jointly bring the radiation community closer to that goal: (1) joint evidence-based summaries of late effects scientific evidence (e.g. QUANTEC 2010 and pediatric QUANTEC, *in progress*) to reach a common standard of terminology across the radiation research disciplines, including, radiation oncology, physics, radiobiology, epidemiology, biostatistics etc.; (2) reach international consensus about standards for real-time, *prospective* data registration of patients treated for cancer now, by including radiation dose and chemotherapy characteristics , short-term and long-term health outcomes, and set-up such registries where feasible. Since such registries cannot, by definition, answer questions about long-term effects, it is essential that we strengthen the retrospective study arena as well, by (3) including added measures (crude or detailed) of exposed organ volume and fractionation to existing retrospective study databases (e.g. de Bruin et al 2009) to enable international pooled analyses of joint dose-volume effects for the very long-term late effects for which outcome data are already available. Finally, (4) novel 2D-to-3D dose reconstruction methods to derive DVH-based doses recently proposed for Hodgkin lymphoma survivors (Ng et al 2010) should be validated and further developed for more general application in retrospective late effects studies to quantify the very long-term dose effect relationships according to current standards of dose estimation. By working together more closely we can overcome current gaps between clinical radiation oncology and population-based studies.

SP-0025
Late cardiac damage: Integrating radiotherapy, dosimetry, and epidemiology
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Background: Long-term follow-up of women irradiated for breast cancer in both randomised trials and observational studies has revealed that past breast cancer radiotherapy regimens have increased the risk of heart disease. Assessment of the relationship between heart radiation dose and heart disease requires detailed dosimetry. In women irradiated for breast cancer, measures of their cardiac dose can be combined with outcome information on subsequent heart disease to create dose-response relationships. These can then be used to predict the likely cardiac risk for women irradiated today.
Methods: A large database of internationally used breast cancer radiotherapy techniques from the 1950s onwards was compiled using information from practising and retired radiation oncologists from several different countries, from radiotherapy textbooks, and from breast cancer radiotherapy protocols.
Each breast cancer radiotherapy regimen was reconstructed using "virtual simulation" which involved the construction of a virtual 3-dimensional patient representation using CT scan data from a representative patient. Radiotherapy beams were designed and applied to this patient representation. Following this, the radiation beam and patient information were analysed using a CT planning system. For each regimen, dose volume histograms were generated and used to calculate a number of different measures of dose including mean dose and mean dose in equivalent 2 Gray fractions. Doses were estimated for the whole heart and for the three main coronary arteries. The main sources of variability associated with the dosimetry method were assessed.
Cardiac doses were applied to women irradiated for breast cancer in two different studies. The first study included around 40,000 women irradiated in 76 randomised trials of radiotherapy in the Early Breast Cancer Trialists' Collaborative Group Overview. In this study, mean heart dose was related to death from heart disease. The second study was a case control study including around 2,000 women. It investigated incident ischaemic heart disease (myocardial infarction, coronary revascularisation or death from ischaemic heart disease) in population-based registries in Denmark and Sweden. Mean heart radiation dose was related to risk of developing a major coronary event.
Results: Radiation fields that were used to treat the internal mammary lymph nodes delivered the highest mean heart doses, particularly for left-sided irradiation. Of the cardiac structures considered, the left anterior descending coronary artery generally received the highest doses, due to its proximity to the left breast. Assessment of the effect of patient anatomy on heart dose showed that, although there was some interpatient variability in dose, there was greater dose variation between tumour laterality and between different regimens.
In both the randomised and observational data, the risk of developing heart disease increased with increasing mean heart dose. In the randomised data, there was a 5% increase in heart death per Gray (SE 1%, 2p<0.00001). In the population-based data, there was a 7% increase in incident ischaemic heart disease per Gray (95% confidence interval 2-13%; 2p=0.0001).
Conclusions: Virtual simulation and CT planning enable the measurement of detailed estimates of cardiac radiation dose.
The risk of developing heart disease increases with increasing mean heart dose, with no evidence of a threshold below which there is no risk.
For women with no cardiac risk factors a mean heart dose of 1 Gray from breast cancer radiotherapy is likely to increase her absolute risk of an acute coronary event by around 0.5%, while for a mean heart dose of 2 Gray, the increase is likely to be around 1%. Absolute risk increases will be larger for women who are already at increased cardiac risk prior to radiotherapy.

DEBATE: BRACHYTHERAPY IS THE OPTIMAL MODALITY FOR DOSE ESCALATION IN H&N RADIO-THERAPY

SP-0026
Brachytherapy: een optimal tool for dose escalation of radiotherapy in oropharyngeal cancer
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Brachytherapy (BT) can be used for patients with early-stage head and neck cancer (HNC) from different subsites: oropharynx, nasopharynx, lip, check, and nasal cavity.
Until recently, 5-year survival rates for locally-advanced HNC were reported to be 40% even with early multimodality approaches. Since 1990s, the treatment of HNC has changed dramatically. Different strategies were implemented in order to improve loco-regional control (LRC) and overall survival (OS). However, the improvements in oncologic outcomes achieved by these efforts have come at the cost of increased toxicity and deterioration of QoL, mostly because of the increasing incidence of dysphagia and xerostomia. In order to reduce the incidence and severity of these complications and to improve QoL without jeopardizing outcomes, highly-conformal RT techniques are required.
Given the increasing incidence of HPV-related oropharyngeal cancer (OPC) in the last decades, especially among young patients and the ongoing discussion in which group of patients dose escalation of RT is really necessary, we will limit our discussion on the potential role of dose escalation in patients with OPC.
Is dose escalation really necessary in patients with OPC?
In the last decades different new strategies have significantly improved LRC and OS. The 5-year Kaplan-Meier estimate of LC was 78% for patients with locally-advanced OPC treated at our institution by accelerated scheme of chemo-IMRT. In these patients, feeding-tube dependence was needed in 65% and the incidence of grade ≥2 late toxicities was 44%. Despite the gains achieved, further improvement in oncologic outcomes and reduction of late toxicity is needed in all patients with OPC, in particular patients with locally-advanced and HPV-negative disease. As a result of using highly conformal RT techniques (IMRT, BT, SRT) and the recent introduction of promising imaging techniques to predict the final outcome (DCE-MRI, DWI, and FDG-PET), dose escalation of RT become appealing. The implementation of different image-guided techniques, for instance cone-beam CT, will further facilitate such risk-adaptive approach to escalate the dose of radiotherapy, when needed.
The current scheme of the Rotterdam Organ-Function Preservation Protocol consists of 46 Gy of (chemo)IMRT to all patients followed by a boost using BT or Cyberknife SRT for patients with T1-3N+ or IMRT-boost for large tumors. The combination of 46 Gy of IMRT followed by a BT boost in 167 patients with OPC has resulted in excellent LC-rates (94% at 5 years) with low toxicity and satisfactory QoL scores. Only 26% patients needed tube feeding. Grade ≥2 late xerostomia and dysphagia were seen in only 11 % and 8%, respectively. Besides T-stage, the incidence of LRC was also significantly correlated with HPV-status (p=0.05) and boost technique (BT, Cyberknife vs. IMRT, p<0.001) in our patients.
Improvements of LRC-rates in high-risk OPC might be achieved by escalating the dose of RT to the GTV. Raktoe et al (2012) showed that 70% of all LFs after RT for OPC were seen in the GTV, suggesting radioresistance in these tumor parts and might advocate for escalating the dose to the GTV.
Our group is almost ready to launch a risk-adaptive dose escalation protocol for patients with OPC. DWI will be performed at baseline and after 40 Gy, in order to predict response on RT. Patients with poor response (ADC increase of <25%, compared to baseline threshold) would be the target for such dose escalation protocol. According to our protocol, OPC-patients receive 22 Gy of PDR-BT. In case of poor response to the initial treatment, the dose of the PDR will be escalated from to 30 Gy.