A compelling body of non-randomized evidence has showed that SABR is a safe and efficient way to control multiple metastatic sites. However, when treating metastatic patients (even if “oligometastatic”), selection criteria are a pivotal issue. In general, clinical indications are the same as those for metastasectomy (pulmonary and/or liver metastasectomy), but without the limits regarding patients unfit for surgery.

Current literature has showed promising long-term survival outcomes after SBRT for limited metastases. Future studies are, and will be, addressing: 1) what (if any) benefit SBRT (and other local therapies) should offer for patients with limited metastases, 2) which patients are most likely to benefit from SBRT (host-related factors underlying the oligometastatic state, i.e. miRNA), 3) optimal dose and fractionation schedules, 4) what radiobiologic mechanisms are relevant in the treatment of the target tumor (i.e., SBRT as “immunomodulator”).

**SP-0313**

**SABR versus surgery in extracranial oligometastatic disease: (lung, liver other sites)**

M. Cengiz1

1Hacettepe University Ankara Faculty of Medicine, Radiation Oncology, Ankara, Turkey

Standard treatment of metastatic cancer is systemic therapies. Local treatments for oligometastatic patients may have significant role since a large majority of patients treated with systemic chemotherapy experience progression mostly in initial sites of tumor burden rather than new sites of progression. Surgical excision of metastatic sites usually from liver and lung that have been shown to prolong survival in colorectal cancer, sarcomas, melanoma, breast cancer and many other tumor types.

Currently surgery is considered to be standard approach for these groups of patients. Surgical series of hepatic metastasectomy of primary colorectal cancer resulted 18-51 % 5-year survival rate with 2-7% operative mortality and 6-13 % serious morbidity risk. Most of the metastasectomy data are based on single institutional series and had many confounding factors such as patient selection that cause some doubts about the results. It should also be considered that many tumors are inoperable due to tumor location or medical inoperability of the patient.

Stereotactic treatment was developed by a neurosurgeon Lars Leksell to treat inoperable deeply seated lesions in the brain. SABR recently become popular to extra-cranial sites with technological improvements. Its strengths include high rates of tumor eradication via non-invasive, convenient, short outpatient treatment course, favorable toxicity and no recovery time. It yielded very good results for treatment of primary and metastatic tumors in various body sites in properly selected patients. However despite potential advantages, there are few published retrospective or phase II studies with limited patient number. These studies about metastatic liver disease that have been treated with SABR yielded 70-82 % 2-year local control rate without any serious toxicity. So there is great hope that SABR may find prominent place in treatment of metastatic cancer. There are also few literature data with favorable results on lung, adrenal, lymph node metastasis treated with SABR.

There is no randomized study comparing efficacy and toxicity of surgery and SABR in oligometastatic setting. Many authors consider surgery as the standard treatment for local management of metastatic sites. However, SABR is promising approach as a complementary or alternative regimen to surgery. Until well-designed randomized studies comparing these two regimens, selection of treatment should be individualized to the patient with the guidance of available data.

Individualization of treatment is dependent on patient factors and metastatic sites. Performance status, comorbidities of the patient, location and number of metastatic sites, previous treatments, underlying prognosis, tumor biology and experience of the team are all important factors for consideration of local treatment.

**OC-0314**

Can SBRT be a viable therapeutic option for unresectable pancreatic adenocarcinoma? Results of phase II study

T. Comito1, E. Clerici1, G.R. D’Agostino1, P. Navarra1, A. Tozzi1, C. Ifode1, C. Franzese1, E. Villa1, F. De Rose1, A.M. Ascolese1, F. Lobefalo1, A. Zerbi1, L. Rimassa1, C. Carnaghi1, M.C. Tronconi1, M. Scorsetti1

1Istituto Clinico Humanitas, Radiotherapy and Radiosurgery, Rozzano (Milan), Italy

1Istituto Clinico Humanitas, Pancreatic Surgery, Rozzano (Milan), Italy

1Istituto Clinico Humanitas, Oncology, Rozzano (Milan), Italy

**Purpose/Objective:** To assess the safety and efficacy of stereotactic body radiotherapy (SBRT) in patients affected by inoperable locally advanced pancreatic adenocarcinoma and local recurrence after surgery.

**Materials and Methods:** Patients with unresectable locally advanced tumor or local recurrence disease were treated with exclusive SBRT. All cases were evaluated by multidisciplinary team. Irradiated lesions had a diameter less than 5 cm and no metastatic disease was present at the time of SBRT. Prescription dose was 45 Gy in 6 daily fractions of 7.5 Gy. SBRT was delivered using the volumetric modulated arc therapy (VMAT) by RapidArc technique. Primary end-point was freedom from local progressions (FFLP) and secondary end-points were overall survival (OS) and toxicity. Local control was defined according to RECIST criteria. Acute and late toxicity was scored according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

**Results:** Between January 2010 and October 2012, 62 patients were treated. Forty five patients (74%) had unresectable locally advanced disease and 17 patients (26%) had local recurrence after surgery. Median follow-up was 12 months (3 - 48 months). Nineteen (30%) patients were alive at the time of analysis. Median follow-up was 17 months in this group of patients (range 12-48 months). In patients with inoperable locally advanced disease, FFLP was 90% at 1year. Median progression free-survival was 8 months. Median OS was 13 months, with 1-year OS rate of 51%. Ca 19.9 value increased in 28 cases (62% of this subgroup) and Ca 19.9 value was less than 300 U/ml in 12 patients (43%) while it was more than 300 U/ml in 16 patients (57%). Univariate analysis showed that Ca 19.9 < 300 U/ml was closely correlated (p = .055) to a better OS. In those patients with local recurrence after surgery, FFLP was 85% at median follow-up. Median progression free-survival was 9 months. Median OS was 19 months, with 1-year OS rate of 53%. In all the cases, toxicity rates were satisfactory with no patients who experienced acute grade 3 toxicity or greater.

**Conclusions:** SBRT is a safe and efficacy treatment to improve local control in patients with unresectable locally advanced or recurrence pancreatic adenocarcinoma, in absence of grade 3 toxicity or greater. Our results suggest that SBRT may be a promising therapeutic option in the multi-modality treatment of these patients.
Purpose/Objective: Treatment planning for Stereotactic Body Radiation Therapy (SBRT) of liver tumours is often challenging due to large respiratory motion and a close vicinity of OARs such as great vessels and duodenum. In such cases a section of the PTV is edited to spare nearby OARs. We evaluated a PTV-less probabilistic planning technique which directly incorporates respiratory motion and other geometric uncertainties of the GTV in the dose optimization process. An improved balance between OAR exposure and the confidence of proper target dosage is expected, as well as a more efficient planning procedure since less human interaction is required.

Materials and Methods: Four liver SBRT plans (3x20 Gy prescription) for which clinical planning had been problematic due to OAR constraints were re-planned using an in-house developed research plug-in for Pinnacle (version 9.100). The plug-in combines the tumour trajectory extracted from the 4D planning CT (~1 cm amplitude for this case) with the Gaussian distribution of random errors (0.25 cm) into a dose blurring kernel, and incorporates a Gaussian distribution of systematic errors as GTV offsets (0.34 cm). Our probabilistic objective assumes shift invariance and aims for a set confidence (e.g. 90%) of GTV minimum dose. Clinical and probabilistic plans were compared using in-house software that accurately simulates the effects of motion and uncertainties on an optimized dose distribution by explicitly sampling three daily errors for each systematic error (10000 were simulated), and 100 positions along the breathing trajectory for each daily error. OARs were evaluated via a traditional DVH.

Results: In three out of four cases the probabilistic plan showed a clear clinical benefit compared to the conventional plan. In two cases the clinical PTV coverage was lowered to spare the great vessels and duodenum, here probabilistic planning significantly increases GTV coverage, while maintaining a low enough dose on the OAR (e.g. Fig. 1). In a third case a higher dose to the great vessels was tolerated in the clinical plan in favour of getting proper PTV coverage. Using probabilistic planning we were able to reduce the great vessel dose while still reaching 90% target dose confidence. In the fourth case all clinical constraints were met both in the clinical and probabilistic plan.

Conclusions: Probabilistic planning can make a valuable contribution to treatment planning in those cases in which it is difficult to meet all clinical criteria.

Figure 1. Isodose lines for a clinical (left) and probabilistic (right) plan. Due to the overlap of the duodenum (blue) with the PTV (pink line), clinical optimization was done only on the dashed part of the PTV, leading to reduced GTV dose confidence (99% of the volume received 87.5% of the dose with a probability of 90%). Probabilistic planning did not use a PTV, and led to sufficient GTV coverage (99% of the volume received 95% of the dose with a probability of 90%) while still sparing the duodenum.

OC-0316
Normal lung tissue reaction to stereotactic body radiation therapy
M. Miften1, Y. Vinogradskly1, B. Kavanagh1, Q. Diot1
1University of Colorado Denver, Academic Department of Radiation Oncology, Aurora, USA

Purpose/Objective: Stereotactic body radiation therapy (SBRT) is becoming the standard of care for early stage lung cancer patients. Toxicity data of lung injury after SBRT remains sparse. Our work evaluated toxicity by analyzing lung density changes for lung cancer patients that underwent SBRT.

Materials and Methods: From 2003 to 2009, 63 patients received SBRT treatments in 3-5 fractions for a total median dose of 54 Gy (range 30-60 Gy). RT-induced lung density changes were evaluated after registration of the planning CT with post-RT CT scans acquired at 3, 6, 12, 18, and 24 months after treatment. A comprehensive dose-response analysis was performed including 1) CT number (HU) changes as a function of dose, 2) spatial analysis of lung fibrosis location, and 3) correlation of lung tissue changes with clinical end-points. We generated patient specific dose-response curves (DRC) by binning voxels into 10 Gy dose bins, calculating the average HU for each dose bin, and evaluating the HU change as a function of dose. Spatial analysis was performed by contouring regions of fibrosis and analyzing the centroid movement of the fibrosis volume relative to the gross tumor volume (GTV) centroid. Airway or vessel branches inside the lung were paired on the pre- and post-RT CT scans to guide the spline based deformable registration of the lung. Regional density increases were classified as local lung collapse or fibrotic based on the local volume changes calculated using the deformation field Jacobian.

Results: DRCs exhibited a linear HU increase up to 35 Gy and a plateau beyond 35 Gy. The response of the 4-5 fx (high toxicity risk) and 3 fx (lower toxicity risk) groups were notably different as the 4-5fx group experienced HU changes twice the increase seen in the 3fx group. The average radial movement of fibrosis centroids relative to the GTV centroids was 2.6 cm with movement greater than 5 cm occurring in 11% of patients questioning the direct exposure of the fibrotic tissues to high doses. 30% of patients with a large fibrotic tissue displacement showed concurrent local lung volume contraction (according to the Jacobian) compatible with radiation-induced regional lung collapse.

Conclusions: The current study presents a comprehensive dosimetric, spatial, and clinical analysis of lung density changes after SBRT. In addition to characterizing dose response after SBRT, we demonstrate certain unexpected observations including a dose-response plateau at 35 Gy and fibrosis volume travel outside of the high dose region. Our clinical analysis suggests some of these abnormalities may be explained by regional lung collapse due to high SBRT doses to the proximal airways. Although current clinical toxicity rates with SBRT are low, as treatments become more aggressive, toxicity rates will increase and better prediction of lung response will be needed. Our work presents important data towards the mechanical and clinical understanding of lung injury after SBRT.