1.1 Optimization of breast cancer patient treatment plans using artificial intelligence

*Background*: Patients with cancer can be treated in various ways, usually with a combination of surgery, chemotherapy, immunotherapy and radiotherapy. With radiotherapy, a high radiation dose is given to the tumor while sparing the surrounding tissue as much as possible. For breast cancer patients, the dose given to the breast needs to be balanced against the dose given to the lungs and the heart. Based on international guidelines, the number of irradiation fractions and the nominal dose per fraction is harmonized. However, in current clinical practice often no use is made of previously generated treatment plans and associated dose distributions to generate plans for new patients. In an ongoing research line, we have already developed Convolutional Neural Networks (CNNs) to include this information, thereby improving plan consistency and decreasing planning time. However, in current practice plan optimization does not explicitly take the position of the primary tumor into account or patient related lung or cardiac morbidity risk factors.

*Objective*: To automatically, through the use of CNNs, determine the optimal individual breast cancer radiotherapy treatment plan based on the position of the primary tumor and the individual lung and cardiac morbidity risk factors.

*Study design:* to develop and implement methods to optimize treatment plans based on the location of the primary tumor and the individual lung and cardiac morbidity risk factors. This includes some scripting in python and developing and testing of CNNs. To quantify the reduction in lung and cardiac toxicity resulting from this individualized optimization. To develop and validate the generation of new plans based on previously generated plans using a large clinical database of plans and artificial intelligence solutions (based on software tools available in the research version of our planning system) and finally to compare the results with similar results as reported in the literature and to improve the new AI models that are under development in the ongoing cooperation between the Catharina Hospital, the manufacturer of the treatment planning system and the TU/e.

*Student background*: Masters student in biomedical engineering or physics or Data Science and Artificial Intelligence.
*Availability*: 9-12 months
*Student skills*: Phyton programming, data analytics, AI modeling, signal processing
*Location*: Radiation Oncology Department, Catharina Hospital Eindhoven.
Involved supervisors: Coen Hurkmans (clinical physicist), Ward Cottaar (professor Applied Physics).

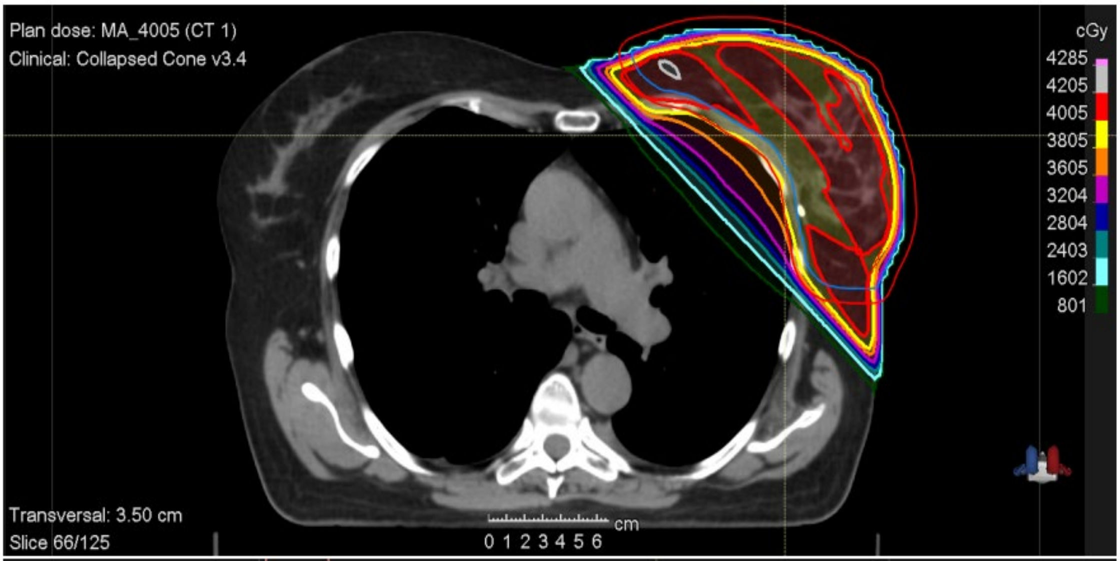


Figure: An axial CT slice through the middle of the breast

1.2 Machine learning for automated organ contouring on CT and MRI

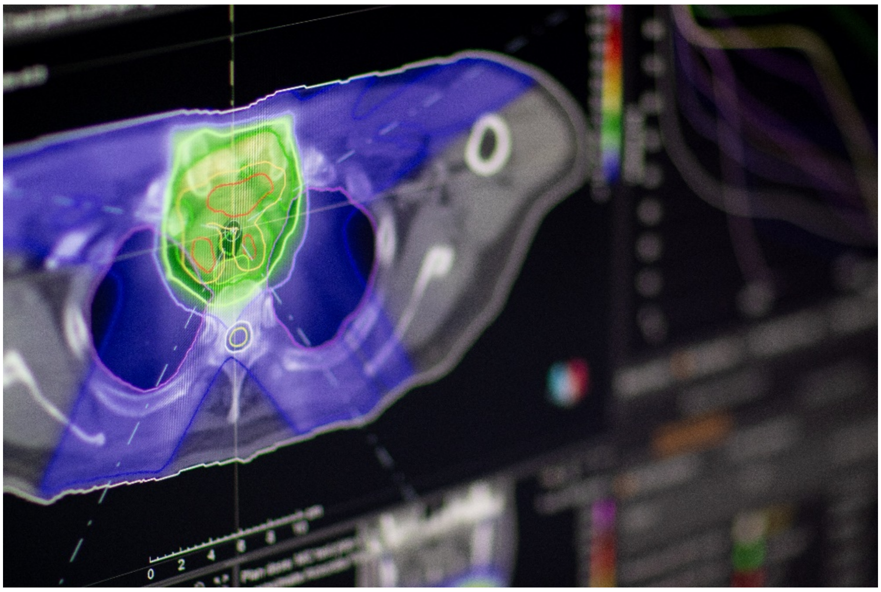
*Background*: Approximately 50% of all cancer patients receives radiotherapy treatment at some stage during their treatment. The goal of radiotherapy is to deliver a high dose of ionizing radiation to the tumor, while sparing the surrounding healthy tissue as much as possible. To accomplish this an individualized ‘treatment plan' is designed based on a pre-treatment CT scan in which the optimal beam angles and shapes are determined. The first step of this process is the manual contouring of the target (i.e., the tumor) and the surrounding organs to avoid. This manual step is very time-consuming, and subjective to variation. Machine learning has the potential to automate and possibly improve the quality of this step. We recently upgraded our treatment planning system, Raystation, to include Deep Learning based auto-contouring. However, in order to safely introduce this new method into the clinic, they need to be carefully evaluated.

*Objectives:*

1. The aim of this project is to evaluate the performance of DL-based auto-contouring and to investigate whether having multi-modality image information (CT + MRI) provides higher quality delineations than CT alone.
    a. First, the (multi-institutional) models as provided by the vendor will be tested against human generated delineations.
    b. Next, the benefit retraining the model using local (institute specific) data will be assessed. We will compare the use of 3 different training sets (CT alone, CT + MRI, and MRI alone). The latter will provide useful information for MR-guided radiotherapy treatments on a MR-linac system, which the department is planning to purchase.
    c. Time permitting, there will be an opportunity to design a custom network architecture based on the latest literature and compare this against the commercial tools offered by Raystation.

*Study design:* Technical development and observational study based on available clinical data. Machine learning models (in Raystation/Python) will be used to generate auto contours and evaluate against the gold standard (expert delineations). In the second part of the project, the model will be fine-tuned and new network architectures will be explored.

*Student background:* Master student biomedical engineering, applied mathematics or physics.
*Duration:* 9-12 months
*Student skills:* Python programming, data analytics, modeling, and interest in radiotherapy.
*Location*: Catharina ziekenhuis Eindhoven.
*Involved supervisors*: Rob Tijssen (medical physicist); Hanneke Bluemink (medical physicist);



*Screenshot treatment plan created in RayStation (RaySearch stock image)*

## 1.3 Optimization of cone-beam CT imaging for adaptive radiotherapy

*Background*:

Radiotherapy is delivered in a fractionated fashion (i.e., the dose is typically given in 3 to 30 daily treatment sessions). Most treatment devices (i.e., linear accelerators, or Linacs) are equipped with onboard cone-beam CT (CBCT) imaging to provide the image guidance that is needed to ensure the target (i.e., tumor) is positioned correctly each day. The image quality on our current CBCT Linacs, however, is sub-optimal and in need of improvement. We want to use the images clinically to adapt our treatment plan for every treatment session. This is now hampered by the inaccuracy with which the tumour and organs can be defined on the CBCT scans and with the uncertainty in the calculation of the dose due to the inaccurate electron density information in the CBCT images.

In a research cooperation with the vendor, Catharina Hospital defined the following objectives.

*Objectives:*

With the by the vendor newly developed reconstruction algorithms CBCT scans will be generated from clinically obtained image acquisition data. These new CBCT reconstructions will be inspected and analysed in terms of:

- Visual comparison and quantitative scoring with respect to original CBCT scans
- Image quality comparison and its applicability to plan-of-the-day for rectal cancer treatments
- Accuracy of dose calculations
- Suitability of the new CBCT scans for (automatic) delineation purposes
- Validation of (deformable) registration tools using the new CBCT scans.

The data from rectum, lung and oesophageal cancer will be used in this project

*Student background:* Master student biomedical engineering, applied mathematics or physics.
*Duration:* 9-12 months (within the full project also a PhD student will be appointed)
*Student skills:* Python programming, data analytics, modeling, and interest in radiotherapy.
*Location*: Catharina ziekenhuis Eindhoven.
*Involved supervisors*: Paul van Haaren (medical physicist); Coen Hurkmans (medical physicist);

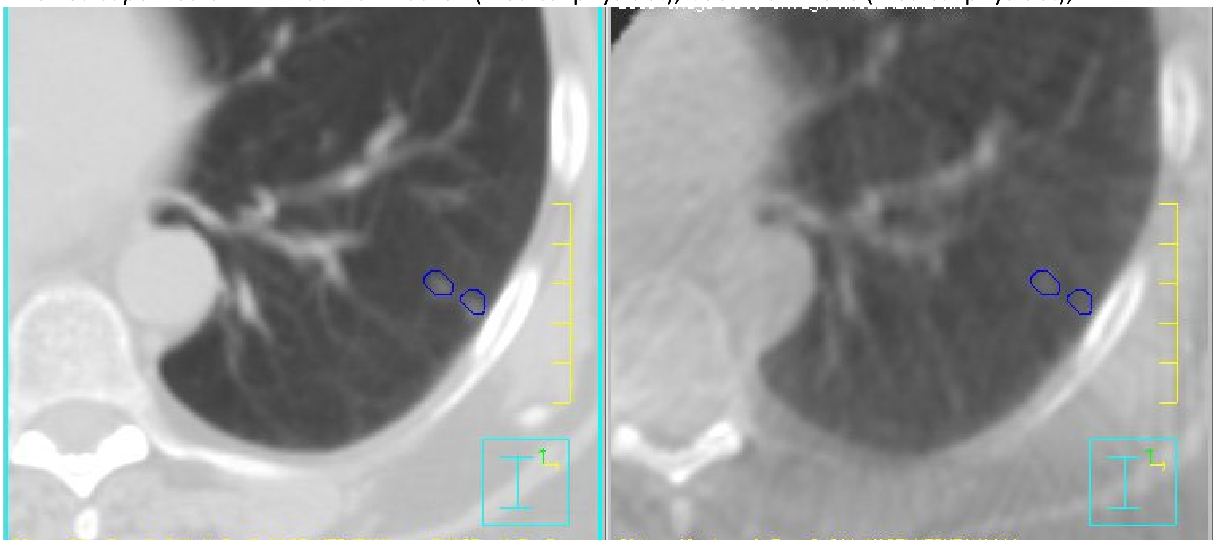


Figure: example of an axial image through the lungs showing 2 lung cancer nodules on CT (left) and on Cone-beam CT (right). Note the poor image quality of the Cone-beam CT.

### 1.4 Compressed Sensing and Deep Learning based Cone-Beam CT (CBCT) reconstruction for improved treatment guidance.

*Background*: Radiotherapy is delivered in a fractionated fashion (i.e., the dose is typically given in 3 to 30 daily treatment sessions). Most treatment devices (i.e., linear accelerators, or Linacs) are equipped with onboard cone-beam CT imaging to provide the image guidance that is needed to ensure the target (i.e., tumor) is positioned correctly each day. The image quality on our current CBCT Linacs, however, is sub-optimal and in need of improvement. In the field of MRI a lot of progress has been made with the advent of compressed sensing, and -more recently- deep learning based image reconstruction. Mathematically, the synergy between MR image reconstruction and CT is strong. We therefore believe that onboard CBCT imaging could greatly benefit from the research developments in MRI.

*Objectives:*

1. The aim of this project is to implement and evaluate a compressed sensing algorithm for cone-beam CT, which will be complemented with a Deep learning based image reconstruction in the second phase of this project.
    a. First, existing code for compressed sensing MRI will be adapted and made suitable for CBCT image reconstruction including scatter correction terms, etc.
    b. When successful on the first part of the project an (open source) deep learning network will be implemented, trained, and tested/evaluated.
    c. The final evaluation will be based on a comparison between the two implemented methods, the vendor provided reconstruction and the pre-treatment (fan beam) CT image. Images will be scored on image artefacts, reconstruction speed, and conspicuity of features of interest.

*Study design:* Technical development and observational study based on available clinical data. Raw data from existing CBCT scans will be used for the assessment of the implemented reconstruction methods.

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| *Student background:* | Master student in biomedical or electrical engineering, or applied physics. |
| *Duration:* | 9-12 months |
| *Student skills:* | Matlab/Python programming, mathematics, radiation physics, signal processing. |
| *Location*: | Catharina ziekenhuis, Eindhoven. |
| *Involved supervisors*: | Rob Tijssen (clinical physicist); Paul van Haaren (clinical physicist); |

### 1.5 Optimized quantitative and 4D-MRI for MR-guided radiotherapy of liver tumors on the MR-linac.

*Background*: The hybrid MR-linac, a Dutch invention, offers direct tumor visualization while the patient is being irradiated. The Catharina hospital is in the process of purchasing this promising new treatment device. One of the benefits of real-time image guidance is the ability to track tumors that move due to respiration, thereby minimizing the damage to surrounding healthy tumors. Patients with liver metastases are believed to benefit a lot from this new treatment strategy. Liver metastases, however, are often difficult to image as the imaging sequence needs to be robust against motion and it is not always obvious which contrast (T1-, or T2-weighted) provides the best tumor conspicuity. We have recently developed quantitative imaging methods (Magnetic Resonance Fingerprinting) and 4D motion robust imaging methods for the MR-linac. In this study we want to assess these techniques in liver patients in order to design a lean imaging protocol for MRI-simulation (that is, pre-treatment acquisition on a diagnostic MRI in preparation of treatment on the MR-linac) and the MR-linac. This study is a collaboration between the Catharina hospital and the UMC Utrecht.

*Objectives:*

2. The aim of this project is design a pre-treatment MR imaging workflow for MR-guided radiotherapy of liver tumors.
    a. First, the recently developed pulse sequences (MRF and 4D-MRI) will be piloted on phantoms (to assess the accuracy and precision of the quant. MRI) and healthy volunteers.
    b. Next, quantitative and 4D-MR imaging will be acquired prospectively in a group of patients. The added benefit of the quantitative MRI scans is assessed as well as the image quality of T2w and T1w 4D-MRI in collaboration with radiologists and radiation oncologists [acquisition in Catharina hospital as well as UMC Utrecht].
    c. Time permitting, the optimized protocol will be ported to the MR-linac and tested in a smaller cohort. The acquisition of these data will take place in Utrecht.

*Study design:* prospective observational study. Two new pulse sequences will be optimized and assessed on a group of patients on a diagnostic MRI scanner as well as an MR-linac system.

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| *Student background:* | Master student in biomedical engineering |
| *Duration:* | 9-12 months |
| *Student skills:* | MR physics, image processing, data analytics, strong communication skills. |
| *Location*: | Catharina ziekenhuis, Eindhoven / UMC Utrecht. |
| *Involved supervisors*: | Rob Tijssen (clinical physicist, CZE); Tom Bruijnen (PostDoc MR Physics, UMCU); |

*Hybrid MR-linac with coronal MR image of the liver showing the onboard imaging capabilities.*

## 1.6 Obtaining the actual delivered dose for image-guided online adaptive radiotherapy

*Background*: The radiotherapy treatment nowadays is mainly based on a treatment plan derived from a single CT "snapshot" of the patient anatomy, and then performing daily treatment without accounting for changes in this anatomy. For organs with large deformations, such as the bladder, this can result in a mistreatment of the tumor or complications due to the irradiation of healthy tissue. By estimating the shape variations at the start of treatment (e.g. by using an empty and full bladder scan), creating a library of plans accounting for these variations, and selecting the appropriate plan based on daily pre-treatment imaging, a more effective treatment can be given. With the introduction of online MR-guided radiotherapy, further possibilities are opening up for applying this online adaptive approach. Adding the daily delivered doses to obtain the total dose given to the patient is not a straightforward problem. Using deformable image registration, displacements of each voxel in an organ can be determined, and an accumulated dose can be calculated.

*Objectives*: To implement improvements to our clinical online adaptive radiotherapy treatment (specifically for bladder cancer), and develop and validate a method for calculating the total delivered dose to a patient from the daily selected plans.

*Study design: To d*evelop a method to create synthetic CTs of intermediate organ shapes based on empty and full bladder scans, and validate these using daily cone-beam CT images. To use deformable image registration and dose accumulation to determine the actual delivered dose for patients treated clinically with this online adaptive procedure. To validate the dose accumulation by looking at registration uncertainties and their effect on the accumulated dose. To create an efficient workflow for calculating these dose accumulations using Python scripting. And to evaluate the gains from these adaptive treatments, and explore possibilities for further improvement.

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| *Student background*: | Masters student in biomedical engineering or physics. |
| *Availability*: | 9-12 months |
| *Student skills*: | Matlab programming, data analytics, modeling, signal processing |
| *Location*: | Radiation Oncology Department, Catharina Hospital Eindhoven. |
| *Involved supervisors*: | Coen Hurkmans (clinical physicist), Hanneke Bluemink (clinical physicist) Ward Cottaar (professor Applied Physics). |