Editorial

Dear Reader

Welcome to this edition of our bi-annual newsletter from the RAPTOR (Real Time Adaptive Particle of Cancer Therapy) project.

The RAPTOR program is on track, having successfully achieved all objectives and milestones set for this year, as it advances toward its scheduled conclusion in September 2025. All 15 RAPTOR PhD students have demonstrated remarkable progress, with one student already successfully defending his PhD. Collectively, their contributions in 2024 have included numerous presentations at national and international conferences, as well as 11 peer-reviewed journal publications, underscoring the program's growing impact on the scientific community.

Inside this issue

The program has fostered collaboration and knowledge-sharing through three training schools, open to both RAPTOR students and external participants. These events enhanced the consortium's outreach and contributed to the professional development of participants.

A key highlight of this year, and the focus of this newsletter, was the final RAPTOR conference held in Dresden, Germany. This event not only provided a platform for RAPTOR students to showcase their findings from the past three years but also included a grant-writing workshop designed to equip them with valuable skills for future career opportunities. The ESR got an exclusive tour through OncoRay including the proton therapy facility and could get a first-hands impression on how OncoRay fosters its focus on translational research and bringing innovations to the patient. A very special highlight for many ESRs was also the meeting with a local patient representative who gave very personal but also meaningful insights in her experience as patient and as patient representative. Despite challenges posed by travel strikes, the conference successfully attracted 48 participants, who provided very positive feedback on the experience.

This newsletter offers a review of the final RAPTOR conference, with a special focus on the grant-writing workshop, as shared by participants. It also features abstracts from all 15 RAPTOR students, showcasing their achievements and results from the past three years. Additionally, the newsletter includes remarkable scientific updates and secondment reports.

For more information and updates on future progress, please visit the official RAPTOR website (RAPTOR Consortium) or follow our LinkedIn page (RAPTOR LinkedIn).

Enjoy reading!

Stefanie Bertschi & Christian Richter

Review of final conference

Author: Beatrice Folia

Towards the end of their project, the RAPTOR students gathered with senior researchers and invited speakers from 3 to 5 October for the RAPTOR final conference in the picturesque city of Dresden.

Dresden is the capital of the German state of Saxony, framed by the Elbe river. Despite being heavily bombed in 1945, the city is very well-known for its baroque-rococo beauty, such that the artist Canaletto represented it in some of his paintings.

On the first day, the participants where hosted by OncoRay - the National Center for Radiation Research in Oncology. Inspired by this innovative environment, the young researchers took part in a grant writing workshop, given by Scriptoria, a consultancy recognized for its expertise in sustainable development and knowledge management, which already partnered with RAPTOR in past events. Grant writing is an important skill for those wishing to continue working academia and aiming to lead their own projects, and it is not

an easy task for fledgling researchers. During this workshop, young researchers learnt how to properly draft a grant, not only highlighting the problem and the research aim, but also focusing on the general methods which would be exploited to reach said aim and on the likely outcomes, posing attention to benefit to the society and aligning to the funder's objectives (more details in the following report).

At the same time, senior researchers met to discuss details about the future of RAPTOR, conveyed into the RAPTOR+ project. The consortium wants to continue its work on real-time adaptive particle therapy, and the meeting had the aim to strengthen the position within the research community working on online-adaptive particle therapy, opening up for new members.

The day's activities concluded with an engaging tour of the OncoRay facility, where Prof. Dr. Christian Richter showcased the center's collaborative approach to translational research, emphasizing the essential role of interdisciplinary communication.

On the following days, participants were hosted in the majestic Schloss ("castle") Eckberg, built on the right of the Elbe river between 1859 and 1861 on behalf of the merchant Johann Daniel Souchay.

Day two was mostly dedicated to the RAPTOR students, who presented the status and outcomes of their projects. Three sessions were assigned to the presentations, one per RAPTOR work package. The progresses made by each student clearly came out, not only related to results which were shown, but also from the ability to present and stand in front of public. Summing up the work of 3 years in 15 minutes was not an easy task, but it was carried out excellently.

In between presentations, people could get an insight of some work carried out outside RAPTOR, looking at research posters realized by some participants. Moreover, a couple of parallel sessions were held. During one of these sessions, Dr. Jakob Ödén from RaySearch Laboratories talked about his personal experience, going from academia to a company, and highlighted perks and drawback of the industry environment. At the same time, Daniela Kunath from Dresden University

Hospital (UKD) described the role of a Medical Physicist and how the education to this profession works in Germany. She outlined how the work of a Medical Physicist foresees research involvement, and she mentioned the challenges of recruiting new qualified candidates.

Meanwhile, a small group had the opportunity to converse with a former patient and now patient representative. The outcomes of this conversation were reported to all the participants afterwards. For some, it was the first time being involved in a more human atmosphere, listening to the other side of proton therapy. She talked about her experience and her treatment. She mentioned about being more curious about why things were happening, other than what was about to happen, but she also underlined how this feeling could be different for other patients, who might need more emotional assistance and support. Follow-ups represented one important aspect of her treatment, during which she felt well taken care of.

During another session, young participants applied their grant-writing skills acquired from the previous day. After brainstorming, three groups' representatives explained their ideas about solutions for "Cost-effective realizations of Online-Real time adaptive therapy", "Technological improvements for online adaptation at different tumor locations" and "Concepts beyond anatomy-based adaptation", three of the topics which will be tackled within the RAPTOR+ program.

The last day started with three presentations from invited speakers. Dr. Sergej Schneider from OncoRay gave a broad overview about MR-guided proton therapy and its advancements, followed by Dr. Francesca Albertini's case study on Paul-Scherrer-Institute's successful implementation of an online adaptive proton therapy workflow. Eventually, Prof. E. Sterpin summarized the achievements of the ProtOnART consortium.

The event concluded with a scenic hike in the wonderful Sächsische Schweiz ("Saxon Switzerland"), a hilly climbing area and national park in the Elbe Sandstone Mountains.

Participants enjoyed breathtaking views and reinforced relationships built over the past few years.

The RAPTOR Final Conference represented the culmination of years of hard work and the potential for future collaborative innovations. As the students look toward their next steps, the lessons learned and connections made within RAPTOR will undoubtedly shape their careers, contributing to the advancement of radiation research.

Detailed review of the grant writing workshop

Author: Anestis Nakas

In the final RAPTOR school in Dresden, the students participated in a grant writing workshop, an enriching experience aimed at building foundational skills in securing research funding. The workshop provided structured training on effectively presenting research ideas, writing compelling proposals, and understanding the intricacies of the grant application process. Given the competitive landscape of academic funding, these skills were invaluable for the students looking to establish themselves in their respective fields.

Throughout the workshop, the students learned how to align their proposals with the priorities of funding agencies, articulate the significance of their research, and emphasize its broader societal impact. Practical exercises, such as drafting sections of a proposal and peer-reviewing other researchers' work, not only enhanced their writing skills but also fostered a sense of collaboration and mutual support among participants. Participant feedback underscored the workshop's value, with an overall rating of 4.6 out of 5, expectations met with a score of 4.8 out of 5, and the trainer receiving a perfect score of 5.0 out of 5. Comments such as, "Will be very helpful when actually writing a grant application to recap. But also for other interviews and applications," and, "The trainer did his best to keep the participants engaged and added personal anecdotes... I think it added a lot," highlighted the engaging and practical nature of the experience.

By the end of the workshop, the students reported feeling more confident in their ability to pursue funding opportunities. This experience is expected to have a lasting impact, empowering them to initiate and sustain independent research projects, increase their academic visibility, and contribute more effectively to their respective fields. Overall, the workshop proved to be a crucial step in developing the grant writing proficiency essential for a successful academic career. By equipping young researchers with these vital skills, the RAPTOR program fosters their growth while empowering them to pass on this knowledge, driving a continuous cycle of innovation.

Abstracts RAPTOR students

Dose accumulation and uncertainty estimation

Author: Andreas Smolders

Aim and Motivation:

Online adaptive proton therapy aims to reduce setup and anatomical uncertainties so that the dose can be delivered more accurately, better covering the tumor and sparing the surrounding healthy tissue. Currently, only one clinical implementation has been reported, solely focusing on non-deforming anatomies (e.g. skull-based). However, anatomical deformations arguably cause the largest delivery errors, and online adaptation would especially benefit cases with substantial deformations. In my PhD thesis, titled Towards online adaptive proton therapy in deforming anatomies, we developed and analyzed multiple algorithms supporting online adaptation in deforming patients, and demonstrated their quality and applicability.

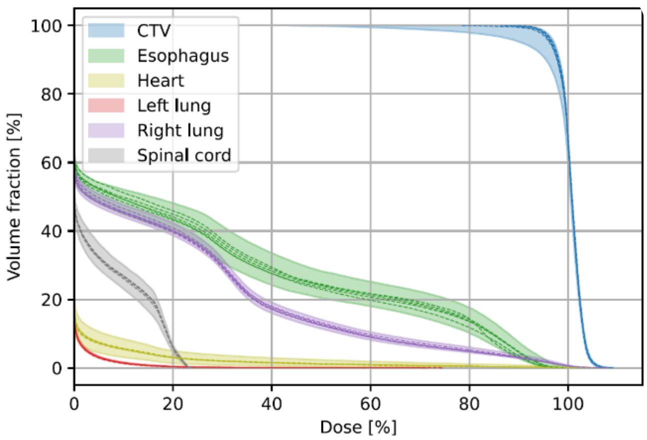
Approach & Achievements:

First, the impact of increased imaging dose on secondary cancer risk was assessed. We showed that, for patients with head-and-neck cancer, a 1 mm reduction in setup robustness would compensate this effect. Thus, online adaptation will likely reduce secondary cancer risk, alongside other, better-established benefits. Second, a specialized technique for automatic contouring was introduced, combining the speed of deep-learning segmentation with the quality of deformable image registration (DIR). A dosimetric analysis showed that the influence of using automatic organ-at-risk contours was usually small, comparable to commonly accepted dose deviations. The effect of automatic target contouring was more pronounced, yet we showed that target coverage was significantly better with online adaptation despite inaccuracies in automatic contouring. In later work, we compared methods to explicitly account for contouring uncertainties in robust optimization. Efficient, dedicated consideration of contour uncertainties was possible, with less dose to healthy tissue than current methods.

A specific advantage of online adaptation is its potential to account for previous delivery inaccuracies when optimizing the daily plan. Dose accumulation is necessary for this, but for deforming anatomies, it requires DIR, introducing dose accumulation uncertainties. In a retrospective analysis of lung cancer patients, we showed that these uncertainties were substantial and should be included in decision-making. Therefore, a deep learning based DIR uncertainty prediction model was developed, applicable for dose accumulation and contour propagation. This model predicts uncertainty based on image contrast and deformation magnitude and the uncertainty could be efficiently propagated into contouring and dose accumulation uncertainties (Fig. 1). The model showed promising quantitative results when compared to manual landmark and contour annotations. However, such evaluations are sparse, considering only a few points or regions. Comprehensive evaluation in real patient images is impractical; thus, virtual phantom models were developed, where an anatomically plausible deformation was generated and applied to a single image. These models, based on denoising diffusion probabilistic models, produced high-quality deformations consistent with those observed in real patient images, but the application for DIR uncertainty evaluation was not yet been performed.

Impact and Outlook:

Throughout our analyses and using our developments, we identified no major barriers preventing the transition toward online adaptive particle therapy in deforming anatomies. Moreover, our findings indicate that patients will benefit from swift implementation in practice, despite current algorithmic imperfections. Additionally, the work on dose accumulation uncertainty provides the first steps toward advancing beyond basic online adaptation.



Automated segmentation and contour propagation

Author: Luciano Rivetti

Aim and Motivation:

A major source of uncertainty in conventional radiotherapy stems from anatomical changes that patients experience during treatment. One approach to mitigating these uncertainties is by developing anatomically robust treatment plans that remain effective despite such changes. However, this approach is challenged by the knowledge of all possible anatomical variations that a patient may undergo. An alternative approach to mitigate anatomical uncertainties is to adapt the treatment plan daily based on the patient's current anatomy. While promising, this method is constrained by the need for fast algorithms to update plans in real-time. One key bottleneck in this workflow is the generation of daily anatomical structures, which is slowed by algorithmic inefficiencies and the need for physician review of the structures before treatment optimization.

In this work, we aim to develop a method to predict likely anatomical changes in head and neck cancer and evaluate how these predictions can improve the robustness of treatment plans. We will also develop a fast deformable image registration (DIR) algorithm to generate the daily structures and its uncertainty by propagating the treatment planning structures. Finally, we will implement a probabilistic robust optimization algorithm that incorporates structure uncertainties generated with our DIR algorithm, aiming to reduce the time required for physician intervention and thus the time of the re-adaptation.

Approach & Achievements:

We developed a model that predicts likely anatomical changes in radiotherapy using denoising diffusion probabilistic models (DDPMs). This model takes a reference cone-beam CT (CBCT), the fraction number, and the delivered dose distribution as input and predicts possible anatomical changes for each treatment fraction (Fig 1. a). The model was then used to optimize a proton therapy plan, accounting for these predicted changes. This work, conducted during the secondment of Andreas Smolders at the University of Ljubljana, led to a short paper presented at ICCR 2025 and a peer-reviewed publication in Physics in Medicine & Biology (PMB) in 2024.

The DIR algorithm was developed using a probabilistic multi-resolution approach that employs convolutional neural networks (CNNs) to estimate a dense displacement field (DDF) with multivariate normal distribution (Fig 1. b). We evaluated the performance of our approach against three other uncertainty-predicting DIR algorithms—VoxelMorph, Monte Carlo dropout, and Monte Carlo B-spline—assessing both deformation quality and the reliability of uncertainty estimates. The results of this study were presented as the first deliverable of the project at the AAPM 2023 conference and published in PMB in 2024.

The structures generated by our DIR method were used to simulate two different online adaptive treatments: one based on the most likely propagated structures, and the other using probabilistic optimization of the uncertainty map derived from the structures. The performance of these treatments was compared to the gold-standard DART workflow, which relies on physician-reviewed structures. The results of this study were published as part of the project's second deliverable in 2024.

Impact and Outlook:

Our algorithm for predicting anatomical changes can significantly improve dose coverage in regions where minimal anatomical variation occurs, offering a practical alternative to traditional adaptive radiotherapy. This approach can reduce radiotherapy's clinical burden by reducing the re-adaptation frequency. For cases where substantial anatomical changes are anticipated, combining our fast DIR algorithm and probabilistic robust optimization could reduce physician intervention during the re-optimization process. This would not only speed up treatment re-planning but also increase the overall efficiency of adaptive radiotherapy, reducing the burden on clinical workflows while maintaining treatment accuracy.

Figure 2: a) Overview of a single step of the DDPM model. At each diffusion step t, the noisy image x_t, the conditional CBCT, and the dose distribution are concatenated and inputted to a 3D U-Net that denoises the image. This model denoises pure Gaussian noise images during inference time and generates a new likely anatomy. b) Illustration of the training workflow used in our supervised and unsupervised models. The solid lines show the data flow for the unsupervised model, and the solid lines plus the dash lines show the data flow for the supervised model.

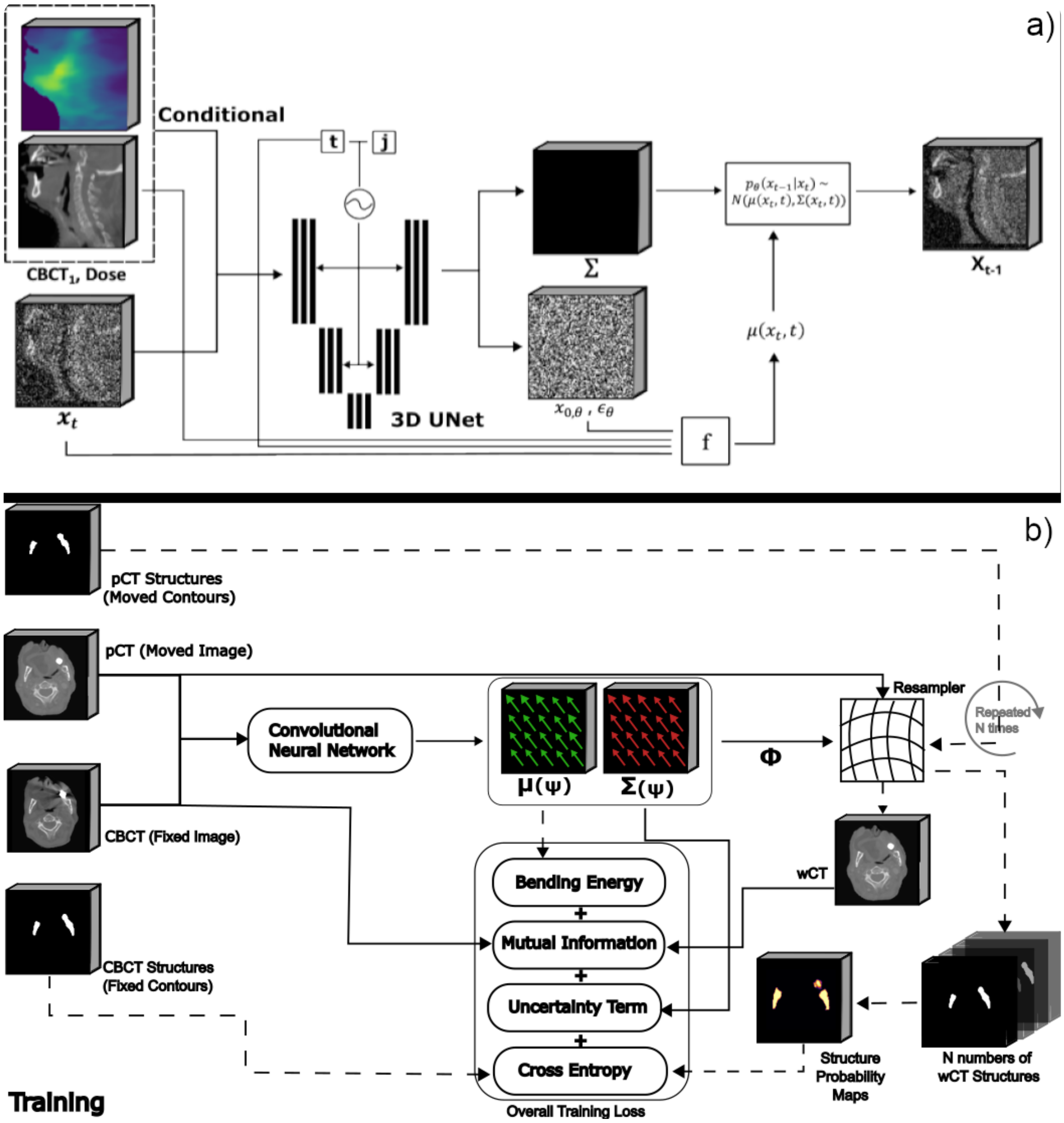


Figure 2: a) Overview of a single step of the DDPM model. At each diffusion step t, the noisy image x_t, the conditional CBCT, and the dose distribution are concatenated and inputted to a 3D U-Net that denoises the image. This model denoises pure Gaussian noise images during inference time and generates a new likely anatomy. b) Illustration of the training workflow used in our supervised and unsupervised models. The solid lines show the data flow for the unsupervised model, and the solid lines plus the dash lines show the data flow for the supervised model.

CBCT enhancement strategies for adaptive ion beam therapy

Author: Francesco Maria Russo

Aim and Motivation:

The goal of this project is to improve the quality of Cone Beam Computed Tomography (CBCT) images to enable their use in adaptive particle therapy workflows. CBCT is commonly used for patient positioning, but due to issues such as scatter radiation, detector lag, and cone-beam artifacts, the Hounsfield Unit (HU) values obtained are not reliable enough for treatment replanning. This is particularly true in particle therapy, where accurate knowledge of electron density is crucial to determine particles range. Improving CBCT image quality to make it suitable for treatment replanning would offer significant clinical benefits in terms of sparing healthy tissue and fully exploiting the precision achievable with particle therapy.

Approach & Achievements:

Our approach focuses on both software and hardware-based corrections. On the software side, we have developed an algorithm that utilizes low-frequency information from an AI generated synthetic CT (sCT) to correct shading artifacts in CBCT, while preserving the anatomical fidelity of the original CBCT image. This method mitigates the risk of "hallucinations" associated with AI sCTs and was presented at ICCR 2024 conference in Lyon. Parallel to this, we are investigating projection-based correction methods to further enhance image quality starting from the same sCT. Close collaboration between medPhoton, MedAustron and the Ludwig Maximilian University of Munich enables us to test these pipelines in clinical settings while ensuring academic rigor. Additionally, we have begun testing a hardware-based correction approach, exploring the use of Anti-Scatter Grid (ASG) technology to reduce scatter radiation from reaching the detector, which has shown potential for improving HU accuracy and enabling dual-energy CBCT.

Impact and Outlook:

This project has the potential to significantly impact clinical workflows in adaptive particle therapy by enabling CBCT images to be used for treatment replanning. Our close collaboration between medPhoton, LMU, and MedAustron ensures that our solutions remain clinically relevant and focused on patient safety. The combination of software post-processing and hardware means aims to provide a robust solution that bridges the gap between current imaging limitations and the demands of adaptive therapy, while always considering the clinical applicability and safety for patients.

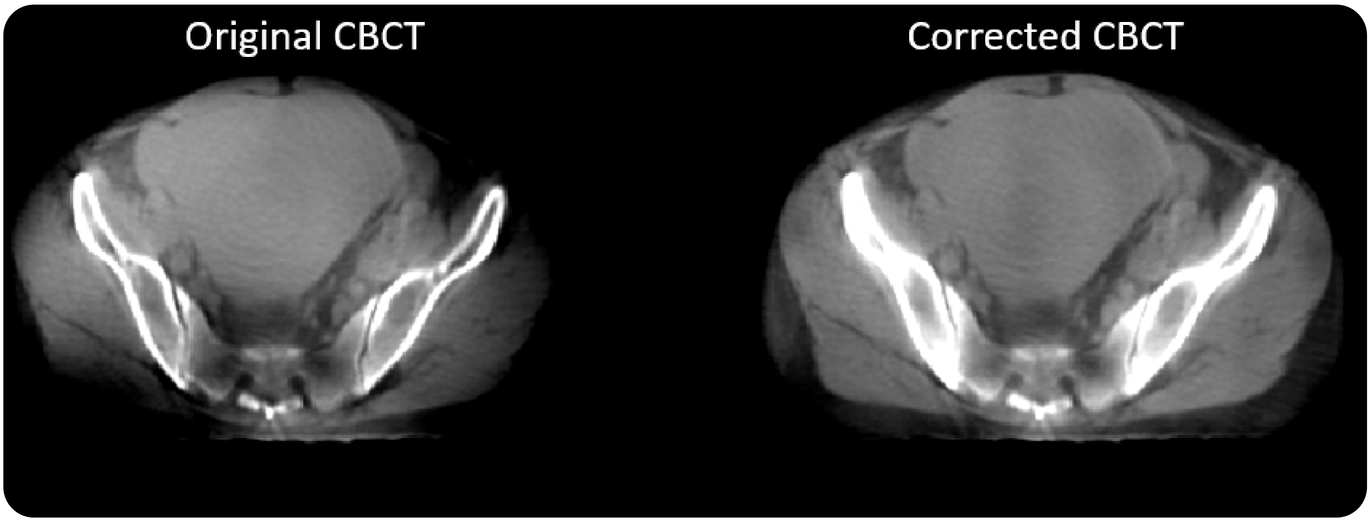


Figure 1: Example of the corrected CBCT after the shading correction pipeline. W/L [400,0]

Advanced use of MR Imaging in Adaptive Intensity Modulated Proton Therapy

Author: Arthur V. Galapon Jr

Aim and Motivation:

Online adaptive radiotherapy can significantly benefit from the rapid and precise conversion of in-room volumetric imaging modalities, such as cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI), into diagnostic-quality synthetic computed tomography (sCT). Generating sCT images from these modalities is crucial for streamlining the adaptive radiotherapy workflow, enabling faster processes by eliminating the need for verification CT scans (rCT) and allowing CBCT and MRI images to be used directly for dose calculations.

Advancements in deep learning (DL) algorithms and the availability of large datasets have greatly enhanced the speed and accuracy of CBCT/MRI conversion into sCT, making sCT-based workflows increasingly viable in clinical settings. However, the successful integration of sCTs into clinical practice requires the development of robust quality assurance methods. Since ground truths may not always be available, developing reliable quality assurance (QA) tools using uncertainty maps may serve as a surrogate for evaluating the quality of DL-based sCTs.

Approach & Achievements:

A. Two deep-learning models were trained to generate sCTs from paired MR-CT images using a dataset of 101 head and neck cancer patients. A deep convolutional neural network (DCNN) was trained with paired inputs, while a cycleGAN utilized unpaired inputs for training. The results showed an average mean absolute Hounsfield Unit (HU) difference of 56.34 ± 8.6 HU for the DCNN model and 86.66 ± 7.9 HU for the cycleGAN model. Each patient's clinical plan was used to assess the dosimetric performance of the generated sCTs. Dosimetric evaluation demonstrated high similarities tot he actual clinical plan with a gamma analysis of 99.29% and 97.39% pass rate for the DCNN cycleGAN, respectively.

B. The clinical implementation of sCTs requires reliable quality assurance tools to ensure their performance is consistent with that of the planning CT images. In the absence of ground truth data, uncertainty maps may serve as a surrogate for evaluating sCT quality. Using Monte Carlo dropout (MCD), uncertainty maps were generated alongside the sCTs. These maps were found to be highly correlated with the actual Hounsfield Unit (HU) errors between the sCT and planning CT (pCT). Additionally, regions with high uncertainty showed a positive correlation with the range errors between the sCT and pCT [1].

C. Transfer learning strategies were used to assess the sustainability of using DL-based models in the presence of changes in the input image quality, particularly following improvements in the reconstruction software algorithms of imaging devices. Results indicate that transfer learning with a small number of datasets is sufficient to reduce the downtime of sCT-dependent workflows due to the limited availability of new data from post-upgrade sources [2].

Impact and Outlook:

With all the necessary tools in place, the clinical integration of sCT-dependent workflows for adaptive proton therapy will be one step closer. However, achieving seamless integration of all components—including model training, quality assurance methods, and clinical sustainability—will require further effort. Additionally, the overall impact of using sCTs in clinical practice must be evaluated to highlight the benefits of transitioning to an sCT-dependent adaptive workflow.

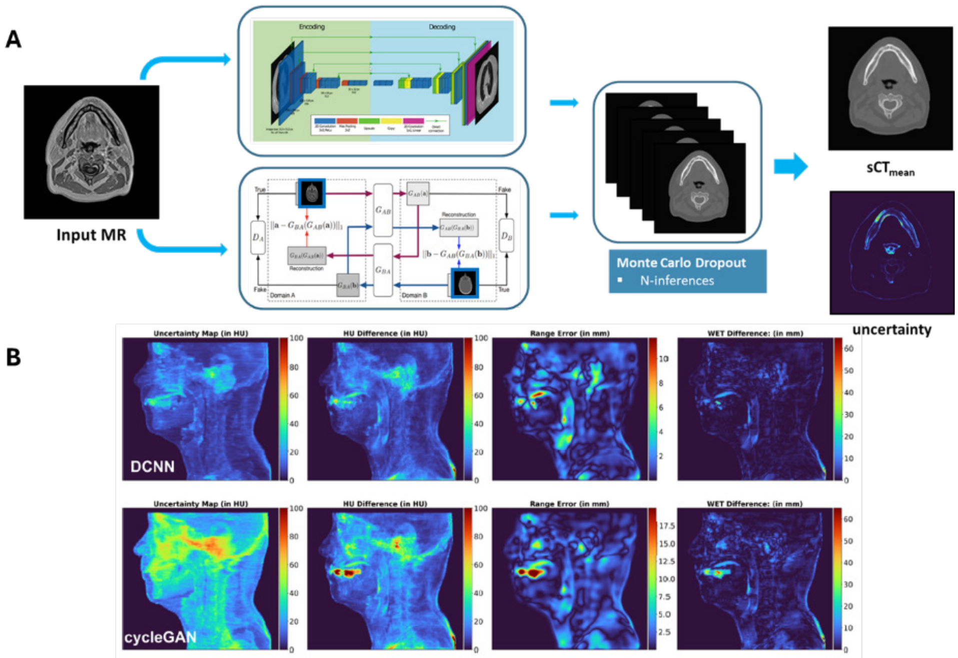


Figure 1: (A) Synthetic CT generation workflow using DCNN and cycleGAN and model uncertainty prediction using Monte Carlo Dropout. (B) Comparison of Uncertainty maps to HU difference, range error difference, and WET difference.

[1] Galapon AV, et al., Med Phys. 2024; 51: 2499–2509. https://doi.org/10.1002/mp.16838,

[2] Galapon AV, et al., under review Medical Physics

4DMRI and motion management in adaptive particle therapy

Author: Anestis Nakas

Aim and Motivation:

Carbon Ion Radiotherapy (CIRT) requires high treatment precision, which is a challenging task for tumours subject to respiratory motion. As such, motion should be considered both in treatment planning and delivery. For treatment planning, 4DMRI could address motion and its induced uncertainties by creating and exploiting virtual or synthetic 4DCT (4DsCT) using Deformable Image Registration (DIR) or deep learning. For treatment delivery, 4DMRI data could be used to assess the efficacy of different 4D dose delivery methods. Motion compensation could be achieved via the integration of optical motion monitoring with 4D delivery by means of patient – specific correlation models.

Approach & Achievements:

A. A conditional GAN (cGAN) was trained and tested on abdominal 4DCT and virtual T1-weighted 4DMRI (v4DT1-w) data of 26 patients undergoing CIRT at CNAO, to generate 4DsCT (See Figure). A 4D computational phantom was used to validate the cGAN's performance. Generated volumes were evaluated with respect to the original 4DCT based on motion analysis, similarity metrics and dosimetric criteria, by recalculating clinically optimized CIRT plans on the 4DsCT. The cGAN could generate accurate 4DsCT of the abdominal site, allowing CIRT dose calculations comparable to clinical plans. Additionally, a comparison analysis is underway to test the performance of different deep-learning networks in 4DsCT generation.

B. Time-resolved virtual CT (TRvCT) volumes were created for 5 patients by warping the planning end-exhale CT on 2D cine-MRI frames after 3D motion estimation, to generate dynamic vCT datasets animated with the motion derived from cine-MRI data. Treatment plans were created using different optimization techniques, on the TRvCT and planning 4DCT. Multiple 4D delivery techniques were used, with the planned and delivered doses calculated on planning 4DCT and TRvCT, compared. The study was also verified experimentally in CNAO and the results are currently under processing.

C. The exploitation of an integrated platform, developed at CNAO, that provides real-time respiratory information, acquired by an Optical Tracking System (OTS), to the 4D Dose Delivery System (4D-DDS) for the 4D delivery of a moving target, was investigated, using a linearly moving pixel-array detector. OTS-derived motion data were used in the delivery of 4D CIRT plans with the 4D-DDS. Simultaneously, motion information was communicated to a GPU-based, real-time dose calculation system, interfaced with the 4D-DDS, named RIDOS. A correlation model was used within RIDOS to generate in real-time new CTs along with the reconstructed the delivered dose. Planned and delivered dose distributions were compared to assess the dosimetric accuracy of the dose engine and test the motion model. Overall, the results demonstrated the feasibility of the OTS-DDS-RIDOS framework in a quasi-clinicatoel environment.

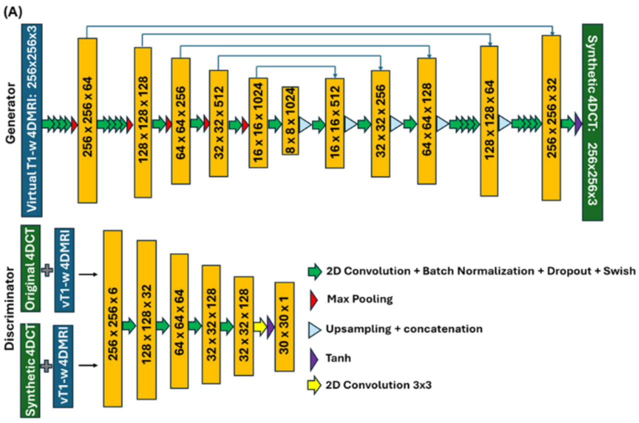


Figure: The cGAN used to generate 4DsCT as described in section (A)

Impact and Outlook:

The generation of 4DsCT and TRvCT could be put forward to support treatment planning evaluation and robustness in CIRT by complementing 4DCT. The OTS-DDS-RIDOS framework tested in a quasi-clinical environment shows potential for on-line adaptive treatments with full motion compensation.

Optimizing the plan of the day

Author: Zihang Qiu

Aim and Motivation:

As patients experience daily anatomical variations, using on the initial treatment plan, which is designed based on their pre-treatment anatomy, becomes suboptimal throughout the treatment course. Misalignment between the treatment plan and the patient's actual anatomy during irradiation can lead to compromised target coverage and insufficient sparing of normal tissues.

The goal of this project is to develop fast algorithms that enable treatment plans to be optimized for daily anatomy. The primary challenge in generating a daily treatment plan is the limited time available. A typical daily radiation therapy session lasts only tenths of minutes, whereas manually creating a treatment plan can take hours for a medical physicist. As a result, human intervention in daily treatment plan optimization is highly constrained.

To address this, it is essential to develop highly automated, yet effective, treatment planning algorithms that can optimize plans efficiently for daily treatment.

Approach & Achievements:

The ESR has developed a highly automated workflow for daily treatment plan optimization, as shown in Figure 1. This workflow optimizes daily treatment plans based on the objective values of the initial plan while accounting for cases where the initial planning constraints cannot be met due to daily anatomical changes.

The daily treatment plan optimization algorithm, the Reference-Point Method (RPM), is constructed using the initial plan's objective and constraint functions, which are selected by a medical physicist before treatment and deemed appropriate for the patient. The RPM replicates the objective values of the initial plan, as these values correspond to critical dose-volume histogram (DVH) parameters. Consequently, the optimized daily treatment plan is expected to have similar DVH values to the initial plan.

One challenge addressed by the workflow is the infeasibility of initial planning constraints. Since these constraints are designed based on the patient's initial anatomy, they may not always be achievable during daily re-optimization, which can prevent the optimizer from finding a feasible solution. The conventional approach to this issue involves relaxing the planning constraints through trial and error until a feasible solution is found. However, this process is time-consuming and therefore unsuitable for daily adaptive radiation therapy. To overcome this, we developed an optimization method that identifies the most challenging initial planning constraints and converts them into objectives, effectively resolving the issue of planning constraint infeasibility.

The efficiency and effectiveness of the developed workflow were demonstrated in a study involving four breast cancer and six head and neck cancer patients.

The ESR's project has so far resulted in

Two published peer-reviewed papers:

1. Qiu Z, Olberg S, den Hertog D, Ajdari A, Bortfeld T, Pursley J. Online adaptive planning methods for intensity-modulated radiotherapy. Phys Med Biol. 2023 May 11;68(10):10.1088/1361-6560/accdb2. doi: 10.1088/1361-6560/accdb2.

2. Qiu Z, Depauw N, Gorissen BL, Madden T, Ajdari A, den Hertog D, Bortfeld T. A reference-point-method-based online proton treatment plan re-optimization strategy and a novel solution to planning constraint infeasibility problem. Phys Med Biol. 2024 Jun 3;69(12). doi: 10.1088/1361-6560/ad4a00.

One conference oral presentation:

1. Qiu Z, Depauw N, Gorissen B, Madden T, Ajdari A, Den Hertog D, & Bortfeld T. (2023, June 14). Online adaptive planning for proton therapy using the reference point method [Talk]. PTCOG61, Madrid, Spain.

Impact and Outlook:

The ESR's work has shown that the RPM is a viable algorithm for daily treatment plan optimization using clinical data. However, current research on the RPM remains limited. Given the positive outcomes of our study, we anticipate further research will emerge to explore its potential for daily treatment plan re-optimization. Additionally, the solution we developed for addressing planning constraint infeasibility offers a novel approach to a challenge that has been under-explored in the context of daily treatment plan re-optimization.

In the future, the ESR will look into improving robust treatment plan which is crucial to account for anatomical uncertainties. The ESR is currently researching on the K-adaptability project to investigate the gain from having multiple robust treatment plans instead of one, which is current state-of-the-art. In the project, the uncertainty scenarios are grouped by a mixed-integer optimization problem and a robust solution is created for each scenario group. We expect to reduce the conservativeness in the robust solutions with this approach.

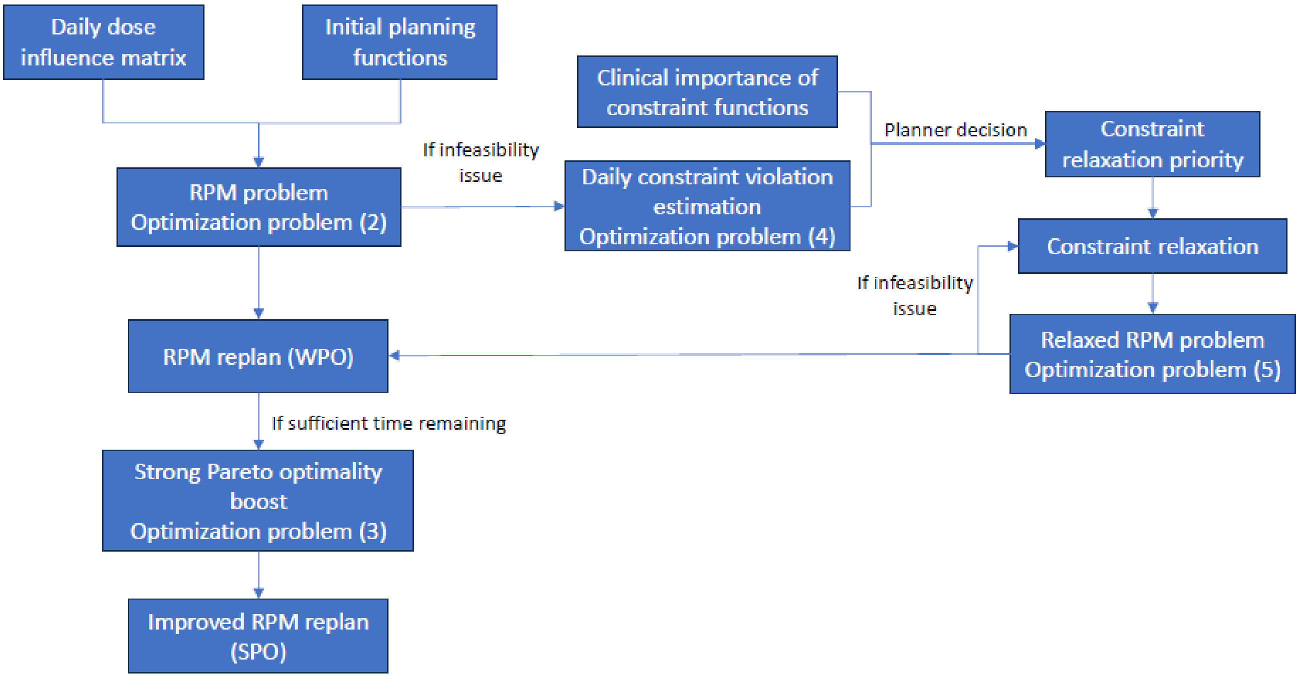


Figure 1: The schematic of developed daily treatment plan optimization workflow.

Robust optimization for anatomical variations

Author: Nadine Vatterodt

Aim and Motivation:

This project explored robust treatment planning solutions to address anatomical variations and their impact on target coverage and dose delivered to organs at risk (OARs) in head and neck cancer proton therapy. These solutions aim to facilitate the implementation of online adaptive particle therapy and provide alternative treatment approaches, especially for institutions with limited resources.

Approach & Achievements:

A population-based principal component analysis model was developed for a retrospective cohort of oropharyngeal cancer patients. The model allows to create images representing likely anatomical changes for individual patients and was used to assess the feasibility of anatomical robust plan evaluation prior to treatment. Our findings indicated that anatomical robust plan evaluation achieved comparable or superior accuracy compared to robust evaluation methods for setup and range uncertainty, particularly when analyzing plans with varying robustness.

For sinonasal cancer patients we tested a simplistic approach to simulating varying cavity fillings for initial robust planning. However, this approach did not necessarily improve target coverage in the presence of actual daily variations. In contrast, scheduled robust plan adaptation using synthetic CTs of the previous fractions resulted in enhanced robustness, with weekly adaptations improving coverage compared to a single adaptation.

For oropharyngeal cancer patients we investigated a triggered robust adaptation framework. By including the triggered fraction's CBCT alongside the planning CT for re-optimizing and introducing additional robust objective functions for respective OARs, this approach offers an individualized and progressive treatment strategy. Interestingly, including multiple images did not substantially enhance robustness compared to a single additional image.

Impact and Outlook:

This research represents an initial step towards clinically feasible robust planning methods to account for anatomical variations in particle therapy. Given that full online adaptation is resource intensive, anatomical robust evaluation may serve as a selection tool to assign patients to either online adaptation, initial robust planning, scheduled robust adaptation or triggered robust adaptation based on their individual needs.

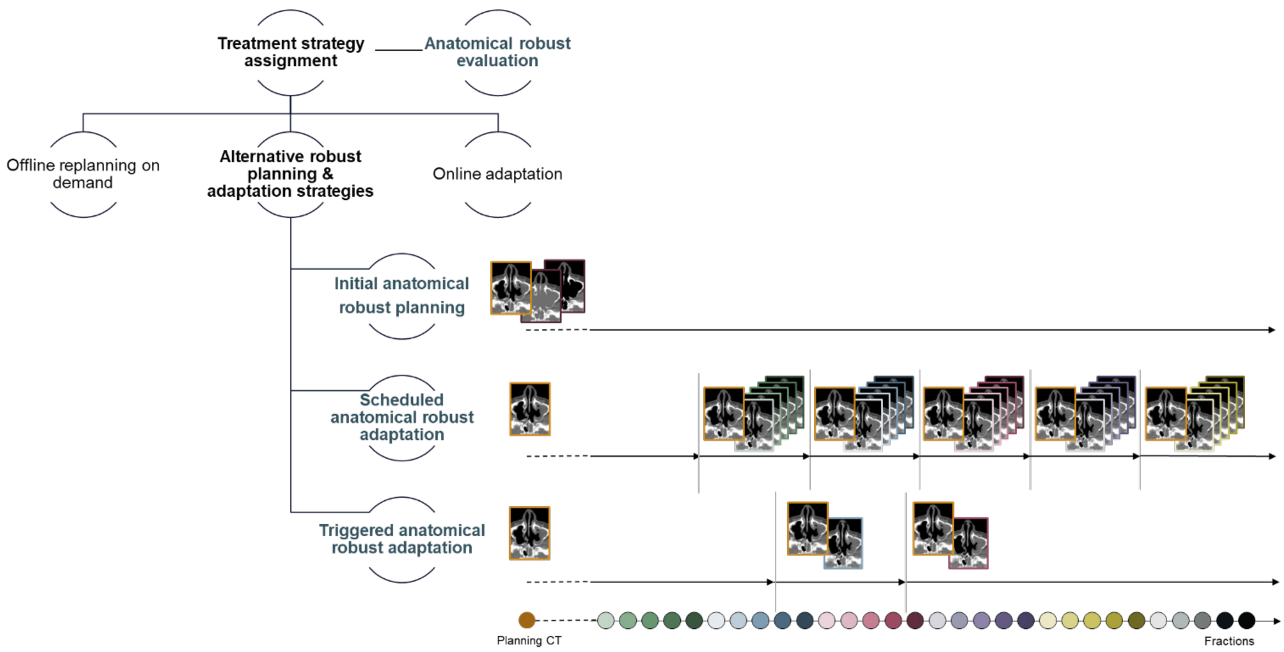


Figure 3 Overview of the PhD project addressing treatment strategy assignment and alternative robust planning and adaptation strategies

Real-time 4D-dose calculation to assess the efficacy of motion mitigation strategies

Author: Cosimo Galeone

Aim and Motivation:

Real-time adaptive therapy is a promising approach to improve the accuracy of treatment delivery and handle patients' intra-fractional motion. For such a strategy, estimating dosimetric errors between planned and delivered doses is essential. This project presents a real-time 4D-dose reconstruction system, synchronized with the treatment delivery and motion of the patient, able to provide prompt feedback on the quality of the delivery, Fig.1.

Approach & Achievements:

A. The RIDOS [1] system for reconstructing static delivered doses has been first verified. We built a new hardware and software interface with the research version of the CNAO and GSI Dose Delivery System (DDS), to receive beam characteristics (MU, beam position) during the delivery. In particular, we developed a new Graphical User Interface (GUI) managing the data transfer between DDS and RIDOS, visualizing the reconstructed delivered and planned doses and performing an estimation of the treatment quality, Fig.1;

B. The algorithm has been extended to handle 4D calculations (4D-RIDOS) and improve time performances. The new system has been tested at CNAO, proving the accuracy of the reconstruction with an average gamma-index passing rate (3%/3mm) of 98.3% against detector measurements, and an average reconstruction time per spot one order of magnitude smaller than the delivery [2].

C. Finally, an external-internal correlation model has been included within 4D-RIDOS to handle 4D irregular motion scenarios. We updated the quasi-clinical framework, interfacing the system with the Optical Tracking System, receiving motion parameters (respiratory phase and 1D-amplitude), synchronized with beam characteristics provided by the DDS. We conducted an experimental campaign to prove the accuracy of the new system, resulting in an average gamma-index passing rate (3%/3mm) of 97.5% against detector measurements, and an average reconstruction time per spot of 0.4 ms.

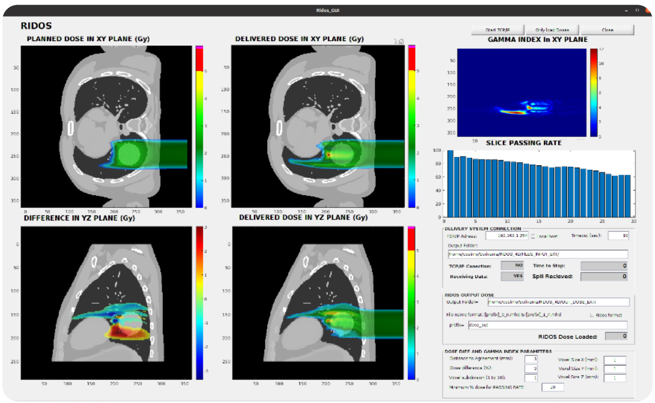


Figure 1: 4D-RIDOS GUI at the end of an interplay delivery. In the lower section delivered dose and the difference between planned and delivered doses in the YZ plane. In the upper section, planned and delivered doses in XY plane. On the right-hand side, gamma-map in the same XY plane, and below the gamma-index passing rate for each energy slice delivered during the treatment. The GUI is updated at the end of each energy slice. Picture from [2].

Impact and Outlook:

We extended the 4D-capabilities of RIDOS and tested in a clinical scenario, meeting the requirements in terms of speed and accuracy. The integration of the system with the CNAO DDS and OTS paves the way for a swift transition to the clinics.

1. S. Giordanengo, et al., "RIDOS: A new system for online computation of the delivered dose distributions in scanning ion beam therapy," https://doi.org/10.1016/j.ejmp.2019.03.029

2. C. Galeone, et al., "Real-time delivered dose assessment in carbon ion therapy of moving targets," https://doi.org/10.1088/1361-6560/ad7d59

Automated and fast machine and delivery log-file based QA

Author: Sergei Diuzhenko

Aim and Motivation:

Particle therapy (PT) Pencil Beam Scanning (PBS) technique treatment plans include thousands of beams, defined by a set of parameters optimized so that the resulting dose distribution maximises the probability of curing the disease and spares the healthy tissues. However, during the dose delivery beam parameters can deviate from the planned values due to dynamic effects as well as random noise in the accelerator beamline components, resulting in deviations from the desired dose distribution.

Therefore, to fully exploit the dosimetric benefits of PBS, it is essential to minimise the impact of machine delivery parameter deviations. The aim of this project is to improve the robustness of PBS treatment to machine parameter deviations and to support daily dose adaptation with a model of machine delivery deviations and a correction strategy.

Approach & Achievements:

The implementation of the deviation model and correction strategy requires a deep understanding of machine specifics, such as the magnitude of deviations, their systematicity and consequently their dosimetric impact. We have developed a methodology and a dedicated software platform to derive such information from retrospective analysis of machine log files. The platform was designed to automatically reconstruct the delivered dose distribution from machine log files using a fast GPU-based dose calculation algorithm. Platform has been clinically validated using patient CT, treatment plans and machine delivery log files from the PSI Gantry 2 machine in collaboration with ESR1 Andreas Smolders. Validation was performed on a cohort of 20 patients with typical indications treated with PT, and different treatment plan modalities. We identified two machine parameters with the highest impact on the delivered dose specific to the PSI Gantry 2 machine: patient couch position and spot positions. Statistical analysis of the delivery log files also revealed a strong positive correlation between the deviations of both parameters measured in the first delivery fraction and all subsequent fractions. Validation results confirmed that the proposed methodology is a viable strategy for characterising uncertainties in specific machine delivery parameters.

Based on the clinical validation results we defined a model of machine parameter deviations and a deviation correction strategy for the daily dose adaptation. In the proposed support strategy the daily treatment plan adaptation objective function is constructed using the baseline plan's objective and constraint functions. Additional objective term is introduced to penalise the weights of the spots with highest deviations from the planned position. The distribution of spot position deviations is extracted from the delivery log file of the first treatment fraction and is assumed in our model to be similar to the distribution in the next fraction. The computational results showed that with an appropriate weighting of the penalty objective, it is possible to restore the quality of the initial treatment plan even in the presence of spot position deviations (Figure 1).

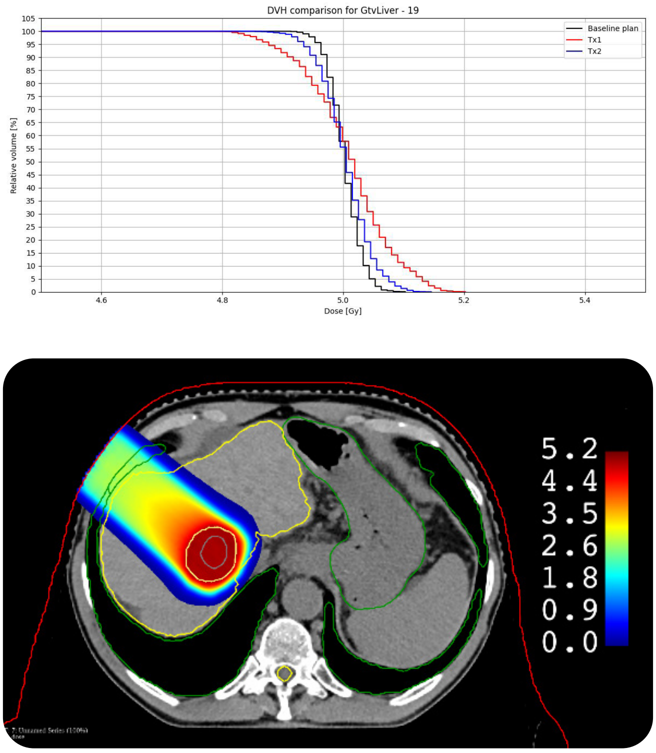


Figure 1. Results of deviation correction in the daily adaptive framework. Left: dose distribution for selected treatment plan. Right: Dose-volume histogram for the CTV, black line shows histogram for nominal dose distribution, red line shows dose distribution for the first fraction with introduced spot position deviations, and blue line shows dose distribution for corrected treatment plan in fraction two.

Impact and Outlook:

With this work, we have developed a methodology to assess deviations in individual machine parameters, providing a deeper understanding of delivery robustness in the PBS. With this project, we are also investigating the possibility of improving the robustness of PBS dose delivery to machine uncertainties, which is particularly important for adaptive PT, while the dosimetric impact of other major uncertainties is expected to be less dominant. The aim of the ongoing work is to experimentally validate the proposed correction strategy. Further efforts will focus on generalising the machine parameter deviation model to allow pre-treatment correction of expected deviations.

Plan Approval for daily plan adaptation

Author: Choulilitsa Evangelia

Aim and Motivation:

Adaptation in proton radiotherapy has been increasingly investigated in recent years to address uncertainties in patient positioning and anatomical changes, aiming to enhance target coverage and reduce radiation toxicity. Different institutions are exploring various daily adaptation strategies—such as dose restoration, reoptimization, plan libraries, and online re-planning—to tailor treatment plans based on each patient's daily anatomy. While studies within single institutions have shown that adaptive methods generally outperform non-adaptive approaches, there is a growing need for multi-institutional studies to validate these results and determine the most effective strategies. At PSI, the Daily Online Adaptive Proton Therapy (DAPT) developed workflow utilizes a rapid full re-optimization process that generates plans in under a minute. A key step for DAPT's clinical implementation involves defining quality assurance (QA) tests and thresholds to facilitate daily plan approval without extending treatment times.

Approach & Achievements:

This study compares two well-established adaptive proton therapy workflows: i) PSI's DAPT workflow, which uses a fast ray casting dose algorithm to fully reoptimize the daily plan, and ii) the online dose restoration approach from MGH, which uses a GPU-based Monte Carlo method to adjust beamlet weights while keeping their positions fixed. The experimental comparison was conducted using an anthropomorphic phantom, delivering adaptive plans across multiple fractions with different anatomical changes. Additionally, an in-silico study was performed on a cohort of 10 head and neck (H&N) patients previously treated at both institutions, with daily images acquired following clinical protocols. Both the experimental and in-silico studies confirmed the dosimetric advantages of these adaptive workflows over non-adaptive approaches. In most cases, dose restoration successfully maintained the original plan quality, while the DAPT workflow consistently ensured the highest plan quality. PSI's DAPT workflow was successfully implemented in a clinical setting, generating adaptive plans without increasing treatment times compared to non-adaptive treatments. My contribution focused on establishing QA thresholds to ensure safety and quality. This QA work formed part of the first deliverable for the Raptor Consortium, with the clinical implementation itself being a major deliverable, marking a critical step toward real-world adoption of adaptive proton therapy.

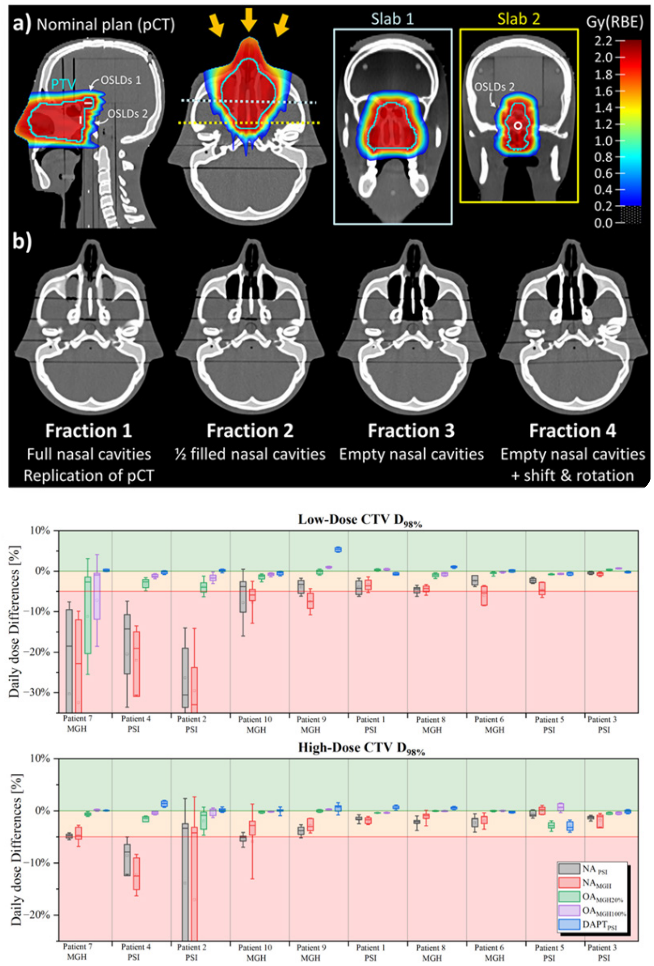


Figure 4. Left: The anthropomorphic head-and-neck phantom, used in the multi-institutional experimental validation of PSI's and MGH's adaptive proton therapy workflow (DOI 10.1088/1361-6560/ad6527). Right: Dosimetric results of the in silico multi-institutional comparison of the two adaptive approaches with patients from both institutions (manuscript in preparation)

Impact and Outlook:

Moving forward, the focus is on maximizing the benefits of full reoptimization in adaptive proton therapy. Our ongoing efforts aim to refine these workflows, including exploring unconventional beam arrangements, to provide patients with the most effective, personalized treatments.

Robust optimization considering uncertainties in the frame of proton adaptive radiation therapy

Author: Suryakant Kaushik

Aim and Motivation:

Addressing uncertainties such as those arising from anatomical variations is crucial for precise treatment. Although adaptive proton planning (APT) using daily CBCT image correction is an effective strategy, it may introduce some uncertainties, such as those related to image correction and auto-contouring. This project aims to quantify and develop strategies to address such uncertainties and thereby improving APT workflow.

Approach & Achievements:

1. An anatomy-preserving virtual CT (APvCT) approach was proposed as a hybrid method for CBCT correction and virtual CT generation. Robustly optimized proton adaptive plans were created on APvCT and other methods for CBCT correction. The results were dosimetrically evaluated using gamma-index passing rate and isodose volume comparison. The APvCT method with CT-like image quality handled the changes in anatomy even in scenarios of substantial anatomical deformations and found superior to other methods.
2. A 4D robust optimization (4DRO) method that relies on dose mimicking planning (MA) was proposed for automated adaptive proton planning (Figure 1). Furthermore, a biologically consistent dose accumulation (BCDA) and a variable RBE analysis were performed to address non-linear biological effects and RBE uncertainties. Results indicate that MA planning is better than template-based planning (TA) in terms of target coverage and sparing organs-at-risk, effectively managing respiratory motion and anatomical changes. BCDA in conjunction with variable RBE-weighted dose evaluation offered additional information to improve clinical decisions on the need for adaptive planning.

Impact and Outlook:

An automated 4DRO with dose-mimicking can significantly decrease the clinical workload in adaptive proton therapy, especially for thoracic tumours. The preservation of anatomy in APvCT aids accurate adaptive planning and dose accumulation, thereby reducing uncertainties. Moving forward, a crucial focus will be to assess the feasibility of the APvCT method for the head and neck region, which often requires frequent adaptive planning.

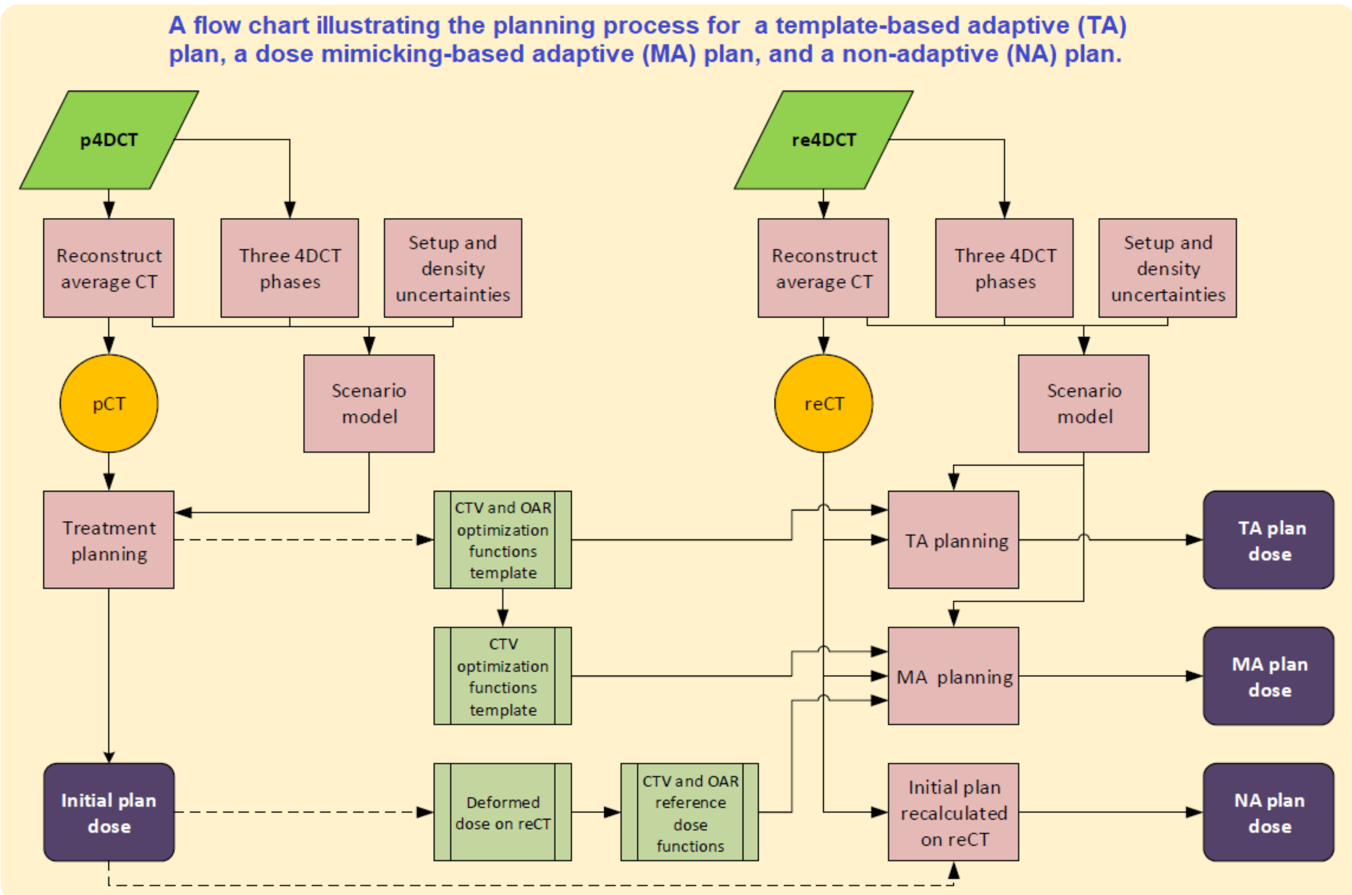


Figure 1: A flowchart illustrating the planning process for a template-based adaptive (TA) plan, a dose mimicking-based adaptive (MA) plan and a non-adaptive (NA) plan.

Development of an end-to-end test workflow for all RAPTOR real-time adaptive PT components

Author: Jacob Brunner

Aim and Motivation:

The RAPTOR project at its core aims to develop novel tools, techniques or approaches for adaptive particle therapy and bridge the gap between the concept of adapting the patient's treatment on a daily basis and its successful clinical application. To overcome the inherent resistance to the introduction of new technologies, its essential to ensure that any deviation from the tried and true standards is predictable and safe. One way of building such trust is conducting end-to-end tests, where a scenario is mimicked completely from the beginning to the end as close as possible to the clinical reality. In lieu of a patient end-to-end tests often use phantoms – task specific, artificial patient stand-ins. The aim of this project was to develop a workflow to conduct end-to-end tests for the RAPTOR adaptive components, build a phantom that was fit for the task, and conduct the end-to-end tests at participating centres.

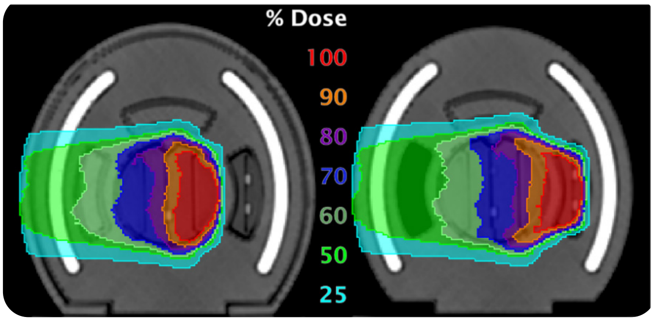
Approach & Achievements:

An end-to-end test phantom, which works at multiple centres and with various centre-specific tools or devices posed design challenges which led to the following requirements:

1. Robustness – to withstand the strain of transport
2. Reproducibility – to easily and reliably change between configurations
3. Adaptability – to fulfil different requirements (e.g. dosimetric) in different institutions

Considering the above requirements, a modular approach with multiple exchangeable inserts to mimic anatomical variations (e.g. changing cavity filling) was selected. The phantom was built using additive manufacturing (3D-printing) as a cost-effective and quick method produce different modular inserts where necessary. The characterization of the utilized materials' interaction with radiation and stopping power prediction for particle beams was determined [1]. An in-depth dosimetric characterisation of the phantom using photons, protons and carbon ions depicted in figure 1 is currently being finalized.

The planned end-to-end tests took place between Mai and September 2024 at six different centres. Treatment scenarios were simulated, in which the novel adaptive tools and devices developed in the RAPTOR project were tested with the developed phantom and workflow.



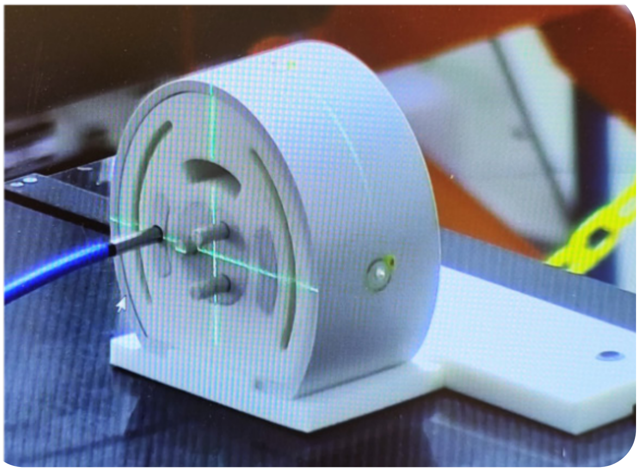


Figure 1: Dosimetric impact of anatomical change (removed shell and cavity) is depicted in the left and middle picture. The right picture shows the phantom in treatment position with a dosimeter positioned to the left of the central target.

Impact and Outlook:

This project contributed to the growing field of using 3D-printed phantoms as cost-effective tools in particle therapy. The end-to-end tests at six European centres demonstrated the feasibility of a harmonized workflow to test adaptive particle therapy components and build trust in these systems. Future efforts will focus on refining the testing strategies and finding meaningful metrics for evaluation. This will help the community to build evidence for the safe and effective use of adaptive particle therapy strategies.

[1] Brunner J et al. 2024 Dosimetric characteristics of 3D-printed and epoxy-based materials for particle therapy phantoms Front. Phys. 12 1323788

Towards automated prompt-gamma treatment verification: Identification and classification of clinically relevant deviations

Author: Stefanie Bertschi

Aim and Motivation

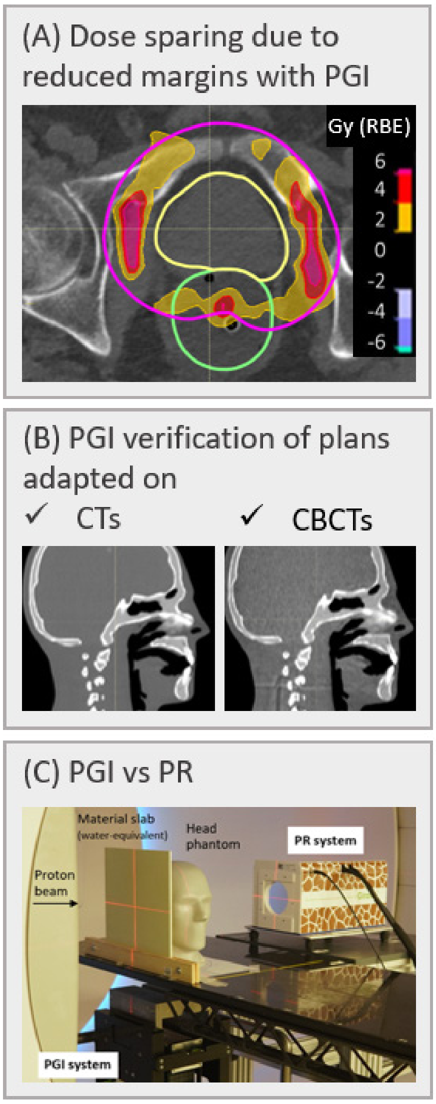
Treatment verification (TV) systems, such as prompt-gamma imaging (PGI), are crucial in online-adaptive proton therapy (OAPT) for detecting anatomical changes, reducing current range uncertainty margins and serving as safety net during treatment. PGI has proven to be functional in real-world clinical treatments and will be employed in an upcoming interventional study to provide patients with the benefit of reduced margins. To incorporate PGI also into future OAPT workflows, three projects were explored.

Approach & Achievements

A. In a first step, the potential reduction of current clinical margins when using PGI was assessed by analyzing clinical PGI data of 10 prostate cancer patients. Using the current trolley-mounted PGI system for online TV to trigger an adaptation would allow a reduction of range uncertainty margins from 7 mm to 3 mm (-57%). Furthermore, for prostate cancer patients, dose reduction due to reduced range margins was shown to be substantially larger compared to reduced setup margins when using pre-treatment volumetric imaging [1].

B. Online TV with PGI requires a reliable reference simulation of the expected PGI profiles on the planning image to which measurements are compared to. Cone-beam CTs (CBCT) are a promising solution for 3D in-situ imaging in OAPT, however at the cost of increased uncertainties in determined CT numbers. Hence, in this second project, it was investigated whether CBCTs can provide a reliable PGI reference simulation and thus whether PGI can also serve as TV tool for plans that were adapted based on CBCTs. Our study has shown for phantom as well as for patient data, that PGI simulations on CBCT depend mainly on the reliability of depth dose distributions on the planning image while additional uncertainties from PG emission spectra were negligible. For CBCT-based plan adaptations, a correct depth dose distribution is a crucial requirement and deviations would be detected by PGI as a systematic mismatch between measured and simulated PGI profiles. Hence, PGI is a promising TV tool for CBCT-based OAPT [2].

C. Lastly, in a collaboration with Giuliano Perotti Bernardini (ESR 15), for the first time, the performance of PGI was compared to proton radiography (PR), two different yet complementary TV methods, using a simultaneous setup in Dresden. Both systems detected mimicked anatomical changes and setup errors for an anthropomorphic head phantom precisely and accurately. PGI enables TV during field delivery, detecting range deviations relevant for the treatment field, while PR enables pre-treatment range verification after setup imaging (CBCTs) with a low-dose PR-field. Due to the complementary information and partly different use cases, a combined application of both systems can be beneficial in OAPT [3].



Towards PGI treatment verification in OAPT

Impact and Outlook

By demonstrating the benefit of reducing current clinical margins, confirming the applicability of PGI also in CBCT-driven OAPT and showing differences and potential combinations with other TV systems, the substantial potential of online TV with PGI in OAPT has been further validated. Alongside ongoing investigations on workflow improvements, these findings pave the way for PGI to serve as an online TV tool in OAPT.

[1] Bertschi et al., phiRO 2023 (https://doi.org/10.1016/j.phro.2023.100447), [2] Bertschi et al., submitted, [3] Bertschi & Perotti Bernardini et al., manuscript in preparation

Dose quantification from prompt gamma imaging for adaptive planning

Author: Beatrice Foglia

Aim and Motivation:

In proton therapy, multiple factors can cause range uncertainties. Reducing such uncertainties would open new possibilities in promoting tighter conformation of the dose delivery to the intended tumour target. A promising technique developed for in vivo range verification is prompt gamma (PG) imaging. PG are emitted in a timescale below nanoseconds, which makes them suitable for real-time adaptive particle therapy applications. This project aims at a fast dose reconstruction of few exploratory pencil beams from the original treatment plan. In case of detected deviations from the originally intended dose, the information can be in turn fed to the adjustable RAPTOR treatment adaptation framework to enable adapting the remainder of the planned delivery.

Approach & Achievements:

Dose reconstruction algorithms, which have already been used in the literature mostly for the case of positron emission tomography (PET) data, were evaluated: the analytical deconvolution method [1], the evolutionary algorithm [2][3][4] and the maximum likelihood expectation maximization (ML-EM) algorithm [5][6]. These techniques are based on the forward filtering approach, firstly developed by Parodi and Bortfeld [7] for PET monitoring and recently extended to PG monitoring by Pinto et al. [8]. The feasibility of the application of the mentioned techniques to emitted PG distributions was assessed in silico performing simulations of protons interacting with homogeneous and inhomogeneous (slab) phantoms, and patient data (figure 1). Dose reconstruction from in silico detected PG distributions considering a model of a knife-edge slit camera response [10] is in progress. The aim is to move towards benchmarking the algorithms with measured PG data with this type of camera, available through national and international collaborations.

The higher the number of protons delivered, the more PG are created, therefore high statistics make PG monitoring more reliable [11]. However, this is not currently considered during clinical treatment plan optimization. A research version of the commercial treatment planning system (TPS) RayStation was created, in order to robustly re-optimize plans by increasing the number of protons delivered to selected spots (boosting) [12-14].

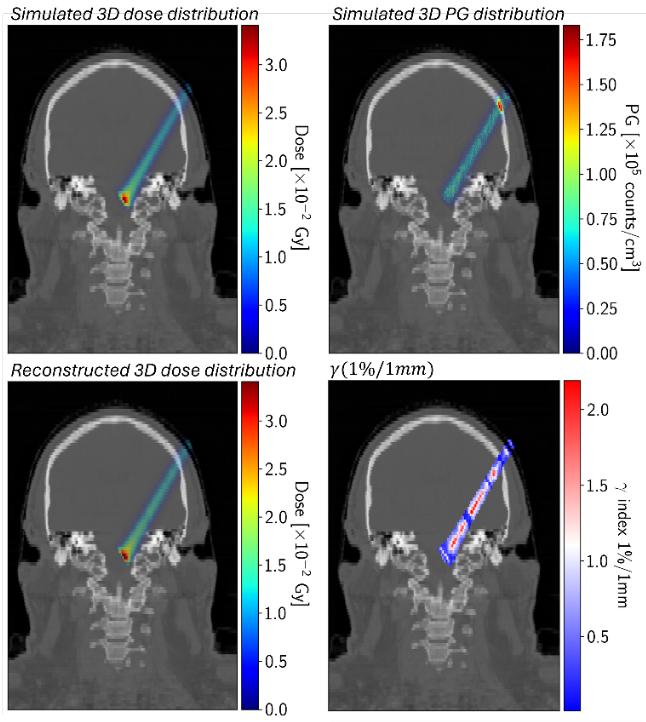


Figure 1: Results of protons irradiating a H&N patient [8] with initial energy of 132.3 MeV and incident angle of 210 degrees. Upper: simulated 3D dose and PG distributions. Lower: 3D dose reconstructed with the evolutionary algorithm (reported as example), and corresponding γ(1%/1 mm) index analysis [9]. Clinical data courtesy of J. Bauer, J. Debus, Heidelberg University Hospital.

Impact and Outlook:

Within this work, the applicability of the investigated dose reconstruction techniques to PG distributions at emission is verified. Ongoing work addresses in silico the influence of detection response, efficiency, attenuation in the tissue and patient anatomy, prior to experimental validation. Moreover, the feasibility of boosting spots in a treatment plan without changing its quality was verified using a research version of a clinical TPS. The resulting high statistics spots can be exploited for a more reliable PG monitoring and to enhance dose reconstruction.

[1] Remmele, S. et al., Phys. Med. Biol. 56 (2011); [2] Schumann, A. et al., Phys. Med. Biol. 61 (2016); [3] Hofmann, T. et al., Phys. Med. Biol. 64 (2019); [4] Yao, Z. et al., Nucl. Sci. Tech. 34 (2023); [5] Masuda, T. et al., Phys. Med. Biol. 64 (2019); [6] Masuda, T. et al., Phys. Med. Biol. 65 (2020); [7] Parodi, K. and Bortfeld, T., Phys. Med. Biol. 51 (2006); [8] Pinto, M. et al., Phys. Med. Biol. 65 (2020); [9] Low, D. A. et al., Med. Phys. 25 (1998); [10] Sterpin, E. et al., Phys. Med. Biol. 60 (2015); [11] Xie, Y. et al, IJROBP (2017); [12] Tian, L. et al., Phys. Med. Biol. (2018); [13] Tian, L. et al., Phys. Med. Biol. (2020); [14] Tian, L. et al., Phys. Med. Biol. (2021)

Proton Radiography for real-time Intensity Modulated Proton Therapy plan verification

Author: Giuliano Perotti Bernardini

Aim and Motivation:

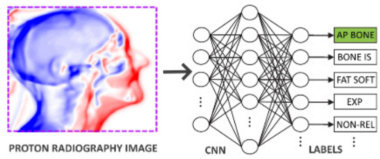
Treatment deviations in the proton range can result in overdoses in healthy tissues and imprecise dosages in target volumes. Imaging techniques can pinpoint uncertainties in proton therapy, such as patient misalignment, anatomical changes, and CT image conversion issues. For in vivo proton range verification, proton radiography (PR)/range probing (RP) has been proposed as a quality control (QC) method. However, generating and interpreting PR images remains challenging in the fast-paced and complex clinical workflow, its performance comparison against different yet complementary imaging methods remains unexplored and its application for moving targets is yet to be addressed, which all those findings will contribute to the incorporation of PR into online-adaptive proton therapy (OAPT) workflows.

Approach & Achievements:

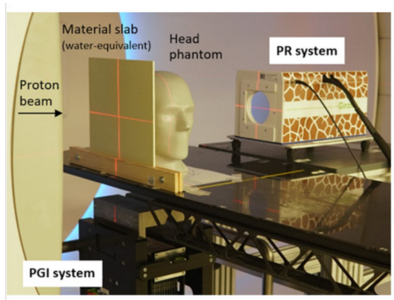
A. An AI-enhanced PR tool was developed to automatically and quickly evaluate PR images, recognising multiple sources of error modifying the proton range, including synthetic weight changes for head and neck cancer patients driven by deformable image registration [1]. The tool successfully identified setup errors, calibration curve errors, and anatomical changes. The tool also demonstrated a rapid processing ability, analysing PR images in just six seconds. A retrospective analysis of PR showed a good agreement between simulated and measured integral depth doses (IDD) in anatomically stable areas, adding further confidence to the model [2].

B. The capability of proton radiography to detect treatment deviations was evaluated for the first time in collaboration with Stefanie Bertschi using Prompt Gamma Imaging (PGI) in a simultaneous setup. PR verifies range before treatment with low-dose PR-field imaging. The combination of both systems in OAPT can be advantageous because of their complementary information and different use cases [3]. PR performance was also assessed by conducting a simultaneous measurement in Groningen using a PET detection system. Additionally, the End-to-End phantom was employed in collaboration with Jacob Brunner (ESR12) to further evaluate the PR performance.

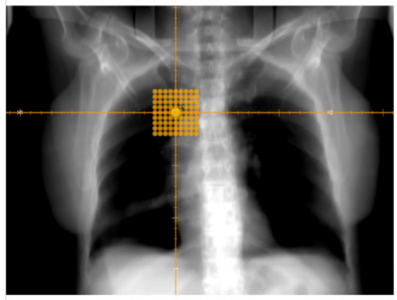
C. For the first time, we used range probing as a patient-specific quality control (RP-QC) procedure on moving targets for lung cancer (LC) patients. Seven LC patients with 10mm motion in middle/upper lung tumours received two RP-QC sessions in this study. Patients' mean relative range errors (RREs) in the first RP session were all within ±3% range uncertainty. Four out of seven patients had mean RREs values within ±3% in the second RP session. Anatomical changes and setup errors cause the most RRE variations, especially for the three RP fields exceeding ±3% margin [4].



(A) AI-Enhanced PR Tool for treatment deviation detection



(B) PR vs PGI simultaneous setup measurements



(C) RP-QC for moving targets on lung cancer patients

Impact and Outlook:

Our AI-enhanced PR tool has shown potential for improving the speed and accuracy for detecting setup and calibration curve errors, and anatomical changes. The successful validation against simulated and measured data reinforces its potential for clinical application.

Combining proton radiography with other imaging techniques like PGI and PET systems offers a comprehensive approach for treatment verification. Applying PR to moving targets, allow us to verify the uncertainties we assign to LC treatments. Future efforts will focus on integrating these advancements into online-adaptive proton therapy workflows to further improve treatment precision and patient outcomes.

[1] Perotti Bernardini et al.,to be submitted [2] Perotti Bernardini., to be submitted, [3] Bertschi & Perotti Bernardini et al., manuscript in preparation [4] Perotti Bernardini et al., manuscript in preparation

Scientific contributions

Peer-reviewed journal publications

- Galeone C., Real-time delivered dose assessment in carbon ion therapy of moving targets, Physics in Medicine and Biology 2024
- Kaushik S., Adaptive intensity modulated proton therapy using 4D robust planning: a proof-of-concept for the application of dose mimicking approach, Physics in Medicine and Biology 2024
- Qiu Z., A reference-point-method-based online proton treatment plan re-optimization strategy and a novel solution to planning constraint infeasibility problem, Physics in Medicine and Biology 2024
- Smolders A., Robust optimization strategies for contour uncertainties in online adaptive radiation therapy, Physics in Medicine and Biology 2024
- Smolders A. Rivetti L., DiffuseRT: predicting likely anatomical deformations of patients undergoing radiotherapy, Physics in Medicine and Biology 2024
- Bobic M., Choulilitsa E., Multi-Institutional Experimental Validation of Online Adaptive Proton Therapy Workflows, Physics in Medicine and Biology 2024
- Rivetti L., Uncertainty estimation and evaluation of deformation image registration based convolutional neural networks, Physics in Medicine and Biology 2024
- Brunner J., Dosimetric characteristics of 3D-printed and epoxy-based materials for particle therapy phantoms, Frontiers in Physics 2024
- Kaushik S., Generation and evaluation of anatomy-preserving virtual CT for online adaptive proton therapy, Medical Physics 2024
- Smolders, A., The influence of daily imaging and target margin reduction on secondary cancer risk in image-guided and adaptive proton therapy. Physics in Medicine and Biology 2024
- Nakas, A., Modelling strategies to enable time-resolved volumetric imaging. Imaging in Particle Therapy: Current practice and future trends. Bristol, UK: IOP Publishing, 2024. 9-1.

Conference participation

Author: Zihang Qiu

2024 was a fruitful year for our RAPTOR students in terms of conference participation. Our students participated in various national and international conferences in 2024. We have set our foot on ESTRO, PTCOG, AAPM, ICCR, and many more.

Eight students contributed to ESTRO 2024. Among them, five RAPTOR students presented their cutting-edge research projects. Sergei Diuzhenko discussed the dosimetric impact of deviations in machine delivery parameters. Evangelia Choulilitsa shared her study on the impact of CT selection on dose accumulation in adaptive radiotherapy for head and neck patients. Giuliano Perotti Bernardini presented his work on AI-enhanced proton radiography. Arthur Galapon discussed the clinical sustainability of deep learning-based sCT models after CBCT image software upgrade. Stefanie Bertschi talked about the feasibility of prompt-gamma verification for CBCT-based adapted plans. Andreas Smolders, Nadine Vatterodt, and Jacob Brunner were invited to disseminate and summarize the scientific progress of the three work packages of the RAPTOR consortium (imaging, intervention, and verification) to publicity.

At PTCOG 2024, we again had eight RAPTOR students representing the consortium. Two students addressed the robustness consideration in treatment planning. Nadine Vatterodt and Suryakant Kaushik talked about robust plan evaluation using a population-based anatomical model and 4D robust planning based on dose mimicking, respectively. Andreas Smolders exhibited his research on secondary cancer risk in CT-guided adaptive head-and-neck particle therapy. Sergei Diuzhenko discussed the dosimetric impact and systematicity of proton therapy machine delivery. Arthur Galapon and Giuliano Perotti Bernardini presented their work on range probing. Finally, Choulilitsa Evangelia shared multi-institution investigations of daily adaptive proton strategies for head and neck cancer patients between Paul Scherrer Institute and Massachusetts General Hospital.

Secondment Reports

Suryakant Kaushik

Who:
Suryakant Kaushik in collaboration with Dr. Stine Korreman.

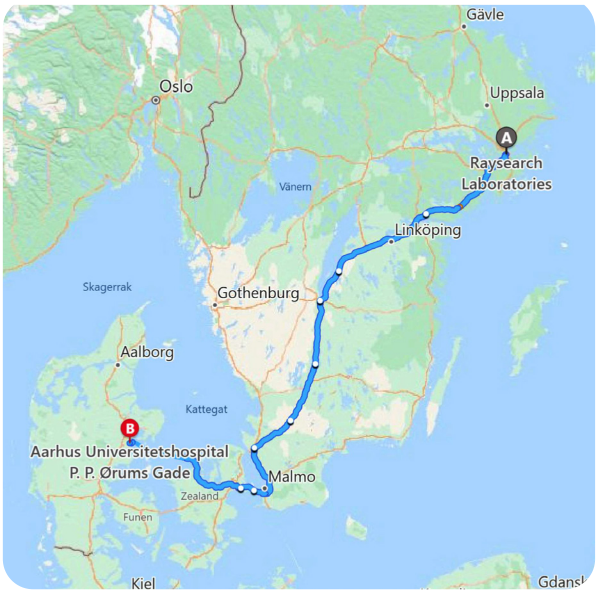
Where:
Danish Centre for Particle Therapy, Aarhus, Denmark

When:
12th August 2024 to 30th August 2024

Why:
Feasibility of daily image correction methods for adaptive head and neck planning.

Aarhus, which boasts a vibrant city life alongside its rich cultural heritage, provided a wonderful setting for my secondment. I visited captivating locations such as the ARoS Aarhus Art Museum, known for its iconic rainbow panorama and housing Ron Mueck's impressive "Boy" sculpture (1999). Other memorable visits included trips to the Aarhus Docklands, the historic Old Town (Den Gamle By), and the intriguing Moesgaard Museum. After finishing my secondment, I took the opportunity to visit Copenhagen en route to Stockholm, where Rosenborg Castle stood out as a stunning example of Renaissance architecture, and home to the Danish crown jewels.

Professionally, my experience at the Danish Centre for Particle Therapy was rewarding. I had the chance to apply different CBCT image correction methods to head and neck patient datasets. This experience enhanced my comprehension of the challenges inherent in each method and allowed me to formulate recommendations for their implementation. The project yielded promising results, highlighting the substantial potential of daily image correction methods in clinical settings and will surely enrich my doctoral research.



How would you describe your secondment in one word?
Productive

What did you take home from your secondments (message, object, recipe....)?
A wealth of professional insights and cultural enrichment.

Which song describes your secondment best?
"Here Comes the Sun" - The Beatles

Jacob Brunner, *MedUni Wien, Vienna (AT)*

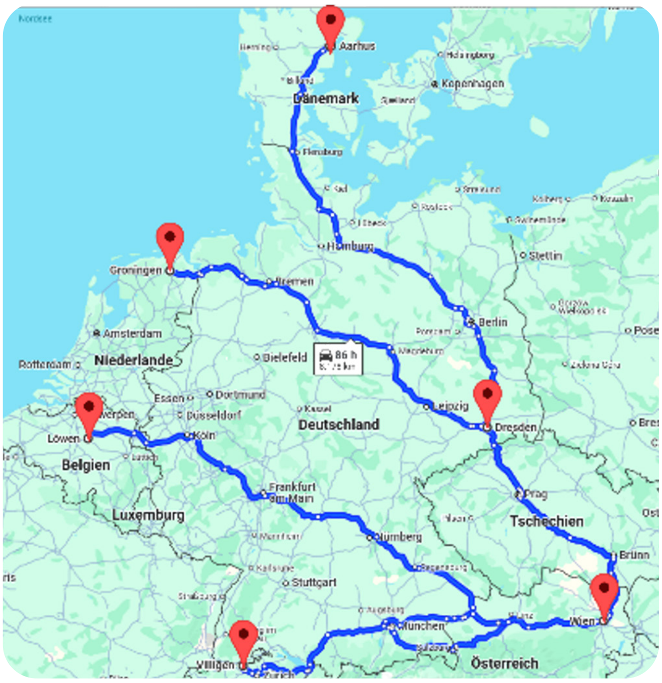
Who:
Jacob Brunner, collaborating with friends and colleagues from the participating centres

Where:
Paul-Scherer-Institute (CH), Proton Therapy Center Leuven (BE), University Proton Therapy Dresden (DE), University Medical Center Groningen (NL), Danish Centre for Particle Therapy (DK), MedAustron Ion Therapy Centre (AT)

When:
June – September 2024

Why:
End-to-end tests of adaptive particle therapy components

For the last leg of my PhD journey we planned to take my phantom and end-to-end test workflow to various different particle therapy centres across Europe. Over the course of last summer I visited colleagues in Germany, Austria, Switzerland, Belgium, Netherlands and Denmark. During brief yet intense 1.5 to 2 week stays I tried to pack in all the research, social and culinary experiences I could. I'm very happy to report that I could complete all my travels via train. Good for the planet and some very cool experiences! My favourite mode of transport certainly was the capsule cabin on the new night trains between Vienna and Hamburg, just enough space for one person to enter the train in Vienna in the evening and wake up close to Hamburg in the morning. Speaking of railway connections: whenever I considered all the travel back and forth between Vienna and the various centres, I always imagined a star with Vienna in the centre and the branches reaching out to our collaborators. Looking at the map above, it reminds me more of a kraken and it's tentacles reaching out across Europe. In my memory travelling back and forth seemed a lot shorter than they were, after all looking up the trip on Google Maps the suggested travel time by car is a short 86 hours. I suspect the positive memories make the places feel a lot closer to home. I studied for my masters degree in Dresden, so the stop in Germany was essentially me enjoying home field advantage, meeting new and old colleagues alike. Nevertheless, the next stop in Villigen was just as pleasant and memorable. I can now claim to have completed an obligatory dip into the Aare during summertime. The third destination, Leuven, received me with open arms, typically Belgian mussels & fries, and plenty of open air music during their summer city festival. My fourth visit took me back to beautiful Groningen, the destination of my very first secondment! This time around my stay was considerably shorter, but I felt right at home again and was very happy to catch up with people I hadn't seen in a while. The fifth and last stop took me all the way north to Aarhus, where I meet Zihang and Eva during their Secondments there. The city showed off her strong cultural programme during our visit, which I think we all thoroughly enjoyed. Without picking any favourites I can say I'm looking forward to visiting all these places again. Maybe next time without work, an action packed schedule and a little more sleep. Please?



With regards to research, the visits were very productive. A huge thank you to everyone involved at this point! It is difficult to put into words the willingness and effort it took to coordinate and execute beam time at five different therapy centres in clinical operation. Thank you to everyone who helped with equipment, expertise and time! As for our goals: I came prepared with a plan for our adaptive scenarios, what components we wanted to test and the framework we wanted to use for testing. In my luggage I also brought a custom-made phantom, including anatomical changes, to provide a platform for adaptive strategies. Now, no matter how good, no plan survives first contact with the enemy realities of beamtime at an unfamiliar institute. But we adapted (just like our workflows :)) and all measurements were successfully completed. As for the results themselves, I need to ask you to be patient for a while longer. In the future you will see our evaluations, comparisons and results with my phantom and various tools, e.g. logfile-based dose reconstruction, prompt gamma imaging and proton radiography. Stay tuned!

How would you describe your secondment in one word?
Whirlwind

What did you take home from your secondments (message, object, recipe….)?
Culinary experiences from the different countries

Which song describes your secondment best?
The Proclaimers – I'm Gonna Be (500 Miles)

*Listed in alphabetical order.

Layout and Design:
Valentina Margaria, Tanja Gerkman

RAPTOR project has received funding from the European Union's Horizon 2020 Marie Skłodowska-Curie Actions under Grant Agreement No. 955956