Status of the Ph.D-project:

Risk of radiation induced heart disease in early breast cancer patients

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In the first paper, Risk of coronary artery disease after adjuvant radiotherapy in 29,662 early breast cancer patients: A population-based Danish Breast Cancer Group study, we evaluated the risk of cardiac events (coronary artery disease and valvular heart disease) in a cohort of 29,662 women diagnosed with early breast cancer between 1999 and 2016. Information on cardiac events was reached from the Western Denmark heart register which contains detailed information on type and localization of the cardiac event. In total, 22,056 received RT. For patients irradiated during a non-CT-based-period (1999-2007), the incidence rate ratio (IRR) was 1.44 (CI 1.14-2.0) and a trend towards an increased risk for left-sided compared to right-sided was observed within the first 5 years after RT. For patients irradiated during the CT-based period (2008-2016), the IRR was 0,90 (0.69-1-16) and no trend towards an increased risk for left-sided patients was observed within the first 10 years after RT. However, information on cardiac event 10 or more years after RT was limited. Furthermore, information on RT doses to the heart and cardiac substructures is needed. This paper is submitted.

The second paper concerns development and validation of Danish national guidelines for delineating the heart and cardiac substructures across four Danish Multidisciplinary Cancer Groups (DMCG) where RT dose to the heart may be of concern. Consensus regrading guidelines was reached during a 2-day workshop with participation of 15 observers representing the four DMCGs. During the workshop, the guidelines were validated by individual contouring of the heart and cardiac substructures. At the end of the workshop we had 5 individual contouring-set on 12 CT scans from breast cancer patients. The inter-observer variation was evaluated by DICE similarity coefficient for larger structures and distance between the center of mass for smaller structures. The highest inter-observer overlap was seen for the heart and heart chambers and decreased with smaller structures. The national guidelines will ensure consistency in the delineation of the heart and cardiac substructures across the different DMCGs with an acceptable inter-observer variation. This paper is published.
https://pubmed.ncbi.nlm.nih.gov/32544606/

In the third paper, we validated an automatic CT-based atlas for the heart and cardiac substructures. Experts in oncology delineated the heart and cardiac substructures according to the Danish guidelines, on non-contrast enhanced RT planning scans of breast cancer patients. The MIM software was used to generate an atlas consisting of the 40 CT-scans representing different anatomy. In the process of delineating the heart and cardiac substructures on a new CT-scan, the MIM software automatically select the 5 CT-scans with the best anatomical match. The automatic CT-based atlas was tested on the 12 CT scans generated during the workshop regarding guidelines. The atlas-based delineation was tested against the delineations of the experts. This manuscript is under preparation.

In study four, we conducted a nested case-control study of cardiac events in a population-based cohort of 16,058 BC patients irradiated between 2005 and 2016 and treated with CT-based RT. The cohort included 273 cases diagnosed with cardiac event after BC irradiation and 546 controls. The controls were matched on age at BC diagnosis, year of breast cancer diagnosis and an index time, where the controls should be without cardias event at least as long as their matched case. The heart and cardiac substructures were delineated by using an automatic CT-based atlas and dose-volume histograms were used to extract the mean and maximum RT doses for each structure. The dose-response relationship will be estimated by modeling the cardiac event rate as $K_m(1+\beta d)$ where K_m is a constant specific to each matched set of case and controls, β is the excess relative risk of cardiac event per unit increase in dose and d is the RT dose in Gy to the relevant cardiac substructure of an individual patient. This work is in progress.

Publications:

Milo MLH, Offersen BV, Bechmann T, Diederichsen ACP, Hansen CR, Holtved E, et al. Delineation of whole heart and substructures in thoracic radiation therapy: National guidelines and contouring atlas by the Danish Multidisciplinary Cancer Groups. Radiother Oncol 2020;150:121–7. https://doi.org/10.1016/j.radonc.2020.06.015.

Milo MLH, Thorsen LBJ, Johnsen SP, Nielsen KM, Valentin JB, Alsner J, Offersen BV. Risk of coronary artery disease after adjuvant radiotherapy in 29,662 early breast cancer patients: A population-based Danish Breast Cancer Group study
This work is submitted

Presentations/lecture:

Presentation of the study; Delineation of whole heart and substructures in thoracic radiation therapy: National guidelines and contouring atlas by the Danish Multidisciplinary Cancer Groups at Odense University Hospital, Department of Oncology in August 2020

Presentation of cardiac toxicity at webinar in Aalborg. Arranged by Pfizer. October 2020

Presentation of the study; Risk of coronary artery disease after adjuvant radiotherapy in 29,662 early breast cancer patients: A population-based Danish Breast Cancer Group study at ESTRO congress, November 2020

Presentation of the study: Risk of coronary artery disease after adjuvant radiotherapy in 29,662 early breast cancer patients: A population-based Danish Breast Cancer Group study at DCCC webinar, November 2020

Lecture in cardio toxicity at a meeting in FYO (foreningen af yngre onkologer) in January 2020

Poster presentations at Ph.D day at the university, January 2020

Poster presentations at ESTRO congress November 2020

Activities in 2021

Poster presentations at Ph.D day at the university, January 2020
Abstract submitting to ESTRO 2021 in Martz
Submission of the dissertation in June 2021