AARHUS UNIVERSITY

Project description

Project title: Comparison of radiation treatment plans, for patient selection and establishment of best practices

Aim

The aims of the project are to establish a framework of advanced metrics for radiation treatment plan comparison, to enable patient selection between radiation modalities (e.g. photon vs proton), and to support the development of national consensus guidelines for optimal treatment planning in general.

Background

Radiotherapy (RT) is an important tool in the treatment of cancer. The past decades have seen a rapid development of new, improved RT treatment techniques including e.g. intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and intensity modulated proton therapy (IMPT). At the same time, dose optimization and calculation algorithms used in treatment planning have become increasingly more accurate. These technical improvements have made it possible to deliver highly conformal radiation doses to the tumor.

RT treatment planning consists of many steps, including both target and organ delineation performed by radiation oncologists, and the actual creation of treatment plans performed by medical physicists. The details in each step of the planning process can vary greatly between institutions, making the comparison of treatment and outcome data difficult. It is the goal of the Danish Multidisciplinary Cancer Groups (DMCG) to establish uniform national guidelines for cancer treatment, including RT treatment planning and delivery [1].

In the coming years, new RT modalities will be introduced at Danish cancer clinics, including proton therapy (PT) at the Danish Center for Particle Therapy (DCPT. In addition, new knowledge-based planning software is becoming widely available, introducing more automated use of treatment planning software [2,3]. For both of these developments it is pertinent that assessment of plan quality can be consistently performed, based on quantifiable parameters [4].

Comparison of treatment plans is not a trivial issue. There are many degrees of freedom in plan creation, multiple organs are involved, and accumulation of dose over the treatment course is highly affected by patient-specific factors and cannot easily be calculated. At the present time, the available metrics to compare treatment plans are highly simplified (e.g. dose-volume parameters, see fig. 1), and do not account for several of the factors involved. A great number of metrics describing more detailed aspects of treatment plans are currently in use, although there is little consensus on which are the most appropriate [5].

The comparison of RT and PT treatment plans is an example of a situation that is difficult to quantify with current standard metrics. A proton beam, unlike a photon beam, delivers a highly focused radiation dose within a small volume of tissue, at the location of the so-called Bragg peak, near the end of the proton beam track (see fig. 2) [6]. The ability to quantitatively compare such different treatment is necessary in order to guarantee the best choice of treatment plan for a given patient. A metric that is used to evaluate photon treatment plans is the dose to the planning target volume, which has no true equivalent in a proton plan. Different metrics must therefore be developed for these situations and the performance of these metrics in plan comparison must be assessed.

Quantifying the differences arising from varying planning practices is a necessary step towards optimizing the processes and establishing inter-institutional consensus. Together with the establishment of consistent metrics for comparison of RT treatment plans, this will facilitate research collaborations and the dissemination of knowledge, and ultimately further improve RT treatment outcomes.

Plan for the project

Materials and methods

The goal of this project is quite ambitious. The subject of treatment plan evaluation covers a vast amount of differing approaches, and a key part of this project is thus to gain an overview of current knowledge and from that distill methods that will be useful in clinical practice.

All patient data necessary for carrying out the project will be available within the CIRRO national imaging and dose plan bank [8]. Software will be available at Aarhus University Hospital (AUH), and participating physicists and oncologists are experienced in treatment planning and evaluation for both RT and PT. The study will be performed using photon and proton treatment planning with standard techniques as well as IMRT, VMAT and IMPT performed retrospectively. The various plan metrics will be calculated for the generated plans and compared using relevant statistical tests.

Data:

The studies will be performed using planning computed tomography (CT) scans from patients previously treated with RT at all participating centers in Denmark. Investigated treatment sites will include: brain, head and neck (divided into naso-pharyngeal and laryngeal tumors), breast, lung, oesophagus and prostate. Twenty to fifty patients for each treatment site are expected to be sufficient to obtain a representative diversity in e.g. patient size, tumor position and size, and other site-specific anatomical characteristics [2,3].

The access to patient data is guaranteed through the framework of the new national Danish Comprehensive Cancer Center (DCCC) research center for RT. Participating centers have already committed to delivering the data within this framework and have agreed upon a time frame for doing so.

Software:

Treatment planning will be performed primarily in two treatment planning systems; Eclipse version 13.7 (Varian Medical Systems, Inc), which is available at AUH through an existing dedicated research license, and Raystation (RaySearch Laboratories), which will be acquired in a stand-alone research license for the purposes of this project. Both systems include the option of custom-made scripting.

Data analysis (calculation of treatment comparison metrics etc.) will be carried out either in MATLAB (a dedicated research license is available) or Python (open source). Statistical analysis will be carried out in SPSS or similar (a license is available through our department).

Structure of the project:

The study addresses four specific research questions, as stated in the description below, each concerning a different aspect in which RT treatment plans can differ. The predicted timeline can be seen in fig. 3.

Q1. Development and test of metrics in simulated scenarios of planning protocol variations.

Method:

Available patient CT scans will be used for treatment plan simulation and dose calculation. In this study the parameters to be varied in simulations are those related to treatment planning protocols. They include:

1. The use of knowledge-based treatment planning algorithms
2. Variations in target and organ delineation
3. Different application of margins
4. Differences in the prioritization of plan objectives during plan creation

Metrics to be investigated include dose-volume parameters, dose distribution metrics and plan complexity metrics as well as metrics describing the robustness of plans toward geometrical uncertainties and anatomical variations. All delineation and planning will be performed at AUH according to local and national guidelines and resulting treatment plans will be examined by experienced radiation oncologists.

Q2. Development of metrics to compare plans for photon versus proton therapy.

Method:

Metrics to compare doses to the CTV over the course of treatment for photon and proton treatment, respectively, will be investigated. This includes the use of treatment field margins to account for uncertainties and variations (which is used in photon treatment) versus direct incorporation of these parameters in probabilistic optimization (which is often used in proton treatment).

Various RT and PT treatment plans will be simulated on a number of available patient CT scans, and various metrics will be calculated. The accumulation of dose over a full treatment course will be simulated either by using daily setup cone-beam CT scans for calculating the dose given at each fraction (if available) or by artificially simulating geometric shifts and deformations in the planning CT scan. Robustness of treatment plans to such changes will be evaluated from the individual calculations. The focus will lie on tumors of the brain and the head and neck region. Metrics deemed to be suitable will be implemented in future prospective protocols for patient selection for proton therapy at DCPT.

Q3. Test of metrics in plans generated at different clinics.

Method:

The metrics developed under Q1 and Q2 will be used to compare treatment plans generated for the same patients at different clinics throughout Denmark. To obtain these, a collection of exemplary patients will be gathered for each treatment site. These patient data sets will be sent out once yearly to all participating centers, for structure delineation and treatment planning according to national and local guidelines and plan evaluation criteria. The performance of the metrics will be evaluated by the PhD student by performing statistical analysis, and if the performance of certain metrics is judged to be poor they will be adjusted and re-evaluated.

Q4. Investigation of geographical variations and development over time.

Method:

Using the data acquired in Q3, variations in treatment plans generated at the different clinics will be quantified and compared to identify potential trends in variation between clinics. In addition to this, each clinic's development over time will be investigated, as data from several consecutive years will be available.

Personnel:

This applicant will carry out the tasks of the research plan (listed above) with input from local experienced oncologists (co-supervisor Dr. Jesper Grau Eriksen) and clinical medical physicists (co-supervisors Drs. Lone Hoffmann and Ditte Sloth Møller) to ensure proper assessment and evaluation of patient anatomies and treatment plan quality and with the overall supervision of Professor at Aarhus University Stine Sofia Korreman.

Collaborators:

The project is a part of Work Package (WP) 5 in the new national research center for RT under the DCCC, led by Stine Korreman and Christian Rønn-Hansen from Odense University Hospital. WP5 aims to develop national strategies for automated image segmentation and treatment planning. Through this work package, funding is provided for local scientists at all Danish RT clinics to supply necessary data and treatment planning efforts. The work will hence be done in collaboration with all Danish RT clinics and all DMCGs. Through these collaborations access to data and expertise in all aspects of RT will be guaranteed.

Expected results and impact:

Based on the results of this PhD study, we expect that a set of valid metrics for treatment plan comparison will be ready for use in all Danish RT clinics, including DCPT. These metrics will greatly facilitate comparison of treatment and outcome data from different clinics and will thus aid in the conduct of nationwide research studies and in the DMCGs' effort to establish uniform national RT guidelines.

During the course of this study the effect of variations in treatment planning procedure will be investigated. The resulting knowledge will help in the optimization of the planning process, leading to improved plan quality and clinical outcomes.

The developed metrics will also be useful in comparing treatment plans utilizing different modalities, and thus aid in determining the optimal treatment for each individual patient. In particular they will be of great use in determining which patients will benefit from receiving proton therapy at the DCPT instead of photon RT.

Ethical considerations:

As only retrospective data will be used there are no relevant ethical considerations for prospective subject inclusion.

References:

1. http://dmcg.dk/en/welcome/
2. Hazell I *et al.* (2015) Automatic planning of head and neck treatment plans *J. Appl. Clin. Med. Phys.* **17**(1):272-282
3. Chang ATY *et al* (2016) Comparison of planning quality and efficiency between conventional and knowledge-based algorithms in nasopharyngeal cancer patients using intensity modulated radiation therapy *Int. J. Rad. Oncol. Biol. Phys.* **95**(3):981-990
4. Moore KL *et al.* (2012) Quantitative Metrics for assessing plan quality *Semin. Radiat. Oncol.* **22**(1):62-69
5. Yaparpalvi R *et al.* (2018) Evaluating which plan quality metrics are appropriate for use in lung SBRT *Br. J. Radiol.* **91**: 20170393
6. Newhauser WD, Zhang R (2015) The physics of proton therapy. *Phys. Med. Biol.* **60**:8 R155-R209
7. www.shi.co.jp
8. Westberg J *et al.* (2013) A DICOM-based radiotherapy plan database for research collaboration and reporting *J. Phys. Conf. Ser.* **489**: 012100

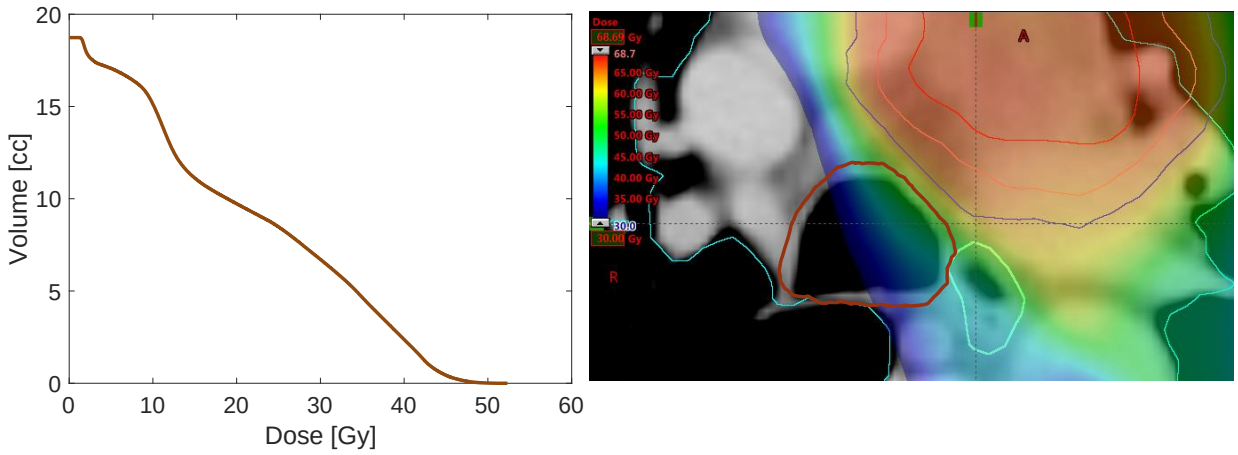

Figure 1: Left: Dose-volume histogram for the bronchi of a lung cancer patient. Right: Part of an axial CT slice depicting the bronchi for the same patient. The delivered radiation dose is shown as an overlaid color wash showing doses from 30 Gy (blue) to a maximum of 68.7 Gy (red).

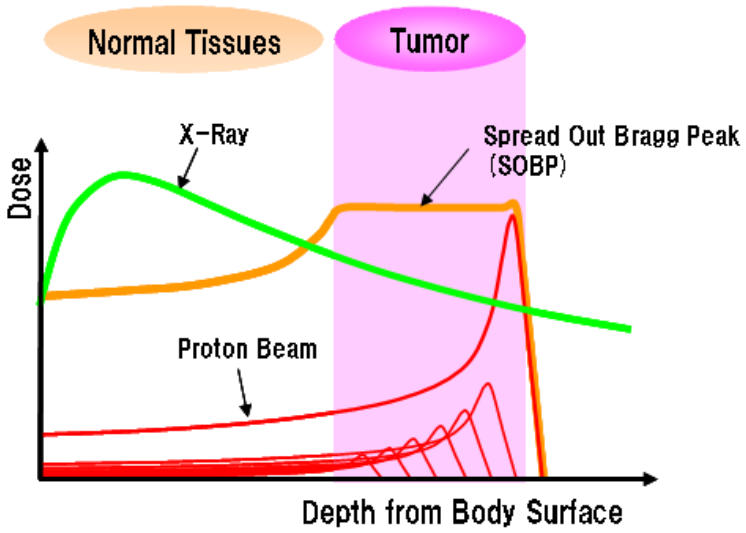

Figure 2: Delivered dose as a function of depth inside the target for a high-energy photon beam (green) and proton beams of different energies (red). In practice, many proton beams are overlapped to create a so-called spread-out Bragg peak (orange) which covers the intended target. Source: [7]

	1st semester	2nd semester	3rd semester	4th semester	5th semester	6th semester
Literature review					.	
Training in treatment planning using Eclipse						
Evaluation of RT plans made with different planning algorithms and by different planners; subsequent choice of appropriate metrics.						
Treatment planning using Eclipse and RayStation.						
Evaluation of RT plans utilizing varying margins for targets and organs at risk, and varying plan objectives and planning systems.						
Evaluation of RT plan differences using different modalities; subsequent choice of appropriate metrics.						
Test of plan deliverability						
Test cases are sent out to participating centers						
Evaluation of variations in delineations and RT plans from participating clinics.						
Thesis						
Publication		Comparison of plan quality metrics		Systematic approach to comparison of plans utilizing different modalities	Quantification of inter-observer and inter-planner differences on a national scale	

Figure 3: Projected timeline for the work and expected publications included in this PhD study.