Project description: PhD student Daniella Østergaard

Expanding the use of optimal radiotherapy planning and image guided treatment delivery in children and adolescents

- The life-threatening toxicities associated with radiotherapy (RT) can be reduced with simple technical solutions such as breath-hold and the implementation of modern image guidance and RT planning
- To ensure patient equity and a safe delivery of RT throughout Denmark, a standardization of RT strategies in children and adolescents should be implemented for both photon and proton treatments

Follow-up studies of childhood cancer survivors have documented a substantial treatment-induced increased mortality and morbidity, primarily from cardiovascular disease and secondary cancers, many related to RT. To limit the healthy tissue exposure among children and adolescents, the margins used to account for random and systematic uncertainties during RT must be reduced. The potential for margin reduction by applying image-guided RT (IGRT), introducing motion compensating techniques such as deep inspiration breath-hold (DIBH), and optimizing treatment delivery techniques will be investigated in a pediatric and adolescent setting as margins cannot be extrapolated from adults. In this project we will develop the first evidence-based "child-size" RT margins. In addition, we will explore the potential of well-recognized strategies for reducing margins in adult RT, e.g. IGRT and DIBH, and tailor them specifically for use in children and adolescents.

Finally, we will demonstrate how these new margins can lead to optimized treatment delivery techniques based on systematic analyses.

Research questions and hypotheses

1) **What is the lowest possible daily CBCT dose for IGRT in children and adolescents?** IGRT by daily CBCT must provide sufficient image quality for visualization of soft tissues and bony structures in order to ensure correct positioning of the patient prior to each daily treatment, however, with lowest possible radiation exposure.
   Hypothesis 1: Pediatric and adolescent patients can be safely evaluated for RT delivery using a 10 fold reduced CBCT imaging dose.
2) **What are the uncertainties during RT delivery for children and adolescents in DIBH, for both photon and proton therapy, compared to free-breathing?** A RT delivery margin specific for children and adolescent should be calculated for both free-breathing and DIBH planning using the van Herk formula, based on results from the TEDDI trial, the only prospective trial investigating DIBH in children and adolescents.
   Hypothesis 2: DIBH will mitigate uncertainties in RT delivery compared to free-breathing with age-specific margins for children and adolescents.

3) **How have children and adolescents in Denmark been irradiated from 2010 to 2020?**
   A national database of retrospective cross-country documentation of target definition, RT delivery techniques and dose exposure will enable the development of future national guidelines. *Hypothesis 3: RT has changed over time with an increase in the use of more conformal techniques, incl. proton therapy, leading to an overall decrease in dose exposure to the normal tissue.*

Methods:

The project will be based on retrospective data such as CT scans, RT plans and computer-based simulation of RT plans with modern techniques readily available on Rigshospitalet and Christie NHS Foundation Trust, UK retrieved from patient journals. Data from the TEDDI trial relevant for this project has already been collected and further analysis will be retrospective.