

AbstractID: 9825 Title: Introduction to Extracranial Stereotactic Radiosurgery: III.
Radiobiological Considerations and Future Directions

Extracranial stereotactic radiosurgery (ESR) provides fertile ground for investigations across a range of radiobiological and clinical topics. Because ESR involves the administration of tightly constructed dose distributions targeting discrete tumor nodules in a shortened, hypofractionated course of treatment, the relationship between radiation dose and tumoricidal effect may be studied without the same potential concerns regarding tumor cell repopulation that apply during conventionally fractionated external beam radiotherapy. Careful longitudinal observations of tumor control and normal tissue complications following ESR can yield insight into true *in vivo* radiosensitivity parameters. However, the frequently substantial inhomogeneity of ESR dose distributions obliges careful thought in the interpretation of dose-response relationships. It can be argued that a composite description of the dose-volume histogram, for example the equivalent uniform dose (EUD), is essential to control for widely variable dose hotspots provided by different techniques of ESR. Among the many possible avenues for future investigations of ESR would be the combination of ESR with a radiosensitizer, for instance an enhancer of oxygen delivery such as RSR13, to exploit the typical fraction size dependence of radiosensitization via oxygen delivery enhancement or other chemical modification. Clinical trials currently underway at the moment, of course, address more straightforward phase I/II endpoints, and the rationale and design of lung and liver ESR protocols currently ongoing at several institutions will be presented. In conclusion, planned cooperative group protocols in ESR will also be discussed.