The Radiosurgery Society (RSS) Public Comment Invitation: Consensus Guidelines for the Design of Clinical Trials in Spatially Fractionated Radiation Therapy (SFRT) for Head and Neck Cancer

Consensus Guideline Development Methodology

To advance the development of clinical trials in the field of SFRT, the Clinical Working Group of the *RSS GRID/Lattice, Microbeam and Flash Radiotherapy Working Groups* is developing a guideline/recommendations for clinical trial design through a consensus effort among experts in individual malignancies that may be considered for treatment with SFRT, and among the SFRT community.

This description provides a general overview of the consensus development methodology. The process includes a systematic review of evidence in the literature, voting on clinical trial criteria among experts in the field, and development of the guideline by a multi-disciplinary disease-site specific Expert Panel. Disease-specific Expert Panels are selected based on their scientific output and clinical practice record in SFRT and in SFRT for the specific disease site.

The consensus guideline for clinical trial design are developed according to the following structured process:

1. Literature review and development of initial criteria for clinical trial design through an expert group:
   A comprehensive review of the literature is carried out, and an initial group of nationally/internationally recognized experts is convened to develop proposed criteria for clinical trial design that address the general clinical trial elements (e.g. eligibility, treatment, outcome assessments).

2. First voting round: Rating of the appropriateness of proposed trial design criteria:
   Based on the proposed trial design criteria (as determined by the initial expert group) a voting survey is conducted among SFRT experts within the respective primary tumor disease site (e.g. head and neck cancer). The proposed criteria are voted upon with a voting survey that uses a scale of 1 through 9 (“not appropriate” through “highly appropriate”) and solicits additional recommendations and comments.

3. Review and discussion of voting results by disease-specific SFRT Expert Panel:
   The aggregated anonymized results of the initial vote are reviewed and discussed by a disease-specific Expert Panel in iterative consensus calls/communications according to

the modified Delphi process. Iterative voting rounds (see section 4) are conducted as needed. The disease-specific Expert Panel consists of 3 clinicians with expertise in SFRT in the specific disease site (e.g. for SFRT in head and neck cancer), a physicist and a basic scientist.

4. Iterative voting:
   Additional voting round(s), focused on areas where consensus is not achieved or for additional clinical trial design considerations, are held as decided upon by the disease-specific Expert Panel. Voting results are reviewed and discussed by the Expert Panel as described in section 3.

5. Repeat literature review:
   The comprehensive literature review (described in section 1) is repeated to assess the literature for interval publications. Any additionally identified publications are reviewed by the disease-specific Expert Panel.

6. Development of draft guideline/recommendations and review:
   The consensus guideline is drafted and the draft is reviewed and discussed by disease-specific Expert Panel.

7. Posting for comment:
   The draft Consensus guideline for clinical trial design is posted for comment. All comments are reviewed by the Expert Panel to inform the final guideline. Decisions on the specific content of the final guideline resides with the SFRT experts' review.

8. Final recommendations:
   The Expert Panel formulates the final guideline.