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POSTER

# Comparison of Three Approaches to Delineate Internal Gross Tumour Volume Based on Four-dimensional CT Simulation Images of Non-small-cell Lung Cancer

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**Background:** To compare positional and volumetric differences of internal gross tumour volume (IGTV) delineated separately by three approaches based on four-dimensional CT (4DCT) for the primary tumour of non-small cell lung cancer (NSCLC).

**Materials and Methods:** Twenty-one patients with NSCLC underwent big bore 4DCT simulation scan of the thorax. IGTVs were delineated using three approaches as followed: gross tumour volumes (GTVs) delineated on ten bins of 4DCT were fused to produce IGTV<sub>10</sub>; GTVs delineated separately based on end-inspiration (EI) and end-expiration (EE) phases were fused to produce IGTV<sub>EI+EE</sub>; the visible tumour on the MIP images were delineated to produce IGTV<sub>MIP</sub>. The position of the target center, the volume of target, the degree of inclusion (DI) and the matching index (MI) were compared reciprocally among IGTV<sub>10</sub>, IGTV<sub>EI+EE</sub> and IGTV<sub>MIP</sub>. The definition of DI of volume X included in volume Y [DI (X in Y)] is the percentage of the overlap between volume X and Y in volume X.

**Results:** The mean centroid shifts among IGTVs in the LR, AP and CC directions were less than 1 mm, with no statistically significant difference. The IGTV<sub>10</sub> size was larger than IGTV<sub>EI+EE</sub> size, the difference was statistically significant ( $t=2.37$ ,  $p=0.028$ ); the IGTV<sub>10</sub> size was larger than IGTV<sub>MIP</sub>, but the difference was not statistically significant ( $t=1.95$ ,  $p=0.065$ ). The mean size ratio of IGTV<sub>EI+EE</sub> to IGTV<sub>10</sub>, IGTV<sub>MIP</sub> to IGTV<sub>10</sub> were  $0.85\pm0.08$  and  $0.92\pm0.11$ , respectively. The mean DI of IGTV<sub>EI+EE</sub> in IGTV<sub>10</sub>, IGTV<sub>MIP</sub> in IGTV<sub>10</sub> were  $84.78\pm8.95\%$  and  $88.47\pm9.04\%$ . The mean MI between IGTV<sub>10</sub> and IGTV<sub>EI+EE</sub>, IGTV<sub>10</sub> and IGTV<sub>MIP</sub> were  $0.85\pm0.09$ ,  $0.86\pm0.09$ , respectively.

**Conclusions:** The centroid shifts among IGTVs delineated by the three manners based on 4DCT images are not obvious; IGTV<sub>EI+EE</sub> and IGTV<sub>MIP</sub> can not replace IGTV<sub>10</sub>, however, IGTV<sub>MIP</sub> is closer to IGTV<sub>10</sub> comparing to IGTV<sub>EI+EE</sub>. The size ratio of IGTV<sub>EI+EE</sub> to IGTV<sub>10</sub> is correlated to the tumour motion vector. As the vector increases, the size ratio of IGTV<sub>EI+EE</sub> to IGTV<sub>10</sub> decreases.

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# Phase 2 Study of Nimotuzumab in Combination With Concurrent Chemoradiotherapy (CRT) in Patients With Locally Advanced Non-small Cell Lung Cancer (NSCLC)

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**Background:** Nimotuzumab (Nimo), a humanized IgG<sub>1</sub> monoclonal EGFR antibody, is approved and widely used in patients (pts) with head and neck cancer or malignant glioma in combination with radiotherapy in several countries. In previous clinical studies, Nimo has demonstrated a very mild and low incidence of skin toxicity compared to other EGFR antibodies. On nonclinical models using NSCLC cell lines, Nimo showed a radiosensitizing effect.

**Material and Methods:** This open-label, multicenter phase 2 study evaluated the tolerability and efficacy of Nimo in combination with concurrent CRT in pts with unresectable locally advanced NSCLC. All eligible pts received concurrent thoracic radiotherapy (60 Gy, 2 Gy/day, 6 weeks from day 1) and 4 cycles of chemotherapy (cisplatin 80 mg/m<sup>2</sup> on day 1, vinorelbine 20 mg/m<sup>2</sup> on days 1 and 8) once every 4 weeks as scheduled. Nimo (200 mg) was administered once a week from cycle 1 to 4. The primary endpoint was tolerability in combination with concurrent CRT, which was measured by the percentage of pts who completed 60 Gy of radiotherapy within 8 weeks, completed 2 cycles of chemotherapy and received more than 75% of Nimo.

**Results:** Between June 2009 and May 2010, 40 pts were enrolled from 7 sites in this study in Japan, and 39 eligible pts received the study treatment. The pts characteristics (n=39) were as follows: 62 years (median); male/female, 34/5; stage IIIA/B, 21/18; PS0/1, 25/14. Thirty-four pts (87%) met the criteria for treatment tolerability, and 38 pts (97%) completed

60 Gy of radiotherapy within 8 weeks. Infusion reaction,  $\geq$ grade 3 skin rash,  $\geq$ grade 3 radiation pneumonitis, or  $\geq$ grade 4 nonhematological toxicity were not observed. For the preliminary efficacy analysis, 37 pts were evaluable with appropriate radiotherapy planning. The response rate (CR+PR) was 70%; the median PFS was 11.1 months; and 92% pts were alive at the cutoff date (Jan 2011). There was no correlation observed between PFS and the above-mentioned pts characteristics. However, the PFS was longer in pts with squamous cell carcinoma (n=16) than that in pts with adenocarcinoma (n=14) (mPFS: not reached vs 9.9 months  $p=0.014$ ; progression free at the cut-off date: 71% vs 13%). Analysis of molecular markers and further survival followup is ongoing and will be presented and discussed.

**Conclusions:** Nimo's addition is feasible to the concurrent CRT consisting of cisplatin and vinorelbine. The preliminary efficacy result observed in pts with squamous cell carcinoma is interesting and further investigation is needed.

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# Advanced Lung Cancers – Combined Use of Stereotactic Body Radiation Therapy for Primary Tumour and Three-dimensional Radiotherapy for Mediastinal Nodes Versus Standard 3DRT: an Intra Individual Dosimetric Comparison

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**Title:** Advanced lung cancers: combined use of stereotactic body radiation therapy for primary tumour and three-dimensional radiotherapy for mediastinal nodes versus standard 3DRT. An intra individual dosimetric comparison.

**Background:** Radiation tolerance of lungs, spinal cord, heart and oesophagus does not allow to deliver efficient doses of irradiation in advanced non-small-cell lung cancers (NSCLC). The aim of the present study is to show a possible dosimetric gain for these organs at risk (OAR) when including only the nodal planned target volume (PTV-N) in the field of standard radiotherapy and covering the tumour planned target volume (PTV-T) by stereotactic body radiation therapy (SBRT), using Cyberknife®.

**Methods and materials:** Nine patients with peripheral stage III NSCLC were selected. They were simulated, planned, and treated with involved field 3DRT using a dose of 66 Gy in 33×2 Gy. Retrospectively, plan of primitive tumour irradiation by SBRT at a dose of 48 Gy in 4×12 Gy and plan of mediastinal lymph nodes irradiation by 3DRT were realised, optimized separately and coregistered (=combined plan). Dosimetric parameters of the two plans were considered for PTV-T, PTV-N, lung, heart, spinal cord and esophagus.

**Results:** Similar coverage of the PTV-T was observed between the two plans ( $p=0.23$ ). Coverage of the PTV-N was significantly improved in the combined plan ( $p=0.01$ ), with a mean increase of 3%. The combined plan minimized the lung V20 and V30 doses with a respective mean decrease of 14.8% ( $p=0.008$ ) and 32.4% ( $p=0.008$ ). MLD was similar between the two plans ( $p=0.37$ ). The V30 of the heart was significantly decreased in the experimental plan ( $p=0.04$ ). There were no significant differences in the maximal dose delivered to the spinal cord and the length of esophagus irradiated at 46 Gy between the two plans (respectively  $p=0.21$  and  $p=0.41$ ).

**Conclusion:** Compared to the conventional approach, the combined plan, in advanced lung cancers, reduces significantly the V20 and V30 of the lung and the V30 of the heart. It also increases biological equivalent dose of the PTV-T and coverage of the PTV-N. These findings encourage us to conduct a phase I-II.

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# Radiation Pneumonitis and Treatment Outcome in Radical Radiotherapy of Stage III Non Small Cell Lung Cancer

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**Background:** The aim of the study was to investigate the relationship between different clinical and dosimetric factors contributing to the development of radiation induced pneumonitis (RP) as well as its possible influence on patients' survival.

**Materials and Methods:** Data from 103 consecutive patients with non-small-cell lung cancer (NSCLC) receiving curative radiotherapy (RT) from 2007 to 2009 were analysed. RP was graded by CTC version 3.3. Median follow-up was 16 months. The clinical and dosimetric parameters related to RP were analysed using SPSS. Median age was 66 (43 to 81); 55% were male, 47% had adenocarcinoma, while 34% had squamous cell carcinoma;