RT, is an effective way of achieving intrathoracic local control. Patients with locally advanced or metastatic disease frequently experience morbidity or mortality due to the consequences of local disease progression. Patients with large, central disease or compression of major bronchi or vessels were found to have worse overall survival (OS) in a pooled analysis of patients enrolled in clinical trials involving first-line, platinum-based chemotherapy, suggesting that improvement in local control with the addition of thoracic RT to systemic therapy could improve OS. (2) Preclinical data suggests that the combination of molecularly targeted agents and RT increases radiation responsiveness. To date, the combination has not improved outcomes in clinical trials in patients with locally advanced NSCLC (3). Studies addressing the choice of agent to be used in combination and in particular the optimal sequencing of modalities are required.


SP-0014
Liver: Role of RFA, chemo-ablation and SBRT for liver metastases
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Resection of liver metastases from colorectal carcinoma (CRC) is associated with 5 year survival rates of approximately 50% with the possibility for cure. Although long term survivors have also been reported following resection of liver metastases from sarcoma, renal cell carcinoma, breast cancer and melanoma (5 year survival up to 36%), resection is not routinely accepted as standard of care. As the risks of surgery increase, and the benefits of surgery decline, alternative local ablative therapies such as radiofrequency ablation (RFA) and stereotactic body radiation therapy (SBRT) are more attractive treatment options.

Hepatic arterial directed chemotherapy (or chemo-ablation) has been used to treat liver metastases from CRC with better than expected results compared with systemic therapy in single institutional series, but there are no comparative studies with modern chemotherapy for CRC or other liver metastases. This therapy is not considered ablative, with the potential to cure.

Radiofrequency ablation (RFA) is an effective ablative technique for liver metastases treatment. Local control is highest (> 80%) in selected metastases < 3 cm in maximal diameter. Recurrences are common in metastases > 5 cm, or in metastases adjacent to large vessels that may act as a heat sink. Primary toxicities include infection and bleeding. RFA of lesions near the common bile duct or diaphragm are associated with increased risks of serious toxicity.

Stereotactic body radiation therapy (SBRT) is an attractive option for patients with liver metastases. Short course, outpatient SBRT delivered in 1 to 10 fractions is convenient for patients, with little ‘downtime’, and short systemic therapy break. Liver SBRT requires a planning CT simulation scan with IV contrast and/or contrast-enhanced MRI for target delineation. Breathing related liver motion should be assessed by respiratory correlated (or 4D) CT, cine-MR imaging or 2D kV fluoroscopy to determine appropriate planning target volume (PTV) margins. Highly conformal dose distributions are desirable using multiple beams or arcs, in coplanar or non-coplanar geometries. Immobilization of the liver using controlled breath holds, abdominal compression, gating of the RT beam during specified phases of the respiratory cycle, medications, or tumor tracking may help reduce the adverse effects of breathing motion. Image guided RT (IGRT) based on volumetric imaging such as kV cone beam CT, is required at every fraction in order to reduce PTV margins. MR IGRT is an area of active research that may benefit liver SBRT.

A Toronto SBRT study (24 - 48 Gy in 6 fractions) in 107 patients with 172 inoperable liver metastases from colon, breast cancer or other sites (median volume 75 cc) had a median survival of 18.1 months. Survival was worse in patients with extrahepatic disease (present in 43%), improved local control was seen with breast cancer and higher doses. Some patients appear cured > 5 years post SBRT. Other SBRT series (30-60 Gy in 1-6 fractions) for < 5 metastases (maximal size ≤ 6 cm) have reported median survival rates from 18 to 37 months, and local control of 67% to 100%. A dose response has been observed in most series, with increased chance of sustained local control (80 - 90% at 2 years) when doses higher than 42 Gy in 3 fractions are used. Local control is also improved in patients with metastases less than 3 cm in maximal size and in breast cancer metastases compared to colorectal cancer metastases. Local control may be reduced in metastases adjacent to luminal gastrointestinal tissues. SBRT has low acute and late toxicity (transient fatigue, nausea, gastritis or duodenitis), and very low risk of liver toxicity. Chest wall and rib fractures have also occasionally been seen. Studies have shown that quality of life is preserved 3 - 12 months post SBRT. The most suitable patients are those with 5 or fewer metastases, < 6 cm, with no extrahepatic disease. More research is required regarding optimal dose-per-fraction, as well as most appropriate patient selection and sequencing with systemic therapy.

Joint Symposium with Proffered Papers: ESTRO-ESR: Metabolism and imaging, planning

SP-0015
Tumour metabolism is a critical factor for molecular imaging
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Radiotherapy induced tumor cell kill relies on induction of oxidative stress. The response to irradiation of malignant tumors vary as a consequence of resistance mechanisms taking place at the molecular level. The hypoxia-inducible factor 1 (HIF-1) pathway is involved in various of these processes. With respect to metabolism HIF-1 is an important regulator of glycolysis and the pentose phosphate pathway. This aberrant cellular metabolism, responsible for maintaining stable intracellular ATP levels without oxygen consumption even under normoxic conditions, increases the antioxidant capacity of tumors, thereby counteracting the oxidative stress caused by irradiation. Interestingly, analysis of glucose transporter (GLUT1) and monocarboxylate transporter (MCT4) expression on the histological level suggested a different metabolism for adenocarcinomas and squamous cell carcinomas of the lung. Results showed that adenocarcinomas rely mainly on aerobic glycolysis, whereas the energy metabolism of squamous cell carcinomas is more physiologically, i.e. mitochondrial
oxidation with glycolysis only under hypoxic conditions. This indicates that adenocarcinomas exhibit glycolysis under normoxic conditions, whereas squamous cell carcinomas are exposed to diffusion-limited hypoxia resulting in a very high anaerobic glycolytic rate. Consequently, FDG-PET should be interpreted in relation to histology. The FDG PET interpretation based on histology improves its prognostic and predictive potential prior to treatment and allows monitoring of treatment efficacy during treatment.

**SP-0016 How much biological information can be extracted from MRI in solid tumours**

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Imaging biomarkers are defined as objective characteristics extracted from medical images that are related to normal biological processes, diseases, or the response to treatment. Imaging biomarkers evaluate the in vivo properties by in silico modelling of different tissue and lesion properties. These patient specific features are resolved in space (parametric images) and time (longitudinal changes), and can be compared to normal population based data. To develop an imaging biomarker, it is necessary to carry out a series of steps to evaluate reproducibility, technical standardization, validation of the relationship with the studied object and situation, and finally checking its clinical meaningfulness. This process includes defining proofs and tests for the concepts and mechanisms; obtaining standardized and optimized anatomic, functional, and molecular images in a multimodality approach; analyzing reconstructed data with computer and statistical models; displaying the parameterized data appropriately; obtaining the different statistic measures and histogram distribution; and finally conducting tests on the principle, efficacy, and effectiveness of the biomarker.

To further develop this strategy, medical imaging biobanks with oncology data are needed. These virtual biobanks recently emerged for advancing on the study of rare diseases, the identification of early biomarkers and surrogates, and the development of population studies.

Oncologic imaging biobanks will evaluate the impact of new biomarkers on early disease diagnosis, disease phenotyping, disease grading, targeting therapies and evaluation of disease response to treatment. In this presentation, I aim to explain the steps that must be established to enable oncologic biomarkers to be correctly applied, from their theoretical conception to their clinical implementation. The learning objectives are:

- To recognize the qualitative and quantitative information of the different modalities.
- To learn about the commonly applied imaging tools in assessing neoplasm size, volume and extension.
- To know the current applied method for quantification of tumor aggressiveness and response to treatment.
- To go through a critical review of criteria actually used in oncologic stratification and management.
- To become familiar with the most appropriate functional imaging biomarkers of tumor activity (perfusion, diffusion, oxygen).
- To appreciate the clinical role of these techniques in planning therapeutic strategies.

**OC-0017 Correlation analysis of combined functional PET/MR data in head and neck tumors**

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**Purpose/Objective:** Combined PET/MRI may be highly beneficial for the individualization of radiotherapy (RT) due to the provided anatomical, molecular and functional information. The purpose of this study was to perform a correlation analysis of functional PET/MR images in head and neck (HN) tumors. Functional imaging data comprised apparent diffusion coefficient (ADC) maps from diffusion-weighted (DW)-MRI, dynamic contrast-enhanced (DCE)-MRI and FDG as well as FMISO-PET.

**Materials and Methods:** N=8 HN patient datasets from combined FDG-PET/MRI (n=8 STIR, i.e. anatomical T2w MRI; n=8 ADC) acquired 1h post injection (p.i.) as well as M=7 HN patient datasets from combined FMISO-PET/MRI (m=7 STIR; m=7 ADC; m=5 DCE) acquired 3h post p.i. were available. Moreover, for each FMISO-PET/MR patient also an FDG-PET/CT dataset was available. For the FDG-PET/MR patients, tumor volumes were manually defined by a radiation oncologist based on FDG as well as STIR images. For the FMISO-PET/MR patients, tumor volumes were transferred from the planning CT to the PET/MR datasets by deformable registration, using the STIR image as reference. Similarly, the FDG-PET/CT data was transferred to the FMISO-PET/MR datasets by deformable registration. From the DCE data, parametric maps were derived according to the extended Tofts model, yielding the volume transfer constant Ktrans as well as the extravascular, extracellular fraction ve and the blood plasma fraction vp. For each patient, voxel-based correlations within the tumor were assessed by Spearman coefficients for all possible pairs of functional data and parameter maps. Two ADC datasets from FMISO-PET/MRI were excluded from the analysis due to geometrical distortions.

**Results:** For each of the pairwise combinations of functional parameters, obtained Spearman correlation coefficients varied strongly between patients. Resulting median correlation coefficients of the patient cohort are shown in Table 1. Highest correlations were observed for the combinations ve/Ktrans (median: 0.58; range: 0.49 - 0.84), FDG/FMISO (0.57; 0.09 - 0.79), ADC/FDG (-0.38; -0.85 - 0.15), ve/vp (0.36; 0.23 - 0.61), Ktrans/FDG (0.31; 0.11 - 0.59) and ADC/FMISO (-0.31; -0.72 - 0.2).