Figure: Stoichiometric calibration curve. The HU shift for the dosimeter needed for a correct SPR estimation based on the curve is indicated with a red arrow.
Conclusion: The stoichiometric method overestimates the measured SPR by 13%. Using DE this error is reduced, to an overestimation of 3%. If the stoichiometric method is used for the 3D dosimeter its HU must be corrected in the treatment planning system.

Keywords: Stoichiometric calibration method, Dual Energy CT, 3D dosimetry

References:
[1] E. M. Høye, P. S. Skyt, E. S. Yates, L. P. Muren, J. B. B. Petersen and P. Balling, "A new dosimeter formulation for deformable 3D dose verification", Journal of Physics: Conference Series 573, 012067 (2015).
[2] Y. De Deene, R. Hill, P. S. Skyt and J. Booth, "Flexydos3D: A new deformable anthropomorphic 3D dosimeter readout with optical CT scanning", Journal of Physics: Conference Series 573, 012025 (2015).
[3] U. Schneider, E. Pedroni and A. Lomax, "The calibration of CT Hounsfield units for radiotherapy treatment planning", Phys. Med. Biol. 41, 111-124 (1996).
[4] N. Hünemohr, B. Krauss, C. Tremmel, B. Ackermann, O. Jäkel and S. Greilich, "Experimental verification of ion stopping power prediction from dual energy CT data in tissue surrogates", Med. Phys. 59, 83-96 (2014).
[5] D. C. Hansen, J. Seco, T. S. Sørensen, J. B. B. Petersen, J. E. Wildberger, F. Verhaegen and G. Landry, "Beyond the stoichiometric method: A comparison of dual energy CT and proton CT for stopping power estimation", submitted to Med. Phys. (2014).

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Organizational response of the hypothalamus and pituitary to external beam radiation
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Purpose: Hypothalamic-pituitary axis (HPA) dysfunction is a dose-dependent sequela of brain irradiation. Meta-analysis of studies on non-pituitary central nervous system tumours performed by Appelman-Dijkstra et al. [*The Journal of Clinical Endocrinology & Metabolism*, 8, 2330 (2011)] found estimated doses of 25-97 Gy to the HPA and 0.54 prevalence of pituitary deficiency. However, no included study reported the site-specific doses to the hypothalamus or pituitary. As the hypothalamus is thought to be more radiosensitive than the pituitary, greater understanding of the structural organization and normal tissue tolerances of these two structures is necessary to better describe the relationship between HPA radiation dose and secondary insufficiency. The purpose of this study is to characterize the radiation dose to the HPA in adults treated for non-pituitary brain tumours.
Materials/Methods: Twelve patients, 3 males and 9 females, have been enrolled in our prospective VoxTox study that will continue to recruit until 2017. Primary diagnoses included meningioma (7), pineal tumor (3), and glioma (2). Patients were treated with TomoTherapy® and received 50-60 Gy to the tumour bed in 30 fractions. Digital Imaging and Communications in Medicine radiotherapy data, including dose cubes, contours and planning imaging, were retrieved from TomoTherapy® archives using an in-house software and imported into ProSoma virtual simulation software. Quality assurance of hypothalamus and pituitary contours was performed. Parametrisation of dosimetric data from planning computed tomography scans was used to determine mean radiation doses to the hypothalamus and pituitary separately. Dose volume histogram data were exported to Matlab®. Equivalent uniform doses (EUDs) for a parallel structure (a=1) and serial structure (a=20) were calculated utilizing a freely available program and normal tissue tolerance parameters for the lung and spinal cord, respectively.
Results: The mean radiation doses to the hypothalamus and pituitary were 35 Gy and 34 Gy, respectively. Serial and parallel EUDs for each patient are presented in Figure 1. The mean EUDs for a=1 and a=20 were 30 Gy (range 14-52) and 33 Gy (range 19-52), respectively, for the hypothalamus and 29 (range 8-46) and 31 Gy (range 8-46), respectively, for the pituitary. The mean difference between serial and parallel EUD values was 3 Gy for both the hypothalamus and the pituitary.
Conclusions: The organization of the hypothalamus and pituitary into serial or parallel structures may not be predictive of HPA response to radiation. Future studies are necessary to isolate the dose-volume effects of these two organs.

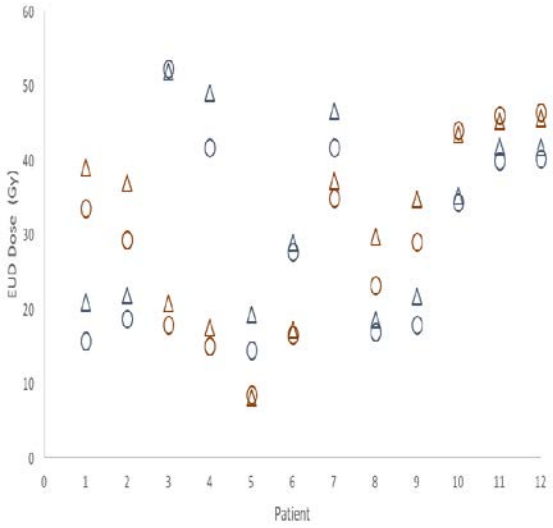

Figure 1. EUD doses to the hypothalamus (blue) and pituitary (red) are presented for parallel (circle) and serial (triangle) structures for each patient.

Keywords: brain tumours; pituitary; hypothalamus

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Response-based Bayesian Network Approaches for Adaptive Radiotherapy of Non-Small Cell Lung Cancer (NSCLC)
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Purpose: In NSCLC radiotherapy, personalized radiation treatment is intended to deliver an appropriate amount of dose to control the tumor while reducing radiation-induced toxicities such as radiation pneumonitis, esophagitis, carditis. The outcomes of radiation treatment may depend on radiation dose and patients' physical, clinical, biological and genomic characteristics before and during the course of radiotherapy. We intend to find hierarchical biophysical relationships influencing the observed outcomes from retrospective data and develop practical Bayesian Networks (BN) for adaptive radiotherapy of the NSCLC.
Materials/methods: Our study includes 79 NSCLC patients treated on prospective protocols under IRB approval. In addition to dosimetric information, each patient had 179 features from five categories including clinical factors (10) (e.g., age, KPS), cytokines before (30) and during (30) the treatment course, microRNAs (49), and single-nucleotide polymorphisms (SNPs) (60). A large-scale Markov blanket based on the HITON algorithm is employed for selecting relevant biophysical predictors of outcomes. The corresponding BN structure is obtained using the hill-climbing algorithm implemented in the R programming environment.

The BN is guarded against overfitting using k-fold cross validation.
Results: BNs representing the biophysical relationships before and during the course of radiotherapy behind the radiation outcomes are identified and designated as "biophysical BNs''. They can be adjusted to "practical BNs" for adaptive therapy purposes, with a possibility of minor compromise of estimated prediction power. Given a patient's pretreatment data, an appropriate treatment plan can be chosen from a practical BN to control the tumor and keep the radiation toxicities under a certain level. When the patient's during treatment information is available, the planned dose can be adjusted in the BN according to his/her responses, to better control tumor without increasing the chance of the complication. Cross validation is employed to measure the prediction power of the BNs. For example, while the performance of a pretreatment BN to predict radiation pneumonitis ≥G2 is 0.80 with 95% CI: 0.69-0.90 based on 2000 stratified bootstrap replicates, the AUC of the BN with patients' responses during radiotherapy can reach 0.84 (95% CI: 0.78-0.92).
Conclusions: We developed clinically practical systems to predict the radiation outcomes in NSCLC patients before and during the course of radiation treatment based on retrospective data. The prediction performance of the BN improves by incorporating during treatment information. Our approach can handle high dimensional predictors and can be an important component of decision support for personalized adaptive radiation treatment. However, it still needs to be validated in external independent data.

Keywords: Adaptive Radiotherapy, Radiation Outcomes Prediction, Bayesian Networks

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Experimental dosimetric comparisons of protons, helium, carbon and oxygen ion beams

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Purpose: The interest in particle therapy is growing worldwide with clinical applications focused on protons and carbon ion beams. Moreover, at the Heidelberg Ion Beam Therapy Center, helium and oxygen ions are available for research purposes with an active scanning beam delivery system. While most of the planning studies comparing these four ions are based on non-experimentally validated calculations, this work is focused on the basic experimental dosimetric characterizations and comparisons of these ions at the same facility.
Material/methods: Laterally integrated depth-dose distributions of pencil-like beams, for 10 different energies in the therapeutic range have been experimentally studied, with a range in water similar for every ion. Several parameters were evaluated, as the range, the entrance-to-peak ratio, the width of the Bragg peak, the distal fall-off and the tail-to-peak ratio, and this with and without ripple filter (used to broaden the pristine peaks). The measurements were performed using a water column, by delivering quasi-monoenergetic pencil-like beams on the central axis.
The lateral dose profiles of these ions, at low, middle and high beam energy, were investigated at different depths in water (without ripple filter). Along with the acquisition of these data, a double-Gaussian parametrization was performed and the evolution of its components along the depth in water was examined. The measurements have been done in a water tank coupled with 24 motor-driven PinPoint ionization chambers by delivering a vertically scanned beam.
Results: For the depth-dose characterization, the evolution of the investigated parameters presents a different behavior depending on the energy, the ion and the presence or not of ripple filter. Helium ions present interesting intermediate characteristics with a distal fall-off smaller than protons and a reduce fragmentation tail compare to heavier ions. These characteristics suggest different advantages and/or drawbacks for the ions depending on the situation, and a compromise among them has to be found for later treatment planning.
The lateral profiles and their double Gaussian parametrizations present net advantages of the heavy ions compared to protons with intermediate results for helium ions.
Conclusions: Our experimental results indicate that helium ions could be a good candidate for further particle therapy improvements, with intermediate properties between the clinically used proton and carbon ions. The main features are the favorable physical characteristics, especially a smaller lateral scattering than protons and a very low tail-to-peak ratio compared to carbon ions. This study was used to create the first helium ions database, allowing biological experiments needed to ensure proper treatment planning and future fair comparisons for planning studies between the ions.
We acknowledge funding from DFG (KFO Schwerionentherapie 214).

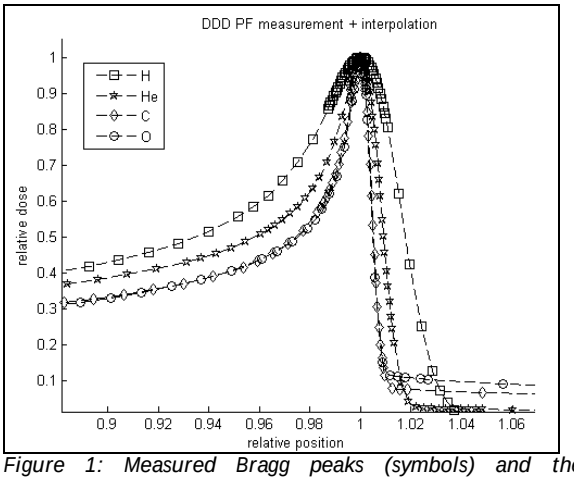

Figure 1: Measured Bragg peaks (symbols) and their interpolation (lines), normalized to maximum and to the peak position, for a range in water of ~15cm.

Keywords: Particle therapy, Experimental dosimetry, Ions comparison

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Orthotopic tumor models for glioma and NSCLC

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Over the last decades, survival rates for most cancer patients have only marginally increased. One reason for the limited decline in this death rate is the lack of effective treatment strategies especially in advanced cancers. In oncology research, drug development processes have proven to be very inefficient and this has been partly attributed to the lack of adequate preclinical testing modalities. Research in our lab is specifically focused on lung and brain cancer, both amongst the most malignant and difficult to treat neoplasms with very poor overall 5-year survival rates. In advanced disease most patients receive chemo- and radiotherapy (CRT), but response to treatment is generally poor with only minimal effects on survival while decreasing the patients' quality of life. Tumors almost invariably recur or are intrinsically resistant to chemotherapy. Improvement of tumor control at primary and distant locations is compulsory. The goal of our research is to identify novel treatment combinations that will result in improved outcome for patients with advanced lung or brain malignancies.