image-guided radiation therapy could improve the treatment accuracy of high precision stereotactic radiosurgery.

**P3-043**

**Protons and C-ions for the treatment of non-small cell lung cancer (NSCLC): What is published the evidence?**

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**Background:** The prognosis of patients with NSCLC is still poor. Amongst distant metastases, also local tumour recurrence is still a problem. Because charged particles (protons and C-ions) have a better dose-distribution than the currently used photons, at least from a theoretical point of view, they should lead to superior results compared to photons. On top of the physical superiority of protons over photons, C-ions also display a biological advantage.

**Aim:** In this review, we searched for clinical evidence that protons or C-ions also display a biological advantage.

**Methods:** We performed a review based on published literature by means of a standardized query using the following electronic databases (up until January 31, 2007): CINAHL, EMBASE and MEDLINE. There was no limit applied to publication year, language or study design. Search terms (using free text words as well as MESH terms) were used alone or in combination, related to lung cancer and charged particle treatment. This included the following terms: neoplasm, cancer, carcinoma, lung cancer, proton, ion, charged particle and hadron.

**Results:** Six fully published series (protons:3, C-ions:3), all dealing with NSCLC, mainly stage I, were identified. No phase III trials could be identified. On proton therapy, weighted means of 2-5 year local tumour control rates varied between 68% and 84%. The weighted mean for 2 year/5 year overall survival and 2 year/5 year cause specific survival were 53%/23% and 66%/46% respectively. Radiation induced pneumonitis was observed in about 10% of the patients. On C-ion therapy, the local tumour control rate was 77% and the 5 year overall survival and cause specific survival rates were 42% and 60% respectively.

**Conclusion:** The results with charged particles, at least for stage I disease, seem to be better than that which is generally achieved by conventional radiotherapy. However, they seem to be similar to what may be achieved with hypofractionated “stereotactic” photon techniques, with which in several phase I/II studies, local tumour control rates of 90% and more were reported. Due to the overwhelming theoretical data on the beneficial properties of protons and light ions, further investment in the infrastructure needed to perform large trials in patients with different lung cancer stages, is warranted.

Until these results are available, for lung cancer, charged particle therapy should be considered as experimental.

**P3-044**

**Image guided gated setup and treatment with implanted fiducials**

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**Background:** Radiotherapy of tumors in the lung is often limited by the relatively low dose tolerance of the lung. One method to reduce the toxicity of these treatments is to reduce the volume of lung irradiated by using image guided setup and/or gating. The current generation of medical linear accelerators have both kVp imaging and gating, allowing the implementation of image guided gated radiotherapy. Tumors, however, are often not evident on kVp projection images, but this limitation can be overcome by the use of implanted fiducials.

**Methods:** A patient was broncoscopically implanted with 4 fiducials. All but one was lost within the first few days after implantation, and the last one remained for the entire treatment. On each day the patient was imaged using the kVp on-board imager. The imager was triggered with the same respiratory gating system used to the gate the treatment. The fiducial was used to align the patient; if a shift was made a 2nd set of kVp images was taken to validate the shift. The fiducial was aligned using both a point matching tool (ISOLOC, CIVCO, Kalona, IA) and an image overlay tool (4DTC, Varian, Palo Alto, CA). We also validated the setup by examining the projection of the fiducial on cine images acquired during the delivery of one the treatment fields.

**Results:** We were able to analyze shift data from 24 of 30 treatment days. The values of the initial shifts were -1.4±1.9, 5.3±2.2 and 0.5±2.2 mm in the lateral, cranial-caudal, and AP directions, respectively. The values of the residual error after the initial shifts calculated from the 2nd set of kVp images were -0.4±1.4, -0.6±3.5 and -0.6±1.3 mm in each direction. The point matching and image overlay systems were consistent at the 1 mm level. The cine images were taken in the AP direction and data could only be extracted for the lateral and cranial-caudal directions. These results were 0.1 ± 1.1 and 1.1 ± 2.2 mm respectively. These data suggest that the uncertainty in the gating represented about 4 mm of tumor motion.

**Conclusion:** Fiducial-based setup of lung patients using either a point-based or image-based system is practical using existing commercially available tools. Gating, however only reduces and does not completely eliminate tumor motion. An internal margin (IM) must therefore be included in the treatment plan to account for the uncertainty in the gated motion.

**P3-045**

**Lung tumor tracking during 4-dimensional stereotactic radiotherapy treatment with the CyberKnife: early results**

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**Purpose:** Synchrony, the respiratory tracking system of the CyberKnife requires the insertion of markers in or close to the tumor. However, in this group of inoperable patients, it is associated with high risks like pneumothorax. To reduce the risks, 4 different methods of marker placement were used: 1) intravascular coil placement, 2) percutaneous intrapulmonal, 3) percutaneous extrapulmonal placement (for fixed tumors to the thorax), and 4) the bronchoscopic placement. To evaluate these techniques, we investigated the toxicity of the marker placement and the tumor response of the treatment. Until now 70 tumors are treated, but because the follow up is too short, we report the results of the first 55 patients with 60 tumors.

**Methods and Materials:** Markers were placed in or around 60 tumors in 55 patients. Forty eight patients were treated with curative intention: 40 patients had a T1-3N0MO lung cancer and 8 patients had 13 solitary metastases in the lung. Seven patients were treated with palliative.
personnel. 5 with recurrent lung cancer, and 2 with metastasis from lung cancer). Platinum fiducials and intravascular embolization coils were used as markers. In total, 180 markers were placed: 67 intrapulmonary in 26 patients (median: 3 markers per tumour), 84 intravascular in 28 patients (median: 3 markers per tumour), 25 extrapulmonary in 5 patients (median: 5 markers per tumour), and 4 markers in 1 patient with the bronchoscopic method. Seven days after marker placement, a planning CT scan was made and the GTV was contoured on a 4D CT scan. The PTV equaled the GTV plus 5 mm. For early stage lung cancer, a total dose of 36 to 60 Gy, (median dose: 60 Gy) was given in 3 fractions. Solitary metastasis to the lung were treated with a total dose of 45 to 60 Gy (median dose: 45 Gy) in 3 to 5 fractions. For palliative treatment, a total dose of 30 to 49 Gy was given in 3-7 fractions (median dose: 40 Gy). The dose to the PTV was prescribed to the 70-85% isodose line. The response was evaluated according to the RECIST criteria with a CT scan 6-8 weeks after the last treatment and routinely thereafter. The median follow up with CT scan was 6 months (range: 2-18).

Results: Six patients (11%) had a pneumothorax after intrapulmonary placement. One patient had no symptoms. A thorax drain was placed in the 5 other patients. One patient complained of severe intrathoracic pain several hours after intravascular coil placement and 5 patients complained of haemoptoe, one after the intravascular coil placement and 4 after the intrapulmonary placement.

The local control was 97%. Seven tumours had a complete response, 38 tumours had a partial response, 13 tumours had stable disease and 2 tumours (both early stage lung cancer) were progressive, one after 8 months and the other after 15 months.

Conclusion: Low toxicity of marker placement was seen due to the 4 methods. CyberKnife tumor tracking with markers is feasible and resulted in excellent tumor response.

P3-046 NT: Radiation Posters, Wed, Sept 5 – Thur, Sept 6

Personalized High-Dose Continuous Hyperfractionated Accelerated Radiotherapy (HI-CHART) of non-small cell lung cancer (NSCLC) based on normal tissue constraints: a prospective clinical trial

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Background: Local recurrence is a major problem after (chemo-)radiation for NSCLC. We hypothesized that for each individual patient the highest therapeutic ratio could be achieved by increasing the total tumor dose (TTD) to the limits of the normal tissues, delivered within 5 weeks. In a theoretical model this resulted in an increase in tumor control probability from approximately 5% for a classical scheme (60 Gy in 6 weeks) to 25% for the study scheme. Here, we report the first results of a prospective clinical trial.

Methods: Twenty-nine patients with medically inoperable (stage I, n=2) or locally advanced NSCLC (stage III, n=27), in a good general condition (WHO-PS 0-1) and with a reasonable lung function (FEV1 >50% of predicted) were included. Most patients (25/29) received induction chemotherapy. All patients were irradiated using an individualized prescribed TTD, based on normal tissue constraints (mean lung dose 19 Gy, maximal spinal cord dose 54 Gy, no constraints for esophagus) up to a maximal TTD of 79.2 Gy. Radiotherapy was delivered in 1.8 Gy fractions, twice daily. Acute and late (>3 months) toxicity was scored using the CTCAE-criteria. A FDG-PET-CT scan (n=27) was performed to evaluate (metabolic) response 70 days after radiotherapy according to EORTC-criteria (PET) and RECIST-criteria (CT). The Kaplan-Meier method was used to compute overall survival.

Results: The mean delivered dose was 62.7 Gy (range 46.8-79.2 Gy). This corresponds to a mean biological equivalent dose of approximately 80 Gy (2 Gy fractions, once daily, in 8 weeks). Most patients experienced mild acute toxicity, while only 2 patients (6.8%) developed acute grade 3 toxicity (n=1 dysphagia, n=1 cough) as depicted in figure 1. Concerning late toxicity, 93% of patients (n=25) showed radiographic changes (75% in <25% and 18% in >25% of the lungs), while 12 out of 28 patients (43%) had clinical symptoms (>gr 1 pneumonitis). One patient (3.4%) died 51 days after radiotherapy due pneumonitis (treatment related mortality).

The post-radiotherapy PET-CT showed in 18 patients a metabolic response (41% complete metabolic response, 26% partial metabolic response), whereas only in 9 patients (33.3%) a response was seen on CT (p=0.01). Eight patients (29.6%) showed progressive disease, consisting of loco-regional progression (n=4), metastases (n=3) or a combination of both (n=1). With a mean FU of 13 months the mean overall survival was 16.7 months and a 1-yr survival of 65%.

Conclusions: Personalized HI-CHART radiation prescription based on normal tissue constraints is tolerable and initial results are promising.

P3-047 NT: Radiation Posters, Wed, Sept 5 – Thu, Sept 6

NSCLC: Primary tumor size - radiation dose related accelerated, twice daily radiotherapy by target splitting, preceded by 2 cycles of chemotherapy: First results of a prospective study

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The post-radiotherapy PET-CT showed in 18 patients a metabolic response (41% complete metabolic response, 26% partial metabolic response), whereas only in 9 patients (33.3%) a response was seen on CT (p=0.01). Eight patients (29.6%) showed progressive disease, consisting of loco-regional progression (n=4), metastases (n=3) or a combination of both (n=1). With a mean FU of 13 months the mean overall survival was 16.7 months and a 1-yr survival of 65%.

Conclusions: Personalized HI-CHART radiation prescription based on normal tissue constraints is tolerable and initial results are promising.