Editorial

Dear Reader,

Welcome to this edition of our Newsletter on the RAPTOR "Real-Time Adaptive Particle Therapy Of Cancer" project.

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In the following pages you will find the results relevant to Workpackage WP2 "Imaging" describing the activities that our brilliant ESRs conducted to achieve the objectives of this scientific WP2.

Up to now Computed Tomography (CT) is the clinical standard for treatment planning in particle therapy (PT), but it is not representative of the anatomo-pathological configuration of the patient, which is subject to inter and intra-fraction organ motion, throughout all the treatment workflow. As such, repeated CTs are usually acquired off-line to account for organ motion and adapt the treatment. This results in a slow clinical workflow, where multiple imaging acquisitions are acquired outside the treatment room, requiring contours delineation for plan optimization and adaptation as well as delivering additional non-therapeutic dose to the patient. Repeated CTs can be also supported by other imaging modalities such us on-board Cone Beam CT (CBCT) or near-room radiation-free Magnetic Resonance Imaging (MRI), but these image modalities do not provide the electron density information needed for dose calculation and adaptation.

The main aim of WP2 is to enable on-board volumetric image guidance suitable for daily (and in the future real-time) adaptive PT planning. To achieve this aim, two main pillars are currently investigated in WP2, that are (i) automated contour propagation and dose accumulation and (ii) generation of synthetic CT from CBCT and MRI towards daily adaptive PT.

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The first study conducted by ESR1 proposes a deep-learning approach to evaluate the uncertainty of Deformable Image Registration (DIR) for contour propagation and dose accumulation, whereas ESR2 shows an alternative to DIR for contour propagation in poorly segmented organs based on deep-learning. The two activities can be used for fast automatic segmentation and uncertainty estimation in contour propagation on daily images.

ESR3 and ESR4 instead report strategies for the generation of synthetic CT from CBCT and MRI for static anatomy (e.g. head and neck cancers). Here, methods based on DIR and deep learning are investigated. ESR5 finally explores the potential of dynamic MRI to support treatment planning and delivery in organs that move with respiration treated with carbon ions (e.g. thoraco-abdominal tumors).
The results of our brilliant ESRs, their motivation and enthusiasm are demonstrated by participation in national and international conferences and submission of their work in high-ranked scientific journals. The ESRs activities are also supported by secondments, which confirm the high connectivity among RAPTOR members.

With all these scientific achievements and the excellent collaboration within RAPTOR, we aim at pushing towards the development of innovative solutions to support the clinical implementation of online adaptive PT, paving the way to improved workflows and patient care.

Enjoy the reading!

Deep learning based uncertainty prediction of deformable image registration for contour propagation and dose accumulation in adaptive radiotherapy

ESR1: Smolders Andreas Johan, Center of Proton Therapy (CPT) at Paul Scherrer Institute – PSI, Switzerland.

Supervisor: Francesca Albertini, Tony Lomax

Background and aim : In online adaptive proton therapy, the treatment plan is reoptimized each fraction based on an image acquired shortly before delivery. This reoptimization requires delineation of the organs-at-risk (OARs) and the (clinical) target volume (CTV). Since manual contouring would be too time-consuming, automatic methods are used. One promising method is deformable image registration (DIR), which maps the planning contours to the daily image by a deformable vector field (DVF). Apart from contouring, DIR is also used for dose accumulation, i.e. the process of summing up doses related to different time points on one reference anatomy. Clinical use of DIR is however limited, because different algorithms generally yield different solutions and because it is hard to evaluate the accuracy of a result. This work presents and evaluates a deep-learning method to predict the uncertainty of a DVF and its effect on contour and dose accumulation uncertainty.

Materials and Methods: A 3D UNet was trained on 52 CT pairs to predict the variance of a given DVF, using the fixed and moving image and DVF as input. The training combined an unsupervised loss [1], yielding high uncertainty where contrast is low and inversely, with a supervised loss [2], yielding high uncertainty in regions with large or non-deformable anatomical transformations, e.g. nasal cavity filling. Samples of the resulting probabilistic DVF can be used to warp contours and dose distributions, yielding contour and dose samples. The method was evaluated on the DIRLAB dataset, containing 10 patients with in- and exhale CTs with 300 landmarks. Additionally, for 5 lung cancer patients with 9 repeated manually contoured CTs, the planning contours were propagated with 50 DVF samples to each repeated CT, yielding voxel-wise probabilities p to be inside a contour. Ideally, p is equal to the proportion of voxels with probability around p that are within the manual contour, and the average error between the two is called the *expected calibration error (ECE)*.
For these patients, the treatment was further reoptimized on all repeated CTs yielding daily dose maps. These were warped back to the planning CT and accumulated with 50 DVF samples per repeated CT. The resulting accumulated dose samples were used to generate *probabilistic accumulated dose-volume-histograms (DVH)* with 95% error bounds. To evaluate their quality, we accumulated the dose with 5 different DIR algorithms and evaluated the volume fraction for which the DVHs of these accumulated doses lay within the error bounds of the probabilistic DVH, hereafter referred to as the *encompassed volume fraction (EVF)*.

Results: The DIRLAB landmark registration errors are on average indeed large in regions with high predicted uncertainty and low in regions with low uncertainty. Quantitative evaluation shows good agreement between the root-mean-squared registration error and the predicted uncertainty. The method predicts contour uncertainty with ECE=2.5%, i.e. the predicted voxel-wise probabilities differ on average 2.5% from the actual proportion inside the contour. The probabilistic contours were generated in less than 25 seconds. The EVF=97.8%, which is close to the expected 95% given the 95% error bounds.

Discussion and conclusion: The method predicts DIR uncertainty accurately on average and can efficiently translate this into accurate contour uncertainties [3,4]. These could be used for prioritizing manual contour adjustments, or directly in combination with robust optimization. The method further allows estimation of accumulated dose uncertainty, without the need for running multiple DIR algorithms.

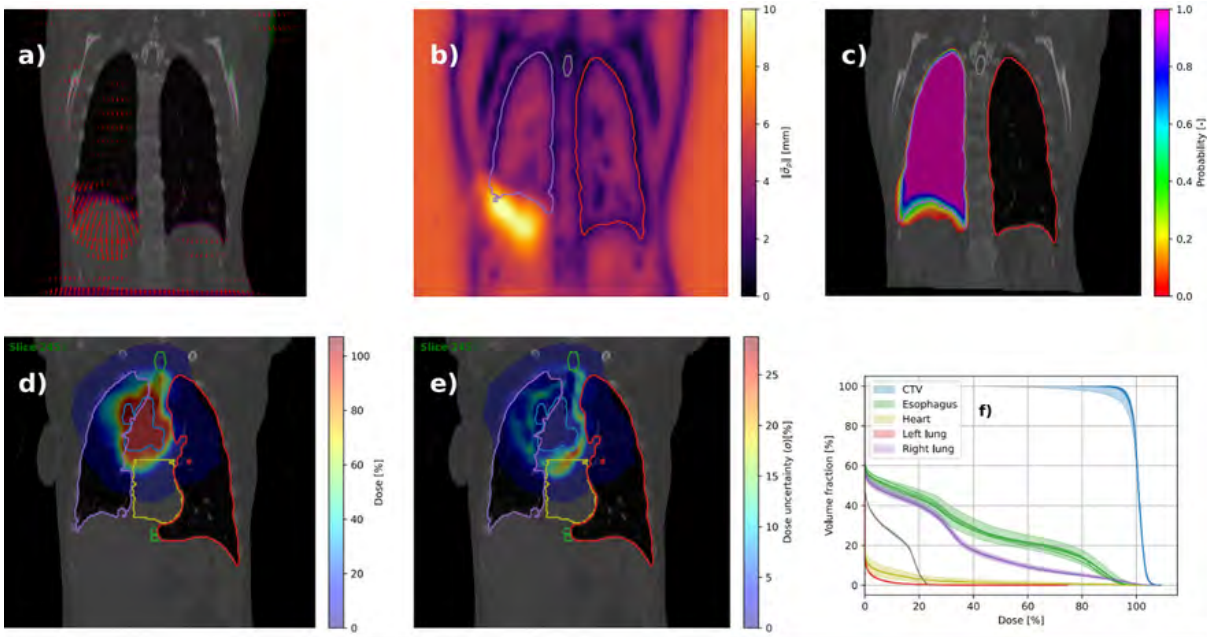


Figure 1: Example inputand results of our method.a) Input to the network:fixed (purple) and moving (green) image together with the mean DVF (red arrows); b) predicted DVF uncertainty; c) probabilistically propagated contourof the left lung, togetherwith ground truthmanual contours; d) mean accumulated dose over all samples; e) standard deviation of the accumulated dose; f) 95% bound probabilistic DVH, together with the DVH for 5 different DIR algorithms (solid lines).

Conferences and Publications

1. Smolders A., Lomax T., Weber D. C., & Albertini F. (2022). Deformable Image Registration Uncertainty Quantification Using Deep Learning for Dose Accumulation in Adaptive Proton Therapy. In A. Hering, J. Schnabel, M. Zhang, E. Ferrante, M. Heinrich, & D. Rueckert (Eds.), *Biomedical image registration* (pp. 57–66). Springer International Publishing.
2. Smolders A., Amstutz F., Zhang Y., Weber D. C., Lomax T., & Albertini F. (2022). Fast deformable image registration uncertainty estimation for contour propagation in daily adaptive proton therapy. *Medical Imaging with Deep Learning.*
3. Smolders A., Lomax A., Weber D. C., & Albertini F. (2023). Deep learning based uncertainty prediction of deformable image registration for contour propagation and dose accumulation in online adaptive proton therapy. *Submitted to: Physics in Medicine and Biology.*
4. Smolders, A., Weber D. C., Lomax T., & Albertini F. (2023). Deep learning based uncertainty prediction of deformable image registration for contour propagation and dose accumulation in adaptive radiotherapy. *61st Particle Therapy Cooperative Group.*

Secondment

UMCG, July 2022, 4 weeks – Dose accumulation for ΔNTCP validation in lung cancer

Estimating segmentation accuracy in poorly automatic segmented organs using deep-learning contour propagation uncertainty

ESR2: Rivetti Luciano, Faculty of Mathematics and Physics of the University of Ljubljana (UL), Slovenia.

Supervisor: Andrej Studen and Robert Jeraj

Background and aim : In daily adaptive radiotherapy, fast and accurate acquisition of the daily structures is needed. Deformable image registration (DIR) speeds up this process by propagating the planning structures to the new daily anatomy. However, classical DIR doesn't estimate the accuracy of the structures leading to the time-consuming task of identifying and reviewing the structures which were not accurately segmented. In this work, deep learning was used to develop a fast and accurate DIR method for contour propagation that predicts the structure uncertainty and allows the estimation of the structure segmentation accuracy in poorly segmented organs in head and neck radiotherapy.

Materials and Methods: This work was carried out in a head and neck dataset which consisted of 9 patients (216 CTs and CBCTs) for training, 2 patients (66 image pairs) for validation, and 3 patients (98 image pairs) for testing. An uncertainty score (UCS) obtained from the structure uncertainty was defined and validated to identify propagated structures that were prone to errors. The method's performance was assessed by calculating the surface dice similarity coefficient (SDSC) between the propagated structures and their ground truth. In addition, the results were compared using a reference DIR method based on b-splines (Elastix). Results: The results showed that the presented method has a median SDSC higher than Elastix for six of the ten structures analyzed ($p>0.05$) (Fig 1).

Our method achieved the lowest median SDSC in the submandibular glands (0.93) and the highest for the spinal cord (0.96). The metric showed a strong Spearman anticorrelation (<-0.7) with the median and standard deviation of the SDSC for poorly segmented structures, i.e., structures with a low mean and high standard deviation of SDSC (Fig 2, 3).

Discussion and conclusion: In conclusion, a fast and predictive Deep Learning method to propagate contours with competent accuracy with physician-delineated contours was developed [1,2]. The method allows estimating the structure segmentation accuracy in poorly segmented organs without compromising the performance of the contour propagation. This method could be used in the future to guide physician's review to poorly segmented organs and save time in an adaptive radiotherapy workflow.

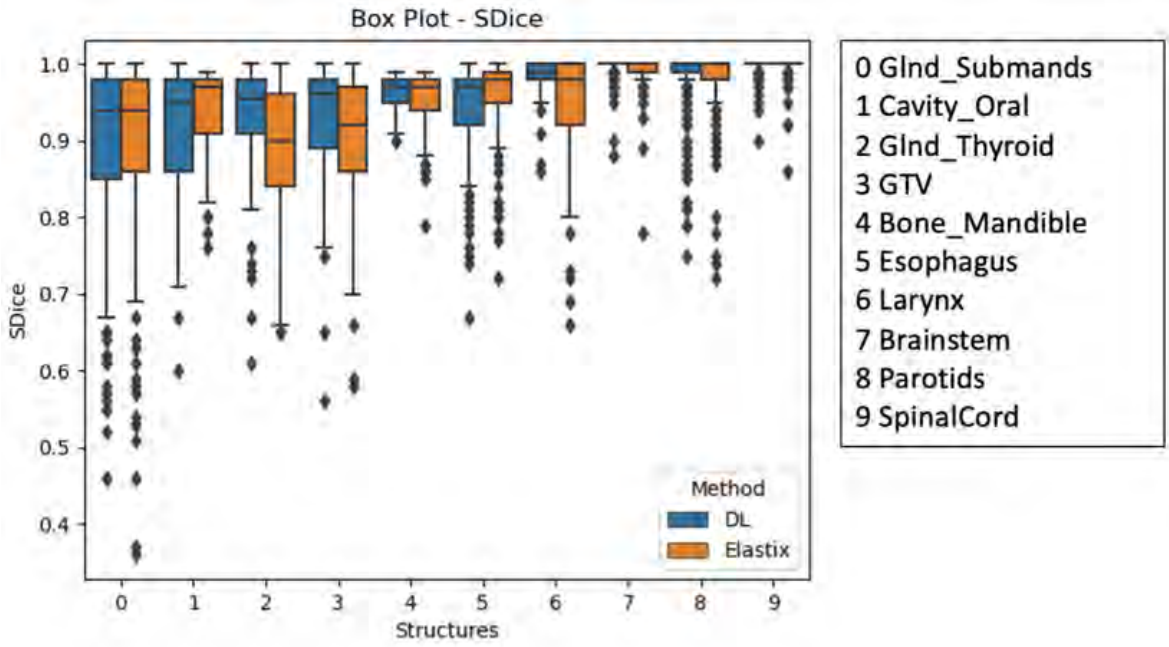


Figure 1: Surface Dice Coefficient (SDCS) calculated with the presented method (DL) and Elastix for different structures of the test set.

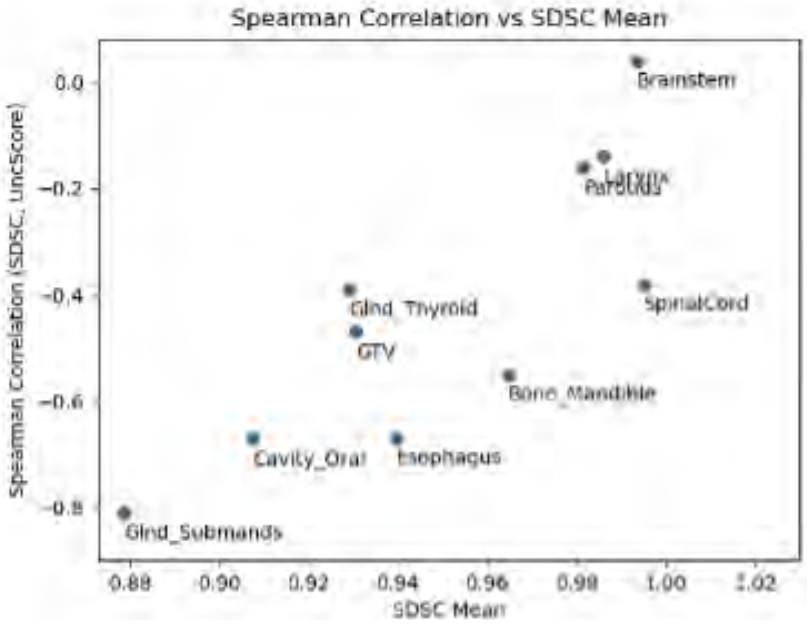


Figure 2: Spearman correlation vs the mean surface dice coefficient (SDCS) calculated for different structures. The Spearman correlation was calculated with the distribution of the SDCSs and the uncertainty scores for each structure.

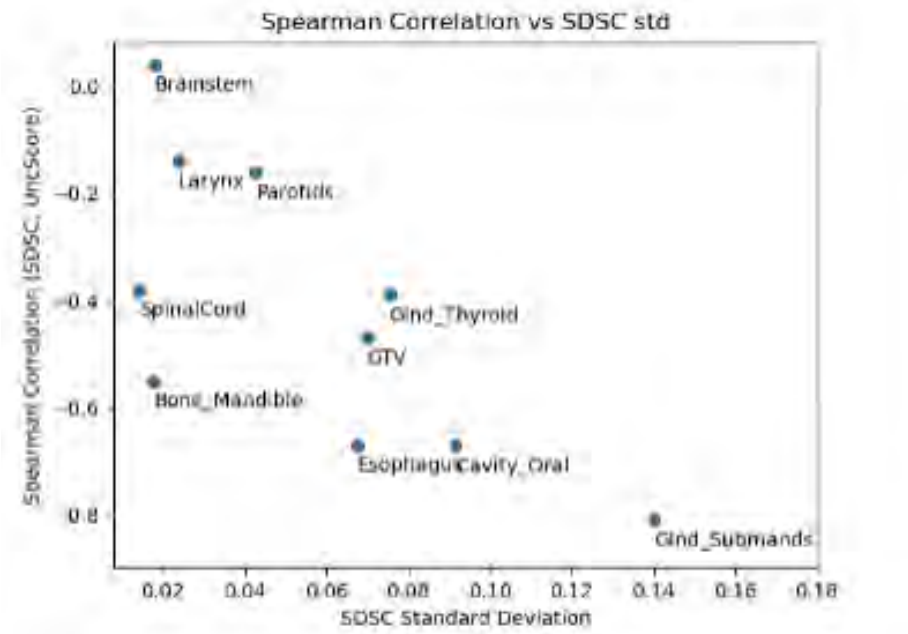


Figure 3: Spearman correlation vs the standard deviation of the surface dice coefficient (SDCS) calculated for different structures. The Spearman correlation was calculated with the distribution of the SDCSs std and the uncertainty scores for each structure.

Conferences and Publications

1. Rivetti L., Studen A., Sharma M., Chan J., Jeraj R. "Contour propagation and uncertainty estimation using deep learning in head and neck treatments" – ESTRO 2023
2. Rivetti L., Studen A., Sharma M., Chan J., Jeraj R. "Estimating segmentation accuracy in poorly segmented organs using deep-learning contour propagation uncertainty" – PTCOG 2023

Secondment

Cosylab (Ljubljana), December 2022, 12 weeks – Studying parallel programming paradigms and associated complexity of interconnected systems.

Towards synthetic CT generation from CBCT using a robotic, mobile CBCT scanner

ESR3: Saba Hussain (till January 2023), Francesco Russo (from May 2023), MedPhoton, Austria.

Supervisors: Phil Steininger, Katia Parodi

Background and aim : Cone-Beam Computed Tomography (CBCT) scanners, such as the mobile ImagingRing (IRm) from medPhoton, are affordable and flexible for patient position verification in radiation therapy. However, CBCTs often produce images with inferior quality due to Compton scattering, beam hardening, and other machine-specific factors, resulting in inaccurate CT numbers and reduced soft tissue contrast. As a result, conventional fan-beam CT images are usually required for treatment plan adaptation and dose calculation in particle therapy.
A literature review revealed two main approaches to generating synthetic CTs (sCTs) from CBCTs: non-AI-based methods involving deformation of CT to CBCT or "scatter correction" in projection domain, and AI-based methods using deep learning techniques. In this first study, we conducted initial investigations on enhancing the image quality of CBCTs of IRm using a non-AI-based method, with the aim of achieving a closer match to the image quality of corresponding CT datasets.

Materials and Methods:
CBCT scanner: The IRm consists of a ring gantry with two independently rotating arms, where the first positions an X-ray source with a dynamic collimator, and the second positions an image detector. This enables that the region of interest in the patient can be off-centered with respect to the ring isocenter, and the size of the Field Of View (FOV) of the CBCT acquisition can be selected freely.

Synthetic CT generation: The chosen approach is an a-priori CT-based scatter correction method based on the work of Ludwig Maximilian University (LMU) but modified to cope with the dynamic imaging geometry of the IRm. The method consists of several steps, including registering the corresponding planning CT image to the CBCT by Deformable Image Registration (DIR), generating corrected CBCT projections by subtracting derived scatter map estimates from the CBCT raw projections, and reconstructing the volumetric CBCT image using the scatter-corrected projections as input to obtain a corrected CBCT (i.e. sCT) as output.

Phantoms: The study used a RANDO phantom with planning CT (Siemens) and CBCT (IRm) data, respectively, using a standard full-fan FOV to cover the head and neck region of the phantom.

Results: The abovementioned datasets, CBCT and corresponding CT, were processed as described, and the following image instances were compared (Figure 1): Uncorrected CBCT (reconstruction from raw projections without any further scatter or beam hardening correction), Virtual CT (planning CT deformably registered to the CBCT), Heuristic CBCT (reconstruction involving heuristic corrections as integrated into the IRm product), Scatter corrected CBCT (reconstruction result from applying the method described in this work).

Conclusion: The study compared the quality of scatter-corrected CBCT images with uncorrected ones and found that the corrected images showed improved quality with reduced cupping artifacts, caused by inconsistencies in low-frequency data due to scatter contamination. However, the heuristically corrected CBCT had less noise in some regions, albeit with artifacts close to strong intensity gradients. The study also identified two prominent residual artifacts: a data truncation artifact at the superior end of the skull due to non-optimal phantom positioning and FOV definition, and residual beam hardening artifacts that neither correction approach could eliminate.

To improve the accuracy of the a-priori planning CT scatter correction method, the approach's parameters need further optimization on more datasets with different energies and IRm's flexible imaging trajectories to optimize smoothing kernels, energy- and filtration-dependent rescaling factors as well as edge-preserving denoising techniques.

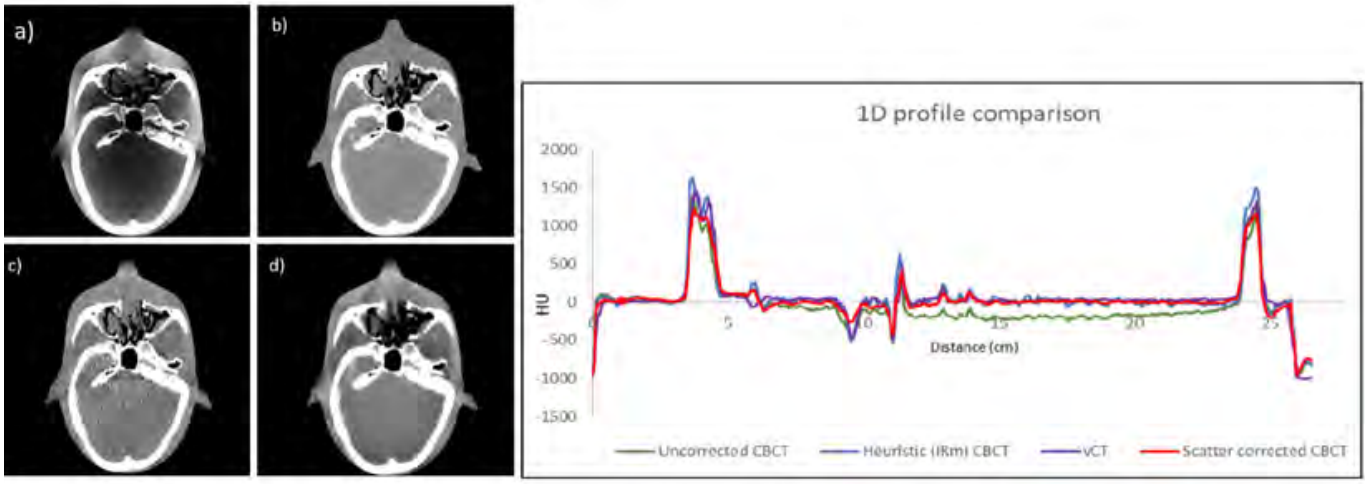


Figure 1. Left: Reconstructed images of the RANDO phantom (trans-axial view). Display window: [-250, 250] HU; a) Uncorrected CBCT; b) virtual CT (vCT); c) Heuristically corrected CBCT; d) Scatter corrected CBCT. Right: Line profile comparison between vCT (ground truth) and corresponding instances of differently corrected CBCTs measured in Hounsfield Units (HU).

Synthetic CT from MR images using DCNN and cycleGAN

ESR4: Arthur Galapon - Cancer Research Center Groningen (CRCG) Research Institute of the University Medical Center Groningen – UMCG, Netherlands.

Supervisor: Stefan Both, Dirk Wagenaar

Background and aim : Adaptive radiotherapy (ART) promises personalized treatment of cancer patients by accounting for daily changes in the tumor geometry while minimizing the exposure of the surrounding healthy tissues. Daily imaging is a crucial aspect of ART, which can be achieved through on-board CBCT or MRI. Although MRI provides superior soft tissue contrast, it cannot be used to determine proton dose the same way CT-based images can. To overcome this challenge, deep learning techniques can be used to convert MRI into synthetic CTs (sCTs) for treatment planning purposes.

Materials and Methods:
The generation of sCTs from MR images involves the use of two deep-learning models: a deep convolutional neural network (DCNN) and a cycle-consistent generative network (cycleGAN). The DCNN requires paired CT-MR images to generate a one-to-one mapping of the conversion. On the other hand, the cycleGAN model can learn the mapping between the MR and CT domain without the need for paired input images. Both models were trained using a cohort of 101 head and neck cancer patients. Image preprocessing was applied to ensure optimal training of the models. The final sCT was obtained using the Monte Carlo dropout method by performing 10 inferences with the average as the final sCT, and the corresponding uncertainty was represented by the variance.

The quality of the generated sCTs was assessed by comparing them with the reference planning CTs (pCTs) using the mean absolute error (MAE), structural similarity index measure (SSIM), Dice coefficient (DCE), and 95% Hausdorff distance (95HD). The dosimetric analysis comprised evaluating the dose difference for the target volume (D99, D95, D50, and mean dose) and the organs at risk, and a gamma analysis using 2%/2mm and 3%/3mm criteria. The correlation between the actual Hounsfield unit (HU) difference was also determined to evaluate the uncertainty map.

Results: DCNN-based sCTs resulted in higher image quality in all evaluation metrics with an average MAE of 56.34 ± 8.6 HU, while 86.66 ± 7.9 HU for the cycleGAN (Figure 1). In terms of proton dose calculations, no significant difference was observed between the two models. The DCNN-based sCT had an average dose difference (DD) of 0.14 ± 0.13% for the D95 of the target volume and 0.28 ± 0.23% average DD for the cycleGAN. A higher gamma pass rate was also observed for the DCNN model for both gamma criteria, with an average pass rate of 99.29 ± 0.81% for the 2%/2mm criterion and 99.76 ± 0.43% for the 3%/3mm criterion. Evaluation of the uncertainty map (Figure 2) also showed a positive correlation for each of the evaluation metrics used, with an average r-value of r = 0.74 ± 0.04 and r = 0.86 ± 0.03 for the uncertainty and HU difference for DCNN and cycleGAN, respectively.

Conclusion: We investigated the use of deep learning models for generating synthetic CTs from MRI images. Results showed that the DCNN model performed better in terms of image quality compared to the cycleGAN-based sCTs. Both sCTs were found to be suitable for dose calculations, with the DCNN exhibiting a closer agreement with the ground truth planning CT dose distribution.

Additionally, we introduced a model-generated uncertainty map method for evaluating the quality of sCTs. The addition of uncertainty quantification provides a certain level of confidence in the generated sCT, particularly for scenarios with no available ground truth for comparison [1,2,3].

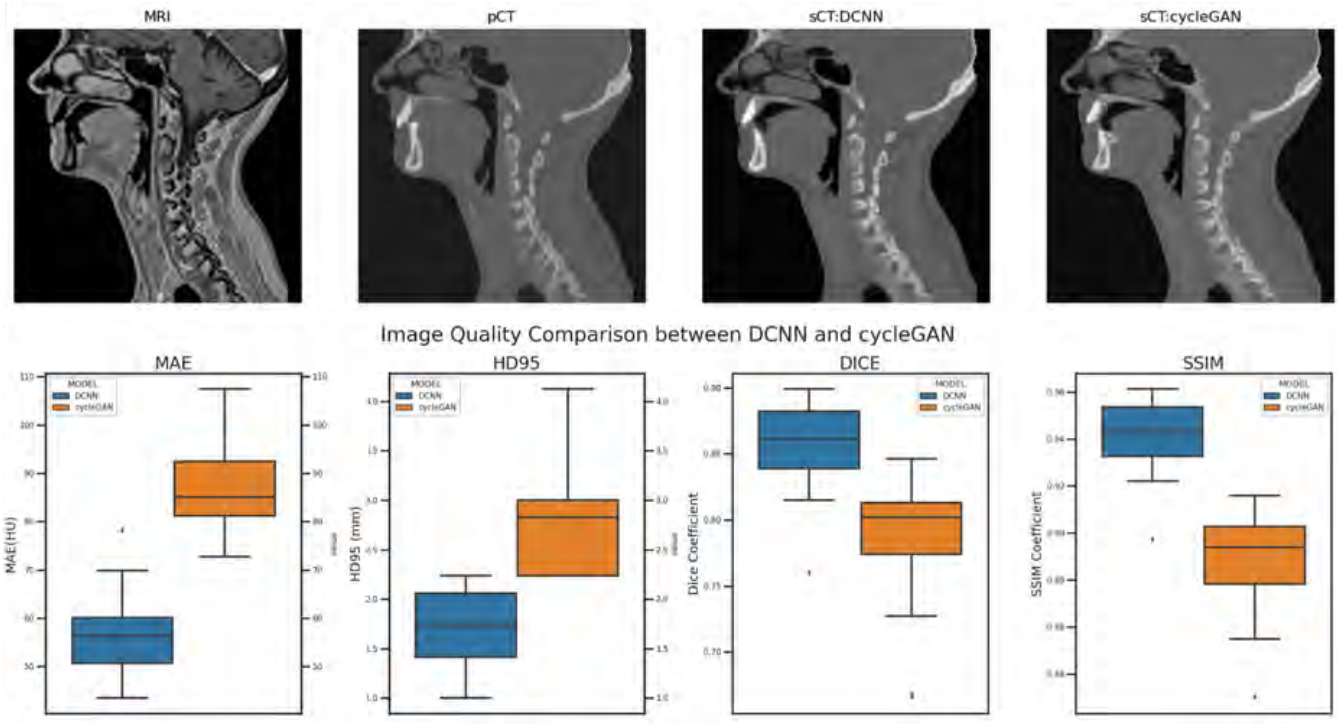


Figure 1. (top): Comparison of MR, pCT, sCT generated using DCNN model, and sCT generated using cycleGAN model. (bottom) Boxplot summary of the MAE, DCE, SSIM, and HD95.

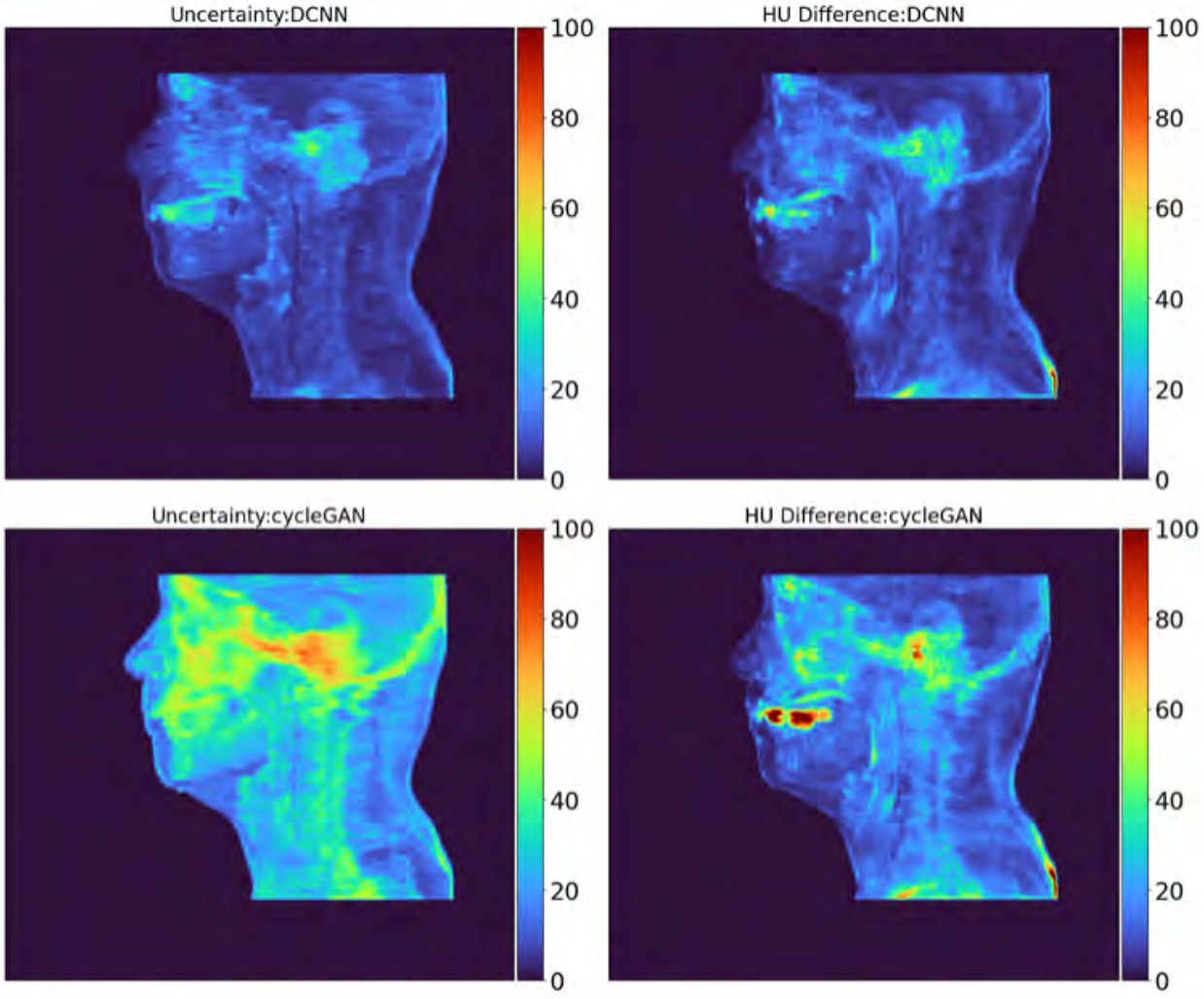


Figure 2. Projected uncertainty along the left-right direction and projected image difference

Conferences and Publications

1. Galapon A., Thummerer A., Wagenaar D., Steiu M., Langendijk J., and Both S.QA of deep learning-based synthetic CTs for adaptive proton therapy using uncertainty estimation. ESTRO 2023
2. Galapon A., Thummerer A., Wagenaar D., Langendijk J., and Both S. Investigation of uncertainty maps to assess deep learning-based synthetic CT quality for adaptive proton therapy. PTCOG 2023

Secondment

Raysearch Laboratories, February 2023, 3 weeks – Familiarization with modern treatment planning systems and optimization of cycleGAN network

Time-resolved MRI and 4DMRI for treatment plan optimization and verification

ESR5: Anestis Nakas – Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano, Milano, Italy

Supervisors: Chiara Paganelli, Guido Baroni

Background and aim : High precision planning and delivery in particle therapy is challenging for tumors subject to respiratory motion. To achieve tumor control and treatment adaptation, respiratory motion should be accounted for. MRI provides advanced imaging for motion management along with fast, radiation-free acquisitions and excellent soft tissue contrast. It lacks, however, electron density information. In this work we propose the use of time-resolved (TR) MRI and 4DMRI for plan optimization and treatment verification in Carbon Ion Radiotherapy (CIRT).

Materials and Methods:
MRI data were acquired on abdominal tumor patients treated with CIRT at the National Center for Oncological Hadrontherapy (CNAO, Italy) in correspondence to planning/re-evaluation 4DCTs. Acquisitions consisted of T1-weighted (T1-w) end exhale 3DMRI, interleaved 2D cine-MRI centered at tumor location and dynamic T2-weighted (T2-w) 4DMRI.

A. Synthetic 4DCT generation from 4DMRI
Virtual T1-w 4DMRI were generated by applying the deformation vector fields (DVFs) obtained through Deformable Image Registration (DIR) among T2-w 4DMRI phases, to the T1-w 3DMRI. Previously we trained a network on end exhale T1-w 3DMRI and correspondent CT data to generate 3D synthetic CT (sCT) [1]. Here, we tested our network implemented in [1] on virtual T1-w 4DMRI data of 3 patients to generate s4DCTs [2]. Multiple metrics were used to evaluate the generated s4DCTs such as the Mean Absolute Error (MAE), Root Mean Squared Error (RMSE), Normalized Cross Correlation (NCC), Structural Similarity Index (SSI) and Peak Signal to Noise Ratio (PSNR).

B. Dose accumulation based on TR MRI
TR virtual CT (TRvCT) volumes were created for 8 patients by warping the planning CT on 2D cine-MRI frames after 3D motion estimation. Then, the planning dose map as optimized on end exhale was used to generate TR dose distributions [3]. The dose to the 95% (D95%) of Clinical Target Volume (CTV) was calculated and accumulated for TRvCTs reconstructed within the gating window. The difference between the accumulated and planned dose was evaluated in terms of CTV ΔD95% variation. Similarly, the accumulated D1% dose was calculated on organs at risk (OARs) and compared with the planning dose, to evaluate whether the D1% constraint of 43 Gy (RBE) was violated.

C. Comparison of 4D delivery methods based on TR MRI
TRvCT data of one pancreatic patient were created consisting of 18 respiratory cycles with 8 phases each, as done in B. Treatment plans aiming for target D95>95% and V75<1% in the duodenum were optimized using all 4DCT phases (4DITV), optional lateral beam tracking (4DtITV), increased spot weights for 8x rescanning/retracking and the single phase uniform dose (SPUD) approach. Delivery techniques entailed multi-phase 4D delivery (MP4D) with optional residual tracking (MP4DRT), while rescanning and retracking plans were also delivered with MP4D and MP4DRT to enforce breath-sampling (BS). Planned (4DD) and delivered (4DDD) doses were calculated on planning 4DCT and TRvCT data, respectively [4].

Results and Discussions:

A. Quantitative results are summarized in Table 1. The accuracy of the used test set was in agreement with other studies concerning sCT generation. This demonstrates the good performance of our network in generating s4DCT of the abdominal site. These could be used to support treatment planning and adaptation within the CIRT workflow of abdominal tumors eliminating the need of re-evaluation 4DCTs. Our network's performance will be tested with larger patient datasets and a dosimetric analysis will be performed.

B. CTV coverage was robust with ΔD95% values being below 5%. Accumulated D1% remained within dose constraints only for patients whose dose constraint was not already violated from the treatment plan. This approach could be used to evaluate CTV coverage and exposure of OARs (Figure 1). The results demonstrated the robustness of the gating treatment at CNAO for CIRT and could be used as a treatment verification tool. A larger patient population will be used in the future in order to validate the results.

C. Target D95, V75 in duodenum, and delivery time are listed in Table 2. Real-time adaptive MP4DRT and lateral beam retracking with sufficient number of rescans lead to conformal dose distributions with a slight trade-off between conformity (MP4DRT) versus robustness and treatment time (retracking). Both modalities out-performed ITV deliveries and MP4D alone. The study will be expanded to more patients and verified experimentally.

Conclusions: Our results showed that TR MRI and 4DMRI could be used to generate synthetic/virtual 4DCT – thus eliminating the intrinsic lack of density information – to be utilized for treatment plan optimization and treatment verification as well as for testing the efficacy of different 4D delivery methods.

Table 1. Metric calculated to evaluate the generated s4DCTs. Average and standard deviations are shown for the three tested patients

	MAE	***RMSE***	***SSI***	***PSNR***	***NCC***
Our study	70.49 (6.46)	130.49 (16.69)	0.63 (0.10)	25.77 (1.78)	0.85 (0.43)
Liu et al., Phys Med, 2019	72.48 (18.16)	-	-	22.65 (3.63)	-
Qian et al., J. Grid Comput, 2020	-	106.43 (11.45)	-	-	0.87 (0.03)

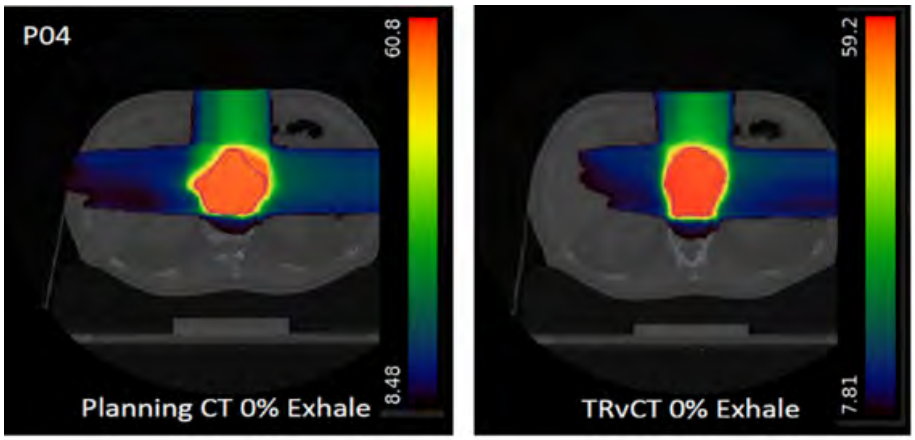


Figure 1. Planning 0% exhale CT overlayed with planning dose map (left); generated TRvCT volume overlayed with accumulated dose distribution (right). Corresponding CTV contours are shown in dark red colour.

Table 2. Planned 4DD on 4DCT and delivered 4DDD on TRvCT

Modality	Optimization	Target D95 (%)		Duodenum V75 (%)		Delivery time (minutes)
		Plan	TRvCT	Plan	TRvCT	
MP4D	SPUD	96.55	90.25	0.91	1.04	10.92
MP4DRT			92.98		1.00	10.92
Tracking	4DtITV	96.17	86.75	1.00	1.04	3.25
8xRetracking		96.38	90.39	1.00	1.01	3.25
8xBS-Retracking			96.21		1.12	10.79
Interplay	4DITV	95.29	85.98	1.33	1.38	3.48
8xRescanning		96.06	85.98	1.35	1.55	4.02
8xBS-Rescanning			91.51		1.34	19.65

Conferences and Publications

1. Parrella G., Vai A., Nakas A., Garau N., Meschini G., Camagni F., Molinelli S., Barcellini A., Pella A., Ciocca M., Vitolo V., Orlandi E., Paganelli C., Baroni G. Synthetic CT in Carbon Ion Radiotherapy of the Abdominal Site – Bioengineering 2023
2. Nakas A., Hladchuk M., Parrella G., Vai A.,Molinelli S., Ciocca M., Pella A., Barcellini A., Vitolo V., Imparato S., Orlandi E., Baroni G., Paganelli C. Synthetic 4DCT generation from 4DMRI of the abdominal site in Carbon Ion Radiotherapy - ESTRO 2023
3. Nakas A., Vai A., Molinelli S., Pella A., Barcellini A., Vitolo V., Imparato S., Ciocca M., Orlandi E., Baroni G., Paganelli C. Dose accumulation based on time-resolved MRI for treatment robustness evaluation in gated carbon ion radiotherapy of pancreatic lesions - 4D Workshop 2022
4. Steinsberger T., Nakas A., Martire M. C., Volz L., Vai A., Ciocca M., Vitolo V., Baroni G., Paganelli C., Graeff C. Comparison of 4D beam delivery methods for pancreatic cancer based on time-resolved 3DCT-MRI images - PTCOG 2023

Secondment

CNAO, Italy, October 2022 – April 2023, 6 months – gained expertise in a clinical particle therapy environment and on alternative fast dose reconstruction strategies

Scientific *Contributions*

Last year, many scientific contributions were made by the ESRs, despite most ESRs just getting started with their project. In the first half of 2023, our ESRs clearly became very productive, with a wide variety of scientific works presented on conferences and even published in high quality journals. Hereunder, you can find a summary:

Journal publications:

WP2:

- Smolders A. et al. Inter- and intrafractional 4D dose accumulation for evaluating ΔNTCP robustness in lung cancer (2023), Radiotherapy and Oncology (ESR 1)
- Smolders A. et al. Patient-specific neural networks for contour propagation in online adaptive radiotherapy (2023), Physics in Medicine and Biology (ESR 1)
- Smolders A. et al. Dosimetric comparison of autocontouring techniques for online adaptive proton therapy (2023), Physics in Medicine and Biology (ESR 1)

WP3:

- Qiu Z. et al. Online adaptive planning methods for intensity-modulated radiotherapy (2023), Physics in Medicine and Biology (ESR 6)

WP4:

- Bertschi S, et al. Potential margin reduction in prostate cancer proton therapy with prompt gamma imaging for online treatment verification (2023), Physics and Imaging in Radiation Oncology (ESR 13)

Conference contributions:

ESTRO 2023:

- Smolders A (ESR 1): Dosimetric comparison of autocontouring techniques for online adaptive proton therapy (mini-oral presentation)
- Rivetti L (ESR 2): Contour propagation and uncertainty estimation using deep learning in head and neck treatments (digital poster)
- Galapon A (ESR 4): QA of deep learning-based synthetic CTs for adaptive proton therapy using uncertainty estimation (digital poster)
- Nakas A (ESR 5): Synthetic 4DCT generation from 4DMRI of the abdominal site in Carbon Ion Radiotherapy (digital poster)
- Vatterodt N (ESR 7): Proof-of-concept: Novel CBCT-based adaptive robust optimization in sinonasal cancer proton therapy (poster discussion)
- Galeone C. (ESR 8): Real-time absorbed 4D-dose calculation for carbon ion therapy (mini-oral presentation)
- Kaushik S. (ESR 11): The effect of different optimization function templates on daily online adaptive proton therapy planning (digital poster)
- Brunner J. (ESR 12): Characterization of 3D printed material for end-to-end test phantoms in proton therapy (poster discussion)
- Bertschi S. (ESR 13): Towards clinical application: Potential margin reduction in proton therapy with prompt-gamma imaging (digital poster)
- Foglia B. (ESR 14): Evaluation of strategies for dose reconstruction from prompt-gamma radiation in proton therapy (digital poster)

PTCOG 2023:

- Smolders A. (ESR 1): Deep learning based uncertainty prediction of deformable image registration for contour propagation and dose accumulation in adaptive radiotherapy (oral presentation)
- Smolders A. (ESR 1): Inter- and intrafractional 4D dose accumulation for evaluating DeltaNTCP robustness in lung cancer (poster)
- Rivetti L. (ESR 2): Estimating segmentation accuracy in poorly segmented organs using deep-learning contour propagation uncertainty (oral presentation)
- Galapon A. (ESR 4): Investigation of uncertainty maps to assess deep learning-based synthetic CT quality for adaptive proton therapy (poster)

- Nakas A. (ESR 5): Comparison of 4D beam delivery methods for pancreatic cancer based on time - resolved 3DCT - MRI images (oral presentation)
- Qui Z. (ESR 6): Online adaptive planning for proton therapy using the reference point method (oral presentation)
- Galeone C. (ESR 8): Real-time expected DVH for carbon ion therapy (oral presentation)
- Kaushik S. (ESR 11): Anatomy-preserving virtual CT generation for online adaptive proton therapy (poster)
- Brunner J. (ESR 12): 3D-printed materials for end-to-end test phantoms in particle therapy (poster)
- Foglia B. (ESR 14): Dose reconstruction methods using secondary prompt-gamma radiation in proton therapy (poster)
- Perotti Bernardini G. (ESR 15): AI-assisted proton radiography interpretation for fast detection and classification of treatment deviations (poster)

BigART 2023:

- Vatterodt N. (ESR 7): Cross-platform assessment of CBCT-based dose evaluations for head and neck cancer proton therapy (poster discussion)
- Choulilitsa E. (ESR 10): Advantages of Online daily adaptive proton therapy for head and neck patients (poster discussion)

DCCCRT 2023:

- Vatterodt N. (ESR 7): The potential of including anatomical error scenarios for nasal cavity filling in robust optimized proton therapy treatment plans (oral presentation)

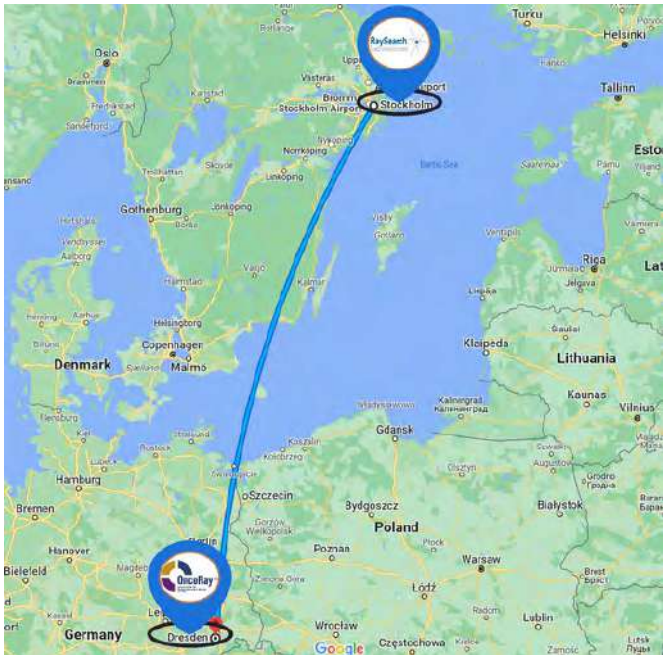
AIFM 2023:

- Galeone C. (ESR 8): Real-time expected DVH for carbon ion therapy (oral presentation)

Secondment
Reports

Suryakant Kaushik, *RaySearch*

Who: Suryakant Kaushik in collaboration with Dr. Christian Richter and Dr. Kristin Stützer
Where: OncoRay, Dresden, Germany
When: 3rd April 2023 to 30th June 2023
Why: Analyse patients' data to test various online adaptive approaches and RBE models in proton therapy



How would you describe your secondment in one word?
Lovely

What did you take home from your secondment?
Oncoray bottle

Which song describes your secondment best?
'Yun Hi Chala Chal' Song by Udit Narayan, Hariharan and Kailash Kher

As we bid farewell to the captivating city of Dresden, I can't help but reminisce about the mesmerizing view of historic buildings along the Elbe River. The sunny days brought much-needed refreshment after the freezing winters. My heart was filled with joy during the "Sommer Fest," especially the entertaining human foosball game that united us all. Among the cherished memories were the Friday group lunches fostering lasting bonds.

My academic journey in Dresden was full of invaluable learning opportunities. I implemented two approaches of 4D adaptive proton therapy planning and RBE models on the patient data. With the unwavering support of supervisors at OncoRay, I was able to overcome obstacles and achieve meaningful results. Sharing knowledge with fellow PhD students from diverse fields enriched my learning journey. The "Dresden Long Night of Science" fortunate me with a long-awaited visit to the MRI Linac.

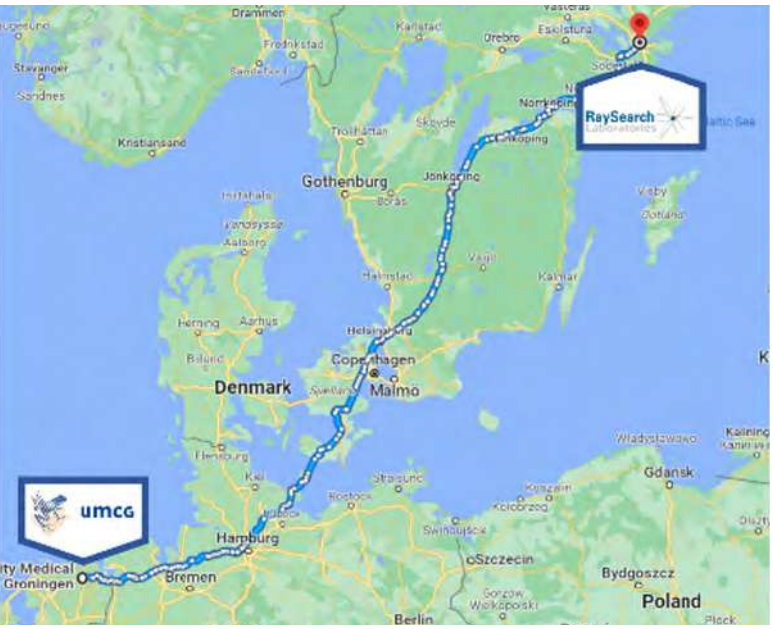
Arthur Galapon, *University Medical Center Groningen*

Who: Arthur Galapon collaborating with Albin Fredriksson and Suryakant Kaushik
Where: RaySearch Laboratories, Stockholm, Sweden
When: February 13 – March 2, 2023 (3 weeks)
Why: Familiarization with the Raystation Treatment Planning System and optimization of the cycleGAN model for synthetic CT generation

Stockholm is a lovely city. Despite being accustomed to the Netherlands' flat lands, I enjoyed strolling to a vantage point during snowy days while watching the city lights. Gamla Stan's quaint cobblestone streets took me on a nostalgic journey back in time. Yet, the highlight of my stay was witnessing a faint aurora gracefully illuminating the night sky—one thing off the bucket list.

During my time at Raysearch, I engaged in a highly productive discussion about optimizing the cycleGAN model. This experience provided valuable insights into a developer's problem-solving approaches. Additionally, I had the opportunity to have fruitful discussions with ESR11 Suryakant, where we explored automating processes in Raystation using scripting. Implementing these automation techniques allowed me to streamline most of my workflows, freeing up more time to focus on other crucial aspects of the project.

I may have stayed for three weeks, but the ideas and insights I've gained during this short time will undoubtedly impact how I approach my work and problem-solving.



How would you describe your secondment in one word?
Cool(d)

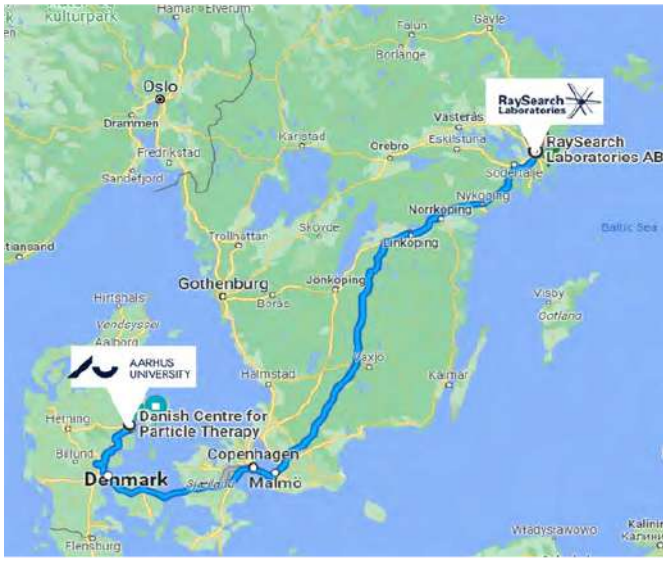
What did you take home from your secondment?
Photo of the aurora and an Arctic fox

Which song describes your secondment best?
Sparkle - Radwimps

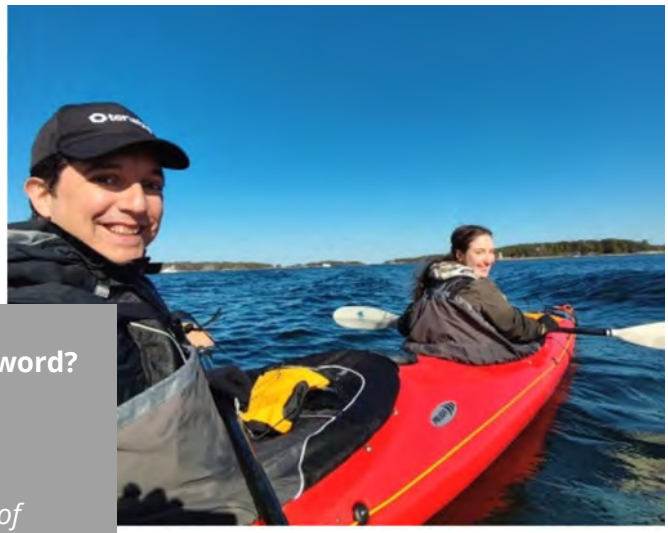
Nadine Vatterodt, *Aarhus University*

Who: Nadine Vatterodt collaborating with Albin Fredriksson
Where: RaySearch Laboratories, Stockholm, Sweden
When: 27. Feb – 2. June 2023
Why: Robust optimization and evaluation strategies for anatomical changes within the TPS RayStation

Moving to rainy and windy Denmark was already a big step for me, being someone who is always freezing. However, Stockholm in February was next level. Nonetheless, I am grateful RAPTOR is pushing me to discover the beauty of Nordic countries. I'm in love! A highlight was the kayaking tour in the Archipelago with ESR Giuliano, who, among others, happened to be visiting RaySearch during my stay.



The secondment allowed me to gain impressions of the private sector and the research team in a company. Since I am far from a software developer, I was quite intimidated by the many brilliant people I met. It was the internal R&D day that helped me overcome some self-doubts. I realized my understanding of the many aspects of radiotherapy and approaching topics from a more clinical perspective are indeed of advantage, too. I had fruitful discussions, followed inspiring presentations and a great Swedish PhD defense on optimizing patient scheduling by Sara Frimodig. Thanks to Albin for the support and guidance that led us to an exciting project on robust evaluation. I hope to return for a short visit to present our findings and discuss them with the entire research team.



How would you describe your secondment in one word?
Enlightening

What did you take home from your secondment?
A study I'm eager to move on with & the embarrassment of knowing that all Germans mispronounce Köttbullar

Which song describes your secondment best?
Thinking of Sunshine by Daniel Adams-Ray

Stefanie Bertschi, *OncoRay*

Who: Stefanie Bertschi collaborating with Stine Korreman, Anne Vestergaard and Ulrik Vindelev Elstrøm
Where: Aarhus University
When: March-April 2023 (2 months)
Why: Investigate possibilities of prompt-gamma-imaging (PGI) simulations based on cone-beam CT (CBCT) based data by performing CBCT scans of phantoms as well as using patient data.

Denmark was a great experience. Being Swiss, I had to visit the highest 'mountain' with 147m, which was very cute. However, it was a very nice trip, followed by many more discovering the beautiful country. Highlights were definitely hunting for polar lights, surfing in Klitmøller, called 'cold Hawaii' and going to pub quizzes.

During the two months in Aarhus, I made use of the CBCT scanner as well as patient data including CBCT scans available at DCPT (Danish Center for Particle Therapy). I met the medical physicists Anne Vestergaard and Ulrik Vindelev Elstrøm, who helped me taking CBCT and CT scans of two phantoms I brought. Based on those scans, I verified the accuracy of simulation of the expected PGI signals based on CBCTs. I extended those investigations to patient data. The first comparison shows promising results, which I will follow up on in an additional secondment in Groningen.

For me, these two months were great success, both in terms of research results as well as meeting and connecting with colleagues. A special thank goes to Anne and Ulrik for supporting me and making everything possible.

How would you describe your secondment in one word?
Successful

What did you take home from your secondment?
CBCT scans and extended general music knowledge (pub quizzes)

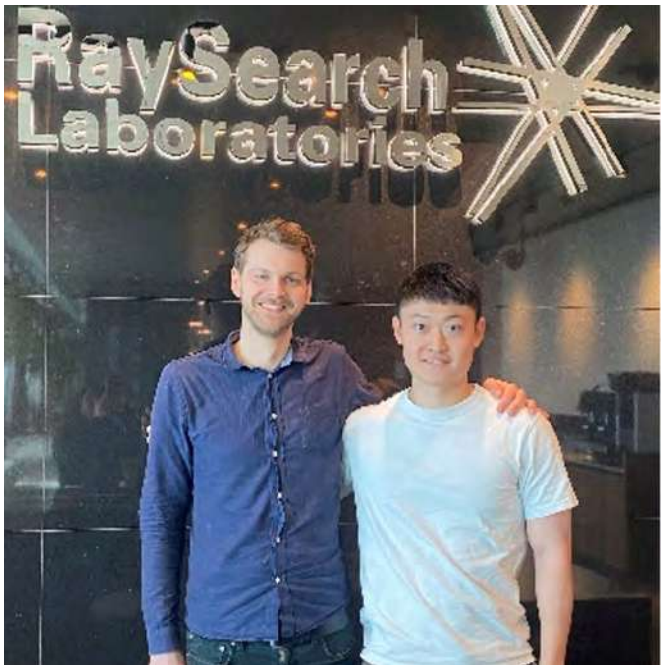
Which song describes your secondment best?
Wheels – Foo Fighters

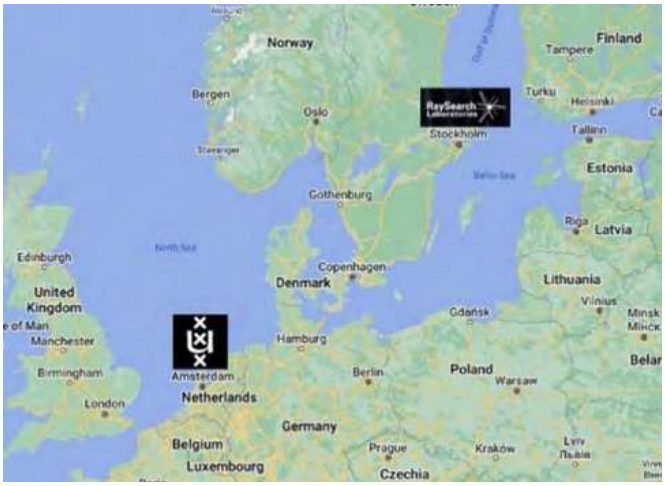
Zihang Qiu, *University of Amsterdam*

Who: Zihang Qiu, with Albin Fredriksson
Where: RaySearch lab, Stockholm, Sweden
When: June - October 2022
Why: Get familiar with RayStation treatment planning system

As I am working on treatment planning for proton therapy, Raysearch is a must-visit for me for their successful Raystation treatment planning system. There, I had the opportunity to access and play with the Raystation treatment planning system, which can be used in my future research. Also, I had the opportunity to get to know the present research studies at Raysearch, understanding what is important and new coming in the proton therapy field.

Besides, Raysearch is an exemplary combination of research and business. I am very glad that I was able to network with people from the product development and business sides and got an idea of how they translate research outcomes into commercial products and make an impact on the real world.





Finally, I have to say, to me, Stockholm is a city of contrast for the people living there. I initially found the city so restrained because people there seemed uninterested in general. They look down on the ground when they walk, barely any eye contact. However, after spending a few days there, I adapted to the vibe, started talking to the locals, and met many interesting people. I would love to visit it again when there is no snow!

How would you describe your secondment in one word?
Restrained

What did you take home from your secondment?
A name tag of Ivar Bengtsson

Which song describes your secondment best?
Koop Island Blues - Koop

Next Events and Important Dates

The 3rd RAPTOR School - Loop Engagement
10 - 15 September 2023
Monte Verità, Ascona, Switzerland
More information here.

The 3rd RAPTOR School will take place in Ascona, Switzerland.
The school is co-sponsored by ETH GRANT "Support for scientific meeting" and will be combined 4D-workshop. **Save the date!**

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