adverse events were observed in 39% of pts; most frequently nausea (6%), diarrhea, dizziness, and rash (4% each). Dyspnea, syncope, raised GGT and sepsis (each 5%) were the most common grade ≥3 AEs. Among 29 evaluable HNSCC pts for efficacy, 4 pts had a partial response. Numerous anti-PD-1/PD-L1 agents are currently tested in HNSCC. First randomized trial with nivolumab vs standard of care in second line after platinum based first line therapy has just closed. Randomized trials testing pembrolizumab and durvalumab in first-line or second-line treatment for R/M HNSCC patients are ongoing. Beside evaluation of efficacy, these studies should help define the best population (HPV status, prior therapies) and more useful biomarkers than threshold of PD-L1 expression, to select patients who can benefit from these new agents. Flare-up reaction with increase of tumor volume and immune-related adverse events may occur: new guidelines are needed to define criteria of response, time to stop treatment and management of toxicities. Some patients may have a fast progression under monotherapy and mechanisms of resistance are unclear. New approaches combining anti-PD-L1/PD-1 agents and other immune-modulators, chemotherapy and radiotherapy are currently explored. Abscopal effect related to anti-PD-L1/PD-1 agents seems promising. For locally advanced HNSCC, trials testing combinations with anti-PD-L1/PD-1 agents in induction regimen and concurrent CRT are ongoing. The story of immunotherapy as a new paradigm in HNSCC is just beginning…

SP-0410
Proton therapy in HNSCC: better than IMRT?
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Abstract not received

Symposium: SBRT in lung - choices and their impact on related uncertainties

SP-0411
Dosimetric aspects and robustness in treatment plan optimisation of small tumours
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Stereotactic radiation of small brain targets provides high spatial resolution and accuracy for positioning of patient and radiation fields, almost on submillimeter ranges. This is not matched by equally sharp dose gradients, since finite source size, collimator design limitations and transport of electrons in the irradiated tissue all diffuses the dose. Not surprisingly, the dose prescriptions evolving for small brain tumors aimed for a specified dose to the target periphery, accepting whatever resulting dose to the target center. A kind of standard evolved aiming for a ratio of approximately 65% relative dose at the periphery versus the maximum target center dose (or 154% center-to-periphery ratio). This dose heterogeneity was considered favorable, as to more effectively treat presumably hypoxic cells at the tumor center. The stereotactic treatment methodology for brain treatments were in the early 1990s transferred to radiation of liver metastasis. Through use of stereotactic body frame high target positioning reproducibility was achieved, and similar dose prescriptions of heterogeneous dose were applied, with a center-to-periphery dose ratio of approximately 154%. Soon the technique was also applied to peripheral lung tumors.
Following the development of 3D treatment planning systems in the late 1980s, ICRU responded to the need for consistent handling of geometrical uncertainties and launched in 1993 the ICRU 50 report recommending the use of GTV, CTV and PTV to capture the uncertainties. Specifically, the role of PTV was to "ensure that the prescribed dose is actually absorbed in the CTV". The normal use of the PTV is to plan a homogenous dose to its interior, through which it is assumed that the CTV gets the same dose as it is located in the PTV. This requires the dose inside the PTV to be both homogeneous and robust with respect to movements involving heterogeneities. The PTV concept was applied also for extracranial stereotactic body treatments, often inheriting a high center-to-periphery prescription. Dose calculations at the time used "class a" algorithms that not account for dose variations due to a varying level of lateral charged particle equilibrium caused by low density regions. Most so called pencil beam algorithms belong to this, class a, category. Accurate dose calculations can now be achieved with "class b" algorithms such as Monte Carlo, Collapsed Cone or Grid based Boltzmann equation solvers. However, for any algorithm that would calculate the dose physically correct, the resulting dose for the PTV is not representative for the CTV when the margin around the latter contains a lower density medium. Hence, the straight forward application of PTV based treated planning together with heterogeneous prescriptions principles (originally inherited from intracranial treatments), has created a confused situation with large uncertainties with respect to the actually delivered doses.
A robust dosimetry can be achieved by realizing that the dose to a CTV surrounded by a low density medium will be independent of movements as long as it is exposed to a uniform fluence. Given that a near homogeneous fluence cover the PTV, dose prescriptions can then be done directly to the CTV based on a dose calculation with a "class b" algorithm (MC, CC or equivalent). As long as the movements of the CTV are kept well inside a PTV with a homogeneous fluence, the dose delivered to the CTV will be much closer to the prescribed dose, thus providing robust dose specification for small tumors. However, tools for optimization of uniform fluence are presently not provided in clinical TPS. Luckily, several workarounds exists that can "cheat" the optimization of homogenous dose to instead yield a effectively homogeneous fluence. From a pure physics point of view, this can be achieved by incapacitating the lateral spread of energy from the rays of the primary beam. In class a algorithms of the pencil beam kind, this can be implemented by changing the pencil beam parameter controlling the lateral spread. In point kernel algorithms such as CC, similar manipulation of kernel data can be done. In essence, in most algorithms fluence is a precursor for dose providing opportunities to access it. Alternatively, the density of the PTV can be set to a high value that shortens the electron transport distance enough to make the dose more fluence like.
In summary, a robust small lung tumor dose can be implemented through a planning process in which the PTV is determined by the common practice addition of a setup margin to a MIP projections ITV, but replacing the common practice dose calculations by a fluence optimization followed by a class b dose calculation with the CC (or similar) algorithm, using absolute dose prescriptions to the CTV rather than the PTV. For a test series of 5 patients this procedure reduced the difference between prescribed and delivered dose to the CTV from 30% to 8% in D98, with a similar reduction for D02.

SP-0412
Does the prescription isodose matter?
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The current practice of cranial and extra-cranial stereotactic radiotherapy is in many ways influenced by Gamma-Knife Radiosurgery (GN-RS). It has been a key component of GN-RS to treat the target volumes without any safety margins (GTV = PTV) and to use inhomogeneous dose profiles within the target volume. The dose was most frequently prescribed to a low isodose e.g. 50% meaning that substantially higher doses are delivered to the central part of the tumor.
This practice of dose prescription to a low target encompassing isodose line has been adopted in extra-cranial stereotactic radiotherapy (Stereotactic Body Radiotherapy