Imaging currently play an important role in routine clinical care and clinical trials in triaging patients to appropriate management and in monitoring patients on therapy. In terms of treatment assessment it is essential for imaging markers to be consistent, reproducible and validated. Standardized response assessment based on morphological change, such as RECIST 1.1 is well established in the clinical trial setting although its limitations for therapies beyond standard chemotherapy are recognised e.g. immunotherapy, and for which alternative response criteria have been proposed. Computed tomography (CT) remains that most commonly performed imaging modality due to its high spatial resolution and its cost-effectiveness, but positron emission tomography (PET) and magnetic resonance imaging (MRI) have advantages in their capacity to image beyond morphology.

Measurement of glucose metabolism, cell proliferation, hypoxia, and vascularisation is now possible in clinical practice as well as quantification of their spatial variation, providing an imaging phenotype that is likely to be more beneficial than simple biomarkers e.g. size in predicting individual patient response to therapy. These imaging methods can also be integrated with genomic and pathological data allowing a comprehensive approach to address the clinical need towards individualisation of therapy in the future.

**SP-0111**

Response prediction in rectal cancer using PET Radiomics

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In personalized medicine, early prediction of pathologic complete response for locally advanced rectal cancer (LARC) patients is essential to tailor treatment. The standard treatment for LARC patients consists of preoperative chemoradiotherapy (CRT) followed by surgery, with a complete response being observed in 15-30% of the patients after the neo-adjuvant treatment. Overtreatment of complete responders could be avoided if an accurate prediction of pCR is available, by selecting a wait-and-see policy instead of surgery after CRT, and thereby reducing treatment related complications. Further treatment strategies based on the prediction of pCR include a radiotherapy boost after CRT for patients with good response to achieve a higher complete response rate, and additional chemotherapy after initial CRT for the worst responding patients.

In recent years, [18F] fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) imaging has been increasingly used for treatment decision support, treatment planning and response monitoring during radiotherapy. Radiomics (www.radiomics.org; animation: http://youtu.be/Tq980GEVP0Y) is a high throughput approach to extract and mine a large number of quantitative features from medical images, characterizing tumor image intensity, shape and texture. The core hypothesis of radiomics is that it can provide valuable diagnostic, prognostic or predictive information. FDG-PET radiomics may therefore facilitate early and accurate prediction of tumor response to treatment to identify LARC patients eligible for a wait and see or organ preserving approach, or patients who may benefit from treatment intensification.

This presentation will focus on the methodology of, and technical challenges in, the development and validation of a predictive PET radiomic model for pCR in LARC patients, illustrated with recent data.

**SP-0112**

MRI imaging of irradiated liver tissue for in vivo verification in particle therapy

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In vivo treatment verification is highly desirable, especially but not only in particle therapy where uncertainties in the particle range can compromise the physical advantage of this treatment modality. Existing measurement techniques for range measurements exploit physical effects, in particular secondary radiation that is produced by the proton beam, for example through activation of positron emitters, or prompt gamma radiation. Also biological effects caused by the irradiation can be used for in vivo treatment verification, if a functional imaging method is available to visualize the effect.

One prominent example for biology-driven range verification is an irradiation-induced change in contrast-enhanced MRI of the liver. A strong systematic decrease in uptake of the hepatobiliary-directed contrast agent Gd-EOB-DTPA has been shown in irradiated healthy liver tissue 6-9 weeks after irradiation [1-3] using different treatment modalities (brachytherapy, stereotactic body radiation therapy with photons and protons). The underlying mechanism seems to be based on a pro-inflammatory reaction of the irradiated liver tissue resulting in a downregulation of the Gd-EOB-DTPA uptake transporters and an upregulation of the respective excretion transporters [4].

In a prospective clinical study, carried out at Massachusetts General Hospital in Boston (USA), we investigated whether MRI of the liver can be used for in vivo dosimetric verification already during the course of hypo-fractionated proton therapy of liver metastases (5 fractions within 2 weeks). In contrast to the previously found late changes weeks after the end of treatment that were seen in all patients, for the early Gd-EOB-DTPA enhanced MR imaging large inter-patient variations were found. For 10 patients, strong or moderate signal changes were detected for 2 and 3 patients, respectively. For 5 patients no dose-correlated early signal change was found at all. This qualitative scoring was consistent with a quantitative voxelwise dose to signal change correlation. The analysis of additional parameters that could potentially explain inter-patient variations (e.g. dose delivered at time of MRI scans, several timing parameters, liver function parameters and circulating biomarkers of inflammation determined from blood samples taken before and during treatment) revealed no clear correlation or trend with the strength of the signal decrease.

Hence, irradiation-induced effects in the liver can be detected with Gd-EOB-DTPA enhanced MRI within a few days after proton irradiation in a subgroup of patients. As all patients possessed a significant decrease in follow-up scans, only the early dynamics of the liver response is influenced by these inter-patient variations. The reason for these large variations in early response is not yet fully understood and needs further investigation.

This presentation will cover a brief overview of biological effects used for treatment verification and will then focus on the irradiation-induced signal change in Gd-EOB-DTPA enhanced MRI of the liver. The hypothesis for the biological mechanism, the available data for late and early MRI signal changes will be presented and open questions will be discussed.