Recommendation for the Frequency of Calibration Audits by a Quality Assurance Center Supporting NCI sponsored Clinical Trials.

This document represents work in progress within the Advanced Technology QA Consortium (ATC). Comments are welcome and should be directed to Marcia Urie, PhD or David Followill, PhD, co-chairs of the ATC Credentialing and QA Committee.

Executive Summary

The focus of this report is to provide data from the Radiological Physics Center (RPC) and the literature from which a consensus opinion could be developed regarding annual reference dosimetry TLD audits. Such audits would be conducted by a recognized quality assurance organization and would be performed by NCI cooperative group members, or their affiliates and collaborators. These institutions are primarily located in the USA and Canada.

After an extensive literature search, this committee was unable to find any peer-reviewed published data assessing the possible resulting impact on clinical trial outcome from a change in frequency (increase or decrease) of reference dosimetry audits. The following report analyzing data from the RPC, however, does provide data that indicate that a reduction in the frequency of TLD audits would likely lead to an increase in the number of institutions with an undetected calibration error. The data provided also indicate that in any given year, photon beam audits failed to meet the 5% agreement criteria at 7-14% of the institutions (3-5% of the photon beams) that enroll the majority of clinical trial patients. Including the impact of the number of patients enrolled onto clinical trials from institutions with TLD discrepancies, the percent of total patients per year potentially affected by photon beams with a TLD audit outside of the 5% criterion range from 5 to 12%.

Published data indicate that dose errors as small as 3% can affect the quality and outcome of a trial unless this is anticipated and the trial is powered appropriately. [3-5] As indicated in the World Health Organization report[1] the majority of radiotherapy errors originate from human error which is the probable cause for the majority of the beam calibration errors since it is the one dosimetry parameter most likely to change with time and subject to human interpretation of the calibration protocols. A reduction in the audit frequency and a corresponding increase in the number of undetected calibration errors may increase the uncertainty in tumor dose of patients entered onto trials. It is the consensus of this committee that uncertainties in the doses delivered to clinical trial patients should be kept small to avoid increasing patient accrual goals. The following recommendations are made:

1. The frequency of the reference dosimetry TLD audit should remain annual for participating instituions within the USA and Canada as is currently the parctice.

2. International institutions (outside the USA and Canada) wishing to participate in NCI sponsored clinical trials will have all of their photon beam calibrations verified using a TLD audit prior to enrolling patients onto the trial. Any new machine put into clinical service at the facility will

also have all of its photon beams audited as well. These audits should be performed at a minimal interval of every two years.

3. The RPC and EORTC will jointly conduct a study to determine the consequences and impact on clinical trial dosimetry of varying the frequency of the TLD audit.

References

[1] "Radiotherapy Risk Profile", World Health Organization, Geneva, Switzerland, 2008.

[2] http://www.usatoday.com/news/health/2005-04-02-radiation-overdoses_x.htm, accessed March 18, 2009.

[3] Bentzen et al, Clinical impact of dosimetry quality assurance programmes assessed by radiobiological modeling of data from the thermoluminescent dosimetry study of the European Organization for Research and Treatment of Cancer., European J. Cancer (36), 615-620, 2000.

[4] Pettersen et al, Quality assurance of dosimetry and the impact on sample size in randomized clinical trials., Radiotherapy and Oncology (86), 195-199, 2008.

[5] Boyer, A. and Schultheiss, T., Effects of dosimetric and clinical uncertainty on complication-free local tumor control., Radiotherapy and Oncology (11), 65-71, 1988.