This analysis found the ARFs for OS to be ≥87 days from surgery to end of RT (HR 3.3; p=0.0025 vs <87 days) and ECE (HR 2.6 vs no ECE; p=0.0133). Adverse events did not differ between the groups.

Conclusions: The present analysis has shown that OTT can be an important factor in DFS. OTT of 87 days is challenging and requires careful coordination of procedures and disciplines between surgery and adjuvant therapy, as well as minimizing treatment delays during RT. Our findings suggest that treatment completed within as short a timeframe as possible appears to be associated with longer DFS and that this should be a goal. Further studies are needed to confirm these findings.

PO-0646
Adaptive and robust FDG-PET-based dose painting by numbers (DPBN) in head and neck tumors: a methodological approach
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Purpose/Objective: To develop a methodology for using FDG PET/CT in adaptive DPBN in locally advanced head and neck squamous cell carcinoma (HNSCC) patients. Issues related to noise in PET and robustness against geometric errors are addressed.

Materials and Methods: Five patients with locally advanced HNSCC scheduled for chemo-radiotherapy were imaged with FDG-PET/CT at baseline and after 5, 10 and 15 fractions of RT (2 patients were re-imaged only twice). The GTV_PET was segmented with a gradient-based method. A double median filter reduces the impact of noise in the conversion from PET uptake to prescribed dose. Filtered FDG uptake values were linearly converted into a voxel-by-voxel prescription from 70 (median uptake) to 86 Gy (highest uptake). To be robust against geometrical uncertainties, a PTV_PET was obtained by applying a dilation of 2.5 mm to the entire prescription. Seven iso-uptake thresholds led to 7 sub-levels compatible with the Tomotherapy HiArt® Treatment Planning System. Planning aimed to deliver a median dose of 56 Gy and 70 Gy in 35 fractions on the elective and therapeutic PTVs, respectively. Plan quality was assessed with quality-volume histogram (QVH) and quality factor (QF, objective: <5%). For organs at risk (OARs), DVH constraints were the following: Dmean < 26-30 Gy for parotid glands, D2 < 30 Gy for PRV spinal cord and brain stem. At each time point, plans were generated using a 1 cm collimator width with a total of 3 to 4 plans for each patient. Deformable image registration was used for automatic propagation of volumes of interest and dose summation of the 3 or 4 treatment plans (MIM vista®) (see figure). Finally, to simulate a treatment that is adaptive to anatomical evolution seen at CT but blind to changes in the PET signal, the pre-treatment dose map was deformed and assessed with QVHs on each per-treatment CT scan after non-rigid image registration.

Results: GTV_PET segmentations were performed successfully until week 2 of RT but failed in 2 patients at week 3. QVH analysis showed high conformity for all plans (mean VQ=0.93; mean VQ=1.05 3.9%; mean QF 2.2%) demonstrating feasibility of the treatment. Good OAR sparing was achieved while keeping high plan quality (see table). When comparing biologic/anatomic adaptation versus only anatomic adaptation, QFs were improved in all cases (range 0.8 - 3.7%) with a median value of 2.1% and 4.7% for the biological adaptive and anatomic only adaptive strategy, respectively.

Conclusions: Our results show that adaptive FDG-PET-based escalated dose painting in patients with locally advanced
HNSCC is feasible while respecting strict dose constraints to OARs. By correcting for morphological and biological tumor changes during RT, higher conformity is ensured between the FDG uptake and the dose distributions. Clinical studies must be conducted to evaluate the acute and chronic toxicities and the tumor response of such a strategy.

**PO-0647**

Target-selective radio-sensitization in head and neck tumors by the novel HYPERcollar3D hyperthermia applicator

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**Purpose/Objective:** Current treatment of advanced cancer of the head and neck is unsatisfactory in terms of outcome and the toxicity of current treatments are severe. Phase III clinical trials have shown that hyperthermia (heating in the range of 40-44°C for one hour) is a potent sensitizing agent of radiotherapy, which is achieved without additional toxicity [1-3]. To enable heat-sensitization also in target regions at deep locations, we developed the HYPERcollar and showed in 45 patients that inducing hyperthermia in tumors located deeply and laterally in the head and neck region is feasible and has potential. Over the years, we further introduced an adaptive hyperthermia strategy based on electromagnetic field simulations. In this study, we analyze the HYPERcollar3D that is a redesigned version of the HYPERcollar aimed at improving heating quality, heating reproducibility and patient comfort.

**Materials and Methods:** In the HYPERcollar3D, patient comfort and treatment accuracy/stability are improved by splitting the waterbolus functions into a stable outer part and a patient conformal inner part. Patient positioning according to the CT resembles that of radiotherapy and is obtained by immobilization and a laser alignment procedure. Based on a mechanical redesign, we performed parameter studies using electromagnetic simulator SEMCAD-X (v. 14.8.6) to investigate further improvement by increasing the number of antennas and their locations.

**Results:** The simulation studies showed that higher number of antennas, and their repositioning, allows for a substantially improved treatment quality. All improvements combined enable a predicted reduction of hotspot importance prominence (hot-spot target quotient (HTQ)) by 32%. Combining all systems improvements, simulations predict that a doubling of the clinically applied power to the target can be achieved. After clinical introduction, two patients (nasopharynx ca. and a neck node metastasis) have been treated with the HYPERcollar3D. Validation of heating performance by invasive thermometry in the tumor proved not possible but, in both patients, the scheduled treatments of 75 minutes could be completed using a mean applied power of 350-400W. In addition, the estimated SAR based on the realtime measured powers/phases of the signals was 90W-200W/kg, which is beyond the long term average applied SAR using the conventional HYPERcollar, i.e. 75W/kg.

**Conclusions:** Although the improvement still has to be validated by invasive temperature measurements in the tumor, these results are very reassuring that the HYPERcollar3D will provide a significant improvement in treatment quality. Hyperthermia is currently used as a standard addition to radiotherapy for patients that are re-irradiated. A protocol for a clinical study in primary tumors is being finalized.


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Patterns of long-term swallowing dysfunction after definitive radiotherapy or chemoradiation

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**Purpose/Objective:** To identify patterns of long-term, radiation-induced swallowing dysfunction after completion of definitive radiotherapy with or without chemotherapy (RT or CRT) and to determine which factors could explain these patterns over time.

**Materials and Methods:** The study population consisted of 238 consecutive head and neck cancer patients treated with RT or CRT. The primary endpoint was grade 2 swallowing dysfunction at 6, 12, 18 and 24 months after treatment. Cluster analysis was used to identify different patterns over time. The degree of swallowing dysfunction at baseline and at all subsequent time points (at 6, 12, 18 and 24 months) were considered for cluster modeling on the basis of their contribution to characterizing the patterns of late radiation-induced swallowing dysfunction. The differences between the dose-volume histograms (DHVs) of the swallowing organs at risk for each pattern were determined by using dose maps.

**Results:** The cluster analysis revealed five patterns of long-term, radiation-induced swallowing dysfunction: low persistent, moderate persistent, severe persistent, transient and progressive (Figure 1). Patients with high dose to the upper pharyngeal, laryngeal and lower pharyngeal region had the highest risk of severe persistent swallowing dysfunction.