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Special Session (Tue, 27 Sep, 11:30–12:30) Stereotactic Radiotherapy for Liver Metastases

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INVITED

Radiobiological Aspects of Radiation-Induced-Liver-disease

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Radiation-induced-liver-disease (RILD) is a dose-limiting complication in abdominal irradiation. This plays a decisive role for example in radio(chemo)therapy for gastric, pancreatic or primary liver carcinomas or liver metastases. The threshold dose for RILD after normofractionated (2 Gy per day, 5 fractions per week) whole liver irradiation without chemotherapy is supposed to be between 20 to 30 Gy. However, in combined radiochemotherapy or in chronic liver disease, the risk of developing RILD is even higher. The acute clinical period of RILD after irradiation tends to be relatively silent, the subacute phase is characterized by the development of anicteric ascites, elevation of liver enzymes, rapid weight gain, and liver enlargement 2 weeks to 4 months after treatment. Finally, liver irradiation above the threshold dose is followed by progressive liver fibrosis and cirrhosis as has been shown in animal studies. Thereby – in contrast to other toxic liver injuries –, the fibrosis may not be followed by restitutio ad integrum. Furthermore, a large volume effect has been demonstrated for RILD: Liver doses associated with a 5% risk of RILD for conventional fractionated IR of one third, two thirds, and the whole liver are estimated to be 90 Gy, 47 Gy, and 31 Gy, respectively. However, several studies implementing modern radiotherapeutic techniques in the treatment of liver cancer/metastases such as stereotactic radiotherapy or brachytherapy have already demonstrated that higher single doses compared to conventional fractionated radiotherapy are tolerable to the liver. On the other hand, clinical studies have shown that liver function may also be influenced by pelvic irradiation when the liver is not included in the target volume. The detailed molecular pathogenesis of hepatocellular damage and RILD after irradiation is still obscure. Cell-cell-interactions via various cyto-, chemokines or adhesion molecules are important for hepatocellular damage, repair and fibrosis development in other toxic liver injuries. Similarly, different cell types interact via such mediators in the development of normal tissue reactions after radiotherapy. Therefore, the molecular mechanisms of RILD might be similar. In the meantime, this hypothesis has been substantiated by several experimental and clinical data. Further detailed knowledge of molecular processes taking place after liver irradiation may in future facilitate their modulation. Such modulations may potentially also protect from radiation-induced liver damage.

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INVITED

Stereotactic Radiotherapy for Liver Metastases

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Resection of colorectal liver metastases results in 5 year survival in 30 to 58% of patients, and long term survivors have been seen following resection of 'oligo' liver metastases from other malignancies. For patients unsuitable for resection, stereotactic radiotherapy is a treatment option. There are 7 published prospective studies of stereotactic radiotherapy for liver metastases (26–60 Gy in 1–6 fractions) and many more single institution series. The majority of patients have had unresectable liver metastases from colorectal carcinoma. A dose response has been observed, 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. Median survival in the prospective studies ranges from 18 months to 30 months. Liver toxicity has only rarely been observed, primarily in patients re-irradiated or with underlying liver disease. Respecting dose-volume guidelines can reduce the risk of liver toxicity (e.g. mean liver dose <18 Gy in 6 fractions, >700 cc <15 Gy in 3 fractions) and toxicity to luminal

gastrointestinal tissues. In a recent review from PMH in Toronto, 93 patients (54 colorectal, 20 breast, 19 other) with 172 liver metastases were treated with individualized IGRT stereotactic radiation therapy. Extrahepatic disease was present in forty patients (43%), and 75% had received prior systemic therapy. The median GTV was 25.6 cc (0.14–3088 cc). The median dose was 39.6 Gy in 6 fractions (range 25–60 Gy). Median follow-up was 17 months (3–74 months). Local control was improved in patients treated with higher doses and in breast cancer vs. other cancers. Accumulated minimum doses to the GTV of <35 Gy, 35–45 Gy and >45 Gy were associated with 18 month local control of 33%, 55%, and 83%, respectively. Median survival was 20.9 months (16.8, 25.1). Shorter time to local progression and extrahepatic disease were associated with worse survival. No radiation induced liver toxicity was observed. Some patients with 1 to 3 colorectal and breast liver metastases (<6 cm) are alive with no active disease more than 5 years following therapy. The most suitable patients with liver metastases for radiation therapy are those with 3 or fewer metastases <6 cm, with no extrahepatic disease and with metastases >2 cm from luminal gastrointestinal tissues. Randomized trials of radiation therapy are warranted.

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INVITED

Stereotactic Body Radiotherapy of the Liver – Physical and Technical Issues

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Stereotactic body radiotherapy (SBRT) of liver tumours and metastases has received increased attention in recent years due to promising clinical outcomes in the early studies of Lax, Blomgren and Wulf. Successful SBRT depends on delivery of high fraction doses to small, localised volumes, involving the use of both narrow margins and narrow beams. SBRT in general therefore has several physical and technical challenges, and also several challenges more specific for treatment within the liver. Like for many other tumour sites, internal organ motion is one of the main challenges in SBRT of the liver, influencing both the planning and delivery phases of the treatment. Tumour definition in treatment planning is therefore usually based on the mid-ventilation phase of an abdominal 4-D CT scan. Image-guidance during treatment is also of great benefit, with approaches including both 2D and 3D kV/MV techniques. Image-guided set-up is usually based on registration of surrogates like bony anatomy, the diaphragm or inserted markers, as the tumour itself is not readily visible. Due to the delivery of very high doses, normal tissue morbidity is also a concern during planning. Severe effects like hepatic failure and bowel perforation/obstruction have been reported. For the normal liver, studies have revealed a heterogeneous pattern of organ function pre-therapy, which could potentially be exploited therapeutically for optimal selection of beam arrangements. A further treatment planning issue is related to the use of small fields where edge and penumbra effects are influencing a large part of the total field sizes, with implications for dose measurements and (hence also) dose calculations. Finally, to further reduce normal tissue irradiation and ultimately enable dose escalation, liver SBRT has been shown to be a promising candidate for proton therapy.

Special Session (Tue, 27 Sep, 11:30–12:30) End of Life Care in Oncology

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INVITED

Recognising Dying and End-of-life Prognostication in Elderly Cancer Patients

Abstract not received

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INVITED

Dying Well – Challenges in Acute Oncology Settings

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Despite advances in cancer treatment and concomitant survivorship in recent years, a significant number of cancer patients will still die as a result of their disease. How the transition to palliative care is managed varies widely, may be influenced on the understanding of aggressive treatment and is often predicated on philosophical, ethical and thanatological arguments on the meaning of dying well. Palliative care itself has undergone a notable transformation from a predominantly terminal care approach to one which works in tandem with acute cancer care where it is evident that disease at