Symposia

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RESECTION: ARE THERE LIMITATIONS?
P.E. Postmus

For non small cell lung cancer surgery is the only treatment with a real perspective of long term survival. Especially patients with stage I and stage II benefit from this approach. Whether additional therapy might be beneficial as well is currently under investigation. In daily clinical practice a number of patients present with roentgenologically occult stage I tumours. For these patients endobronchial therapy can also lead to cure. Indications and limitations of this approach will be discussed. With the improvement of diagnostic techniques the detection of small pulmonary nodules has been improved as well in patients with operable non-small cell lung cancer one often has to face the problem of an additional solitary pulmonary nodule: is this a benign or malignant lesion, is it a second primary or a metastasis? In these patients diagnostic and therapeutic thoracoscopy prevents in a number of cases open-and-close thoracotomies and facilitates post-operative recovery prior to the resection of the pathologically proven primary. Another therapeutic problem is the detection of a synchronous single brain metastasis in a patient with an otherwise resectable primary lung tumour. Results of resection of synchronous or metachronous M1 disease will be discussed. Or if this occurs in the lung what are the problems of differentiating M1 and a second primary and possibilities of resections after an earlier thoracotomy?

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ENDOBRONCHIAL THERAPIES
P. Baas
The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

In the majority of NSCLC cases, the tumour will be located in the central part of the tracheo-bronchial tree resulting in dyspnoea, haemoptysis, infection or stridor. In spite of external irradiation many patients will suffer from local recurrence. For these patients and those with significant impairment of pulmonary function, endobronchial treatments are increasingly important. The Nd-YAG laser is most often used to desobstruct the trachea and central bronchi. It emits at a wavelength of 1,064 nm which can be conducted by quartz filaments. Due to the high power used to evaporate or carbonate the tissue, high temperatures will develop. In endobronchial irradiation (brachy-therapy), a radioactive source (Ir-192) is transported via an endobronchial placed catheter to irradiate the tumour at high local doses. Photodynamic therapy (PDT) is a relatively new local treatment modality which has shown considerable advantages with respect to the preservation of normal tissue. Specific laserlight is used to activate a photosensitizer, retained preferentially in the tumour. In the presence of oxygen the photochemical reaction will lead to the production of highly active singlet oxygen. The local application of light to the tumour will lead to selective necrosis. This form of treatment appears to be especially useful in early stage lung cancer.

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LUNG CANCER—WHAT NOW? ADJUVANT CHEMOTHERAPY IN LIMITED NON-SMALL CELL LUNG CANCER
Thierry Le Chevalier
Institut Gustave-Roussy, Villejuif, France

The main curative treatment of non-small cell lung cancer (NSCLC) is surgery. Nevertheless, after surgical resection, more than 50% of patients will die with local and/or distant relapse. Adjuvant treatments have been widely evaluated during the last decades and none has proven to be clearly efficient. A recent meta-analysis using updated individual data from 4357 patients included in 14 trials investigated the value of adjuvant chemotherapy (CT) in NSCLC after surgical resection. In seven of these trials a cisplatin-based regimen was administered and a relative benefit of 13% in terms of death reduction was observed with adjuvant CT. This constitutes a rationale for large scale trials testing prospectively this hypothesis and several adjuvant studies have already been initiated worldwide. Pre-operative chemotherapy has also been evaluated through numerous phase II studies with promising results. A significant advantage has been observed in 2 recent phase III studies enrolling mainly stage IIIA patients. A large French randomized trial including patients with stage I and II disease is currently ongoing. This study has already included more than 270 patients and should clearly define the role of preoperative CT in this setting.

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HAVE THE NEW AGENTS DEVELOPED IN THE EARLY 1990s CHANGED THE TREATMENT OF LUNG CANCER?
Heine H. Hansen
The Finsen Center, Copenhagen, Denmark

After a decade-long standstill a number of new groups of compounds has been developed showing activity in lung cancer.

These include: Taxanes (paclitaxel, docetaxel)
Topoisomerase inhibitors (topotecan, irinotecan)
Antimetabolites (gemcitabine)
Vinca alcaloids (navelbine)

These agents have all yielded response rates of 15–30% in phase II trials and a number of extended phase II trials are ongoing combining these agents with existing active compounds in SCLC and NSCLC. In addition, several phase III trials have been initiated evaluating the effect of these compounds on survival and quality of life.

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GENE THERAPY IN LUNG CANCER
T. Tursz
Institut Gustave-Roussy (IGR), Villejuif, France

We have initiated a feasibility study to investigate gene transfer in non-small cell lung cancer (NSCLC). Our vector is a recombinant replication-defective adenovirus of the Ad-5 subtype, deleted in the E1 and E3 subregions and containing the reporter bacterial gene β galactosidase (βgal), under the control of the strong ubiquitous promoter of the Rous Sarcoma Virus (RSV). The recombinant adenovirus (Ad-RSVβgal) was constructed by M. Perricaudet (IGR, Villejuif) and produced under GMP conditions by Transgene, Strasbourg, France. Six patients (pts) with non-resectable NSCLC have been included and isolated in TL-2 containment conditions for the duration of the study. They have received an intra-tumor infusion of a viral suspension of Ad-RSV-βgal under fibroscopic guidance (10^7pfu:3 pts, 10^8pfu: 3 pts) and concomitant chemotherapy (Vinorelbine-Cis-Platinum). All have signed an informed consent form. No particular toxicity has been attributable to the viral injection. Ad-RSV-βgal was detected in expectoration or bronchial fluids by PCR analysis for up to 15 days while pts remained in isolation. No transmission of Ad-RSV-βgal to hospital personnel has been demonstrated. No replicative infectious adenovirus has been detected throughout the study neither in pts nor in hospital staff. Effective gene transfer has been demonstrated by histochemical staining of βgal enzymatic activity in subsequent tumor biopsies from 2 pts who received 10^8 pfu.

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PREDICTION OF DCIS SUBTYPE AND EXTENSION ON A MAMMOGRAPHIC BASIS
S. Ciatto
Centro per lo Studio e la Prevenzione Oncologica, Viale A. Volta 171, I-50131 Firenze, Italy

Differential diagnosis between benign and malignant isolated microcalcifications may be difficult at mammography, the B/M biopsy ratio being usually 3:1 or higher in the current practice. Typical calcification patterns associated with comedo/non-comedo DCIS have been described but they are not clinically reliable as the error rate is about 20%. Even prediction of invasive or intraductal nature is unreliable on a radiological basis. DCIS may extend beyond microcalcifications, but X-ray oriented slicing of the specimen is fundamental for proper pathological assessment of DCIS size as DCIS may be asymmetric in shape and orientation cannot be based on palpation as most cases are not palpable even in the fresh specimen.