

## Thoracic Cancer Program

**Melvyn Goldberg, M.D., F.R.C.S.C.,** *Senior Member, Co-Director, Thoracic Oncologic Program*

**Walter J. Scott, M.D., F.A.C.S.,** *Member*

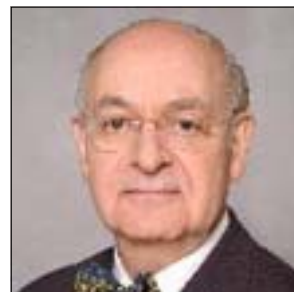
**Patricia Thompson, R.N.,** *Nurse, Outpatient Department*

**Jessie Scholl, R.N.,** *Nurse, Outpatient Department*

**Christine Kappler, M.A.,** *Medical Assistant, Outpatient Department*

**Rose Vickers,** *Administrative Assistant*

The clinical and research programs of the division of thoracic oncology focus primarily on malignancies of the lung and esophagus. The division participates in clinical trials sponsored by three intergroups: ACOSOG, ECOG, and RTOG. We also have initiated several studies that are exclusive to Fox Chase Cancer Center (FCCC), primarily as feasibility and investigative studies that may proceed to intergroup trials at a future date.



**American College of Surgeons Oncologic Group (ACOSOG)** ACOSOG trials Z0030 and Z0040 have been completed and within the year the results of these studies will be reported. In the Z0030 study, random biopsies of mediastinal lymph nodes were compared to radical mediastinal lymphadenectomy with respect to local complications and survival. In the second study, (Z0040), tissues extracted at the time of operative intervention were examined for cytokeratin positive micrometastatic disease utilizing specimens from bone marrow, pleural lavage and mediastinal lymph nodes. Presently we are participating in ACOSOG Z4031 utilizing proteomic analysis of serum samples for detection of non-small cell lung cancers. The objective of this study is to determine prospectively whether the serum proteomic profile can predict the presence of primary non-small cell lung cancer in patients with suspicious lung lesions who are candidates for lung resection. Several secondary objectives include: 1) to correlate the serum proteomic profile with pathologic nodal status and histopathologic features of primary lung cancer in patients with non-small cell lung cancer undergoing lung resection; 2) to correlate the initial serum proteomic profile overall and cancer specific survival; 3) to correlate the follow up serum proteomic profile with overall and cancer specific survival; and 4) to correlate changes in the proteomic profile (preoperative to postoperative) with overall and cancer specific survival.

**Eastern Cooperative Oncologic Group (ECOG).**

We are engaged in ECOG 5597 which is a phase III chemoprevention trial of selenium supplementation in persons with resected Stage I non-small cell lung cancer. The objectives of this trial are: 1) to evaluate the efficiency of selenium supplementation reducing the incidence of second primary lung tumors in patients that have been treated for Stage I non-small cell lung cancer; 2) to evaluate the qualitative and quantitative toxicity of selenium supplementation; and 3) to compare the incidence of specific cancer and mortality from cancer as well as overall survival of patients treated with selenium supplementation versus patients treated with placebo. We also participate in ECOG S9925, which is a lung cancer specimen repository protocol. The objectives of this trial are: 1) establish a central lung cancer specimen repository to serve as a resource for current and future scientific studies; 2) utilize the SWOG clinical data base to perform clinical pathological correlation with the results of those studies; and 3) test new hypotheses as they emerge. ECOG S9900 was a randomized phase III trial of surgery alone versus surgery plus preoperative paclitaxel/carboplatin in clinical Stage Ib (T2N0), II (T1-2N1, T3N0) and selected IIIa (T3N1) non-small cell lung cancer. Recently, in three independent studies there has been evidence of the value of postoperative adjuvant therapy in patients undergoing curative resection for all diseases exclusive of Stage Ia. As a result of that information ECOG S9900 was

prematurely closed since it advocated a new trial utilizing induction therapy rather than adjuvant therapy.

**Fox Chase Cancer Center Protocols.** We are conducting a study that examines trimodality therapy for the treatment of locally advanced potentially resectable non-small cell lung cancer (NSCLC). The objectives are to assess clinical and pathologic response rate, incidence of PCR, resection rate, progression free survival, median survival and overall survival of patients undergoing aggressive trimodality therapy for Pancoast tumors, resectable chest wall tumors, marginally resectable T4N1-0 NSCLC, and IIIa N2 NSCLC. A secondary objective is to determine toxicity and tolerance of combined chemoradiation therapy in this setting. A second study is evaluating esophageal motion by computed tomography during the course of radiation therapy for thoracic malignancies. The primary objective of this study is to determine inter and intra fraction movement of the esophagus. We are performing a phase I study of preoperative chemoradiation therapy (concurrent CPT-11/cisplatin/RT) followed by surgery in limited stage small cell lung cancer. The primary objectives of this study are to determine the safety and feasibility of preoperative chemoradiation therapy followed by surgery in limited stage small cell lung cancer and to determine the pathologic complete response rate utilizing this regimen.

**Radiation Therapy Oncologic Group (RTOG).** RTOG 0246 is a phase II study of a paclitaxel-based chemoradiotherapy regimen with selective surgical resection of local or regionally advanced carcinoma of the esophagus. The objective of this study is to determine the feasibility of a non-operative approach with chemotherapy, concurrent chemoradiation, and selective surgical salvage. Secondary objectives include the determination of standard criteria for salvage therapy with serial CT scan, serial endoscopy, and ultrasound and serial PET scans. The study will also try to estimate the overall survival of patients who have the selective surgical strategy; other efficiency outcomes such as disease free survival will also be estimated. RTOG 0214 is a phase III comparison of prophylactic cranial irradiation versus observation in patients with locally advanced non-small cell lung cancer. The primary objective of this study is to determine

whether prophylactic cranial irradiation (PCI) improves survival after effective locoregional/systemic therapy for patients with locally advanced non-small cell lung cancer.

**Collaboration with Behavioral Science. (Schnoll,<sup>§</sup> Ridge).** R. Schnoll and colleagues are studying correlates of tobacco use among smokers and recent quitters diagnosed with cancer and the longitudinal predictors of continued tobacco use among patients diagnosed with cancer. Other investigations involve relating the trans-theoretical model processes of change to continued smoking among cancer patients and documenting the prevalence and correlates of smoking and readiness to quit among cancer patients. Presently, we are involved in a randomized clinical smoking cessation trial involving bupropion in patients that continue to smoke after a curative pulmonary resection.

**Collaboration with M. Clapper.<sup>§</sup>** A study is being conducted in collaboration with M. Clapper and S. Meireles<sup>§</sup> to assess the contribution of estrogen metabolizing enzymes to risk for smoking-induced lung cancer. Rationale for this study is based on preclinical data from Clapper's laboratory, which indicate that cytochrome P450 1B1 (CYP1B1) is induced dramatically within the lungs of mice exposed to tobacco smoke. In order to determine the clinical relevance of this finding, samples of peripheral blood and lung tissue from lung cancer patients undergoing surgery at FCCC are currently being evaluated for polymorphic expression of CYP1B1 and the transcript levels of several enzymes involved in estrogen biosynthesis and metabolism. The dual role of CYP1B1 in the conversion of both smoke-related carcinogens and estrogen to derivatives that can form DNA adducts suggests that CYP1B1 may contribute significantly to the increased susceptibility of women for lung cancer.

**Summary.** We continue to be actively engaged in discussions regarding future protocols with our intergroups. Future investigations and patient management will include: 1) percutaneous radiofrequency ablation for both primary and secondary tumors in patients that can not undergo resection; 2) a comparison of wedge resection in peripheral non-small cell lung cancer less than 2 cm in diameter with formal lobec-

tomy; 3) evaluation of the survival benefit of radical mediastinal lymphadenectomy; 4) the value of PET scan in evaluating response to induction chemoradiation therapy prior to surgery; 5) the

role of video assisted thoracoscopy lung resection and esophagectomy; and 6) the evaluation of novel and innovative techniques for definitive treatment of high grade Barrett's esophagus.

## Publications

Berger, A.C., Farma, J., Scott, W.J., Goldberg, M., et al. Complete response to neoadjuvant chemoradiation therapy in esophageal carcinoma is associated with significantly improved survival. *J. Clin. Oncol.* **23**:4330-4337, 2005.

Berger, A.C., Scott, W.J., Freedman, G., Konski, A., Weiner, L., Cheng, J.D., Goldberg, M. Morbidity and mortality are not increased after induction chemoradiotherapy followed by esophagectomy in patients with esophageal cancer. *Semin. Oncol.* **32**(9):S16-S20, 2005.

Burkes, R.L., Shepherd, F.A., Blackstein, M.E., Goldberg, M.E., Waters, P.F., Patterson, G.A., Todd, T., Pearson, F.G., Jones, D., Farooq, S., McGlaughlin, J., Ginsberg, R.J. Induction chemotherapy with mitomycin, vindesine and cisplatin for Stage IIIA (T1-3, N2) unresectable non-small-cell lung cancer: final results of the Toronto phase II trial. *Lung Cancer* **47**:103-109, 2005.

Goldberg, M. Multimodality treatment of esophageal adenocarcinoma. *Am. J. Oncol. Rev.* **4**:759-762, 2005.

Goldberg, M., Gupta, D., Sasson, A.R., Movsas, B., Langer, C.J., Hanlon, A.L., Scott, W.J. The surgical management of superior sulcus tumors – A retrospective review with long term follow-up. *Ann. Thorac. Surg.* **79**:1174-1179, 2005.

Henry, L.R., Goldberg, M., Scott, W., et al. Cisplatin and Paclitaxel, followed by combination chemoradiotherapy with 5-FU, Cisplatin and Paclitaxel prior to resection in localized esophageal cancer – A phase II report. *Ann. Surg. Oncol.* **13**:214-220, 2006.

Nguyen, C., Scott, W., Goldberg, M. Radiofrequency ablation of primary lung cancer: Results from an ablate and resect pilot study. *Chest* **128**:3507-3511, 2005.

Schnoll, R.A., Rothman, R.L., Wielt, D.B., Goldberg, M., et al. A randomized pilot study of cognitive-behavioral therapy vs. basic health education for smoking cessation among cancer patients. *Ann. Behav. Med.* **30**:1-11, 2005.

<sup>8</sup> Fox Chase researcher