analyze these effects based on synthetic datasets of anthropomorphic phantoms and suggest an extended optimization scheme which explicitly accounts for these effects. Performance of the method is been tested for various simulated irradiation parameters.
We also investigate the use of a special optimization method to enhance the spatial resolution and the WET accuracy of proton radiographies prior to the HU-RSP re-calibration. The optimization method is designed for imaging systems measuring only the residual range of protons without relying on tracker detectors to determine the beam trajectory before and after the target.
The ultimate purpose of the optimization is to minimize uncertainties in the HU-RSP calibration curve. We therefore suggest and perform a thorough statistical treatment to quantify the accuracy of the optimized HU-RSP curve.
Results: We demonstrate that without extending the optimization scheme, spatial blurring (equivalent to FWHM=3mm convolution) in the proton radiographies can cause up to 10% deviation between the optimized and the ground truth HU-RSP calibration curve. Instead, results obtained with our extended method reach 1% or better correspondence, as shown in Figure 1. We have further calculated gamma index maps for different acceptance levels. With DTA=0.5mm and RD=0.5%, a passing ratio of 100% is obtained with the extended method, while an optimization neglecting effects of spatial blurring only reach ~90%.
Conclusions: Our contribution underlines the potential of a single optimized proton radiography to generate a patient-specific calibration curve and to improve dose delivery by optimizing the HU-RSP calibration curve as long as all sources of systematic incongruence are properly modeled.

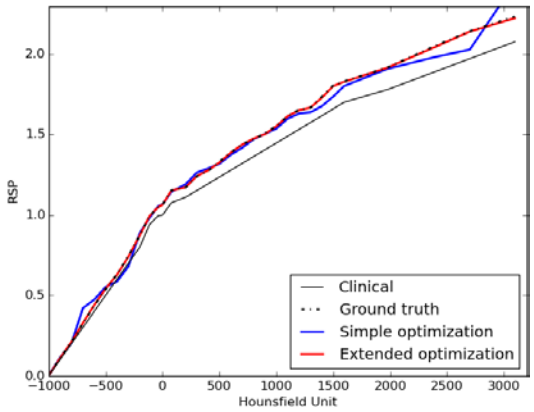

Figure 1: Comparison of optimized conversion curves.

Keywords: proton therapy, proton radiography, image processing

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Overcoming Cancer Radioresistance
Factors of radioresistance in prostate cancer
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Prostate Cancer is one of the leading cancer entities in men, however. In this disease, radiotherapy leads to comparable cure rates compared to surgery. Overall, survival and cure rates of patients with prostate cancer are on average much higher than in many other cancers. Despite this fact, biological individualization of treatment is also an important research topic in this disease. Specifically in the field of personalized radiation oncology important research questions include: 1) pre-treatment identification of patient subgroups with individually very radioresistant tumours that would have a high risk of recurrence after standard radiotherapy alone. 2) pre-treatment identification of subgroups that have a high chance of tumour cure after radiotherapy alone 3) identification of subgroups with a high risk of distant metastasis after local treatment
Definition of biomarkers to identify such patient subgroups need to consider biochemical failure, local recurrences and distant metastases. Biomarkers will in future help to individualize radiation dose, but also combined radiation and systemic treatments. All endpoints need to be compared with surgical patient groups, with the mid-term aim to find decision parameters between the two treatment approaches. The talk will give an overview over current candidate biomarkers in preclinical and translational research.

Keywords: prostate cancer, radiotherapy, personalized treatment, biomarker

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Front-end electronics and hit position reconstruction methods for the J-PET scanner
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Purpose: The J-PET collaboration is developing a novel TOF-PET, whole-body tomography scanner based on polymer scintillators [1-4]. The scanner barrel is made of long scintillators, axially positioned, which are readout from both sides by photomultipiers. This novel approach relies mainly on the timing of the signals instead of their amplitudes for the reconstruction of the Lines-of-Response, therefore a very precise time resolution is one of the main challenges of the project.
Material and methods: For this purpose, novel ultrafast front-end electronics (FFE) allowing for sampling in the voltage domain of the signals with a duration of few nanosecond was developed [5]. The FEE solution is a purely digital implementation, based solely on a FPGA (Field Programmable

Gate Array) device and few satellite discrete electronic components. An additional advantage of the FPGA solution is a very low cost. At present, in the prototype phase, one sample together with digitization costs only about 10 Euro.
Results: The proposed solution provides very good time measurement properties, allowing to probe the signal in the voltage domain with an accuracy below 20 ps (σ) [5]. The input signals are amplified and split into four paths, each having an individual threshold level. This multi-level threshold technique is well suited for the application of reconstruction methods of the hit position of gamma quanta in the scintillator, which results in the improvement of the TOF resolution. We developed several hit reconstruction methods, e.g. compressive sensing technique allows for the recovery of the full signal shape and amplitude based on the samples registered in the PMTs. This information can be used to improve the precision of the hit position reconstruction [6]. Other methods are based on the comparison of detector signals with results stored in a library of synchronized model signals registered for a set of well-defined positions of scintillation points. The hit position is reconstructed as the one corresponding to the signal from the library, which is more similar to the measurement signal. A degree of similarity between measured and model signals is defined as the distance between points representing the measurement- and model-signal in a multidimensional measurement space [7] or as the Mahalonobis distance[8].
In this talk, the developed front-end electronics will be described. Also, the application of the multi-threshold measurement to the hit reconstruction methods will be presented.

Keywords: PET, FEE, hit reconstruction methods

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Utilizing CBCT data for dose calculation in adaptive IMPT
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Purpose: In intensity modulated proton therapy (IMPT), inter-fractional anatomical changes can substantially compromise the treatment quality for cranial and pelvic lesions [1,2], motivating treatment adaptation. The increasing availability of in-room cone beam computed tomography (CBCT) in proton centers enables frequent acquisition of 3D imaging data which may be used for dose calculation and plan adaptation. This work investigates and compares two complementary approaches for correcting CBCT image intensity for dose calculation in adaptive IMPT for head and neck (H&N) and prostate cancer. For H&N patients a mid-treatment replanning CT was used for validating the correction methods.

Material and methods**:** CBCT images and corresponding projections of 3 H&N and 3 prostate cancer patients were used in this study. In the first approach, a so-called virtual CT (vCT) was generated by deformable image registration (DIR) of the corresponding planning CT to the pre-treatment CBCT [3]. In the second approach, the vCT was used as prior for scatter correction of the raw CBCT projections, following the approach of Park *et al.*[4] Reconstruction of the corrected projections yielded a corrected CBCT image ($CBCT_{cor}$). Both approaches were evaluated for CT number accuracy using phantom scans and compared by means of beam eye view 2D range maps of single field uniform dose (SFUD) plans in all patients. For prostate cases, the geometric accuracy of target and OAR structures was also evaluated qualitatively.
Results: For H&N cases, no considerable differences between SFUD dose calculations on vCT and $CBCT_{cor}$ were found, with 97.3% to 99.8% of the 2D range maps showing a range difference below 3 mm (Table 1). Median range differences compared to a diagnostic quality replanning CT acquired within 3 days of the CBCT were below 0.5 mm. For prostate cases, an even higher agreement of SFUD beam ranges between vCT and $CBCT_{cor}$ was observed (Table 1). However, the analysis also showed that the DIR-based vCT approach exhibits inaccuracies in the pelvic region due to the very low soft-tissue contrast in the CBCT. The $CBCT_{cor}$ approach yielded results closer to the original CBCT (Figure 1), promising an improved accuracy in delineation. In general, the $CBCT_{cor}$ approach was not affected by inaccuracies of the DIR used during the generation of the vCT prior. An enhanced agreement of bowel filling with respect to the original CBCT image was observed on the $CBCT_{cor}$.
Conclusions: A DIR-based CBCT intensity correction has been compared to a scatter correction method on basis of the CBCT projections. Both techniques yield 3D CBCT images with intensities equivalent to diagnostic CT and appear to be suitable for dose calculation in adaptive IMPT. For H&N cases, no considerable differences between the two techniques were found, while improved results of the $CBCT_{cor}$ were observed for pelvic cases due to the reduced sensitivity to registration inaccuracies. A detailed quantification based on delineation accuracy using vCT and $CBCT_{cor}$ is under way.

Keywords: IMPT, Adaptive Radiotherapy, CBCT imaging

Acknowledgements: BMBF (01IB13001, SPARTA); DFG (MAP)

Patient	SFUD angle	RD < 3mm (%)	RD < 2mm (%)	Median RD (mm)	IPR RD (mm)
PatHN1	315°	99.7	98.9	0.1	1.1
PatHN2	0°	97.3	91.3	0.1	2.2
PatHN3	270°	99.8	99.2	0.3	1.1
PatPR1	0°	100.0	100.0	0.0	0.6
	270°	100.0	100.0	0.2	0.5
PatPR2	0°	99.8	99.8	0.2	0.7
	270°	100.0	100.0	0.0	0.9
PatPR3	0°	100.0	100.0	-0.3	0.7
	90°	100.0	100.0	-0.1	0.4

Table 1: SFUD BEV range comparison of vCT and $CBCT_{cor}$ for the investigated H&N (PatHN1-3) and prostate (PatPR1-3) patients. The percentage of 2D range maps with a range difference (RD) below 3mm and 2mm is given together with the median range difference and half the 2.5% to 97.5% inter-percentile range (IPR). The SFUD angle is given according to the IEC scale.

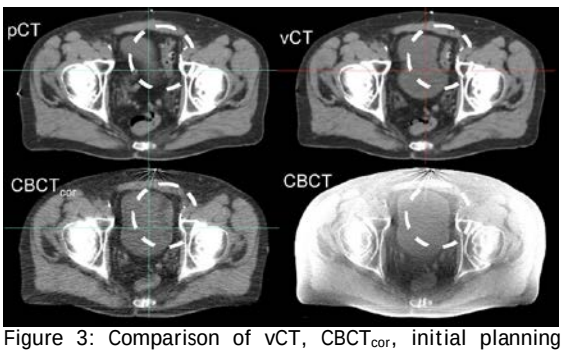

Figure 3: Comparison of vCT, $CBCT_{cor}$, initial planning CT (pCT) and the original CBCT of PatPR3, using the same window for displaying. The original CBCT shows inaccurate