University of Groningen

PV-0477: Early CT image biomarkers change and xerostomia score are strong predictors for late xerostomia

Dijk, L.V. Van; Brouwer, C.L.; Beukinga, R.J.; Schaaf, A. Van de; Laan, H.P. Van der; Burgerhof, H.G.M.; Langendijk, J.A.; Steenbakkers, R.J.H.M.; Sijtsema, N.M.

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2016

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Dijk, L. V. V., Brouwer, C. L., Beukinga, R. J., Schaaf, A. V. D., Laan, H. P. V. D., Burgerhof, H. G. M., Langendijk, J. A., Steenbakkers, R. J. H. M., & Sijtsema, N. M. (2016). *PV-0477: Early CT image biomarkers change and xerostomia score are strong predictors for late xerostomia*. S227 - S228. https://doi.org/10.1016/S0167-8140(16)31726-1
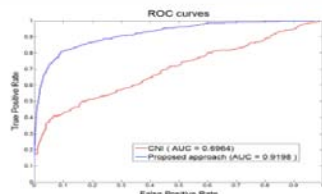
Figure 1 Receiver operating characteristic (ROC) curve for the proposed method (blue) and for the standard CNI approach (red).
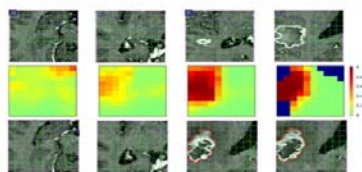

Figure 2 Pre-RT T1-Gd (top), probability maps of GBM relapse generated by the proposed approach (middle) and reference manual contours of the relapse for a given patient (bottom). Each slice represents a slice in the axial view. Dark blue on the probability maps indicate voxels where metabolic information was not available. The areas at risk of relapse predicted by the proposed approach (using MR data acquired before RT) are in clear accordance with the manually contoured relapse regions.

Conclusion: A learning system based on SVM trained with mp-MR data has been presented. Reported results show that this learning scheme can provide a probability map of the area of relapse of GBM in a stable and accurate manner. This study suggests the potential of mp-MR data in addressing specific questions in GBM imaging.

PV-0476
Fractional anisotropy dose-response relationship of the corpus callosum

N. Pettersson[1], H. Bartsch[2], J. Brewer[2], L. Cervino[1], M. Connor[1], A. Dale[2], D. Hagler[2], R. Karunamuni[1], A. Krishnan[2], J. Kuperman[2], C. McDonald[3], N. Farid[2], N. White[2], J. Hattangadi-Gluth[1], V. Moiseenko[1]
[1]University of California San Diego, Radiation Medicine and Applied Sciences, La Jolla, USA
[2]University of California San Diego, Radiology, La Jolla, USA
[3]University of California San Diego, Psychiatry, La Jolla, USA

Purpose or Objective: Diffusion tensor magnetic resonance imaging (DTI) is a non-invasive modality for determination of water diffusion properties. Fractional anisotropy (FA) quantifies the extent of directionality of water diffusion. We investigated absorbed dose as a predictor of FA change in the corpus callosum (CC) following radiation therapy for high-grade glioma.

Material and Methods: Fifteen patients with high-grade glioma underwent DTI scans before, and ten months after radiation therapy to 59.4-60 Gy. Diffusion data were acquired on a 3T MRI scanner. Using an automated white matter fiber tracking technique, 23 fiber tracts were segmented on the baseline and follow-up DTI images. The CT images used for treatment planning and both DTI image sets were aligned using non-linear registration. This way, the baseline FA, the follow-up FA, and the absorbed dose could be determined for each voxel in all 15 patients. For each voxel in the CC, we calculated the FA change as FAfollow-up /FAbaseline and dichotomized the data into a binary outcome variable using 0.5 as cutoff. For all 15 patients, logistic regression was used to determine dose-response curve parameters (D50 and g50) and their confidence intervals (CIs). We used the area under the receiver-operating characteristics curve (AUC) to evaluate the discriminative ability of the voxel dose. Then, we estimated dose-response curve parameters and calculated the AUC for each patient individually.

Results: The median age was 59 (range: 40-85) years. The average CC volume and average CC mean absorbed dose was 62±8 cm3 and 26±14 Gy (1 SD), respectively. Using data from 99 691 voxels, the estimated parameters for the dose-response curve for all patients (upper panel in Figure 1) were D50=88.0±0.1 Gy and γ50=0.80±0.01 (95% CIs). The AUC was 0.71 indicating good discriminative ability. For nine out of 15

patients, the individual AUC was ≥0.60, indicating that higher absorbed dose is associated with higher probability of FA change ≥0.5. Dose -response curves for those patients are shown in the lower panel in Figure 1 and their estimated parameter values in Table 1. Individual D50s varied between 41.3 and 125.9 Gy.

Table 1. Fractional anisotropy and absorbed dose data for the corpus callosum. For patients with an AUC ≥0.6, dose-response curve parameters and their 95% confidence intervals are given.

patient id	# voxels changed ≥0.5	# of voxels	median voxel dose (range) (Gy)	AUC	D50 (Gy)	γ50
All 15	11448	99691	21.5 (0.5-65.9)	0.71	88.0±0.1	0.80±0.01
1	279	7037	3.0 (0.6-20.1)	0.13		
2	156	6428	8.5 (0.7-64.4)	0.49		
3	1159	6417	38.7 (2.5-65.9)	0.69	79.2±0.5	0.80±0.05
4	777	6095	21.0 (4.7-64.2)	0.57		
5	533	6605	39.9 (4.1-64.0)	0.68	104.8±0.7	1.06±0.08
6	816	6232	19.6 (1.5-57.9)	0.70	41.3±0.4	1.02±0.05
7	1137	6688	24.7 (1.0-63.6)	0.76	57.9±0.3	0.86±0.04
8	28	6988	6.7 (0.8-36.1)	0.61	125.9±3.7	1.50±0.16
9	377	6982	21.7 (8.0-64.9)	0.72	92.6±0.6	1.12±0.07
10	113	5767	9.1 (0.5-44.9)	0.56		
11	749	8149	35.5 (2.0-63.9)	0.77	81.1±0.5	1.26±0.07
12	1299	6501	37.8 (5.9-63.1)	0.59		
13	1108	6946	11.2 (1.3-63.0)	0.85	46.0±0.3	0.90±0.04
14	1017	7765	60.9 (7.9-63.1)	0.68	69.1±1.8	3.24±0.42
15	1900	5091	25.4 (6.8-43.8)	0.59		

AUC: the area under the receiver-operating characteristics curve; D50: absorbed dose required for 50% probability; γ50: the normalised dose-response gradient.

Probability of change in fractional anisotropy ten months after radiation therapy
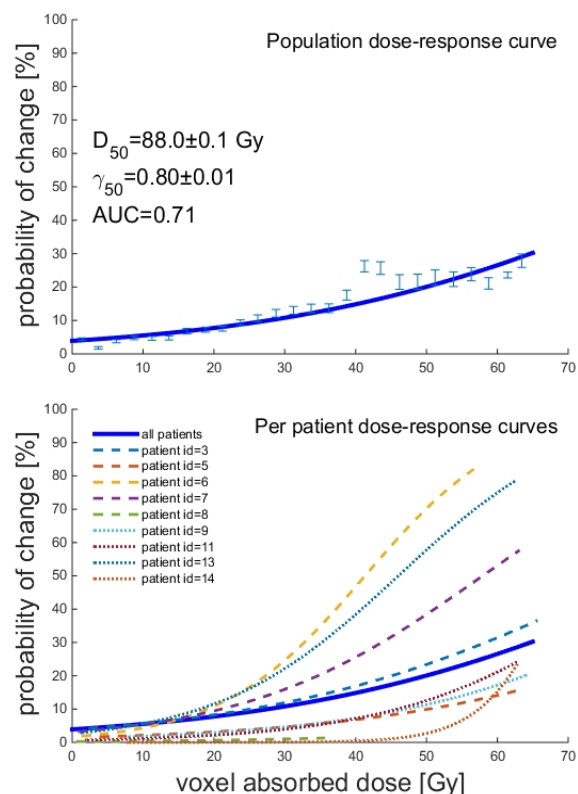
Conclusion: Absorbed dose was a significant predictor of FA change in the CC. This was the case both when all patients were pooled for analysis, and in nine out of 15 patients when analyzed separately. More detailed analyses are needed to better understand the effect radiation has on water diffusion in brain white matter.

PV-0477
Early CT image biomarkers change and xerostomia score are strong predictors for late xerostomia

L.V. Van Dijk[1], C.L. Brouwer[1], R.J. Beukinga[1], A. Van de Schaaf[1], H.P. Van der Laan[1], H.G.M. Burgerhof[2], J.A. Langendijk[1], R.J.H.M. Steenbakkers[1], N.M. Sijtsema[1]
[1]University of Groningen- University Medical Center Groningen, Radiation oncology, Groningen, The Netherlands
[2]University of Groningen- University Medical Center Groningen, Epidemiology, Groningen, The Netherlands

Purpose or Objective: Radiation induced xerostomia is related to the dose given to the parotid glands (PG).

_____

Nevertheless, substantial unexplained variability remains in the development of late xerostomia. To understand this variation becomes increasingly important with the advent of more conformal radiation techniques. Our hypothesis is that the patient-specific late response to radiotherapy (RT) is associated with changes in CT images and xerostomia scores early after RT.

Material and Methods: Parotid gland (PG) image characteristics were extracted from CTs before (T0) and after RT (6 weeks post RT) of 110 HNC patients. The differences between those two time points resulted in potential Δ CT Image Biomarkers (IBMs). These potential Δ CT IBMs represent geometric (20) and CT intensity (24) changes of the PG. Furthermore, the scored xerostomia of the patients before (XER*baseline*) and 6 weeks post RT (XER*6w_post*), tumour, patient and dose characteristics were included. To identify variables that were associated with the endpoint moderate-to-severe xerostomia 12 months after RT (XER*12m*) whilst reducing multicollinearity, variables were first omitted based on inter-variables correlation. Second, multivariable selection was conducted by bootstrapped forward selection based on log-likelihood performance. The performance of the resulting logistic regression models was evaluated with the area under the ROC-curve (AUC) and Nagelkerke R2 index. All models were internally cross validated.

Results: Multivariable analysis was performed with 23 Δ CT IBMs. The primarily selected IBM wasΔ volume (between T0 and 6 weeks post RT) of the PG (figure) (p<0.001). Larger volume change was related to a higher chance of XER*12m*. Furthermore, the XER*6w_post* and XER*baseline* were very prognostic. The performance of the multivariable model was high with an AUC of 0.89 and R2 of 0.54 (table). This model showed to be stable when it was internally validated (AUC-cross=0.88, R2-cross=0.53). Moreover, dose parameters did not add to the performance of the model (AUC-cross=0.88, R2-cross=0.52). Δ Volume made dose parameters redundant, suggesting that PG volume changes are related to the patient-specific response to dose.

Table. Model performance measures

	Baseline model	Post RT model	
	PG dose + XER$_{baseline}$	XER$_{w6\ after\ RT}$ + XER$_{baseline}$	XER$_{w6\ after\ RT}$ + XER$_{baseline}$ + Δ volume
2 log-likelihood	111.47	99.55	81.72
Nagelkerke R^2	0.27	0.47	0.54
Discrimination Slope	0.20	0.38	0.45
AUC (95% CI)	**0.76 (0.66-0.85)**	**0.83(0.75-0.91)**	**0.89 (0.82-0.95)**
AUC-cross validation	0.74	0.83	0.88
R^2- cross validation	0.25	0.47	0.53

XER$_T$: *Patient rated xerostomia at different time points;*
PG dose: *Planned mean dose to contra lateral parotid gland;*
Δ volume: *PG volume change from baseline (T0) to 6 weeks post RT*

Conclusion: Change of PG volume 6 weeks post RT showed to be strongly related to late xerostomia. Moreover, together with xerostomia scores before and 6 weeks after RT, outstanding performance was obtained to predict XER*12m*. We believe that this model can contribute to the understanding of the patient-specific response to RT in developing late xerostomia. Secondly, it can serve as a quantitative measure for late damage to the PG early after treatment. The next step will be to investigate whether Δ PG Volume and xerostomia determined early in treatment can be used to predict late xerostomia, to select patients with a large risk on late xerostomia for proton treatment.
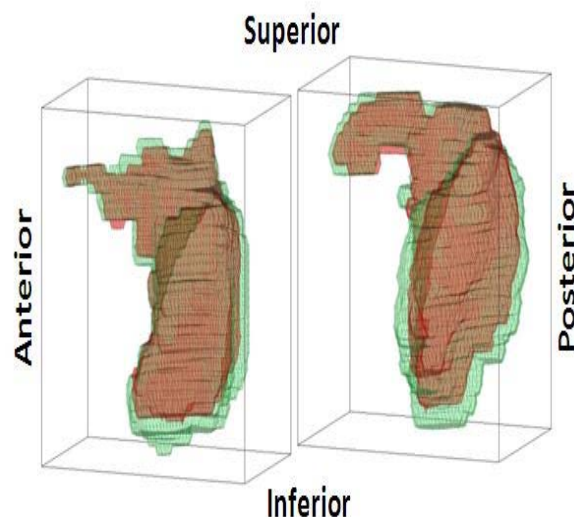

Figure. Examples of PGs with large Δ volume between the start of (green) and 6 weeks after (red) RT

PV-0478
Predicting pulmonary function loss in lung cancer radiotherapy patients using CT ventilation imaging
C. Brink[1,2], J. Kipritidis[3], K.R. Jensen[1], T. Schytte[4], O. Hansen[2,4], U. Bernchou[1,2]
[1]Odense University Hospital, Laboratory of Radiation Physics, Odense, Denmark
[2]University of Southern Denmark, Institute of Clinical Research, Odense, Denmark
[3]The University of Sydney, Radiation Physics Laboratory, Sydney, Australia
[4]Odense University Hospital, Department of Oncology, Odense, Denmark

Purpose or Objective: Pulmonary complications remain a major dose limiting factor for lung cancer radiotherapy. Pulmonary function loss is known to correlate with physical lung dose, but better prediction accuracy is desired. This work investigates the potential of 4D CT-based functional imaging to improve the prediction of radiation-induced pulmonary function loss.

Material and Methods: 80 lung cancer patients each received a treatment planning 4D CT scan prior to radiotherapy. To quantify pulmonary functional loss the patients also underwent spirometry measurements of forced expiratory volume (FEV1) and forced vital capacity (FVC) immediately before radiotherapy and at 3, 6, and 9 months follow-up. For each patient, the pre-treatment regional ventilation was evaluated by performing deformable image registration (DIR) between the CT inhale and exhale phase images. The Jacobian determinant (J-1) of the DIR motion field was used as a ventilation surrogate. The functional mean lung dose (fMLD) was then defined as the regional lung dose weighted spatially by the regional ventilation. The physical mean lung dose (MLD) was calculated without ventilation weighting.Logistic regression was used to compare the ability of fMLD and MLD to predict clinical pulmonary function loss, defined as a reduction of the FEV1 and FVC to less than 90% of their initial values at 6-months post treatment. To minimise noise in the spirometry data, the FEV1 and FVC values at 6 months were estimated based on a fit to the available data up to 9 months post-treatment.

Results: Both functional and physical lung dose correlated with the onset of clinical pulmonary function loss. The figure and table show the logistic regression results and model parameters respectively. We observed a 0.7 Gy decrease in the tolerance dose (D50) when using fMLD as opposed to MLD. However, the difference in log-likelihood between the MLD and fMLD based models was not statistically significant different from zero. Thus we did not observe a significant