

Results: LOC1: deviations < 3 mm increased from 75.5% during PER1 to 81% during PER2 to 83% during PER3. Conversely deviations of 3-5 mm dropped from 19.5% to 13% while deviations of more than 5 mm remained stable around 5%. The actual standard error of the mean deviation observed is 2 mm. LOC2 : deviations < 5 mm were observed in 81% of cases during PER1 and in 91% during PER3 (89.5% in PER2). These good results led to a decrease of deviation of 5 to 7 mm (11% to 6%) and also to a significant drop of deviations of more than 7 mm, 8% to 3% respectively. The actual precision obtained is 2.5 mm +/- 3 mm SD.

Conclusion: The OLP based upon the early correction of the systematic error led to a significant increase of setup accuracy of patients irradiated for brain, head and neck and especially for pelvic lesions.

1005 Quantitation of Acute and Late Toxicities of a Concomitant-Boost Thrice-Daily Dose Escalation Radiotherapy Regimen for Advanced Head and Neck Squamous Cell Carcinomas

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Purpose: This randomized Phase III trial, comparing once-daily (QD) vs. thrice-daily (TID) irradiation for Stages III and IV head and neck squamous cell carcinomas (HNSCC), was based on the comparative analysis of conventional irradiation vs. accelerated hyperfractionated, twice-daily concomitant boost irradiation (AHCRT). The questions of this trial included relative toxicities and effectiveness of standard fraction QD delivery relative to a hyperfractionated regimen using TID irradiation in the concomitant boost setting to achieve significant acceleration and dose escalation to 75 Gy.

Materials and Methods: Based on our institutional experience on case-matched comparisons between QD and twice-daily AHCRT the projected patient number for a trial comparing QD vs. TID irradiation was computed to require 70 patients for a significance at the 10% confidence level. The QD group received 2 Gy to large HN fields followed by reduced field boosting to a cumulative dose of 70 Gy over 54 days. This was compared to a concomitant boost accelerated TID regimen irradiating patients daily with 1.8 Gy fractions for 14 days, followed by 1.5 Gy fractions given thrice-daily at 6 h intervals to reduced fields encompassing gross tumor, and large fields including or excluding the spinal cord. The spinal cord was only irradiated once-daily to a maximum total dose of 45 Gy. Gross tumor and electively irradiated lymph node bearing tissues were irradiated TID to total doses of 75 Gy and 51 Gy, respectively, over 33 days. Treatment volume dependent acute and late radiation toxicities were quantified using RTOG/EORTC toxicity criteria as was the relationship between CT-/MRI-based tumor volume and tumor control.

Results: Between 1993 and 1998, 67 evaluable patients were accrued, 34 to the QD and 33 to the TID arm. The T- and N-Stage distribution in the two groups was balanced, as was the 4:1 male to female ratio. There was also a similar distribution of primary tumors by major subsites of oral cavity, oropharynx, hypopharynx and larynx. The combined primary and nodal gross tumor volume was comparable as well with a median volume of 22 cc (4-218cc) for the QD and 35 cc (7-111cc) for the TID group. All patients experienced grade 1 (G1) mucositis. G2 mucosal toxicity was seen in 70% and 90% (n.s.) of the QD vs. TID patients. There was a significant increase ($p < 0.01$) of G3 mucositis in the TID (75%) vs. the QD (25%) group, and a 5% incidence of G4 toxicity in the TID arm. Acute mucosal reactions occurred earlier and lasted longer in the TID arm. Rates of percutaneous gastrostomies or prophylactic intravenous hydrations during the last treatment week were required at twice the rate in the TID cohort. With these interventions the extents of weight loss, <10%, 10-20%, and >20%, were not significantly different for the two groups. Importantly, the increased acute toxicities did not translate into more severe late sequelae using separate maximum late toxicity scores for mucosa, soft tissues, or salivary glands. Because of the much smaller than expected differences in tumor control between the two arms, the study was discontinued at a patient accrual sufficient to assess acute and late toxicity of the two arms.

Conclusion: Our results demonstrate that the concomitant boost concept can be developed into a thrice-daily accelerated radiotherapy regimen with dose escalation to 75 Gy delivered over 33 days. Careful patient management allows this to be given in the outpatient setting. Quantitative acute and late toxicity data demonstrates expected increases in acute but not late tissue toxicities. This regimen should be considered in comparative radiotherapy fractionation schedules with or without chemotherapy.

1006 Accelerated Fractionation for Head and Neck Cancer Using the SMART (Simultaneous Modulated Accelerated Radiation Therapy) Boost Technique

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Purpose: To update the use of intensity modulated radiation therapy in the definitive treatment of head and neck cancer utilizing the SMART (Simultaneous Modulated Accelerated Radiation Therapy) boost technique. Dosimetry, toxicity, initial response and efficacy are analyzed.

Materials and Methods: From January 1996 to August 2000, 50 evaluable patients were treated definitively for head and neck carcinomas with the SMART boost technique. Using the NOMOS PEACOCK intensity modulated radiation therapy system, primary and secondary targets were treated simultaneously at different fraction sizes. The primary targets included palpable and radiographic disease and were treated at 2.4 Gy fractions to a total dose of 60 Gy. Areas at risk for microscopic disease were defined as secondary targets and treated at 2.0 Gy fractions to a total dose of 50 Gy. A single anterior field was used to treat the lower neck nodes. Treatment was completed in 25 fractions delivered over 5 weeks. Patients were evaluated for acute toxicity using RTOG criteria, dosimetric parameters, time to complete treatment, initial response, locoregional control, and distant metastases. All patients had at least 6 months of follow-up. The median follow-up time was 22 months. Eleven patients

received chemotherapy. Twenty-eight patients had stage IV, 7 had stage III, 7 had stage II and 5 patients had stage I disease. Recurrent disease was treated in 2 patients and one patient had an unknown primary.

Results: Acute toxicity: Fifteen patients (30%) required feeding tubes. Eleven patients (22%) required IV hydration. RTOG grade 3 mucositis was seen in 20 patients (40.0%). RTOG grade 3 or 4 pharyngitis was seen in 10 patients (20%). Grade 1 or 2 xerostomia was seen in 36 patients (72%). Thirty-six patients (72%) completed treatment in less than 40 days, 9 patients (18%) in 40 to 49 days, and 5 patients (10%) in 50 or more days.

Dosimetry: The mean dose to the primary and secondary targets were 63.9 Gy and 54.7 Gy respectively. The mean dose to the spinal cord was 13.6Gy, brainstem 11.5Gy, mandible 29.1Gy, ipsilateral parotid 24.7, and contralateral parotid was 20.9Gy.

Initial response and relapse rates: Complete responses were seen at the primary site of disease in 46 patients (92%) while 4 patients (8%) had partial responses. Nine patients (18%) had local-regional recurrences and seven patients (14%) developed distant metastatic disease. Six patients initially had complete responses but subsequently failed in the head and neck region.

Conclusion: The SMART boost technique offers the opportunity to treat both primary and secondary targets simultaneously with different fractionation schemes. The accelerated treatment regimen provides excellent local control with diminished dose to the parotid glands. The majority of patients completed the treatment in under 40 days despite increased acute toxicity.

1007 Simultaneous Integrated Boost IMRT of Advanced Head and Neck Squamous Cell Carcinomas Using Dynamic Multi-Leaf Collimators

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Purpose: This presentation describes the unique aspects of an IMRT protocol implemented at our institution for the treatment of advanced head and neck squamous cell carcinomas. The objectives of this study are to determine the feasibility of this protocol and to identify maximum tolerable doses for locally advanced disease for which unilateral or bilateral parotid sparing is appropriate.

Materials and Methods: IMRT is designed and delivered using the "simultaneous integrated boost" (SIB) strategy in which the highest (boost) dose to the primary gross tumor volume (GTV), an intermediate dose to the subclinical tumor extensions, and a lower dose to electively irradiated nodal volumes are delivered simultaneously. Total nominal dose is adjusted using linear quadratic formalism to account for the different fraction sizes. Primary dose levels of 68, 71 and 74 Gy, given in 30 fractions (biologically equivalent to 74, 79, 85 Gy respectively if given in 2 Gy per fraction), are to be evaluated. In all cases, the subclinical disease and electively treated nodes are prescribed 60 Gy and 54 Gy respectively. The secondary goal of IMRT is to minimize the doses to parotids and to study the dependence of xerostomia on parotid dose distributions. The doses to all other critical normal tissues are maintained at or below their tolerances. The IMRT planning and leaf sequence generation software, developed in-house and coupled to a commercial treatment planning system (Pinnacle³, ADAC, Milpitas, CA), is used for this study. The patients are immobilized with a perforated thermoplastic mask covering from head to shoulder. The mask is attached to the couch (CT as well as treatment machine) using the indexed patient positioning system (IPPS, MedTec, Orange City, IA). This ensures maximum patient setup reproducibility. Nine 6 MV intensity-modulated photon beams at equal gantry angles are used for the planning. IMRT optimization is based on the dose-volume criteria. Treatments are delivered with a multi-leaf collimator (MLC) using the "sliding window" technique. Limitations of the delivery system such as MLC leakage and head scatter were taken into account. Fields sizes are set to sizes large enough to cover all target volumes including the superclav nodes, and often exceed the inherent limit of leaf travel. Therefore, when necessary, these fields are split using a "dynamic feathering" technique. The final treatment plans are automatically transferred to the delivery system using a data interchange computer program to minimize human error. Dosimetric verification is performed for each intensity-modulated field using a flat homogeneous phantom and film. Treatments were delivered automatically without the need to enter the room between fields.

Results: To date we have completed accruals at the first two dose levels (14 patients). Disease sites were predominantly oropharyngeal. For the required level of tumor coverage, cord and brainstem sparing, a variable degree of parotid sparing has been achieved. Treatment times (excluding set up and field verification) were typically within 15 minutes. Summary of patient dose distributions will be shown in a companion presentation. For dosimetric verification of treatments, films placed at 5 cm depth of the phantom were irradiated with the same intensity modulated field, and the measured dose agrees with the corresponding calculations within 3% for most points.

Conclusion: IMRT of head and neck cancers with SIB IMRT using dynamic MLC is feasible. The planning and delivery processes are efficient. Predicted dose distributions can be delivered accurately. The clinical impact of such accuracy on tumor control and normal tissue toxicity is the subject of ongoing investigation in our department.

1008 "Simultaneous Integrated Boost" (SIB) IMRT of Advanced Head and Neck Squamous Cell Carcinomas - Dosimetric Analysis

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Purpose: This presentation summarizes dosimetric data for patients treated for advanced head and neck squamous cell carcinoma under an IMRT protocol. The objectives of this protocol are to determine the feasibility of the treatment technique and to identify maximum tolerable IMRT doses for locally advanced disease for which unilateral or bilateral parotid sparing is appropriate.

Materials and Methods: IMRT is designed and delivered using the SIB strategy in which the highest (boost) dose to the primary gross tumor volume (GTV), an intermediate dose to the subclinical tumor extensions, and a lower dose to electively irradiated nodes are delivered simultaneously. Primary dose levels of 68, 71 and 74 levels, given in 30 fractions (biologically equivalent to 74, 79, 85 Gy respectively if given in 2 Gy fractions), are to be evaluated in this phase I study. Details of the procedure are described in a separate presentation. Treatment dose distributions were used to compute the following quantitative