AbstractID: 6984 Title: Application of Hypofractionation in the Lung

While some groups are pursuing traditional dose per fraction hypofractionation in treating non-small cell lung cancer (NSCLC), more investigation in recent years has been in characterizing the delivery of ablative dose fractionation using stereotactic body radiation therapy (SBRT) techniques. Ablative treatments by definition disrupt both cellular clonagenic capacity (i.e., cellular division) as well as functional capacity (e.g., secretion from a gland). Ablative treatments given in the thyroid via systemic brachytherapy have been associated with higher rates of ultimate tumor local control than conventionally fractionated radiation therapy (CFRT). The same has been observed in the treatment of lung cancer.

Lung cancer, unlike prostate cancer, constitutes an immediate threat to survival in all stages of presentation. Failure to control local irradiated tumor is common after most schedules of CFRT and typically leads to metastatic spread, suffering, and death. In these circumstances, the balance of treatment related benefit and toxicity would favor more heroic efforts to control tumor as recurrence inherently leads to morbidity. Investigation of ablative dose SBRT has been carried out mostly in medically inoperable patients whose inherent tolerance of therapy is limited at baseline. Still, this therapy has been shown in mostly small phase II and retrospective reports to improve local control dramatically compared to historical CFRT. More surprisingly, even with biologically potent prescription, tolerance has been mostly acceptable. The more potent dose prescriptions have been problematic near serial functioning central lung structures, and more investigation is required for finding adequate therapy for these patients.

Unfortunately, many practitioners insist on applying understanding from CFRT toward SBRT even when observed data is inconsistent. For example, radiobiological models derived from the linear quadratic polynomial fit from CFRT have been shown to grossly overestimate the biological and clinical response to SBRT. Realistically, both new basic science investigation and clinical outcome assessment needs to be performed for dose per fraction 8-30+ Gy. Very importantly, outcomes in patients must be measured with long and mature follow-up. This is true for both assessing local control (failure occurs very late) as well as for the classic late toxicity.

References

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Objective:

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1. Explore the rationale and goals of applying very large dose per fraction radiation delivery for patients with early stage NSCLC
2. Understand variations in toxicity based on tissue architecture (e.g., serial vs. parallel tissues)
3. Be apprised of results of clinical trials using such hypofractionation in lung cancer.