FACULTY OF MEDICINE AND HEALTH SCIENCES

Adaptive Biological Image-Guided Dose-Painting for Head-and-Neck Cancer

From technical feasibility to clinical applications

Luiza Olteanu

2020-2021

Thesis submitted in fulfilment of the requirements for the degree of Doctor in Medical Sciences

Supervisors:

Prof. Dr. ir. Werner De Gersem[1]
Prof. Dr. Indira Madani[2]
Prof. Dr. Frederic Duprez[1]

GHENT UNIVERSITY

Conclusions

The acquisition of new CT images during the treatment course revealed the variation in volume and (biological) properties of the tumor and critical anatomical structures and allowed the adaptation of the patient treatment according to these changes.

It was demonstrated that the accuracy of DIR in correlating the CT images depended on the mathematical validation and visual inspection of an experienced radiotherapist. The developed and tested methods were successfully integrated in the ART process and increased the confidence level in the evaluation of its dosimetrical impact.

The implementation of the IMAT technique led to better structured dose-painted distributions, reduced critical structure doses and improved treatment delivery.

The analysis of the dosimetrical data together with the clinical observations and patient characteristics helped in the formulation of additional guidelines for toxicity reduction in subsequent clinical trials. Furthermore, the added value of ART could be proven on a patient individual basis.

For this reason, we recommend the implementation of ART strategies for the treatment of head-and-neck cancer stressing out the need for adequate validation techniques.

Curriculum Vitae

Luiza Olteanu studied Medical Physics at Bucharest University (Romania) followed by a Master of Biophysics and Medical Physics at the same university. The Master studies were completed with a thesis on the topic of Monte Carlo simulations for high-energy electron beams at Ghent University.

Following specialized courses in the field of radiation therapy and the accumulated experience while working as a medical physicist in the Radiotherapy department of Ghent University Hospital led to the obtaining of the title of Expert in Medical Radiation Physics.

Together with surgery and systemic treatments, radiotherapy is nowadays part of the standard of care for the treatment of head-and-neck cancer. In radiotherapy, geometrical precision is of paramount importance and is obtained by means of non-invasive medical imaging of the patient's internal anatomy. Several imaging modalities are involved in the localization of the tumor and critical structures. The investigations of this thesis include the use of computed tomography (CT) and biological ^{18}F-FDG-PET to define the tumor contour and guide the prescription of the dose within the target volume (i.e. dose-painting).

A radiation treatment for head-and-neck cancer is delivered daily over a time span of several weeks, the applied daily dose and number of fractions varying in function of the disease indication and known effectiveness. New fractionation schemes are studied in clinical trials as a worldwide effort to improve the radiation treatments.

In a local clinical trial, escalated dose levels were focused to small tumor volumes defined on biological images to improve the disease control, while limiting toxicity. To account for the patient's changing internal anatomy during the course of radiotherapy, a treatment strategy in three phases was designed. For this, the treatment was adapted twice according to the biological images acquired after 8 and 18 fractions.

These treatments were delivered by a modern linear accelerator capable to perform intensity modulated arc therapy.

To correlate the information of the CT images taken before and during the treatment, deformable image registration (DIR) was applied. This technique uses mathematical models to interpret the images and follow the 3D changes in shape and volume of the anatomical structures.

The main purpose of this thesis was to assess the technical feasibility of dose-escalated biological image-guided adaptive radiotherapy in comparison to the standard radiotherapy for head-and-neck cancer in clinical practice. To achieve this, the following technical and clinical objectives were set:

- Introduce and apply a validation method for the DIR of the CTs acquired for each adaptive treatment
- Implement treatment dose accumulation methods based on DIR done with certified commercial algorithms
- Study the added value of intensity modulated arc therapy (IMAT) in comparison to the standard step-and-shoot intensity modulated radiation therapy (sIMRT)
- Compare the dosimetric results of biological image-guided adaptive radiotherapy (ART) treatments to the ones of standard non-adaptive treatments
- Use the implemented methods to help in the identification of the factors that cause late grade 4 mucosal ulcers in dose-escalated ART treatments

Examination Board:

Chairman: Prof. Dr. ir. Carlos De Wagter[1]
Prof. Dr. Wouter Huvenne[3]
Prof. Dr. Christian Vanhove[4]
Prof. Dr. Katrien Vandecasteele[1]
Dr. Jan Vandecasteele[5]
Prof. Dr. Jean-François Daisne[6]
Prof. Dr. Nick Reynaert[7]

Guiding committee:
Prof. Dr. Wilfried De Neve

[1]Ghent University, Department of Human Structure and Repair, Ghent, Belgium
[2]University Hospital, Department of Radiation Oncology, Zurich, Switzerland
[3]Ghent University, Department of Head and Skin, Ghent, Belgium
[4]University Hospital, Institute of Biomedical Technology, (IIBiTech), Ghent, Belgium
[5]AZ Sint-Lucas & Volkskliniek, Radiotherapy Department, Ghent, Belgium
[6]University Hospital, Radiation Oncology Department, Leuven, Belgium
[7]Institut Jules Bordet, Radiotherapy Department, Brussels, Belgium

CONTACT
Ghent University Hospital
Faculty of Medicine and Health Sciences
Department of Human Structure and Repair
T +32 9 332 3015

The PhD online public defense will take place on 03/06/2021 at 5 pm

The link to the online defense can be provided upon request at: anamarialuiza.olteanu@ugent.be