

**February 28, 2003 Meeting of the
General and Plastic Surgery Devices Advisory Panel**

Background Information: Ablation of Lung Tumors

Lung cancer is among the most commonly occurring malignancies in the world, and in the U.S., is the leading cause of cancer death in men and women. In the year 2000, there were approximately 164,000 new cases and approximately 157,000 deaths from this disease.¹ Pulmonary metastases are also a significant health care concern and are common in patients with a variety of cancer. Approximately 30% of patients with cancer develop pulmonary metastases.

For patients with primary lung cancer, surgery provides the best chance for a cure. For Stage I and stage II lung cancer, the 5 year survival rate with recurrence exceeds 50% in stage I and 35% in stage II. In completely resected tumors, the 5-year survival rate exceeds 70%. However, many patients are not surgical candidates at the time of diagnosis. This may include patients with poor pulmonary reserve, co-morbid conditions or widespread disease at diagnosis. For these patients, an alternative is radiation therapy. Reported 5-year mortality results for patients treated with radiation therapy alone for early stage lung cancer ranged from 8 to 32%.¹ Chemotherapy alone and in combination with radiation therapy have also been used. For patients with Stage IV primary lung cancer, chemotherapy alone is used to relieve symptoms and provide a minor prolongation of survival time.

For patients with pulmonary metastases, systemic chemotherapy cannot completely eliminate pulmonary metastases arising from many solid cancers, and surgical resection of the metastatic tumor may be used. As in the case of surgical resection of primary pulmonary tumors, there may be patients who are not surgical candidates for resection of the metastatic tumor, due to the presence of co-morbid conditions, recurrent disease, bilateral disease to the lung, or limited extrathoracic disease.

As an alternative to open surgical resection, various localized ablation techniques have been considered to achieve local control of lung tumors. Please note that in the context of this discussion, we consider the term “ablation” to be synonymous with coagulation necrosis. The use of radiofrequency (RF) ablation for the treatment of pulmonary tumors has been described in the literature.²⁻⁹ Copies of relevant articles have been included in this background package.

Devices designed to ablate tissue using RF energy have been approved by the FDA for a variety of different surgical indications. At this time, no ablation device has been cleared by the FDA specifically for the treatment of lung tumors.

The purpose of this panel meeting is to solicit input from the panel members on the type of clinical data that you believe would be needed to support FDA clearance of ablation or coagulation necrosis devices for the specific indication of destruction of malignant

tumors (primary and metastatic) in the lung. Although the literature articles describe the use of RF ablation devices, we are seeking general comments that could be used to support marketing applications for ablation/coagulation necrosis devices using any technology (including cyroablation, microwave ablation, etc.) Your comments on the appropriate study design may be different based on the patient population to be treated and the goals of the therapy.

Questions for the Panel to Consider:

1. Please discuss where you believe that ablation as a means of local control may fit into the current armamentarium of treatments for lung cancer. Local control may mean reduction, stabilization or a decrease in the growth of tumor size. Please describe the specific patients for which this treatment may be appropriate, in terms of extent of disease, size of the tumor(s), and evidence of failure of other treatments.
2. Please discuss what you believe to be the appropriate endpoints for a study to demonstrate the effectiveness of ablation devices for the treatment of primary and secondary lung malignancies, e.g., increase in survival, reduction in tumor size, improvement in symptoms, improvement in quality of life.
3. Please discuss the imaging modalities that you believe would be appropriate to assess tumor size during these studies.
4. The duration of follow-up should allow FDA to adequately assess the safety and effectiveness of treatment with these devices. Please comment on what you believe to be the appropriate duration of follow-up for a pivotal clinical study for these devices.
5. Please describe the appropriate control group, endpoints and duration of follow-up for a clinical study of an ablation device that is to be used in place of surgical resection of lung tumors for patients who would be considered operable.

Background Literature Articles

- 1) Cancer: Principles and Practice of Oncology, Vol 1, 6th edition, Lippincott, Williams and Wilkins, 2001.
- 2) LaVeen, H.H., Wapnick, S., Piccone, V., Falk, G., Ahmed, N. "Tumor Eradication by Radiofrequency Therapy", *JAMA*, 235:20 (1976).
- 3) Dupuy, D.E., Mayo-Smith, W., Abbott, G.F., "Clinical Applications of Radio-Frequency Tumor Ablation in the Thorax", *Radiographics*, 22:S259-269 (2002).
- 4) Rose, S.C., Fotoohi, M., Levin, D.L., Harrell, J.H., "Cerebral Microembolization during Radiofrequency Ablation of Lung Malignancies", *J. Vasc. Interv. Radiol.*, 13:1051-1054 (2002).
- 5) Nishida, T., Inoue, K., Kawata, Y., Izumi, N., Nishiyama, N., Kinoshita, H., Matsuoka, T., Toyoshima, M., "Percutaneous Radiofrequency Ablation of Lung Neoplasms: A Minimally Invasive Strategy for Inoperable Patients", *JACS*, 195(3):426-430 (2002).
- 6) Vaughn, C., Mychaskiw, G., Sewell, P., "Massive Hemorrhage during Radiofrequency Ablation of a Pulmonary Neoplasm", *Anesth. Analg.*, 94:1149-51 (2002).
- 7) Choi, J.Y., Kang, S., Byun, J., Kim, Y., Kim, Y., Lee, S., "Radiofrequency Ablation of Lung Cancer: Preliminary Report", *J. Korean Radiol. Soc.*, 45:271-275 (2001).
- 8) Dupuy, D., Zagoria, R., Akerley, W., Mayo-Smith, W., Kavanagh, P., Safran, H., "Percutaneous Radiofrequency Ablation of Malignancies in the Lung", *AJR*, 174, (2000).
- 9) Karasawa, K., Muta, N., Nakagawa, K., Hasezawa, K., Terahara, A., Onogi, Y., Sakata, K., Aoki, Y., Sasaki, Y., Akanuma, A., "Thermoradiotherapy in the Treatment of Locally Advanced Nonsmall Cell Lung Cancer" *Int. J. Radiation Oncology Biol. Phys.*, 30:5, 1171-1177 (1994).