401 INVITED

Can We Consolidate Medical Response With Local Treatment

Abstract not received

Special Session (Tue, 27 Sep, 11:30−12:30)
Treatment of T1N0M0 Non-Small Cell Lung Cancer in Patients Who Are Not Candidates for Lobectomy

402 INVITED

Alternative Surgical Resections for Lobectomy

Abstract not received

403 INVITED

Role of Stereotactic Radiotherapy

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If non-small cell lung cancer (NSCLC) is detected at early stage, clinical outcome is favourable after lobectomy and systematic mediastinal lymphadenectomy with long term survival. However, about one third of the patients are medically inoperable and conventionally fractionated radiotherapy has been the standard of care for these patients. Stereotactic body radiotherapy (SBRT) has been first described about 20 years ago and is characterized by dose-intensified, hypo-fractionated irradiation: this aggressive irradiation has become possible by advanced radiotherapy technologies, which spare the normal lung tissue and confine the irradiation doses to the tumour.

Most relevant issues of clinical practice and outcome after SBRT will be discussed. Starting with patient selection, histopathological confirmation of disease should be performed; however, if this bears an unacceptable risk, the probability of treating a benign lung nodule is less than 10% after CT and FDG-PET staging. Additionally, FDG-PET is mandatory for nodal staging: the risk of nodal relapse is maximum 10% if contemporary FDG-PET staging had been performed. The effect of SBRT on pulmonary function is very small so that SBRT is safe even for patients with very poor pulmonary function; safety of SBRT has also been demonstrated for the elderly patient population >75 years old and patients with severe pulmonary co-morbidities. Regarding the technique of SBRT, most important aspects are full and consistent consideration of breathing induced tumour motion in treatment planning and delivery, highly conformal dose shaping and image-guided patient set-up.

All published retrospective and prospective studies consistently report excellent local tumour control rates of 90% and higher if sufficient irradiation doses of >100 Gy BED were used; this was achieved with toxicity grade $\geqslant$II of less than 10%. In retrospective and population-based analysis, it has been shown that the introduction of SBRT improved overall survival for medically inoperable patients and consequently, SBRT is considered as the treatment of choice for these patients. Additionally, SBRT seems to be at least equivalent to sublobar wedge resection in terms of oncological outcome offering a non-invasive treatment alternative. If SBRT was practiced in operable patients refusing surgery, overall survival compared well to surgical series; prospective studies are needed for defining the role of SBRT in the operable patient cohort.

Prospective phase II studies	Year published	Radiotherapy dose	2−3 year local control	2−3 year overall survival
Nagata et al.	2005	4 × 12 Gy	98%	75%
Baumann et al.	2009	3 × 15 Gy	92%	60%
Fakiris et al.	2009	3 × 20−22 Gy	88%	43%
Ricardi et al.	2010	3 × 15 Gy	88%	51%
Bral et al.	2010	60 Gy in 3−4 fractions	84%	52%
Timmerman et al.	2010	3 × 18 Gy	98%	38%

404 INVITED

Role of Radio-Frequency Ablation

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Today RFA is used primary lung neoplasms are close to those for surgical resection, in a curative intent in non-surgical or boarderline surgical candidates with T1A or T1B tumours. Inoperability is due to poor either respiratory function in relation do COBP in primary tumours, and iterative surgery or general comorbidities. Pre-ablation imaging work-up must be equivalent to a pre-surgical one, namely with PET-CT. Because, size is strong redictive factor of success, the largest diameter f the tumour should be ideally smaller than 3 cm, and in any manner larger than 5 cm. A review of 17 of the most recent publication demonstrated a median reported rate of complete ablation of 90%, even if high variability exists between publications with a range from 38% to 97% [1]. Most studies report a statistically significant lower success rate of ablation with tumours larger than 2 to 3 cm in diameter [2−5]. Oversizing ablation relative to the tumour improve complete ablation rate up to 96% at 18 months ablation when the ratio between the area of post-RFA ground glass opacity and the tumour area before treatment was at least 4 [2]. Ground glass opacity margins have been reported absent in 85% of post RFA CT of incompletely ablated tumours [6] Contact with a large vessel (>3 mm) has been reported by Hiraki et al and Gillams et al as a negative predictive factor of complete tumour ablation in lung [3,7].

A series of 75 primary NSCLC (75% stage IA and 25% stage IB) patients demonstrated a median survival of 29 months (IC95%: 20−30 months) with a 1, 2, 3, 4, and 5 years overall survival of 78%, 57%, 36%, 27%, and 27% [8]. Median survival for stage IA was 30 months and 25 months for stage IB. Better survival was reported for tumours 3 cm or smaller with a survival rate close to 50% at 5 years [8]. Grieco, et al., combined radiation therapy and RFA in 41 patients with NSCLC (Stage IA: 21; Stage IB: 17, Stage IIB: 3). The 27 patients with the largest tumours received external beam radiation (66 Gy) and the 14 patients with tumours less than 3 cm received brachytherapy through the puncture tract used for RFA. Combination treatment seems to improve results in NSCLC with 57% survival at 3 years. The median survival was 34.6$\pm$7 months for tumours larger than 3 cm and 44.4$\pm$5.4 months for tumours 3 cm or smaller ($p = 0.08$) [9]. Difference between overall survival [70% (95% CI 51−83%) at 1 year and 48% (30−65%)] at 2 years and Cancer-specific survival [92% (78−98%) at 1 year and 73% (54−86%) at 2 years] in patients with NSCLC highlight the comorbidities in the NSCLC patients treated with RFA [10].

The possibility to ablate larger volume gives hope for better rate of complete ablation for larger tumour even if datas about outcomes of MWA of pulmonary malignancies remain relatively scarce. Early reports are promising with the largest available clinical study includes 50 patients, including 30 with a non small cell lung cancer (NSCLC) treated with MWA during 66 ablation sessions for tumours 5 cm or smaller with a mean size of 3.5 cm$\pm$1.6 [11]. Tumour smaller than 2 cm were treated with a single antenna (53%), two antennae were used in 5%, 3 antennae in 27%, four antennae in 9%, and multi-probe loop antenna in 6%. 26% of patients had recurrent disease at the ablation site. This recurrent disease was most commonly found inn tumour large than 3 cm ($p = 0.01$). It is noteworthy that after MWA, on follow-up imaging cavitary changes were found in 43% of ablation and 6% results in documented infectious complications including one abscess and one pneumonia [11].

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

405 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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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.

407 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

408 INVITED

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

Abstract not received

409 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 thier disease. How the transition to palliative care is managed varies widely, may be influenced on the understanding of aggresive 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 predominently terminal care approach to one which works in tandem with acute cancer care where it is evident that disease at