

## **GUIDELINES FOR THE USE OF PROTON RADIATION THERAPY IN NATIONAL CANCER INSTITUTE SPONSORED COOPERATIVE GROUP CLINICAL TRIALS**

There are potential advantages to patients from proton radiation therapy (PRT) but substantial concerns persist at present regarding the actual planning, optimization and execution of PRT in the multi-institutional setting of co-operative group clinical trials. Therefore, there is a need for credentialing and quality assurance procedures that are specific for PRT.

Protons are less tolerant than photons of inadequacies in the planning, optimization and execution of radiation therapy. This reflects the nature of the interactions of protons with matter. The guidelines below are intended to ensure that when PRT is employed in the setting of a multi-institutional co-operative group clinical trial neither patient safety nor the study is compromised. The guidelines only specify the MINIMUM required of any facility that treats with PRT patients participating in any NCI-supported clinical trial that requires or allows PRT; they are not to be construed as prescriptive of standards of care.

### **Guidelines:**

1. Before treating with PRT any patients participating in a cooperative group protocol, an institution must be appropriately credentialed for PRT by the QA center designated in the protocol.
2. Only passively scattered or actively scattered (wobbling) beams shall be employed [1].
3. The IAEA TRS 398 protocol (available at [http://www-naweb.iaea.org/nahu/dmrp/pdf\\_files/CoPV11b.pdf](http://www-naweb.iaea.org/nahu/dmrp/pdf_files/CoPV11b.pdf)) shall be used for beam calibration [2].
4. All doses shall be expressed as Cobalt Gray Equivalent (CGE, e.g. 70 CGE) employing a standard RBE of 1.1 with respect to Cobalt-60 [3].
5. Treatment planning shall be performed on a CT scan obtained with the patient in the treatment position. Correlation between the institutional 'CT treatment planning system Hounsfield Units' (for the specific CT scanners and parameters) and 'relative proton stopping power' must be established at each institution and demonstrated to the satisfaction of the quality assurance center designated in the protocol [4].
6. Doses will be specified to volumes using standard nomenclature, i.e. GTV, CTV, and PTV. The GTV and CTV shall be identical for protons and photons but in specifying the PTV every protocol that allows PRT must explicitly address issues unique to PRT such as range uncertainties and lateral scatter [5].
7. Before treating with PRT any patients participating in a cooperative group protocol, an institution shall undergo a site-visit by the Radiological Physics Center (RPC) for conducting measurements and an audit of its proton facility. In addition, the RPC shall conduct annual remote monitoring of the proton calibrations as they relate to clinical trials in which the facility is participating [6].
8. Every protocol that allows PRT must specify a radiation oncologist actively practicing at a proton facility who will be responsible for incorporating into that protocol the appropriate dose terminology and the specific constraints related to the PTV and OAR [7].

## **Rationale:**

1. *There is substantial clinical experience with passively and actively scattered proton beams in the United States while there is very limited clinical experience with scanned proton beams. Hence approval of the latter for NCI-sponsored protocols will be deferred until this approach matures in the US at which time these guidelines will be updated.*
2. *IAEA TRS 398 will be the recommended protocol by the ICRU in an upcoming report and it is based upon a National Institute of Standards and Technology (NIST) traceable Cobalt 60 calibration. The difference in calibration between the ICRU recommendations, ICRU 59, and the IAEA recommendations is quite small, less than 2%, though it depends upon the ion chamber used.*
3. *This RBE and dose specification has been used historically by each of the facilities within the U.S., so this will allow for clinical continuity of treatment methods and results.*
4. *The conversion of HU to stopping power ratios determines the energy (range) required of the protons and must be performed at each institution. The HU to physical density calibration curve should be independently reviewed.*
5. *The use of the PTV concept is more challenging for protons in that it must incorporate the uncertainties in the distal and proximal range, which are a treatment field specific requirement. Currently, there is no consensus approach to the use of the PTV concept with protons. It is recommended that the use of the PTV concept be based on particular protocol requirements and institutional procedures to account for motion of patient and internal organs as well as variability in set-up and uncertainties in the proton range.*
6. *The RPC is funded by the NCI to maintain uniformity and NIST traceability of all physical dosimetry in NCI clinical trials, both photon and proton. The on-site visit will verify the proton beam calibrations and will capture the data needed by the QA center to:*
  - *assess the accuracy of the CT/ HU to stopping power conversion,*
  - *assess the accuracy of the treatment planning algorithm, and*
  - *assess the adequacy of patient specific immobilization techniques.*

*Each of these factors will be evaluated in the context of the specific protocol requirements.*

7. *The characteristics of protons are unique enough that they are not readily appreciated from the traditional photon experience. Hence, special knowledge and experience is required in order to ensure patient safety and adequacy of the trial design.*