T-regulator cells or myeloid-derived suppressor cells, and overexpression of certain ligands (e.g., programmed death ligand-1 [PD-L1]) that inhibit the host’s existing antitumor immunity. The latter effect is thought to take place by the cancer cells’ overexpressing ligands that can bind inhibitory co-receptors expressed by T lymphocytes (also known as “immune checkpoints”). Recent advances in melanoma research have led to the development of immunotherapies that have substantial antitumor effects in other types of cancer as well, including lymphoma, renal cell carcinoma, and non-small lung cancer (NSCLC). These advances have been paradigm-shifting for several reasons. For example, the observed immune response patterns have led to marked deep tumor regression that often outlasted the period of study. Such responses are unprecedented for disease that has been refractory to other types of treatment. Second, these new forms of immunotherapy have shown activity in tumors traditionally viewed as unresponsive to immune therapies, raising hopes that any type of cancer might be “targetable” by immunotherapies if the right agent can be found. This antitumor activity has been most impressive in NSCLC, particularly among patients with unresectable disease treated with primary radiation therapy, a modality known to stimulate antigen production. It is conceivable that treatment such as this acts as a type of “in situ vaccine” to prime the immune response. Nascent preclinical and early clinical findings have supported this possibility, suggesting that radiation, through its immune-stimulating properties, may eventually be useful as a form of systemic therapy in addition to a means of local tumor control. 

123 Prompt Gamma-ray Timing experiment during different modalities of proton beam delivery
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Purpose: Prompt Gamma-ray Timing (PGT) is a method for range verification in hadron therapy which requires only minor or no interference with clinical routine due to a very low hardware footprint. The principal feasibility of the method for range verification has already been shown in theoretical considerations [1] and in proof-of-principal experiments [2]. Further considerations of the clinical feasibility show that a high-throughput data acquisition system can be realized as a miniaturized instrument [3]. In this work, PGT measurements during phantom irradiation with clinical beam currents - both during pencil beam scanning (PBS) and passive beam formation (double scattering, DS) are presented.

Materials and Methods: By exploiting the time structure of the beam on the nanosecond scale, it is possible to measure the duration of the emission of secondary photons. This duration is linked with the transit time of the projectiles in the target. Longer transit times reflect a longer bunch width, and phase remain constant or are monitored. The shown data do not incorporate any kind of bunch timing correction and the conditions are assumed to be constant. As a photon detector, a CeBr3 crystal in the extends of ø2”×1” coupled to a PMT is used. It is either read out with a CAEN DT5730 waveform digitizer or with a Target Systemelektronik U100 dedicated system which is also a sampling ADC based readout module. Online pulse processing algorithms are applied in both cases to achieve a high throughput rate. The ADCs were synchronized to the RF. Experiments during DS were conducted parasitically during the workflow training with an anthropomorphic phantom. For the PBS measurements dedicated beam time could be scheduled at the therapeutic treatment room. A rectangular dose distribution was impinged on a homogeneous PMMA target. In DS mode, a lead shielding was placed between the detector and the nozzle in order to reduce background radiation which originates from the nozzle.

Results: In both cases, it was possible to identify the individual phases of beam delivery. In DS mode, the periodic modulation at 600 Hz which is synchronized with the beam formation equipment can be seen. In PBS, single layers and single spots can be recognized (figure 1). After data selection, the beam microstructure is revealed in PBS as well as in DS mode although it is considerably less clear in the DS case.

Conclusions: The experimental techniques which are required for a clinical implementation of PGT are being evaluated under clinical beam conditions. The beam delivery mode has major impact on the data quality.

Figure 1: Count rate over time during DS (left) and PBS (right), recorded at 2 Gy/min at different distances.

Keywords: Prompt Gamma-ray Timing, Range Verification, Hadron Therapy

References: