Protocol Requirements for IMRT delivery to mobile lesions:

1. The protocol must require appropriate patient immobilization and localization. The immobilization in this case is not just for the patient's body, but also the tumor. There are a variety of commercially available systems to achieve reasonable tumor immobilization. It will be the responsibility of the protocol PIs to assess the adequacy of these systems for their protocol. For IMRT delivery tumor immobilization with respiration should be limited to 5 mm. In this way the interplay between the dynamic delivery and respiration induced tumor motion is minimized.

2. The protocol must require that a 3-D treatment planning volumetric imaging study be used to define the target volumes and critical structures. The imaging study needs to include an assessment of tumor with the patient in the treatment position. A standard 3D image study may yield in accurate volumes so provisions must also be made to acquire images that do represent the true tumor volume sans motion artifact. This can be achieved using any one of the following: occlusion spirometry, organ motion suppression, 4D CT, inspiration and expiration scans on a fast CT scanner.

3. Protocols permitting IMRT treatment delivery must be written using the nomenclature defined in the NCI IMRT Working Group Report (IMRT Collaborative Working Group: Intensity modulated radiation therapy: current status and issues of interest. Int. J. Radiat. Oncol. Biol. Phys. 51:880-914, 2001) and the International Commission on Radiation Units and Measurements (ICRU) Reports 50 and 62 for specifying the volumes of known tumor, i.e., the gross tumor volume (GTV), the volumes of suspected microscopic spread, i.e., the clinical target volume (CTV) and the marginal volumes necessary to account for setup variations and organ and patient motion, i.e., the planning target volume (PTV). The CTV is potentially affected by organ motions, which should be explicitly accounted for with an internal margin (IM). The IM should compensate for variation in position, size, and shape, of the CTV during treatment. Thus the PTV for a mobile target

represents a volume that encompasses the CTV, a set-up margin (SM) that specifically accounts for spatial uncertainties in patient positioning and treatment delivery, as well as an IM for the residual internal organ motion.
(ICRU Report 62 refines this definition of planning target volume by introducing the concept of an Internal Margin (IM) to take into account variations in size, shape, and position of the CTV in reference to the patient's coordinate system using anatomical reference points, and the concept of a Set-up Margin (SM) to take into account all uncertainties in patient beam positioning in reference to the treatment machine coordinate system. Report 62 defines the volume formed by the CTV and the IM as the Internal Target Volume (ITV). The ITV represents the movements of the CTV referenced to the patient coordinate system and is specified in relation to internal and external reference points, which preferably should be rigidly related to each other through bony structures. The ITV concept is likely to be used mostly by researchers studying internal organ motion. Note however, that the introduction of the ITV concept does not change the global concept and definition of the PTV as a means of accounting for geometric uncertainty. In most cases, the practicing physician can skip having to explicitly define the ITV. However, how the IM and SM should be combined is not at all clear. Simple linear addition of the two margins will generally lead to an excessively large PTV that would exceed patient tolerance and not reflect the actual clinical consequences. Thus, the risk of missing part of the CTV must be balanced against the risk of complications due to making the PTV too large. ICRU states that a quadratic approach similar to that recommended by the Bureau International des Poids et Mesures can be used).

ICRU Report 62 introduced the concept of the planning organ-at-risk volume (PRV), in which a margin is added around the organ at risk (OAR) to compensate for that organ's geometric uncertainties. The PRV margin around the critical structure that must be spared is analogous to the PTV margin around the CTV. The use of PRV concept is even more important for those cases involving IMRT because of the increased sensitivity of this type treatment to geometric uncertainties. The PTV and the PRV may overlap, and often do so, in which case a compromise must be found when weighing the importance of each in the planning process.

4. The protocol must provide a rationale for the choice of margins (IM and SM) to be used by the participating institutions to expand CTV to PTV.

5. The protocol must require that a heterogeneity-corrected dose distribution be prepared for plan evaluation and dose prescription. The protocol must also specify the prescription dose to the volume, for example 60 Gy to cover 95% of the PTV.

6. The dosimetry must be benchmarked for the protocol to verify that the dose algorithms are within accepted ranges of accuracy.

7. The protocol must provide a clear definition of the prescription dose and dose heterogeneity allowed throughout the PTV. If 3D conformal and IMRT treatments are allowed on the same protocol, the dose heterogeneity requirements for the IMRT patients and non-IMRT patients must be similar.

8. The protocol must clearly define the OARs and/or PRVs that are required for each study and provide clear guidelines for contouring each OAR/PRV defined in the study. Dose constraints for each OAR/PRV in the irradiated volume must be defined. Participants are required to be within the protocol specified limits.

9. The GTV, CTV, PTV, OAR (s), PRV(s), and skin contours (to delineate unspecified tissue) must be depicted on all slices of the 3-D volumetric imaging study in which each structure exists.

10. The protocol must require that specific procedures be in place to insure correct, reproducible positioning of the patient. At a minimum, orthogonal (AP and lateral)

digitally reconstructed radiographs (DRRs) and corresponding orthogonal weekly portal images (film or electronic) are to be required.

11. Copies of all images required by the protocol in defining the GTV must be submitted to the cooperative group QA office for review. The intended dose distribution computed by the planning system in the coronal, axial, and sagittal planes that pass through the center of each PTV must be submitted for QA review. Isodose lines superimposed on representative slices of the 3-D volumetric imaging study must be clear and comprehensive. Values for hot spots and cold spots must be specified by the protocol, all hot spots and cold spots must be clearly indicated. Cold spots (protocol specified, but typically <93% of the prescription dose) within the PTV, CTV and GTV must also be indicated. DVHs for the GTV, CTV, PTV, and dose to all PRVs and OARs defined for the study must be submitted for QA review in absolute and relative units.

12. DVHs must be submitted for a category of tissue called “unspecified tissue” that is defined as tissue contained within the skin, but which is not otherwise identified by containment within any other structure. This will help ensure that the IMRT plan does not result in increased doses in normal tissues that were not selected for DVH analysis. This DVH should be submitted in absolute dose.

13. The treatment machine monitor units (MUs) generated using the treatment planning system must be independently checked prior to the patient’s first treatment. Patient specific quality assurance measurements can suffice for a check as long as the plan’s delivered fluence and/or dose distributions can be validated in a phantom geometry.

14. It is strongly recommended that the data from these treatments be archived at either a central QA facility or at the home institution so that they may be made available for later analysis, due to the emergent nature of these IGRT procedures.