Pre-treatment. FEV1 2.75, TLCOc 5.98.



Four months post-treatment. RP worsening. Started on ACE-I FEV1 1.87 TLCOc 4.08



Two months post-treatment. Grade 3 RP Started on steroids



Six months post-treatment. RP improving.



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## 2478 Stability of Implanted Fiducials for X-Ray Localization of Lung Tumors During Radiation Therapy

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**Purpose/Objective(s):** The use of implanted fiducials as surrogates for lung tumor position assumes that the markers are rigidly positioned relative to the tumor volume. To test this assumption, repeat CT scans were performed throughout treatment to test for marker stability.

**Materials/Methods:** The analysis is performed on 11 patients with small non-small cell lung tumors treated with gated radiotherapy using a stereoscopic x-ray system (Exactrac, BrainLab). Prior to treatment, patients were transcutaneously implanted with a 2.0 cm long x 0.7 cm diameter VisicoilTM gold localization marker. All markers were placed within the tumors. After the marker implantation, patients had a treatment planning CT with exhalation breath hold. Treatment planning was performed to treat the tumor plus margin to 70 Gy in 35 fractions. Repeat exhalation breath hold CT scans were performed periodically during the course of treatment. The repeat CT scans were registered with the planning CT scan by matching the implanted marker's position in the two image sets. All CT scans in this study were obtained with 0.9 mm in-plane pixel resolution and 3 mm slice thickness. The gross tumor volume (GTV) was outlined by a single user on each CT scan, and the center of the GTV as defined on each image set was determined in the planning CT coordinate system. Variation in the center of the GTV relative to the implanted fiducial was defined as the important measure of intrinsic marker position variation.

Results: Data obtained by comparing the patients' first and last CT scans were analyzed. The average time ( $\pm$ S.D.) between the two scans was 41 ( $\pm$  9) days, and the average dose ( $\pm$  S.D.) delivered to the lung tumors between the two CT acquisitions was 47 ( $\pm$  9) Gy. The average 3D variation ( $\pm$  SD) in the center of the GTV relative to the marker was 2.5 ( $\pm$  1.5) mm, and the largest variation along any anatomical axis for any patient was less than 5 mm. Studying these repeat scans separated by several weeks, the observed variation is less than the image resolution. Furthermore, marker stability was determined by observing the variation in GTV centroid relative to the marker. The average ( $\pm$  S.D.) GTV volume reduction over the observation period was 27% ( $\pm$  20%). Larger variations in marker position relative to GTV centroid appear to correspond with larger reductions in tumor volumes during treatment. Visual inspection of the images corroborates this assumption; GTVs do not appear to shrink uniformly about the center of the tumor, but rather the GTV shapes deform substantially throughout treatment

Conclusions: In the patients in the current study, fiducials implanted into a lung tumor show no substantial migration during the entire course of treatment. The average 3D variation ( $\pm$  SD) in the center of the target relative to the marker was 2.5 ( $\pm$  1.5) mm. The variation of marker position relative to the center of the tumor volume varied mostly secondary to tumor volume reduction and resulting change in the tumor anatomy. However, the largest variation along any anatomical axis for any patient was still less than 5 mm. Therefore, implanted fiducials can provide reliable and simple localization of lung tumors, even in the presence of substantial tumor volume reduction.

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## **2479** Efficacy and Morbidity of a Novel Induction Treatment in Locally Advanced Non Small Cell Lung Cancer (NSCLC)

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**Prupose/Objective(s):** The disappointing results of surgical therapy in patients with locally advanced NSCLC have led to the investigation of induction treatments. Of these, phase II trial studies have shown that preoperative chemo-radiotherapy yields a down-staging with a significant complete pathological response amount. The results are often linked to enhanced post-surgical toxicities and impact on survival is not clear.

This study was designed to assess, in patients with locally advanced NSCLC, the efficacy and morbidity of a novel chemo-radiotherapy regimen followed by radical surgery when feasible.

**Materials/Methods:** From October 2000 to January 2005, 107 patients (ITT group) (median age: 59 (34–76); PS 0–1) with locally advanced NSCLC (14 IIB, 25 IIIA, 55 IIIB, 13 IV) were proposed induction chemo-radiotherapy. Chemotherapy consisted of 3 cycles of cisplatin 80–100 mg/m2 + ifosfamide 3–4.5 gr/m2 + vinorelbine 25 mg/m2 and was administered on days 1, 2, 8, 15 (1st cycle), 29, 30, 36, 43 (2nd cycle) and daily from day 59 to 64 (3rd cycle). Concurrent thoracic irradiation (40 Gy, 2 Gy / fraction, 5 d / week) was given from day 36 to 64. Three-dimensional dosimetry was performed using CT scan and Isis treatment planning.

At the end of induction treatment, 42 patients (39%) were submitted to surgical resection (19 lobectomies, 23 pneumectomies)(group S). For these patients, planning treatment volume (PTV), V20 and mean lung dose (MLD) were [mean (SD)] 710 (348) cm3, 17 (5) % and 8.3 (2.3) Gy, respectively. The maximal dose delivered to the heart and the esophagus were [mean (SD)] 34 (12) and 41 (2) Gy, respectively.

Among the 65 (61%) remaining patients (group NS), 13 (12%) did not complete the treatment protocol. The other 52 (49%) patients received an additional 20 Gy and the same chemotherapy during the last five sessions. PTV, V20 and MLD were [mean (SD)] 619 (279) cm3, 20 (4) % and 12 (2.5) Gy, respectively. The maximal dose delivered to the heart and the esophagus were [mean (SD)] 41 (20) and 55.4 (9.6) Gy, respectively.

**Results:** Mean follow-up of the 107 patients is 27 (16–67) months. Projected 2 year survival is 62, 69 and 56% in the ITT group, the group S and the group NS respectively. Complete pathological response was observed in 33% of the group S patients. Main side effects include grade  $\geq 3$  esophagitis and febrile neutropenia in 16 and 8% of the patients respectively. TKCO decreased in both groups whereas FEV1 decreased only in group S. Oral steroids were administered in 6 patients. Three patients died postoperatively from ARDS. Postoperative bronchopleural fistula was observed in one patient.

**Conclusions:** This novel treatment yielded good survival with tolerable toxicity. Induction chemotherapy can convert 39% of inoperable locally advanced NSCLC to candidates for surgical resection.

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## **2480** Quantification of Motion for Different Thoracic Locations Using 4DCT: Implications for Radiation Treatment Planning

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**Background:** Lung cancer remains a leading cause of cancer death despite newer, more aggressive treatments. New imaging modalities such as 4-dimension computed tomography (4DCT) are allowing more accurate delineation of radiotherapy targets.

**Purpose/Objective:** To determine the extent of respiratory-related motion for determination of internal target volumes (ITV) for different thoracic locations using 4DCT, and to assess the relationships between tumor location and motion.

Materials/Methods: We reviewed 4DCT scans of 20 consecutive patients with thoracic tumors treated at our institution in the past year. Patient characteristics including age, gender, tumor volume, and N-stage were tabulated. Tumor histologies included non-small cell lung cancer (N=13), small cell lung cancer (N=13), pulmonary neuroendocrine carcinoma (N=1), primary lung sarcoma (N=1), metastatic osteosarcoma (N=1) and thymoma (N=1). 4DCT scans were performed on an eight-slice Lightspeed PET/CT Scanner (GE Medical Systems). Breathing traces were recorded with a commercial respiratory monitoring system (RPM, Varian Oncology). Image processing was performed on an Advantage Workstation 4.1 with 4DCT software (GE Medical Systems). Motion of thoracic contents was measured in up to three directions [anteroposterior (AP), superoinferior (SI), and lateral (LR)] at seven key anatomic sites (diaphragms, bilateral hila, parenchymal lung tumors, carina and aortopulmonary window). Parenchymal tumors were classified as upper versus lower using a transverse plane centered at the bottom of the carina and anterior versus posterior using a coronal plane also centered at the carina.

**Results:** Table 1 shows the mean, standard deviation, maximum and minimum motion of analyzed structures. There was a significant difference in the SI motion for upper vs. lower thoracic lesions (3.7 mm for upper and 10.4 mm for lower tumors, p = 0.029). Posterior tumors exhibited greater movement than anterior tumors in both the SI (4.0 mm for anterior and 8.0 mm for posterior tumors, p = 0.013) and lateral directions (2.8 mm for anterior and 4.6 mm for posterior tumors, p = 0.045).

**Conclusions:** Our study shows that tumors located in the upper thorax exhibit less motion than those in the lower thorax, and anterior tumors exhibit less motion than posterior ones. It also provides pertinent motion data for ITV expansion for different nodal regions for ungated radiotherapy.