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In reply to Drs. Bekelman and Yahalom: Quality Of Radiotherapy Reporting In Randomized Controlled Trials Of Hodgkin's Lymphoma And Non-Hodgkin's Lymphoma

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Drs. Bekelman and Yahalom's (1) paper describing radiation therapy (RT) quality assurance (QA) in lymphoma clinical trials places emphasis for RT standards. Insuring study defined dose/volume constraint compliance, RTQA requires central pre-treatment diagnostic imaging and RT plan review. This letter describes Children's Oncology Group (COG) historical and current RTQA process for Hodgkin's lymphoma (HL) trials.

For 33 years the Quality Assurance Review Center (QARC) has performed RTQA on cooperative group trials. Process improvements demonstrate maturing of clinical trials QA in response to protocol needs. The increasingly crucial role of imaging in clinical trials QA is validated.

Pediatric Oncology Group (POG) protocol 8725 (intermediate/advanced staged HL) required 8 chemotherapy cycles +/− Involved Field RT. Initial publication(2) demonstrated no advantage for RT. Retrospective data review revealed 10% survival advantage for patients receiving compliant RT.(3) 30% of patients had treatment deviations including omission of RT to involved sites. To improve compliance, POG required pre-treatment RT review for next generation advanced/early stage HL studies, P9425/P9426(4,5). Strategy improved RT compliance. P9426 required post chemotherapy imaging response treatment adaptation. Retrospective response-imaging central review established that ~50% of patients had discordance between local and central review.(6) COG AHOD0031 (intermediate risk HL) included patient response-adapted therapy. QARC initiated real time response review with integrated imaging (anatomic and metabolic) and RT review prior to RT start.

Discordant local and central interpretations were resolved in real time. (7,8) 1733 patients from 251 centers worldwide were enrolled. Near uniform data submission compliance has been obtained with >95% RT compliance in ~600 cases reviewed. Process feasibility allows extension of adaptive treatments based on centrally-confirmed response for the next high risk HL study.

QARC-developed an informatics platform and processes that contribute to success of these clinical trials improvements. QARC acquires and manages imaging and RT data in several digital formats(9). The QARC database houses images and RT objects in side-by-side format, enabling remote investigator access. In collaborating with Dr. Purdy and the Advanced Technology Consortium, full digital RT files are received at QARC for review and DVH analysis. Currently strategies to incorporate Dicom compatible pathology objects into the database and use of open-source format for data sharing are being evaluated.

The objectives identified in this paper for developing consensus standards and peer-review are in place for cooperative groups. Applying these established programs at enterprise level insures the objectives of this publication are met.

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