Different biological aspects have to be considered when estimating the effect of radiotherapy on oligometastases:
1) In contrast to current systemic treatments, radiotherapy has a high potential to inactivate cancer stem cells that are able to cause tumour recurrences. In limited disease stages or, in some cancers, limited metastases stages, this is the basis of the curative potential of radiotherapy and also of complete inactivation of macroscopic metastases.
2) Size of the metastases is predictive for in-field-control. This correlation exists in primary tumours as well as in metastases and reflects the impact of the higher number of cancer stem cells to be inactivated in larger tumours and maybe also higher impact of other resistance factors like hypoxia.
3) Metastases develop through vascular spread of tumour cells, i.e. oligometastases always bear a high risk of later development of further metastases. The time to further disease Progression appears to be longest with a longer time interval between treatment of the primary tumour and development of oligometastases. While this is known for a long time, approaches to biologically characterize tumours with low versus high potential for multi- or oligometastatic spread are only recently developed.
4) Single or oligometastases are often treated using hypofractionated-accelerated radiation treatment schedules, i.e. applying high doses per fraction and higher doses per week as compared to conventionally fractionated radiotherapy schedules. These schedules lead to a higher biological efficacy in the tumour, but also in irradiated normal organs. Thus, for application of high radiation doses, from biological reasons the use of high precision radiotherapy techniques is mandatory to take advantage from the volume-effects in normal tissues that can compensate for the disadvantage of the high doses per fraction.
The talk will give an overview on biological considerations for high-dose radiotherapy of oligometastases and on open questions for further improvement of treatment.

SP-0013
A mathematical model of tumor self-seeding reveals secondary metastatic deposits as drivers of primary tumor growth
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Two models of circulating tumor cell (CTC) dynamics have been proposed to explain the phenomenon of tumor 'self-seeding', whereby CTCs repopulate the primary tumor and accelerate growth: Primary Seeding, where cells from a primary tumor shed into the vasculature and return back to the primary themselves; and Secondary Seeding, where cells from the primary first colonize a secondary tissue which then sheds cells into the vasculature returning to the primary. Thesetwo models are difficult to distinguish experimentally, yet the differences between them is of great importance to both our understanding of the metastatic process and also for designing methods of intervention. Therefore we developed a mathematical model to test the relative likelihood of these two phenomena and show that Secondary Seeding is several orders of magnitude more likely than Primary seeding. We suggest how this difference could effect tumor evolution, progression and therapy and several possible methods of experimental validation.

SYMPOSIUM: PET QUANTIFICATION

SP-0014
How much can we trust PET? (PET uncertainties)
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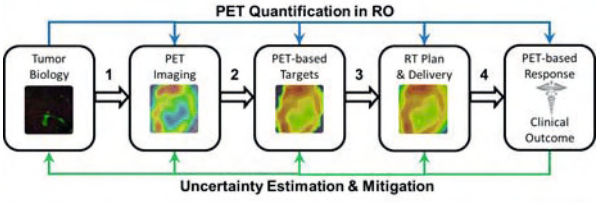
The role of positron emission tomography (PET) in radiation oncology continues to expand beyond the realm of preliminary diagnosis, where FDG PET has directly impacted disease staging in more than 30 % of cancer patients. Radiation oncology clinicians and researchers seek to incorporate PET more objectively into radiotherapy (RT) planning and therapeutic response assessment by leveraging its high sensitivity, tracer specificity, and capacity for absolute quantification. As PET evolves from a qualitative diagnostic tool to a quantitative theragnostic tool, a growing number of clinical trials are evaluating the efficacy of personalized and adaptive RT regimens based on the spatiotemporal dynamics of heterogeneous PET uptake.

However, complex quantitative tasks require the estimation and mitigation of many PET uncertainties. They arise from physical, technical, and biological factors that impact PET lesion signal (contrast) relative to noise, system spatial resolution,and reproducibility. This talk will review uncertainties that determine confidence intervals within which we can trust PET in the context of RT target definition and RT response assessment. In particular, physical uncertainties arising from the image formation process, technical uncertainties from pre- and post-imaging processes, and biological uncertainties from patient-specific tracer kinetics and therapy-induced dynamics will be presented.
The level of trust in PET can be linked to the incorporation of uncertainties into quantification processes. For example, test-retest studies can establish achievable degrees of precision when assessing longitudinal changes in PET metrics. While some uncertainties are mitigated through standardization of imaging procedures within and between institutions, others pose formidable challenges that require innovative technologies and methodologies. Such challenges motivate the need for improved PET quantification and seamless integration into RT planning through multidisciplinary collaboration.



Example workflow of PET quantification tasks in radiation oncology. From tumor biology at the cellular scale to PET-based target definition and therapy response assessment at the image voxel scale, quantitative tasks carry uncertainties that must be estimated and mitigated. This talk will focus on uncertainties in Steps 1 and 2 in the context of their impact on downstream components.

SP-0015
How to make PET more quantitative (PET QA)
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PET is a functional and molecular imaging modality allowing to measure (biological) tumor characteristics quantitatively. The most commonly used parameter to quantify tumor tracer uptake is the so-called maximum standardized uptake value (SUVmax). Yet, various other parameters may be of interest. Metabolically active tumor volume (MATV), total tumor burden (sum of MATV over all lesions) or total lesion glycolysis (TLG, product of MATV and SUV) have shown value as predictive or prognostic factor. Beyond measuring glucose consumption with ^{18}F-FDG there is increased interest in the use of other tracers and/or labeled drugs. Proliferation measured with ^{18}F-FLT or hypoxia measured with e.g. ^{18}F-AZA can be of particular interest in a radiotherapy setting. Specific imaging procedure optimizations may be required when using non-FDG PET tracers. In addition, use of simplified (static) image procedures and data analysis methods may need to be validated against full kinetic analysis to determine use of e.g. SUV as appropriate surrogate for the physiological parameter of interest. Full kinetic analysis can then be helpful to determine which simplified quantitative measure is providing the most accurate and robust results. For example, tumor to blood ratios may be more suitable than SUV measures and SUV normalized by body weight may be suboptimal compared to other normalizations, such as body surface area, depending on the biodistribution of the tracer.
All quantitative PET measures, however, depend largely on the way PET images are collected, reconstructed and analyzed. Moreover, new image reconstruction technologies, that include resolution recovery, can improved image resolution and contrast recovery, but at the same time suffer from increased upward bias when PET images are quantified using the maximum standardized uptake value. Consequently, when implementing new PET imaging technologies one should also adapt data analysis procedures in order to obtain and maintain robust quantitative data.
When quantitative PET studies are performed as part of multicenter studies it is not only essential to optimize the PET imaging and data analysis procedure for the specific question to be addressed, but also to make sure that studies are performed in a standardized manner and that all scanner performances are harmonized to a common standard. There are various organizations that offer scanner validation or accreditation (QC) programs. Most of these programs recognize the need not only to verify the basic calibration and uniformity of the PET