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RADIATION DOSE AND LIMITED SMALL CELL CARCINOMA OF THE LUNG

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Author Roof**

Small cell carcinoma is one of the cancers that are responsive to both chemotherapy and radiation. Years ago it was found to be probably the most responsive to chemotherapy.

Studies have shown that for patients who have radiation and chemotherapy when the cancer is confined to the chest, the survival rate is improved. In general, there are two stages for small cell carcinoma. Another name for small cell carcinoma is oat cell carcinoma.

One stage - when the cancer is confined to the chest - is called limited stage. Beyond the chest cavity, it is called extensive stage. There are a few exceptions. This is important because nearly 200,000 Americans have lung cancer each year. Twenty percent have small cell carcinoma. Most people, about 3 out of 4, with small cell carcinoma have extensive stage cancer. In general, chemotherapy is used for palliation. The remainder had limited stage cancer and were more likely to be cured with aggressive radiation and chemotherapy. This is indeed the standard of care.

There are a variety of issues with those having small cell carcinoma including the radiation dose and the schedule as well as the sequence of radiation and chemotherapy. The addition of radiation to combination chemotherapy improves survival. But local failure rates remain quite high. Therefore, a major issue is how to improve radiation so as to minimize local recurrence.

Many physicians believe that if there is local recurrence that is where the cancer originally arose and can be reduced, then it is possible to have higher survival rate. The cancer has been reduced by giving radiation twice daily versus once daily. A recent study giving the same total dose showed a 75% failure

rate with once-a-day treatment versus 42% with twice-a-day treatment. Overall survival was seen in patients given twice daily radiation with improved local control and improved survival. That would suggest that better local treatment could mean better cancer outcome.

Recently reported by Roof et al in the prestigious International Journal of Radiation Oncology Biology and Physics was a report showing the use of greater than 50gray radiation in limited stage small cell carcinoma. Over a thirteen year span, between 1987 and 2000, 84 patients with limited stage small cell carcinoma were treated with radiation in a single hospital, 54 were in the primary analysis with 30 patients excluded because of low radiation doses of less than 50 gray, others having cancer surgery and palliative intent. Seventeen patients with doses less than 50 gray were excluded because of the lower dose radiation having previously reported.

All reports were reviewed along with radiology reports, pathology reports, operative notes, endoscopy notes, and other important documents. The timing of chemotherapy and radiation were included. Complications were reported as well. Patients received external beam radiation with simulation taking place. Usually the fields were quite simple involving treatment from the front and the back. Chemotherapies had been used during the same time including Cisplatin, Cytoxan, Etoposide, Adriamycin, and other drugs.

The median age was 63 years with a range of 38 to 80. All patients had limited stage lung carcinoma, oat cell type. The most common toxicity was lowering of the white blood count which occurred in 78% of patients and 24% of the patients had fever with white blood count requiring hospitalization. Two patients died of infection during the lowering of the white blood count due to chemotherapy. Treatment related deaths included one with diffuse alveolar damage of the lung after chemotherapy and radiation. Another had scarring of the lung after two cycles of chemotherapy and radiation and a third had pulmonary complications due to infection. One patient died of acute leukemia after being cured of small cell carcinoma and another died of multiple myelomas after being cured of the lung cancer.

The median follow-up for surviving patients was 42 months with a range of 7 to 116. Of 54 patients in this study, 30 patients or 56% died and 7% were lost to follow-up. The median progression-free survival and overall survival for the group was 25 months and 29 months respectively. The median progression-free survival was 25 months and overall survival estimate was 29 months. Progression-free survival at two years was 55% and at 5 years 43%.

When all patients treated with more than or equal to 50 gray were included even those being treated so called palliatively, the two year survival was 61% and five year survival was 46%. Of those 24 patients treated with curative intent who had distal failure, 12 had local failure and 12 had distant metastases. Of 12 patients with local failure, 3 had distant metastases concurrently. Reporting distant metastases free survival was seen in patients who received the greater dose. Patients who had the 63 gray median dose had a trend but did not statistically do better than the group with a dose of 54 gray. It was felt that the patient numbers were too small to be meaningful.

The authors concluded that, "Although we did not find a significant difference in outcome between the lower dose arm and the higher dose arm in this study, the study was not powered to demonstrate such a finding. The study did, however, show that patients treated with a median dose of 57 gray of once-daily radiation did not have excessive toxicity. Furthermore, the prolongation of the overall treatment time did not appear to have a negative affect on the outcomes of these patients because these patients enjoyed survival outcomes comparable to, or better than, those seen with the maximal tolerate dose of twice-daily radiation therapy. These findings suggest that future studies should examine the optimal method of radiation dose intensification by comparing the outcomes of patients treated with the maximal tolerated dose of twice-daily therapy with those of patients treated with higher doses of daily fractionated radiation therapy."

This study is interesting and leads to dose escalation. Our own physicians have offered higher dose radiation to patients through the informed consent process.

Body radiosurgery allows a more precise method of radiation than described in this paper. Patients are placed in the stereotactic frame with custom molding and computerized guidance of radiation beams. Significant higher radiation doses can be used for small cell and non-small cell carcinoma. We can use this technology to boost the radiation dose at the time of diagnosis and in fact even treat people with local recurrence if standard radiation and chemotherapy has not worked.

Our local control rate, that is control in the treated field, is approximately 80%.