Image registration accuracy was <2 mm for all anatomic head and neck landmark displacements in the x, y, and z direction relative to CT. Image quality was found to be comparable to the commissioning benchmark. SNR data for T1 FSE and T2 FSE were not statistically significantly different (p = 0.53, 0.10) from benchmark dataset. However, the benchmark configuration appears to provide more optimized signal across all anatomical structures. For superficial structures closer to the surface, e.g. parotid, the RT coil provides very high signal due to closer proximity to the coil (T1 FSE mean RT 126.1 v diagnostic 99.8). For deeper structures the converse is true, e.g. brainstem (mean SNR RT 33.7 v diagnostic 58.2).

Conclusions: Benchmarking of the system and clinical process has allowed for the development of an MR-IME quality assurance program for this anatomical site, with well defined imaging and image registration metrics.

PROFFERED PAPERS: PREVENT 1: MODELLING AND PREDICTION OF NORMAL TISSUE RESPONSE

OC-0075
Normal tissue complication probability parameters for breast fibrosis: pooled results from two randomised trials
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Purpose/Objective: The dose-volume effect of radiation on breast tissue is poorly understood with few attempts at modeling the Normal Tissue Complication Probability (NTCP). This study estimates the NTCP parameter values for breast fibrosis after external beam breast radiation therapy (RT).

Materials and Methods: Individual patient data of 5282 patients from the multi-centre EORTC 22881-10882 ‘boost versus no boost’ trial and 574 patients from the Cambridge breast IMRT trial were pooled and analysed. All patients received whole breast irradiation (WBI) (40Gy in 15 fractions over 3 weeks or 50Gy in 25 fractions over 5 weeks) followed by tumour bed (TB) boost in some cases. A two compartment model, the best estimated NTCP parameters were BEUD3(50) =136.4Gy, m=0.95 and n=0.01 for the Niemierko model and BEUD3(50)=132Gy, m=0.35 and n=0.011 for the LKB model. A small value of volume parameter ‘n’ suggests that for moderate-severe fibrosis, breast tissue is a serial organ. The observed rates of moderate-severe fibrosis in the START pilot trial were in good agreement to the predicted rates from the above models (x2=0.05; p=0.95 with five degrees of freedom) Figure 1.

Conclusions: This large multi-centre pooled study indicates that the effect of volume parameter is small and the maximum radiotherapy dose is the most important parameter to influence late breast fibrosis. Clinical validation of these results from future prospective studies is suggested.

OC-0076
Second cancer risks after radiotherapy for breast cancer: What is the impact of advanced treatment techniques?
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Purpose/Objective: Breast cancer is the most commonly diagnosed female cancer, and with good survival rates, it is imperative that any potential long term side effects from this effective treatment are reduced. Techniques specific to patient cohorts with differing local recurrence risk factors are likely to be the new standard of care in breast radiotherapy in 5 to 10 years. These techniques include simultaneous integrated boost (SIB) and conformal non co-planar beam arrangements for accelerated partial breast irradiation (APBI). These beam arrangements distribute the dose throughout the body in a different pattern to the standard treatment. This work reports a comparison of the risk for these modern radiotherapy techniques, including the use of image guidance.

Materials and Methods: Five treatment plans were created on a patient CT scan: standard whole breast treatment (WVRT), conformal non co-planar five field plan for an APBI treatment, two volume/two dose level SIB plan with 5 fields, three volume/three dose level SIB plan with 7 fields (forward planned), three volume/three dose level SIB plan with 7 fields (inverse planned). The plans were transferred to a whole body phantom. Regions in the phantom which represented radiosensitive organs were delineated and thermoluminescent dosimeters (TLD) used to measure the dose. Dose from a breast imaging kilovoltage cone beam CT protocol was measured with TLD in the same regions. These dose data were used as input into the Biological Effects of Ionising Radiation Report VII models of second cancer induction and lifetime risks calculated for the five treatment classes and intensive imaging regimes.

Results: The lifetime risk data showed that complex radiotherapy techniques did not increase the theoretical risk of second cancer incidence for organs distant from the treated breast, or the contralateral breast where appropriate constraints were applied. SIB treatments were predicted to increase the lifetime risk of second cancer incidence in the lungs compared to standard breast radiotherapy; this was outweighed by the threefold reduction in 5 yr local recurrence risk with adjuvant radiotherapy for a high risk cohort for whom these treatments are appropriate. A lower lifetime risk of second cancer in the contralateral breast was predicted for the APBI method, compared with WVRT. The contribution of imaging dose to the total dose from both treatment and imaging did not exceed 22% for any measured organ.

Conclusions: Modern complex radiotherapy techniques used in breast cancer treatment were not predicted to increase the theoretical risk of second cancer incidence in organs far from the treated breast. Where increases in the lifetime risk of induced second cancer were predicted, these remained small compared to the large reduction in local recurrence risk from receiving RT as a component of treatment.
The use of image guidance is unlikely to result in an unacceptable increase in second cancer risk.

**OC-0077**
Towards individualized dose constraints: The QUANTEC radiation pneumonitis model with clinical risk factors
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**Purpose/Objective:** Understanding the dose-response of the normal lung in order to minimize the risk of radiation pneumonitis (RP) is of critical importance for optimization of radiotherapy for lung cancer. In this study, we propose a method to combine the dose-response relationship for RP from the landmark QUANTEC paper with clinical risk factors in order to improve individual patient risk prediction. The approach is validated in an independent dataset of 103 patients.

**Materials and Methods:** The prevalence of risk factors (pulmonary co-morbidities, smoking history, age and chemotherapy) in the patient populations underlying the QUANTEC analysis was estimated, and a previously published method to adjust the dose-response relationship for clinical risk factors was employed. Estimates of effect size (odds ratios, OR) for clinical risk factors were drawn from a recently published meta-analysis. Baseline values for $D_{50}$ (the dose resulting in a 50% complication probability) and $y_{50}$ (the normalised slope of the dose-response curve at $D_{50}$) were established. Confidence intervals were estimated using random sampling. The method was tested in an independent dataset (103 non-small cell lung cancer patients), comparing the predictive power of the dose-only QUANTEC model and the model taking risk factors into account. Subdistribution cumulative incidence functions for RP were compared in stratified analyses for patients with high / low risk predictions, based on group medians, from the two models, and concordance indices (c-indices) for the prediction of RP were calculated. C-indices were compared using a Student t-test for paired samples.

**Results:** The logistic relationship between mean lung dose and the risk of RP was described in the QUANTEC paper by $D_{50} = 30.8$ Gy, $y_{50} = 0.97$. From this, a reference dose-response relationship for a patient without pulmonary co-morbidities, no history of smoking, below 63 years old, and not treated with sequential chemotherapy was $D_{50} = 32.3$ Gy (95% CI: 28.9, 36.5), $y_{50} = 1.10$ (95% CI: 0.92, 1.31). ORs for each risk factor were then used to calculate individual patient risk estimates. The cumulative incidences of RP in the validation dataset were not significantly different in high / low risk patients stratified according to the QUANTEC model ($p=0.11$), but were significantly different using the individualized model ($p=0.004$, see Figure 1). The c-indices were significantly different between the dose-only and the individualized model ($p=0.004$ using binary risk allocation, $p=0.04$ using continuous NTCP as predictor).

**Conclusions:** This study presents a method to combine a dose-response function with known clinical risk factors, based on data from large, published meta-analyses. We demonstrate that the predictive power of the combined model is greater than a dose-only model in an independent dataset. This method, although not taking correlations between risk factors into account, allows for individualization of dose constraints and risk estimations, and it can easily be extended to include additional risk factors.

**OC-0078**
Sparing the contralateral submandibular gland in oropharyngeal cancer patients; dose-response analysis.
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**Purpose/Objective:** (1) To prospectively determine the prevalence of patient-reported xerostomia after sparing the contralateral submandibular gland (cSMG) in oropharyngeal cancer patients without contralateral lymph node metastases. (2) To construct a normal tissue complication probability (NTCP) curve for submandibular gland (cSMG) function after radiotherapy (RT) based on mean dose and selective flow measurements.

**Materials and Methods:** 50 oropharyngeal cancer patients (cT1-4N0-2M0) were treated with an optimized IMRT-technique with the intention to spare both parotid glands (PGs) and the cSMG (aim cSMG <40 Gy; cSMG sparing cohort). They were compared with a historical cohort of 52 patients that received only PG-sparing IMRT (PG-sparing cohort). cSMG- and PGflow rates were measured 6 weeks and 1 year post-RT and converted into the percentage of baseline. Patient-reported xerostomia was recorded using the EORTC QLQ-HEN35 single item xerostomia and sticky saliva. For NTCP-analysis, cSMG flow data from a large patient cohort were fitted to the Lyman-Kutcher-Burman model with a complication defined as cSMG flow ratio <25% of pre-RT flowrate (RTDG/EORTC grade 4 xerostomia).

**Results:** cSMG mean dose could be reduced below 40 Gy in 50% and 21% of the patients in the cSMG-sparing and PG-sparing cohorts (mean cSMG dose 39.1 vs 50.4 Gy) respectively. cSMG flow ratio, complication rate and xerostomia scores 1 year post-RT were slightly better in the cSMG-sparing cohort (ns). At 1 year, 56% of the patients from the cSMG-sparing cohort still reported grade 2-3 xerostomia. Post-hoc, patients were re-grouped according to mean cSMG dose above (n= 66) or below (n= 36) 40 Gy. All patients but one in the <40 Gy group had a small (T1-T2) tumor and 53% received only unilateral neck-RT. Significantly higher cSMG flow ratios at 6 weeks and 1 year post-RT in the <40 Gy group translated into lower xerostomia scores at both time points (at 1 yr: 67 vs 42% grade 2-3 xerostomia, p = 0.07). PG function (1 yr) was similar in both groups. LKB-modelling showed substantial shift of NTCP-curve between 6 weeks and 1 year post-RT: the TD50 (mean dose leading to 50% NTCP) was 23 and 35 Gy, resp. Above 40 Gy mean cSMG dose, NTCP worsened between 6 weeks and 1 year post-RT. See figure for the 1 year NTCP-curve.

**Conclusions:** This study concerns the largest group of patients published, for which a dose response curve for cSMG-flow rate after radiotherapy was analysed. cSMG mean doses below 40 Gy resulted in improved cSMG function and reduced patient-reported xerostomia. Above 40 Gy submandibular function worsened in time. cSMG-sparing in oropharyngeal cancer patients(N-stages ≤N2b) is still challenging.