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POSTER

### Improvement of three-dimensional treatment-planning models of small lung targets using high-speed multi-slice CT imaging

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**Purpose:** It is difficult to recognize three-dimensional tumor movement using an ordinary CT scan, but a multi-slice CT scan could provide sagittal and coronal information regarding tumor movement. Respiratory gating technology for imaging and treatment is not yet widely available. The purpose of the current study was to explore an intermediate step to improve the reliability of the patient model and reduce treatment volume by acquiring multi-slice CT data with the patients single holding their breath at normal inhale and exhale.

**Methods and Materials:** We analyzed 9 tumors from 7 patients with small peripheral lung cancers. We used the multi-slice CT scanner GE Light Speed QXi (GE Medical System, Milwaukee, WI). CT scans were performed under 3 respiration conditions: free-breathing (FB), shallow inspiration (SI), and shallow expiration (SE). We created two treatment-planning fields for each tumor with three phase data sets.

1) Two-phase planning: planning target volume was created with a 1-cm margin for all dimensions from mixed CTV, which included SE CTV and SI CTV.

2) Free-breathing planning: with a 1-cm margin (ventro-dorsal, medial-lateral) and a 2-cm margin (cranio-caudal direction) from FB CTV.

To compare these treatment plans, 60Gy crossfire fields and two parallel-opposed fields were set up. These treatment parameters were transferred for use with the two sets of CT data at inhalation and exhalation. Three-dimensional dose calculation was performed with 10-MV photon beam data using Clarkson's summation technique with the 3D-RTP system (FOCUS, CMS, St. Louis, MO).

**Results:** There was no significant difference between minimum doses of the SI and SE CTV in the two plans using two parallel-opposed fields, but there was a significant difference between the minimum doses of the CTV of the two-phase plan and free breathing plan using crossfire fields ( $p=0.04$ ). Comparison of the ipsilateral lung V20 based on inhalation and exhalation CT data revealed that the V20 of the two-phase plan was smaller than the others ( $p<0.001$ ).

**Conclusion:** Compared to current free-breathing CT patient models, modeling lung treatments with two-phase planning using multi-slice CT provide an immediate reduction in the amount of normal tissue treated and improved reliability of patient data for DVH modeling. Spatial information using multi-slice CT has the potential to determine the planning target volume of moving lung tumors more precisely than conventional CT planning.

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### Targeting somatostatin receptor positive tumours with Y-90 Lanreotide

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Targeted radio-therapy with beta emitting labelled peptide Yttrium-90 (Y-90) Lanreotide may be appropriate in patients who have tumours which express somatostatin receptors. Many of these patients, for example, such as those with carcinoid, do not respond to chemotherapy or external beam radiotherapy. The aim of this study is to review our experience in using Y-90 Lanreotide on such tumours

A total of 54 cycles of Y-90 lanreotide have been given to 24 patients over an 18 month period. All patients had failed or found to be unsuitable for other cancer treatments. They all had to have avid uptake of In-111 Octreotide in known tumour sites. All had good or stable markers of renal, liver and bone marrow function. There were 15 patients with carcinoid, 5 with gliomas, 2 fibrolamellar cancers, 1 ACTH secreting cancer and one malignant histiocytoma. The youngest was 19 and the eldest 76.

Patients were infused with 0.8-1.2 GBq on a 3-4 week basis for 3 treatments and if there was response this was repeated after a 3 month gap in one patient. Those with intra-cerebral tumours were treated with 200-400 MBq Y-90 Lanreotide given intra-arterially into the tumour bed via a radiologically positioned catheter.

Most patients had fatigue for 7-10 days post treatment. There has been mild bone marrow toxicity in 4 patients and no renal toxicity. Response as measured by >25% reduction in tumour size on CT has occurred in 6 patients, stability of previously growing disease in 9 patients. All the

remaining 9 patients with progressive disease have died of their disease. Poor prognostic indicators are massive tumour bulk and bone or lung metastases.

Y-90 Lanreotide can induce stability or regression in 58% of patients but may not be appropriate for those with very advanced disease

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### Impairment of immune response after percutaneous low-dose radiation in hepatocellular carcinoma in rats

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**Introduction:** Leucocyte-endothelium interaction by cell adhesion and cell migration is known to determine humoral tumor detection. The aim of our study was to evaluate the effects of percutaneous low-dose radiation on humoral immune response in experimental hepatocellular carcinoma.

**Material and Methods:** In 12 male ACI-rats (weight  $230.0 \pm 39.2g$ ) Morris hepatoma was implanted in the left liver lobe. 10 days afterwards in 6 rats percutaneous single-dose radiation was applied with 6Gy and 12h later intravital fluorescence microscopy performed with respect to tumor vessel diameter, red blood cell velocity and leucocyte adherence. Values were compared with control animals ( $n=6$ , without radiation). Data are given as mean values  $\pm$  standard deviation; significance analysis was done by Wilcoxon-Mann-Whitney-U-Test.

**Results:** Vessel diameter and basal red-blood-cell velocity are comparable in hepatic tumor tissue and liver tissue. In tumor tissue leucocyte adherence was significantly reduced versus liver sinusoids ( $p<0.05$ ). After radiation leucocyte-endothelium interaction was significantly enhanced in tumor tissue and sinusoids ( $p<0.05$ ).

	Liver tissue	Tumor tissue
Vessel diameter	$34.5\mu m \pm 6.5$	$39.0\mu m \pm 3.71$
Red blood velocity [controls]	$1.78 \text{ mm/s} \pm 0.18$	$1.85 \text{ mm/s} \pm 0.14$
Red blood velocity [after radiation]	$1.88 \text{ mm/s} \pm 0.10$	$1.93 \text{ mm/s} \pm 0.14$
Adherent leucocytes/mm2 endothelial surface [controls]	$0.99 \pm 0.79$	$0.32 \pm 0.1^*$
Adherent leucocytes/mm2 endothelial surface [after radiation]	$12.74 \pm 1.64^{**}$	$13.84 \pm 1.21$

\* $p<0.05$  Tumor vs. liver \*\* $p<0.05$  Radiation group vs. controls

**Conclusions:** The results of the current study showed that leucocyte-endothelium-interaction is significantly reduced in tumor tissue.

One of the main mechanisms for modulation of the immune-response in tumor endothelium is to improve the leucocyte-endothelium interaction. Homogeneous activation of liver sinusoids and tumor tissue after radiation indicates that immune response in endothelium cells could be regulated by unspecific inflammation.

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### Comparison of dynamic conformal radiotherapy with micro-multileaf collimator vs arc non conformal radiotherapy vs static conformal radiotherapy

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**Introduction:** In dynamic conformal radiotherapy (DCRT) field shape is being modified during gantry rotation in order to obtain a high dose conformity to planning target volume (PTV) and minimize dose to organs at risk and healthy surrounding tissues. In the Radiotherapy Dept. of the National Neurological Institute 'Besta' (Milan, Italy), DCRT is realized by a dynamic micro-multileaf collimator (DMLC, 3DLine) installed on a Philips SL75-5 linear accelerator: DMLC leaves are being moved during gantry rotation conforming the field shape to the PTV. This DMLC has been designed for the treatment of small and irregular size tumors. In particular it can be used for the fractionated stereotactic radiotherapy of brain tumors.

**Purpose:** To compare the dose conformity to PTV and normal brain dose characteristics obtained with different treatment techniques: DCRT (DMLC, A), dynamic non conformal (arc with fixed square field size, B) and conformal static (MLC conformal field, C). Three types of intracranial tumor have been selected: metastasis, glioblastoma (GBL) and meningioma.

**Methods:** PTV and brain tissue volumes of interest (VOI) are delineated on CT images. Plans for techniques A, B and C are performed: plan A has been performed by DMS software (Ergo, 3DLine) while B and C plans have

been performed by 3D RTS software (Plato, Nucletron). The prescription dose (PD) is referred to the minimum isodose that encompasses almost 99% of the PTV.

For each plan the dose-volume histogram (DVH, 100000 points) has been calculated for the PTV and the brain VOI. Conformity Index (CI) has been evaluated on basis of the definition contained in ICRU 62; over ( $>107\%PD$ ,  $Vo$ ), under ( $<95\%PD$ ,  $Vu$ ) dosage volume in PTV and maximum dose in PTV divided by prescription dose (MDPD) have been evaluated. Non-target volumes brain tissue encompassed in the 50%PD isodose have been evaluated (V50).

**Results:** The average CI is 1.8, 2.9 and 2.3 respectively. The MDPD is 1.26, 1.18 and 1.19 respectively. None of the PTV has been underdosed ( $Vu=0$ ). The average  $Vo$  is 96%, 89% and 92% respectively. For the non-target brain the average volumes V50 are 2%, 5% and 8% for meningioma and metastasi cases respectively; for GBL case V50 are 27%, 48% and 32% respectively.

**Conclusion:** DCRT allows a better dose conformity than conventional arc technique and static conformal for all types of tumor. The overdosage at the PTV is compatible with small volumes of the PTV (6 cm<sup>3</sup>) except for the GBL case. Non target brain is less involved with DCRT in all cases.

From this preliminar analysis, DCRT is particularly indicated for intracranial small size tumor where the dose fall-down outside the PTV is important and dose inhomogeneities on the PTV are not very relevant because of the small size of the volume.

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### Systematic and random set-up errors in patients having postoperative radiotherapy for breast cancer

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**Purpose:** We have previously shown that using different patient positioning for adjuvant breast radiotherapy has a significant effect on cardiac doses and consequently the risk of cardiac radiation damage. Reproducibility of patient positioning and patient movement, including respiratory movement, may dilute this benefit as small variations in physical dose translate to large differences in predicted biological effect. We have investigated the reproducibility of radiotherapy set-up for the best patient positioning (Tgrip method), compared to a standard arm-rest immobilisation technique.

**Methods:** Digital port images were obtained on days 1,2,3 and on the 1st day of each subsequent week of treatment. Medial and lateral images taken each time. The images were scaled and the images were then enhanced to give a clear outline of the treated area. Measurements from skin surface to posterior field border were taken at 1/4, \* and 3/4 intervals from superior to inferior borders at right angles to the posterior border. No adjustments were made during XRT based on these results

**Results:** To date 25 consecutive patients have been assessed 11 with the Tgrip and 14 treated with the armrest. A total of 984 measurements were analysed. The stability of the Tgrip and armrest were not statistically different, SD for set-up error being 0.26cm and 0.28cm respectively. There was a systematic error on day 1 of treatment which disappeared by day 2.

**Conclusion:** There are no difference between techniques in set-up accuracy so the biological benefits of the Tgrip method are not lost by poor reproducibility. The random error for both methods is within acceptable tolerances. Set-ups should not be altered based on day 1 portal images.

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### Impact of intravenous contrast on target definition in radiotherapy of non small cell lung cancer

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**Purpose:** Accurate planning target volume (PTV) definition is critical to achieving local disease eradication in non small cell lung cancer (NSCLC). The impact of intravenous contrast (ivc) on target definition when using three dimensional conformal radiotherapy (3DCRT) was assessed in this study.

**Methods:** Patients with NSCLC (stages Ib -IIIB) underwent CT scanning before and after the administration of ivc. Gross tumour volumes (GTV) for each patient were outlined manually in both ivc and non-ivc scans. 3DCRT plans were generated for PTVivc and PTVnon-ivc. PTVivc was subsequently transferred to the non-ivc study to assess resulting dose distribution to the PTVivc from the non-ivc 3DCRT plan. The impact of ivc on CT based

calculations in 3DCRT plans was also addressed by comparing the dose distribution to an identical test volume in corresponding non-contrast and contrast planning CT plans.

**Results:** When GTVnon-ivc were compared to GTVivc, contrast enhancement reduced the volumes by a range of 22-34%. When the non-ivc 3DCRT plans were used to cover the PTVivc, both the minimum dose in the PTVivc and the volume of the PTVivc receiving  $>95\%$  of the prescribed dose (Vol.95) were significantly reduced. The minimum dose in PTVivc ranged from 85.1% to 43.1% and the Vol.95 of PTVivc ranged from 97.6% to 95.3%. When the contrast and non-contrast scans were assessed for the test volume, the difference in dose distribution to the test volume, spinal cord and lungs ranged from 0-1.6%, 0.7-3% and 0-1.2%, respectively.

**Conclusions:** Use of ivc when defining the GTV reduces the risk of underdosing the target in NSCLC, when using 3DCRT. An added benefit of using ivc is an increase in the potential for dose escalation through reduction in size of the GTV. If ivc scans are used directly for planning, and not just as reference images, the presence of contrast in the scans does not appear to have a major impact on the planning system calculations. However, this warrants further investigation before being used in planning calculations routinely.

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### Stereotactic radiotherapy for lung cancer using gold grain radiomarker and/or active breathing control system

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**Purpose:** A stereotactic radiotherapy (SRT) for lung cancer is not easy due to its internal motion. To overcome this problem, we developed disposable gold grain radiomarker and active breathing control system. The purpose of this study is to investigate the usefulness of newly developed gold grain radiomarker for fluoroscopically invisible lesion and active breathing control (ABC) system.

**Patients and Methods:** Thirty-five patients with metastatic lung cancer (46 lesions) and 19 patients with primary lung cancer (21 lesions) have been treated with SRT since July 1997. To be sure to include the tumor movement due to respiration to planning target volume (PTV), every patients were examined by fluoroscopy and radio-opaque catheters of the same length of tumor movement were attached on the anterior and lateral chest wall before CT simulation. In the case of the tumor which was invisible by fluoroscopy, a gold grain was implanted into the tumor as a radiomarker. This is a very small gold grain with a size of 0.8 x 3mm which is charged in the tip of a sterile disposable long needle with mandril. In the present study, this gold grain radiomarker was used for seven patients. We mainly used a protocol of 60 Gy/8 fractions/2 weeks for the tumors near the mediastinum and pleura (19 lesions), and a protocol of 45 Gy/3 fractions/3-6 days for the tumors in the central region of the lung (32 lesions). Respiration was held at a desired phase at which the tumor was irradiated, by the newly developed ABC system. Six patients were treated using this ABC system.

**Results:** Among 46 lesions of metastatic lung cancer, complete response (CR) was achieved in 37 lesions while 5 lesions had a partial response (PR) so far (1 NC and 3 unknown). All patients developed mild pneumonitis or lung fibrosis about 3 to 6 months after SRT just in the treatment volume. A gold grain was recognized by even linacgram. Internal organ motion was sufficiently suppressed by the ABC system, and the motion was  $\pm 1-1.5$ mm.

**Conclusion:** SRT to primary or metastatic lung cancer provided excellent local control without severe normal tissue damage so far. A gold grain was useful for fluoroscopically invisible lesion for radiotherapy planning and verification of actual irradiation field by linacgraphy. ABC system was also very useful for a tumor with large internal motion by respiration.

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### Interstitial brachytherapy and external beam radiation in patients with locally advanced carcinomas of the head and neck

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**Purpose:** To evaluate the effect of interstitial high-dose-rate (HDR) brachytherapy followed by external beam radiation (Co 60 unit) for locally advanced as well as unresectable tumors of the head and neck.

**Patients and Methods:** Between 1989 and 1996, a total of 68 patients (13 females, 55 males) with squamous cell carcinomas of the head and neck were referred to our Department and consecutively irradiated with