: 1.176-2.543)) remained significant for survival. PS shoved the best discrimination properties for 6-week survival in ROC analysis (AUC 0.81 (CI: 0.76-0.86). If PS ≤2 was used as cut-off to select patients for WBRT, sensitivity and specificity were 53.3% and 96.0%, respectively.

Conclusion:
To avoid unnecessary overtreatment, initial cancer diagnosis, extend of systemic disease, and PS ≤2 can be used to select future patients for treatment.

Pre-trial quality assurance in the Nordic small cell lung cancer trial

Linde S (1,2), Linaa MB (1), Schmidt HH (1), Szejniuk WM (3,4), Lutz CM (1), Knap MM (1), Møller DS (1,2), Hoffmann L (1,2).

(1) Dept. of Oncology, Aarhus University Hospital, Aarhus, Denmark
(2) Dept. of Clinical Medicine, Aarhus University, Aarhus, Denmark
(3) Dept. of Oncology & Clinical Cancer Research Center, Aalborg University Hospital, Aalborg, Denmark
(4) Dept. of Clinical Medicine, Aalborg University, Aalborg, Denmark

Introduction:
Quality assurance (QA) in radiotherapy (RT) trials is a somewhat neglected area, but of high importance. It is crucial to secure viable outcome data, and to catch pitfalls before the trial onset. A Nordic prospective phase III trial of inhomogeneous dose-escalated RT in small cell lung cancer (SCLC), with a primary aim to improve overall survival in patients with limited disease SCLC (LD-SCLC) is planned. Before initiation of this protocol, pre-trial QA has been performed. Here, we report the results.

Materials and methods:
The trial will randomize eligible patients with LD-SCLC to either standard treatment of 60Gy/40fx/10week or inhomogeneously dose-escalated RT as high as possible up to 80Gy/40fx/10week. Seven centers in the Nordic countries participated in the pre-trial QA. All centers made a standard plan (SP) and a dose-escalated plan (EP) for five distributed cases. All centers were informed of constraints and target doses for the trial. Level of dose-escalation and doses to organs at risk (OAR) were examined and presented with medians and range [min-max].

Results:
Mean dose (Dmean) for the EPs was 79.62Gy [76.92Gy-81.00Gy] and 75.83Gy [68.27Gy-81.07Gy] for GTVt and GTVn, respectively. The large variability in GTVn doses between cases were due to the GTVn localization close to OAR. There were three deviations from hard, dose-limiting, constraints. There was a significant (P=0.001) difference in mean lung dose (MLD) of 13.44Gy [6.91Gy-16.96Gy] for SPs and 14.14Gy [7.00Gy-17.57Gy] for EPs. There was no significant (P=0.187) difference between SPs and EPs for mean heart dose (MHD) of 7.30Gy [1.78-20.79] and 6.83Gy [1.91-22.33], respectively.

Conclusions:
Inhomogeneous dose-escalation up to 80Gy/40fx/10week for the GTVt and GTVn is feasible. The dose-escalation can be performed respecting the consensus constraints for OAR in the upcoming trial.

Exploring alternative endpoints after local therapy in patients with EGFR or ALK mutated non-small cell lung cancer

Laursen, MRT (1), Nielsen, AM (1), Jensen, RFG (1), Andersen, JL (1), Persson, GF (1,2)

(1) Copenhagen University Hospital, Herlev and Gentofte, Department of Oncology, Copenhagen, Denmark.
(2) Faculty of Medical Sciences, University of Copenhagen, Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark

Introduction
Local therapies (LT) such as radiotherapy or surgery may be applied in metastatic progressive disease with the intent of prolonging a systemic therapy. In evaluating the efficacy of such a strategy, progression-free survival (PFS) is typically reported. However, it may not fully reflect the longitudinal trajectory for the patients in this setting. We propose the use of an alternative endpoint, the time to failure of LT strategy (TFLS).

Materials and methods
In this retrospective single center study, patients with oncogene-driver non-small cell lung cancer were included if 1) they were treated with any line of tyrosine kinase inhibitor (TKI) at our institution from 2016-2022, and 2) they received LT to any progressive site while maintaining the same TKI. PFS was defined as time from the first LT until progression or death. TFLS was defined as time from first LT until a change in systemic therapy, progression not amenable to a new course of LT, or death. Overall survival (OS) was defined as time from first LT until death. All analyses were evaluated for each TKI regimen, i.e., a patient could be included more than once, and 95 % CI are reported in brackets.

Results
Fifty-four patients were included in the analysis, including 16 patients with ALK rearrangements and 38 patients with EGFR mutations. The median PFS was 4.6 months (2.5-7.0), the median TFLS was 5.6 months (4.4-11.3), and the median OS was 16.9 months (13.6-28.7). A univariable and multivariable Cox regression of TFLS and OS is currently planned.

Conclusion
In the current setting, TFLS may arguably be better suited to evaluate the efficacy of LT than PFS2. However, evaluating this endpoint as a surrogate for e.g., survival or quality of life must be evaluated through prospective randomized trials.

Heart and Lung Dose as Predictors of Overall Survival in Patients with Locally Advanced Lung Cancer. A Danish National Multicenter Study

Olloni A(1,2,3), Brink C (2,4), Lorenzen EL (2,4), Jeppesen SS (1,2,3), Hofmann L (5,6), Kristiansen C (7), Knap MM (5), Møller DS (5,6), Nygård L (8), Persson G (9,10), Thing RS (7), Sand HMB (11), Schytte T (1,2).

(1) Department of Oncology, Odense University Hospital. (2) Department of Clinical Research, University of Southern Denmark. (3) Academy of Geriatric Cancer Research (AgeCare), Odense University Hospital. (4) Laboratory of Radiation Physics, Department of Oncology. Odense University Hospital. (5) Department of Oncology, Aarhus University Hospital. (6) Department of Clinical Medicine, Faculty of Health Sciences, Aarhus University. (7) Department of Oncology, University Hospital of Southern Denmark. (8) Department of Oncology, Rigshospitalet, Copenhagen University Hospital. (9) Department of Oncology, Copenhagen University Hospital, Herlev and Gentofte. (10) Department of Clinical Medicine, Copenhagen University. (11) Department of Medical Physics, Aalborg University Hospital.

Introduction
The impact of lung and heart irradiation on overall survival (OS) following definitive radiotherapy for lung cancer remains a subject of ongoing debate. This study aims to explore the relationship between OS and irradiation of the lung and heart using data from a large national cohort of patients with locally advanced non-small cell lung cancer (NSCLC) who received definitive (chemo-) radiotherapy.

Methods
Treatment plans were collected from six Danish radiotherapy centers, while patient data were obtained from national registries. A hybrid segmentation tool automatically delineated the heart and its substructures. Dose-volume histograms for all relevant structures were extracted and analyzed using principal component analysis (PCA). Parameter selection for a multivariable Cox proportional hazards model for OS prediction was conducted through cross-validation with bootstrapping.

Results
The study cohort comprised 644 patients, with a median survival time of 26 months (95% confidence interval (CI): 24–29 months). The cross-validation process identified two PCA variables for inclusion in the multivariable model. PCA1, which indicated the irradiation dose to the heart, was associated with a negative impact on OS (hazard ratio, 1.14; 95% CI: 1.04–1.26). PCA2 indicated the left-right balance (right atrium versus left ventricle) irradiation, suggesting a better survival for tumors located closer to the right atrium (hazard ratio, 0.92; 95% CI: 0.84–1.00) compared to a lower survival for patients with tumors located close to the left ventricle. Additionally, the multivariable model included age, sex, body mass index, performance status, tumor dose, and tumor volume.

Conclusion
In addition to traditional non-cardiac risk factors, doses of radiation to the lung and heart were found to negatively impact survival. The findings suggest that the left side of the heart is particularly sensitive to radiation. To potentially improve OS, it is recommended that overall heart irradiation be minimized where possible.

Impact of elective target and nodal boost on acute gastrointestinal toxicity in cervix cancer: EMBRACE-II findings

M. Charnalia(1) , K. Tanderup(1,2), R. Pötter(3), S. Chopra(4), M. Pelizzola(1), I.M. Jurgenliemk-Schulz(5), M. Schmid(3), K. Bruheim(6), B. Segedin(7), H. Westerveld(8,18), E. Wiebe(9), M. Valgma(10), L. Velema(11), C.G. Verhoef(12), L. Tan(13), J. Lindegaard(14), R. Cooper(15), H. Mathiesen(16), C. Kirisits(3), M. Serban(17), J. Jain(4), K. Kirchheiner(3), R. Nout(18), S. Spampinato(1)

1. Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark.
2. Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.
3. Department of Radiation Oncology, Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria.
4. Department of Radiation Oncology, Advanced Centre for Treatment Research and Education in Cancer, Tata Memorial Centre, Homi Bhabha National Institute, Navi Mumbai, Maharashtra, India.
5. Department of Radiation Oncology, University Medical Centre Utrecht, Utrecht, The Netherlands.
6. Department of Oncology, Oslo University Hospital, Oslo, Norway.
7. Department of Radiotherapy, Institute of Oncology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.
8. Department of Radiotherapy, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands. Department of Radiation Oncology, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands; Cancer Center Amsterdam, Cancer Treatment and Quality of Life, Amsterdam, The Netherlands.
9. Department of Oncology, University of Alberta, Edmonton, Alberta, Canada.
10. Radiotherapy Centre, North Estonia Medical Centre Foundation, Tallinn, Estonia
11. Department of Radiation Oncology, Leiden University Medical Center, Leiden, The Netherlands.
12. Department of Radiotherapy, Radboud University Medical Center and Radboud Institute for Health Sciences, Nijmegen, The Netherlands.
13. Oncology Centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom.
14. Department of Oncology, Aarhus University Hospital, Aarhus, Denmark.
15. Leeds Cancer Centre, St James's University Hospital, Leeds, United Kingdom.
16. Department of Oncology, Rigshospitalet, Copenhagen, Denmark.
17. Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada.
18. Department of Radiotherapy, Erasmus MC Cancer Institute, Rotterdam, The Netherlands.

Purpose: To assess acute gastrointestinal (GI) toxicity incidence in locally advanced cervical cancer (LACC) patients and association with external beam radiotherapy (EBRT) nodal boosting and elective target volume selections in the prospective international EMBRACE-II study.

Methods: In EMBRACE-II study (2016-2021), patients received EBRT, chemotherapy, and MRI-guided brachytherapy. EBRT included a prescription of 45Gy/25 fractions to elective targets and a recommendation of 55-65Gy for positive nodes. Patients with baseline (BM), 4th week of treatment (RT4W) or end of treatment (RTEND) GI toxicity (CTCAE v3.0) assessments were included. To evaluate the impact of EBRT, patients were grouped based on lymph node (LN) boosting and elective irradiation.

Results: Among 1302 eligible patients, GI toxicity peaked at RT4W and declined at 3 months follow-up (3M). At RT4W, 15.5%, 6.4% and 2.4% of patients experienced grade 2 or worse (G≥2) diarrhea, abdominal pain/cramping and proctitis, respectively, while at 3M incidences were 2.5%, 3.3%, and 0.3%. Node negative (Group1) and node positive (N1) up to two boosted pelvic nodes patients (Group2) had comparable GI toxicity. Pelvic+para-aortic (PAN) elective field in N1 patients without boosted para-aortic nodes (Group3) led to similar or slightly higher GI toxicity. Pelvic+PAN elective irradiation combined with para-aortic node boosting (Group4) was associated with higher GI toxicity, but tolerable with rare severe events (G≥3) compared to other groups.

Conclusion: Acute GI toxicity was higher at RT4W and decreased at 3M, with rare G≥3. Pelvic+PAN elective irradiation with para-aortic node boosting was associated with a higher GI toxicity.

Assessing treatment plan quality in DAHANCA 35: A comparative analysis of photon and proton radiotherapy

Nielsen C.P. (1), Jensen K. (3), Krogh S.L. (1), Brink C. (1), Lorenzen E.L. (1), Smulders B. (2,3), Holm A.I.S (4), Samsøe E. (5), Nielsen M.S (6), Sibolt P. (7), Skyt P.S. (2), Elstrøm U.V. (2), Johansen J. (1), Zukauskaite R. (1), Eriksen J.G. (4), Farhadi M. (5), Andersen M. (6), Maare C. (7), Overgaard J. (4), Grau C. (2), Friborg J. (3), Hansen C.R. (1,2)

1 Department of Oncology, Odense University Hospital, Denmark;
2 Danish Centre for Particle Therapy, Aarhus University Hospital, Denmark;
3 Department of Oncology, Rigshospitalet, University Hospital of Copenhagen, Denmark;
4 Department of Oncology, Aarhus University Hospital, Denmark;
5 Department of Oncology, Zealand University Hospital, Naestved, Denmark;
6 Department of Oncology, Aalborg University Hospital, Denmark;
7 Department of Oncology, University Hospital Herlev, Denmark

Introduction
The primary objective of radiotherapy treatment planning is to achieve optimal target coverage while minimising the radiation dose to critical Organs at Risk (OARs) following relevant guidelines. Ensuring consistently high-quality radiotherapy plans is crucial for patients' survival chances and risk of side effects. The importance of treatment plan quality is emphasised in The Danish Head and Neck cancer Study Group (DAHANCA) 35 trial of proton versus photons, where patients are selected on treatment plan comparisons. This study evaluates the plan quality in DAHANCA 35.

Materials & Methods
193 patients were enrolled from September 2019 to June 2023 based on a simulated benefit in normal tissue complication probability (NTCP) for proton therapy by comparing patient photon and proton treatment plans. A new clinical proton plan was made for patients randomised for proton therapy. All treatment plans followed the DAHANCA radiotherapy guidelines.
Splitting patients into three time-intervals, plans were assessed using NTCP for dysphagia grade 2+, mean dose to 13 OARs relevant to head and neck cancer, and a new metric: Normalised Toxicity Index (NTI), calculating the normalised average of the mean dose to the OARs compared to the recommended thresholds outlined in the DAHANCA guidelines.

Results
99% of the 529 analysed plans met the guidelines for target coverage and critical OAR dose.
There was no significant difference between the three time intervals for both NTCP, mean dose, and NTI for all three plan types. NTI was significantly higher for photon plans than comparative and clinical proton plans.

Conclusions
The results suggest that plan quality remained constant for both photon and proton plans. A consistent treatment plan quality ensures a robust patient selection for clinical trials. It enables transparency in the trial outcome analysis and ensures the reliability of trial results. The ongoing monitoring of plan quality is set in place to ensure consistency.

Proton therapy for second primary breast cancer – first experience and presentation of a new DBCG prospective cohort study

Petersen SE (1), Jensen MF (1), Kronborg CJS (1), Maae E (2), Nissen HD (2), Offersen BV (3), Yates ES (4), Stick LB (1)

(1) Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
(2) Department of Oncology, Vejle Hospital, Vejle, Denmark
(3) Department of Oncology & Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark
(4) Department of Medical Physics, Aarhus University Hospital, Aarhus, Denmark

Introduction
Radiotherapy (RT) for a second primary breast cancer is increasingly common due to high incidence and survival rates of breast cancer (BC). If a patient previously received RT and is diagnosed with a second primary breast cancer in the contralateral breast, it may be difficult to achieve full target coverage without overlapping with previously irradiated tissue. Breast RT with photons typically uses tangential fields whereas RT with protons uses anterior oblique fields, parallel to the previous photon fields, enabling optimal target coverage with minimal overlap. Danish patients have until now been referred for proton therapy (PT) at Danish Centre for Particle Therapy (DCPT) on an individual basis, if the target coverage criteria set by the Danish Breast Cancer Group (DBCG) were not met with photon RT. Here, we present achievable target coverage data for PT of second primary BC.

Materials and methods
All patients treated with proton therapy at the DCPT since 2022 for a second primary BC, where the patient had previously received RT for a prior BC in the contralateral breast. The DBCG RT guidelines recommend that 98% of the breast or chest wall receive at least 95% of the prescribed dose and that 98% of lymph nodes receive at least 90% of the prescribed dose.

Results
31 patients matching the criteria were identified. Patients received their first breast RT between 2001 and 2023. Target coverage criteria for the new contralateral BC were reached according to DBCG guidelines in 23 patients, where no compromises were necessary. In 8 patients target coverage was still compromised with PT with up to 30% (median 7.4%) of the target not receiving the recommended dose.

Conclusions
Most patients met the DBCG target constraints. Based on these data, the DBCG RT Committee created a new prospective cohort study to evaluate proton therapy for previously irradiated BC patients, with the overall aim of evaluating target coverage and late morbidity.