

60 patients were offered and 39 received CT. 38 received RT, which was given adjuvantly in only 5 patients (one of whom later required 2 further courses for the development of biopsy site metastases). RT was given to 12 patients for biopsy site metastases (4 of which were also painful) and to 16 patients for chest wall pain alone.

The median age of those receiving RT was 70 years, 36 were male, 8 (21%) had epithelioid and 5 (13%) sarcomatoid histology. Two were PS 0, 14 PS 1, 10 PS 2 and 4 PS 3. 24 (73%) patients had pleural aspiration, 28 (85%) closed pleural biopsy, 14 (42%) thoracoscopy and 4 (12%) thoracotomy. 13 (39%) also received CT.

**Conclusion:** Age, gender, histology, PS and biopsy procedure did not influence the requirement for RT in our centre. RT was more often delivered for the palliation of pain rather than biopsy site metastases. In our cohort of patients the development of a mass was a relatively uncommon event and this supports a recent Australian study. We suggest that routine prophylactic irradiation to biopsy sites may not be necessary.

## 1172

## PUBLICATION

### First results of a prospective study on safety and feasibility of navigated brachytherapy as a new treatment option for peripheral lung cancer

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**Introduction:** The aim of this prospective study was to prove feasibility and safety of endobronchial high dose rate (HDR) brachytherapy applied as a highly conformal boost for inoperable peripheral non-small-cell lung cancer (NSCLC).

**Material and Methods:** Patients with medically or surgically inoperable stage I-III peripheral NSCLC were prospectively treated with combined external beam radiotherapy (EBRT, 50–66 Gy, depending on nodal status) and navigated brachytherapy (15 Gy). Inclusion criteria comprised tumor localization distant to the second segmental bronchus, tumor diameter <5 cm, written informed consent, and histologically proven NSCLC. Navigated bronchoscopy was performed with an electromagnetic navigation system (superDimension, Israel) for localization of a micro-sensor mounted on the tip of a bronchoscope. The probe can be actively guided by a steering mechanism to the targeted lesion displayed on reconstructed chest CTs. After localization of the NSCLC and placement of a catheter, endobronchial ultrasound (EBUS) was performed to confirm the exact position in the center of the lesion. Then, a 6 french brachytherapy catheter was placed within the tumor and fixed at the nose of the patient for the 5 day treatment period. Primary CT based 3D brachytherapy treatment planning (PLATO, Nucletron, Netherlands) was performed on chest CTs acquired with the inserted brachytherapy catheter loaded with a dummy probe. The brachytherapy PTV comprised the peripheral NSCLC and the draining broncho-vascular bundle. Prior to every brachytherapy repeated CTs were performed to ensure a stable positioning of the brachytherapy catheter. HDR brachytherapy (single dose 5 Gy, 370 GBq 192-Iridium, Nucletron, Netherlands) was applied three times a week. Primary endpoints of this study were safety and feasibility of brachytherapy as well as navigated bronchoscopic catheter placement and primary CT based 3D-treatment planning.

**Results:** After approval of the ethics committee 6 patients have been enrolled so far. Navigated bronchoscopy, catheter placement and CT based brachytherapy proved to be feasible and safe. All patients tolerated the brachytherapy catheter well during the treatment period. Repeated CTs prior to brachytherapy revealed a stable positioning of the catheters with a maximum deviation <2 mm. After a median follow up of 3 months (2 weeks to 9 months) no major side effects or complications have been observed. The first patient treated revealed a partial remission on EBUS and CT, respectively and demonstrated only minor cytological residuals on histology.

**Conclusion:** Navigated brachytherapy of inoperable peripheral NSCLC proved to be safe and feasible. The major advantage of this new approach compared to other highly conformal techniques is the possibility to easily encompass the draining broncho-vascular bundle and to apply highly fractionated treatment schedules with a broad therapeutic index in curative situations or single dose treatments in palliative situations.

## 1173

## PUBLICATION

### Phase II trial of neo-adjuvant gemcitabine-carboplatin-paclitaxel (GCP) chemotherapy for operable non-small cell lung cancer (NSCLC)

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**Background:** The aim of this open-label single-arm phase II study (B9E-MC-S179) was to evaluate the efficacy, feasibility and safety of the GCP combination as neo-adjuvant chemotherapy in patients with operable stage NSCLC.

**Material and Methods:** Major eligibility criteria included histologic or cytologic diagnosis of NSCLC; Stage IB, II or IIIA disease; tumor amenable to curative surgical resection; no prior tumor therapy; ECOG performance status (PS) 0 or 1; and written informed consent. Patients were given 3 cycles of chemotherapy followed by tumor resection. Each 21-day cycle consisted of gemcitabine 1000 mg/m<sup>2</sup> on days 1 and 8, carboplatin AUC 5 on day 1 and paclitaxel 175 mg/m<sup>2</sup> on day 1. The primary endpoint was response rate and secondary endpoints included safety and time-to-event variables.

**Results:** Forty-four patients were enrolled in this multi-national, multi-center study: 39 males, 5 females; mean age 56.4 yr, range 37–67 yr; 18% Stage IB, 16% Stage II, 66% Stage IIIA. All 44 patients received 3 cycles of treatment: 33 patients had a partial response to chemotherapy, for a response rate of 75% (95% CI: 60, 87%). 3 patients did not undergo surgery (1 patient had brain metastases discovered, 1 patient died from the study disease and the tumor of 1 patient was no longer amenable to surgery). 36 patients had a complete tumor resection, 5 of whom had a complete pathological response with no viable tumor cells in the resected tumor on histological examination. Median time to progression and median time to treatment failure were both 13.6 months (95% CI: 8.9, >16 months) and 26/44 patients (59%) have progressed. The one-year survival rate was 86% (95% CI: 72, 95%). Grade 3/4 hematological toxicity was reported for 37 patients (84%), most commonly neutropenia (34 patients, 77%) and thrombocytopenia (11 patients, 25%). Other toxicities included grade 3/4 anemia (4 patients, 9%), febrile neutropenia (1 patient, 2%), bleeding (1 patient, 2%), vomiting (1 patient, 2%), rash (1 patient, 2%), increased alanine aminotransferase (3 patients, 7%) and grade 2 alopecia (35 patients, 80%). Toxicity caused a reduction or delay in gemcitabine for 32 patients (73%) (23% had a reduction or delay at day 1 and 68% at day 8), in carboplatin for 12 patients (27%) and in paclitaxel for 11 patients (25%).

**Conclusion:** The GCP combination showed promising efficacy and appears to be safe and feasible as neo-adjuvant chemotherapy in patients with operable stage NSCLC.

## 1174

## PUBLICATION

### Intrafractional movement of the oesophagus in patients with Non-Small Cell Lung Cancer (NSCLC)

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**Background:** Concomitant chemo-radiation appears to result in a survival advantage in patients with NSCLC compared to sequential therapy. This is at the expense of increased radiation-induced oesophageal toxicity. The extent of oesophageal movement on dose delivered to the oesophagus is not known and needs to be determined before introducing techniques to avoid it.

**Materials and Methods:** CT scans were performed in 7 patients with NSCLC prior to undergoing radical radiotherapy. 2 CT images were acquired of the thorax in inhale and exhale positions. A rigid registration was performed relative to the spine to account for global patient movement. This was followed by non-rigid registration to account for organ motion and deformation. The oesophagus was manually identified on the exhale image and its central point was identified at 4 cm intervals along its length from

the thoracic inlet to the gastro-oesophageal junction. These points were mapped using the registration transformation onto the inhale image which provided a measure of oesophageal displacement between the exhale and inhale breath-holds. Displacements in the right-left (R-L) and anterior-posterior (A-P) directions were measured.

**Results:** A total of 86 measurements were analysed. The range of displacement in each direction was: R-L 0.03 – 7.15 mm; A-P 0.11 – 9.94 mm. The mean and standard deviation (SD) of displacement are shown in the table:

Level of Measurement	Mean Displacement in mm (SD)	
	R-L	A-P
8 cm above the carina	1.92 (1.38)	1.13 (0.60)
4 cm above the carina	2.29 (1.64)	1.43 (1.53)
Carina	1.18 (1.13)	2.98 (3.18)
4 cm below the carina	3.62 (2.49)	4.22 (2.89)
8 cm below the carina	2.05 (2.00)	2.72 (1.57)
12 cm below the carina	1.21 (0.69)	3.23 (1.86)

Displacement of the oesophagus was more marked 4 cm below the carina (range 1.06 – 8.91 mm) and less marked 8 cm above the carina (0.4 – 4.15 mm). The mean SD over all levels in both directions was 1.75 mm.

**Conclusion:** The oesophagus moves during respiration and this needs to be incorporated into a Planning organ at Risk Volume (PRV) using standard margin calculations. Conformal radiotherapy techniques, such as Intensity Modulated Radiotherapy (IMRT), may facilitate avoidance of the oesophageal PRV and reduce radiation-induced toxicity.

## 1175

## PUBLICATION

#### Pilot study of daily low dose cisplatin and radiotherapy for medically inoperable stage I non-small cell lung cancer: long-term follow-up

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**Background:** Previous randomized trials have shown improved outcomes from concurrent radiation and chemotherapy over radiation alone for Stage III non-small cell lung cancer (NSCLC). We carried out a prospective pilot study to assess the feasibility of treating medically inoperable patients with Stage I NSCLC with combination daily low dose cisplatin and small volume radiotherapy.

**Methods and Materials:** From January 1996 to November 2000, 34 consenting patients, median age 73 years, were enrolled. All patients were considered medically inoperable; with tumour size <5 cm (T1-T2, N0) and ECOG status <3. Patients received daily IV cisplatin, 6 mg/m<sup>2</sup>, followed within 30 minutes by radiotherapy. The primary tumor was treated to a dose of 55 Gy/20 fractions/4 weeks (dose calculated with lung correction). No elective nodal irradiation was given.

**Results:** Treatment was well tolerated. One patient had a myocardial infarct during treatment, but was able to complete the regimen. Six patients suffered Grade 3 toxicity (pulmonary: 4, cardiac: 2). Six patients had Grade 1–2 lung toxicity and 18 patients had Grade 1–2 nausea or anorexia. During follow-up, most patients developed in-field Grade 1 pulmonary fibrosis and 3 patients had Grade 1 subcutaneous fibrosis. Twelve patients developed recurrent disease: 7 local recurrence only; 1 simultaneous local and distant recurrence; and 4 distant relapses. No mediastinal nodal recurrences were observed. Actuarial local relapse free survival was 73% at 2 years, 66% at 3 years and 59% at 5 years. Eleven patients died of intercurrent illness. Overall survival rates were 55% at 2 years, 42% at 3 years, and 21% at 5 years. Cause specific survival rates were 71% at 2 years, 67% at 3 years and 44% at 5 years.

**Conclusion:** This regimen of and radiotherapy and concurrent low-dose cisplatin was well tolerated by patients unfit for surgery. These results are superior to those of historical controls from this institution, and compare favourably with other reported series of Stage I NSCLC patients treated with radiotherapy alone. Further study is required to assess the role of chemotherapy in early stage medically inoperable NSCLC and its integration with newer high dose radiotherapy regimens.

## 1176

## PUBLICATION

#### Lung cancer in South-East Scotland: has treatment and survival improved since 1995?

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**Aim:** A national audit of all patients diagnosed in Scotland in 1995 has previously been published, which demonstrated low use of treatment and poor survival. Since 1995 many changes have been made to the organisation and delivery of cancer treatments with the introduction of South-East Scotland Cancer Network (SCAN), treatment guidelines and multi-disciplinary working. This repeat audit has been conducted to assess the impact of these changes

**Methods:** From the Scottish Cancer Registry all cases of lung cancer diagnosed in the SCAN region (population 1.25 million) in 2002, were identified along with demographic and tumour related details. Then using SCAN prospective audit data all treatments with surgery, radiotherapy and or chemotherapy within six-months of diagnosis were identified. The median and one year overall survival were calculated. These data were then compared with the patients identified from this region in the 1995 Scottish National Audit using Chi squared and Log rank tests.

**Results:** In 1995 there were 1082 in the Cancer Registry, of which 904 were included in the audit. In 2002 there were 1017 patients, 888 in the audit.

	1995	2002
Total in audit (% of cases in registry)	904(84%)	888(87.3%)
Pathology type		
SCLC	165 (18.3%)	137(15.4%)
NSCLC	528(58.4%)	520(58.6%)
No pathology	211(23.3%)	231(26.0%)
Age		
Median	70	71
Range	38–96	37–92
Male	58.2%	56.3%
NSCLC + no pathology: Primary therapy	n = 739	n = 751
Resection	88(11.9%)	104(13.8%)
Radical radiotherapy	19(2.6%)	100(13.3%)
Palliative treatment	329(44.5%)	289(38.5%)
No treatment	303(41%)	258(34.4%)
SCLC: Primary therapy	n = 165	n = 137
Chemotherapy (± radiotherapy)	108 (65.4%)	91 (66.4%)
Overall Survival	n = 904	n = 888
Median	4.05 months	5.76 months
1 year	23.4%	30.3%

**Conclusions:** The changes in the organisation of lung cancer services have resulted in a significant increase in the use of potentially curative treatment for patients with NSCLC (P < 0.001), particularly from the increased use of radical radiotherapy. There has been a significant improvement in survival since 1995 (p < 0.01). The impact on the survival of the all lung cancer patients in the Cancer Registry is under investigation.

## 1177

## PUBLICATION

#### Combined CYP1A1/GSTM1 at-risk genotypes are overrepresented in squamous lung carcinoma patients but underrepresented in elderly tumor-free subjects

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**Background:** Polycyclic aromatic hydrocarbons (PAH) are activated by cytochrome P450 1A1 (CYP1A1) and inactivated by glutathione S-transferase mu (GSTM1). Therefore, it is expected that a combination