Quality assurance of proton treatment plans by evaluation of uncertainty doses in brain tumours

The goal in the optimisation of radiation therapy is to give the target the prescribed dose, while minimising the dose to normal tissue as much as possible. According to the guidelines from the Danish Neuro Oncology Group (DNOG), a criterion for dose distribution in proton therapy (PT) is that 98% of the target volume must receive a minimum of 95% of the prescribed dose. DNOG is a clinical national database, the main purpose of which is to gather valid information about the diagnosis and treatment of primary brain tumours in Denmark. The information can be used in research since the database documents the clinical activity of treatments and therefore treatment results can be evaluated.

The unique physical characteristics of PT make it possible to treat tumours that are located close to critical structures such as the eyes, spinal cord and brain. Use of PT can reduce the dose to normal tissue compared with photon therapy, and its use can thereby reduce side effects. According to the Danish Cancer Society, which is an organisation for disease control and patient support, PT may be a more suitable cancer treatment than photon therapy. It is estimated to be more suitable for approximately 10% of all radiation therapy treatments in Denmark. However, the effectiveness of PT is highly influenced by random and systematic uncertainties. The random uncertainties can be associated with tissue heterogeneities, physiological changes, inter- and intra-fractional patient and organ motion, immobilisation and positioning of the patient. The systematic uncertainties can be associated with e.g. image artifacts and the delineation of volumes of interest. Moreover, anatomical considerations, which include the shape, size and location of diseased tissue, can change during the course of treatment as a result of daily positioning uncertainties and the treatment itself. These mentioned uncertainties limit the full potential of PT because they impact on the proton beam range, which affects the dose distribution substantially. The uncertainties may lead to an underdosing of the target and/or an overdosing of the organs at risk. Inadequate dose distribution that results from misalignments, which are caused by setup errors in the patient positioning, should be mitigated to ensure safe treatment for the patient. The setup errors can be mitigated by the use of e.g. image guidance.

Correct alignment is essential for intensity modulated proton therapy treatments because the delivery of the intended treatment depends on accurate alignment of the proton beams. Placement accuracy of 1-2mm or less are important in PT. However, its achievement requires accurate setup of the patient and correct immobilisation. The main purpose of immobilisation is to create a reproducible setup of the patient for daily treatments and therefore reduce the setup uncertainties during the treatment course. In the treatment of brain cancer patients, a customised thermoplastic mesh mask is produced. At the Danish Centre for Particle Therapy (DCPT) of Aarhus University Hospital, the immobilisation of brain cancer patients during a treatment is achieved through use of a base-of-skull frame insert with a Q-fix 3-mask and a Klarity Accu Cushion.

At the DCPT, the patient setup is ensured and verified by use of image-guided radiation therapy (IGRT). The IGRT strategy consists of the capture of one daily cone beam computed tomography (CBCT) image at the start of the treatment with 0o couch angle and the capture of 2D kV-images after every correctional couch shift prior to a treatment field. The purpose of the 2D kV-images is to verify the setup of the patient. When brain cancer patients are positioned at the DCPT, the radiation therapists operate with a setup margin of 3mm. The margin indicates that the patient setup may vary by up to and including 3 mm in the translational directions; vertical, longitudinal and lateral. This setup entails the treatment plans to be robustly optimised and evaluated with +/- 3 mm setup uncertainty.

By reducing the setup margin, the exposure to adjacent tissue and therefore the risks of adverse side effects are reduced. The most common acute side effects for brain cancer patients during PT are skin effects (reddening, soreness, dry skin, itching), pain and swelling in the treated area, fatigue, physical and mental tiredness (concentration difficulty, irritability, reduced memory etc.) and hair loss. The late side effects of PT are usually permanent and occur months to years after treatment. These side effects depend on the location of the area that is treated. The late side effects of PT are considered to be similar to those observed in photon therapy. They include: reduced concentration and memory, learning disability, increased fatigue, endocrine disturbances, impaired vision and brain necrosis. Furthermore, PT can slightly increase the risk of the development of new cancers as can any type of radiation therapy.

In order to reduce setup margins and thereby reduce the side effects of the treatment, the degree of the setup uncertainties during a treatment must be investigated. The purpose of this study was to investigate the deviations in the positioning of brain cancer patients during their treatment at the DCPT.

The data for the first 10 patients with brain tumours who had been treated at the DCPT were included in this study. The robustness of the treatment plans was evaluated with +/- 3 mm setup uncertainty and 3.5 % range uncertainty. Treatment plans of all patients were recalculated on the weekly CT without recalculation of the beamline. The robustness of these plans was evaluated with 0 mm setup uncertainty and 3.5 % range uncertainty in order to verify the impact of anatomical changes on the dose distribution.

The image-guided radiotherapy strategy involved the capture of one daily CBCT image at the start of the treatment with 0o couch angle and 2D kV images after every couch rotation. The kV images from daily treatments were matched in longitudinal, lateral and vertical directions to check the positioning of the patients. The kV matches were analysed by finding the standard deviation for the three cardinal axes.

The results and conclusion of this study will be presented at ESTRO2020.

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