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^2, 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

of proficient *CYP1A1* genotype with deficient *GSTM1* variant would result in particularly elevated lung cancer (LC) risk, especially for squamous cell carcinoma (SCC).
Material and methods: In order to validate whether the *CYP1A1-C*^{3801} (*CYP1A1*2*) allele has an unfavorable significance alone and/or in combination with the *GSTM1* deficiency, we compared the genotype distribution in LC patients (n = 141), healthy donors (HD, n = 204), and elderly tumor-free smokers and non-smokers (ED, n = 246).
Results: *CYP1A1*2* allele carriers demonstrated a clear-cut association with SCC: the adjusted OR were 2.22 (95% CI = 1.06–4.63) and 2.27 (95% CI = 1.14–4.52) when HD and ED were used as referents, respectively. *CYP1A1*2(+)/GSTM1(−)* combined genotypes were overrepresented in the SCC patients (14/70, 20.0%) and underrepresented in the ED (19/246, 7.7%) as compared to the intermediate prevalence in the HD (26/204, 12.7%); the adjusted OR for SCC versus ED reached 3.85 (95% CI = 1.43–10.33).
Conclusions: In agreement with some literature data, our results support the concerted role of *CYP1A1* and *GSTM1* at-risk genotypes in SCC predisposition.

1178 PUBLICATION

Nuclear Factor-kappa B activation by TNF-alpha in mesothelial cells and expression in Malignant Mesothelioma

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Background: Nuclear Factor-kappa B (NF-κB) is a heterodimeric transcription factor central to cellular stress responses and protection against apoptosis, making it a potential target for novel anti-cancer therapies. The role of NF-κB in malignant mesothelioma (MM) is not clear.
Materials and Methods: We evaluated 1) the nuclear translocation of NF-κB in MET5A cells in response to TNFα by immunofluorescence and a nuclear protein factor p65 assay; 2) the degradation of IκBα in response to TNFα, with and without the administration of pharmacological inhibitors; 3) the expression of NF-κB by immunohistochemistry in 146 MM samples and its impact on survival. NF-κB expression was correlated with clinicopathological variables, tumour angiogenesis and necrosis and the expression of the Epidermal Growth Factor Receptor (EGFR). The impact of NF-κB expression on survival was determined.
Results: The pattern of NF-κB expression in untreated MET5A cells was cytoplasmic, with nuclear translocation occurring in response to TNFα administration. Significantly increased levels of nuclear p65 were noted at 8 and 24 hours. Degradation of IκBα was observed in MET5A cells in response to TNFα, but this was not altered by the administration of LY294002, U0126, SB20380, NS398, Iressa or vitamin E. Although cytoplasmic or membranous immunostaining was seen in the majority of tumour samples (96.5%), nuclear localisation of NF-κB was seen in only 11% cases. There was no significant correlation between the level of expression of NF-κB and standard clinicopathological prognostic factors. NF-κB correlated with the expression of EGFR ($p = 0.001$). Survival analysis showed that nuclear NF-κB expression was associated with reduced survival ($p = 0.04$), whereas cytoplasmic expression was not ($p = 0.7$).
Conclusions: NF-κB is activated in MET5A human mesothelial cells in response to TNFα. NF-κB expression is a common feature of MPM and may be a novel prognostic factor. NF-κB may play an important role in the carcinogenesis of MM. NF-κB may be a valid therapeutic target for novel therapies in MPM.

1179 PUBLICATION

EGFR mutation in lung cancers treated by Gefitinib in Thailand

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Background: The sub-group analysis of IDEAL 1 and IDEAL 2 gefitinib studies interested us in that the objective response rate (ORR) of Japanese NSCLC patients fared better than that of Caucasian counterpart. We started our work in Thailand recently by using the mutation study of EGFR gene reported recently by Lynch et al and Paez et al. We ask two questions: 1) Do gefitinib responders of THAI Ethnicity have EGFR mutations as seen in other studies? 2) Is the EGFR mutation rate in THAI NSCLC patients with no gefitinib treatment higher than that of international standard ?
Materials: Fresh lung tumor tissues and or tissue paraffin blocks of six Thai NSCLC gefitinib responders were studied by DNA extraction followed by PCR and DNA Sequencing. Normal DNA pair of each patient was obtained from their own blood leukocytes. DNA from 4 NSCLC patients of our own study who have yet to start gefitinib treatment and 10 additional DNA samples from NSCLC Archives tissue paraffin blocks and from frozen tissue bank were studied for the baseline EGFR mutation rate.
Results:
1. All six gefitinib responders have EGFR gene mutations 6/6 (100%).
2. Deletions and point mutations were among the most commonly found events, however, the base insertions have also been found often in exon 21.
3. Our preliminary data of DNA from 12 NSCLC samples without treatment have mutation rate of 4 /14 (28.5%) in their EGFR genes, exons 19 and 21.

Conclusion:
1. For Non small cell lung cancer, EGFR gene mutations at the Tyrosine Kinase Domain appeared to be required for objective gefitinib response.
2. Our preliminary data, even still small in number, appeared to suggest the high mutation rate in NSCLC in Thai Ethnic patients. Perhaps, this could explain the high success rate of gefitinib treatment in Asian countries. Further study is needed to substantiate our findings.

1180 PUBLICATION

The role of TTF1 as prognostic factor in stage III non-small cell lung cancer (NSCLC)

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Background: The 1997 International Staging System (ISS) separated stage III NSCLC patients into IIIA and IIIB. Stage III NSCLC represents a heterogeneous group and the ISS remains unsatisfactory in term of prognosis prediction. In a previous study, we observed that survival was better predicted when unresectable NSCLC patients were classified into stages IIIβ (T3–4N3) and IIIá (other TN stage III). The aim of the present study was to determine the role of a biological factor, TTF1 (thyroid transcription factor 1) as prognostic factor in stage III NSCLC in addition to stage and other known clinical factors.
Material and methods: All stage III NSCLC patients treated in our hospital were retrieved and searched for biopsy specimens. TTF1 was assessed by immunohistochemistry (Novocastra SPT24).
Results: Between 01/1987 and 07/2003, 108 assessable stage III NSCLC patients, for whom biopsies were available, were included in the study. Their principal characteristics were: median age 64 years (range 37–83), male/female 81/27, squamous/non squamous 52/56, IIIA/IIIB 44/64, III/III 89/16, median Karnofsky PS 80 (range 20–100). They were treated according to the following modalities: chemotherapy alone 44, radiotherapy alone 15, surgery alone 3 and combined treatment 46. Forty-four patients were positive for TTF1 (squamous 25.0% vs non-squamous 55.4%; $p = 0.007$). Nineteen patients were alive at the time of analysis (05/2005). In univariate analysis, good PS, surgery, normal platelet count were found good prognostic factors for survival ($p < 0.05$). In multivariate analysis, including all variables with a p value less than 0.2 in univariate analysis, only 3 factors were statistically significantly associated with better survival: good PS ($p = 0.005$), surgery ($p = 0.004$) and creatinine level ($p = 0.02$). When the analysis was restricted to adenocarcinoma or to non-squamous histology, TTF1 was found a potential prognostic factor for survival in univariate analysis ($p < 0.05$).
Conclusion: In stage III NSCLC patients, good PS, resectability and low creatinine level but not TTF1 are prognostic factors for survival. Nevertheless, TTF1 appears a potential prognostic factor for survival in adenocarcinoma.

1181 PUBLICATION

Bcl-2 family proteins and lymph node metastasis in bronchopulmonary carcinoid tumors

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Apoptosis or programmed cell death is a regulated process responsible for deletion of single cells in normal tissue turnover, allowing the organism to tightly control cell numbers and tissue size. The Bcl-2 family of proteins, which has a crucial role in intracellular apoptotic signal transduction, is composed by pro-apoptotic (Bax) and anti-apoptotic (Bcl-2) members. The objective of this study was to survey the occurrence of apoptosis in