ATC Guidelines for the Use of IMRT (including Intra-Thoracic Treatments)
May 31, 2006

Preamble:

The Advanced Technology Consortium (ATC) has helped to develop general guidelines (*Int. J. Radiat. Oncol. Biol. Phys. 59 (2004):1257-1262*) for protocols that incorporate Intensity Modulated Radiation Therapy (IMRT) as an option. These were communicated to all clinical trial groups by the National Cancer Institute (NCI) and clearly stated that respiratory motion could cause far more problems for IMRT than for traditional treatments. The delivery of IMRT is dynamic as is the effect of breathing motion, therefore the interplay between the two can result in non-reproducible dose distributions due to the variability in how subfields are added. In addition, other patient motions may have significant effects on the summation of subfields whose intensities are based upon a static image. Thus, extra care is required in the acquisition of the CT datasets used in the planning process in order to avoid motion artifacts while still being representative of the average location of the anatomical structures. Those guidelines also explained why accounting for heterogeneities was most important for IMRT since heterogeneities could affect some subfields more than others and result in localized dose distribution differences that could be clinically significant.

The enclosed, updated version of the guidelines explicitly includes IMRT in anatomical regions where target motion can have a significant effect, such as intra-thoracic treatments. While these guidelines are intended to serve only as minimal standards for NCI-supported clinical trials, they do mandate that any protocol that requires or allows IMRT must include the following requirements in either the initial protocol or as an amendment if IMRT is to be subsequently allowed.

Protocol Requirements for IMRT (including intra-thoracic lesions):

1. The protocol must explicitly address the localization and immobilization of both the patient and the tumor. There are several commercially available systems that can help achieve immobilization. The study chair and designated QA Center shall assess the adequacy of those systems for each individual protocol. For IMRT delivery, the residual motion after compensation techniques are applied should be explicitly specified in the protocol. The current literature indicates that with present-day techniques 5 mm of residual target motion is the smallest reasonable limit for intra-thoracic anatomical structures.

2. The protocol must require that a 3-D treatment planning volumetric imaging study be used to define the target volumes and organs at risk (OAR). The imaging studies need to provide an assessment of the target volume with the patient in the treatment position, and provisions must be made to acquire images that represent the target volume without motion artifact. Some of the techniques that can be used for these purposes are: spirometry, abdominal compression, 4D CT, and inspiration and expiration scans on a fast CT scanner capable of imaging the entire planning volume in one scan sequence for each breathing phase. The steps taken to suppress/manage motion and achieve appropriate simulation should be documented and submitted for review to the appropriate QA Center.

3. Protocols must employ the nomenclature defined in the NCI IMRT Working Group Report (*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: 1) the volumes of known tumor, i.e., the gross tumor volume (GTV), 2) the volumes of suspected microscopic spread, i.e., the clinical target volume (CTV) and 3) the marginal volumes necessary to account for setup variations and organ and patient motion, i.e., the planning target volume (PTV). An internal margin (IM) should be used to 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.[i]

4. The protocol should describe the rationale for the choice of margins (IM and SM) to be used for expanding CTV to PTV.

5. The protocol must require that the effects of tissue heterogeneities be included in the dose calculations for plan evaluation, dose prescription and MU calculations.

6. The adequacy and accuracy of the dose algorithms for heterogeneity-corrected dose distributions should be demonstrated by each participating institution to the designated QA Center. The algorithm must meet the criteria of acceptability established by the QA Center.

7. The protocol must provide a clear description of the prescription dose as well as dose heterogeneity permitted in the PTV, recognizing that dose heterogeneity will generally be greater with IMRT. The protocol must also specify the volume to be covered by the prescription dose (for example, the 60 Gy isodose must cover 95% of the PTV). If 3D conformal and IMRT treatments are both allowed in a particular protocol, the dose heterogeneity requirements for IMRT and non-IMRT patients should be comparable.

8. The protocol must clearly specify the organs at risk (OARs) and/or the planning organ-at-risk volumes (PRVs) and include guidelines for contouring each OAR/PRV. Dose constraints for each OAR/PRV must also be specified.

9. The GTV, CTV, PTV, OAR, PRV, and unspecified tissue (see 12. below) must be delineated on each slice of the 3-D volumetric imaging study in which that structure exists.

10. The protocol must specify the procedures that should be in place for documenting correct, reproducible positioning of patient and target. On-board imaging to ensure reproducible positioning is acceptable. Spatially registered volumetric imaging based on kV/MV CT is also acceptable. As a minimum, however, the equivalent of orthogonal (AP and lateral) digitally reconstructed radiographs (DRRs) and corresponding orthogonal weekly portal images (film or electronic) are required.

11. Copies of all images used to define the target and anatomical structures, as well as the RT data (e.g. RT-structures, - dose and -plan) should be submitted electronically to the designated QA center for review. As a minimum, hardcopies or screen captures of the computed dose distribution (in the coronal, axial, and sagittal planes that pass through the center of each PTV) must be submitted. Isodose lines superimposed upon representative slices of the 3-D volumetric imaging study must be clear and comprehensive. Acceptable values for hot spots and cold spots must be specified by the protocol, and images showing the locations and magnitudes of the hot and cold spots must be submitted. DVHs in absolute dose for the GTV, CTV, PTV, and all PRVs and OARs specified in the protocol must be submitted for QA.

12. A DVH in absolute dose must be submitted for a category of tissue called "unspecified tissue" that is defined as tissue contained within the skin, but which is not included within any other structure. This will help ensure that the IMRT plan does not result in unintentionally high doses in normal tissues that were not selected for DVH analysis.

13. The treatment machine monitor units (MUs) generated by the IMRT planning system must be independently checked prior to the patient's first treatment. Patient specific quality assurance measurements can suffice when the plan's delivered fluence or dose distributions are validated quantitatively. The protocol should specify criteria for acceptance of these measurements.

14. Finally, before participating in a cooperative group protocol involving IMRT, an institution must be appropriately credentialed by the QA Center designated in the protocol.

---

[i] *(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 account 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 particularly important for those cases involving IMRT because of the increased sensitivity of this type of 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.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Cancer Institute
Radiation Research Program
6130 Executive Blvd., MSC 7440
Rockville, MD 20892-7440
301-496-6111, 301-480-5785 – fax

July 21, 2006

Dear Dr. (Group Chair)

In January 2005 the NCI had updated its guidelines for using Intensity Modulated Radiation Therapy (IMRT) in clinical trials, reiterating the requirements for a multi-element quality assurance program while also allowing IMRT for intra-thoracic tumors with appropriate corrections for tissue heterogeneity and target motion.

However, the 2005 version did not address the methods for correcting or managing motion. It was assumed that large expansions from CTV to PTV would be used until the techniques became better established.

The attached revision of the guidelines now includes criteria for immobilization and imaging to reduce motion artifacts (criteria 1 and 2) and also recognizes the variability of dose algorithms for heterogeneity correction (criterion 6).

There are potential advantages to patients from IMRT, but justifiable concerns remain concerning the actual planning, optimization and execution of IMRT. Therefore, the need persists for credentialing and quality assurance procedures that are specific for IMRT.

We request that you distribute these revised guidelines to your Clinical Trials Group and affiliates. That will prevent delays in reviewing by CTEP your future protocols that either require or allow IMRT.

If you have any questions please do not hesitate to contact Dr Vikram or Dr James Deye of the Clinical Radiation Oncology Branch at the NCI (vikramb@mail.nih.gov, deyej@mail.nih.gov).

Sincerely,

Bhadrasain Vikram, MD
Branch Chief, DCTD
Clinical Radiation Oncology Branch
National Cancer Institute

Jeffrey Abrams, MD
Branch Chief, DCTD
Clinical Investigations Branch
National Cancer Institute

Cc: Radiation Oncology Committee Chair