Conclusions: The bootstrap provides a statistical analysis of the uncertainty in the estimated dose-response relation. It suggests likely values of $D_{50}$ and $y$ ($m$), their confidence intervals, and how they interrelate for each model. Finally, it can be used to evaluate to what extent data supports one model over another. Both data sets considered here provided fairly strong support to the Lyman model over the Poison-based model.

PD-0189
Multivariate NTCP models for radiation-induced hypothyroidism
L. Cella1, R. Liuzzi1, M. Conson2, V. D’Avino1, M. Salvatore3, R. Pacelli4
1Institute of Biostructures and Bioimaging National Council of Research (CNR), Radiation Oncology, Naples, Italy
2Department of Diagnostic Imaging and Radiation Oncology Federico II University School of Medicine, Radiation Oncology, Naples, Italy

Purpose/Objective: Radiation-induced hypothyroidism (RHT) is a frequent side effect after therapeutic irradiation of the cervical region and it has been described in patients undergoing radiation therapy (RT) for different neoplasms such as lymphoma, head-and-neck cancer and breast cancer. Purpose of this work is to develop multivariate normal tissue complication probability (NTCP) models for RHT and to compare them with already existing NTCP models for RHT.

Materials and Methods: Fifty-three patients treated at our department with sequential chemo-radiotherapy for Hodgkin’s lymphoma (HL) were retrospectively reviewed for RHT events. Clinical information along with thyroid gland dose distribution parameters were collected and their correlation to RHT was analyzed by Spearman’s rank correlation coefficient ($R_s$). Multivariate logistic regression method using resampling methods (bootstrapping) was applied to select model order and parameters for NTCP modeling. Model performance was evaluated through the area under the receiver operating characteristic curve (AUC). Models were tested against external published data on RHT and compared with other published NTCP models.

Results: When we express the thyroid volume exceeding X Gy as a percentage ($V_x(%)$), a two-variable NTCP model including $V_{30}(cc)$ and gender (female=0, male=1) was suggested as the optimal predictive model for RHT ($R_s=0.615$, $p<0.001$, $AUC=0.87$). Conversely, when absolute thyroid volume exceeding X Gy ($V_x(cc)$) was analyzed, an NTCP model based on 3 variables including $V_{30}(cc)$, thyroid gland volume ($V_T$) and gender was selected as the most predictive model ($R_s=0.630$, $p<0.001$, $AUC=0.85$). The three-variable model have a better performance ($AUC=0.914$, 95%CI:0.760-0.984) when tested on external published data on RHT and compared with other published NTCP models.

Conclusions: The absolute volume of thyroid gland exceeding 30 Gy in combination with thyroid gland volume and gender provide an NTCP model for RHT with improved prediction capability not only within our patient population but also on an external cohort.

PD-0190
CT based quantification of radiation induced lung damage (RILD) and the interaction with chemotherapy and cetuximab
H. Sharifi1, W. van Elmpt1, G. Nabanton1, M. Das2, P. Lambin1, D. De Ruysscher1
1MAASTRO Clinic, GROWMaastricht University Medical Center (Department of Radiation Oncology), Maastricht, The Netherlands
2Maastricht University Medical Center, Department of Radiology, Maastricht, The Netherlands
3University Hospital Leuven, Department of Radiation Oncology, Leuven, Belgium

Purpose/Objective: Radiation-induced lung damage (RILD) is one of the most important dose-limiting toxicities in the treatment of lung cancer patients. Prediction models are still unsatisfactory, partly because clinical toxicity endpoints such as dyspnea are influenced by many parameters and difficult to quantitatively objectively. Furthermore, interactions between drugs and radiotherapy (RT) are difficult to assess. We therefore evaluated RILD more objectively, quantitatively and on a continuous scale measuring the regional lung tissue density changes per voxel.

Materials and Methods: Multiple treatment regimens of lung cancer (both SCLC and NSCLC) were retrospectively analysed: radiotherapy alone, sequential and concurrent chemo-radiotherapy with or without the addition of the targeted agent cetuximab. Follow-up CT scans up to 6 months (range, 2-6 months) after the end of treatment were coregistered using deformable registration to baseline CT scans. CT density changes (expressed in Hounsfield Units) in the lungs were correlated to the RT dose delivered in every part (i.e. voxels) of the lungs.

Results: CT scans from 119 lung cancer patients were studied. Patients received a mean dose of 60 Gy (range 45-80 Gy) to the tumor. For the different treatment modalities: patients treated only with RT (N=19), sequential chemo-RT (N=30), concurrent chemo-RT (N=51), concurrent chemo-RT with cetuximab (N=19), the absolute increase in HU for voxels receiving between 40 and 50 Gy was 27 ±26, 38 ± 45, 29 ± 38, and 54 ± 33 HU, respectively. Furthermore, dose-response curves were linear in the dose-region between 0 and 80 Gy with a slope expressed as a lung density increase per dose (HU/Gy), of 0.7 ± 0.7, 1.2 ± 1.2, 1.1 ± 1.2, and 1.6 ± 1.0 HU/Gy. Hence, the dose-response curves for the group treated with the targeted agent cetuximab showed more susceptibility for RILD ($P < 0.03$) compared to (chemo-) radiotherapy.

Conclusions: CT density changes allow quantitative non-invasive assessment of lung toxicity, giving complementary information to standard used clinical endpoints. Patients receiving cetuximab showed a higher increase in HU and a significantly larger dose response compared with the patients not receiving cetuximab.

PD-0191
Time-dependent dose-response relationships for vaginal elasticity after cervical cancer radiotherapy
E. Alevronta1, H. Lind2, M. al-Abany3, A.C. Waldenström1, C. Olsson2, G. Dunberger1, T. Nyberg1, E. Avall-Lundqvist1, G. Steineck1, B. Lind1
1Karolinska Institutet, Department of Oncology-Pathology, Division of Clinical Cancer Epidemiology, Stockholm, Sweden
2Karolinska University Hospital, Department of Hospital Physics, Stockholm, Sweden
3Gothenburg University, Department of Oncology - Clinical Cancer Epidemiology the Sahlgrenska Academy, Stockholm, Sweden
4Karolinska University Hospital, Department of Gynecologic Oncology, Stockholm, Sweden

Purpose/Method: Time-dependent dose-response relationships for vaginal elasticity were determined in patients treated for cervical cancer with pelvic radiotherapy. Vaginal elasticity was assessed by palpation 1 week after the end of RT, and then every 3 months up to 1 year. Tissues from patients receiving radiotherapy were compared to tissues from patients who received no radiotherapy. Elasticity of the vaginal walls was assessed using palpation and viscoelastic properties were determined using dynamic indentation tests. Elastic modulus and damping ratio were calculated for each tissue sample.

Results: In patients treated for cervical cancer, a significant decrease in vaginal elasticity was observed after the end of RT. The elastic modulus and damping ratio were significantly lower in tissues from patients treated with radiotherapy compared to tissues from patients who received no radiotherapy.

Conclusions: Time-dependent dose-response relationships for vaginal elasticity after cervical cancer radiotherapy can be used to monitor the tissue response to radiotherapy and can help in the early detection of radiation-induced changes in vaginal elasticity.
**Purpose/Objective:** Cervical cancer survivors may experience lack of vaginal elasticity after external beam radiation therapy. This late effect of radiation therapy affects the quality of life of the survivors. The aim of this study was to investigate the dose response relationships of vaginal elasticity considering the effect of different follow up times.

**Materials and Methods:** Of the 96 gynecological cancer survivors treated with external beam radiation therapy for cervical cancer, 32 developed the symptom. The survivors were treated between 1991 and 2003. The mean follow up time for this group of patients is 6.4 years. Patients were followed up during 2006 and the occurrence of the symptom was documented with a study-specific postal questionnaire. The vagina was delineated as an organ at risk and the dose volume histograms were exported for each patient. These data were introduced into a maximum likelihood fitting to calculate the best estimates of the parameters using the Relative Seriality model. Splitting the data in two groups, one with an average follow up time of 49 months and one with 105 months we calculated the corresponding dose response relationships using the Probit model with the maximum dose. To model the influence of the follow up time to the dose response relationships we assume that the incident rate is constant over time and the probability of having a persisting complication at time $t$ (the follow up time) after receiving dose $D$ is given by the Probit function $P_t(D)$. Then the symptom prevalence at a time $t$ is given by:

$$P_t(D(t)) = 1 - (1 - P_t(D))^e$$

**Results:** The dose-response parameters for the Relative Seriality model and the vagina were estimated: LL=-54.9, $D_{50}=55.0$ Gy (52.9-56.9), $\gamma_{50}=1.12$ (1.03-1.25), $s=23.8$ (21.3-26.1). The estimated volume parameters indicate that the vagina behave serially for this endpoint. The parameter values of the subgroups with short and long follow up times are $D_{50}=60.9$ Gy, $\gamma_{50}=0.84$ and $D_{50}=58.3$ Gy, $\gamma_{50}=1.04$ respectively. Our data indicates that $D_{50}$ seems to decrease and $\gamma_{50}$ seems to increase with follow up time.

**Conclusions:** In our study, the vagina behaves serially for the symptom vaginal elasticity, which means that maximum dose, describes our data equally well as the relative seriality model. Our data indicates that follow up time influence the prevalence with the outcome vaginal elasticity after radiation therapy.