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OMICS Journal of Radiology

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OMICS Journal of Radiology

Summary of Research work

- Head and Neck malignancies: clinical outcomes and Quality of life measurements (QOL).
- Breast cancer: DCIS.
- Prostate cancer: QOL and clinical outcomes.
- Merkel cell carcinoma: novel prognostic markers and clinical outcomes.
- Thoracic malignancies: NSCLC, SCLC and thymoma: clinical outcomes.
- Extra-nodal lymphoma of different regions and rare case presentations, both Non-Hodgkin's and Hodgkin's lymphomas, & MALT lymphoma of various sites like orbit, stomach.
- Challenging cases in oncology and treatment methods.

Increased recurrences using intensity-modulated radiation therapy in the postoperative setting.

PURPOSE: To determine the pattern of failures following intensity modulated radiation therapy (IMRT) for head & neck cancer.

MATERIAL AND METHODS:

- A retrospective single institution study.
- Between May 2001 & June 2008, 176 patients with head and neck cancer were treated with IMRT.
- Ninety-five (54%) were squamous cell carcinoma treated with curative intent.
- Tumor and nodal stage, tobacco history, definitive versus postoperative therapy (PORT), addition of chemotherapy and RT duration were analyzed for association with patterns of failure.
- In patients treated with definitive radiation, high-risk PTV (PTV1) was prescribed to 70 Gy and low-risk PTV (PTV2) to 56 Gy. In the PORT setting, PTV1 was prescribed to 60 to 66 Gy and PTV2 to 54 Gy.
- Patterns of failure were assessed. Local failure (LF) was defined as the persistence of disease or recurrence within PTV1, marginal failure as recurrence at the region of high-dose falloff, and regional failure as nodal recurrence within PTV2.

RESULTS:

- Median follow-up was 20 months (range: 1-117). Median age was 60 years (range: 28-88), with 80% smokers and 81% stage III or IV.
- PORT was given to 29% and 71% were treated definitively, with concurrent Cisplatin used in the majority.
- Three-year local and locoregional (LR) failure rates were 9% and 16%, respectively.
- Failures occurred in 14 patients: 8 local, 3 regional, 1 LR, and 2 distant. Five of the 8 LF and all 3 marginal failures were observed in PORT cohort.
- On univariate analysis, the only predictor of LF was the use of PORT (P = 0.06).
- LR control was 66% for PORT versus 87%, 97% for definitive RT and chemoRT.

CONCLUSIONS: Local, regional failures were more common following PORT related to an increased risk of marginal failures.

Turaka A, Li T, Sharma NK, Li L, Nicolaou N, Mehra R, Burtness B, Cohen RB, Lango MN, Horwitz EM, Ridge JA, Feigenberg SJ. Am J Clin Oncol. 2010 Dec;33(6):599-603. doi: 10.1097/COC.0b013e3181c4c3cc. PMID: 21063195

Use of a conventional low neck field (LNF) and intensity-modulated radiotherapy (IMRT): no clinical detriment of IMRT to an anterior LNF during the treatment of head-and neck-cancer.

PURPOSE: To determine differences in clinical outcomes using intensity-modulated radiotherapy (IMRT) or a standard low neck field (LNF) to treat low neck.

METHODS AND MATERIALS:

- This is a retrospective, single-institution study.
- Ninety-one patients with squamous cell carcinoma of the head and neck were treated with curative intent.
- According to physician preference, some patients were treated with LNF (Planning Target Volume 3) field using a single anterior photon field matched to the IMRT field. Field junctions were not feathered.
- The endpoints were time to failure and use of a percutaneous endoscopic gastrostomy (PEG) tube (as a surrogate of laryngeal edema causing aspiration), and analysis was done with $\chi(2)$ and log-rank tests.

RESULTS:

- Median follow-up was 21 months (range, 2-89 months). Median age was 60 years.
- Thirty-seven patients (41%) were treated with LNF, 84% were Stage III or IV.
- A PEG tube was required in 30%, as opposed to 33% without the use of LNF. Node 2 or 3 neck disease was treated more commonly without LNF (38% vs. 24%, $p = 0.009$).
- Failures occurred in 12 patients (13%). Only 1 patient treated with LNF failed regionally, 4.5 cm above the match line.
- The 3-year disease-free survival rate was 87% and 79% with LNF and without LNF, respectively ($p = 0.2$), and the 3-year LR failure rate was 4% and 21%, respectively ($p = 0.04$).

CONCLUSIONS:

- Using LNF to treat the low neck did not increase the risk of regional failure "in early T and early N diseases" or decrease PEG tube requirements.

Turaka A, Li T, Nicolaou N, Lango MN, Burtness B, Horwitz EM, Ridge JA, Feigenberg SJ.
Int J Radiat Oncol Biol Phys. 2011 Jan 1;79(1):65-70. doi: 10.1016/j.ijrobp.2009.10.034. Epub 2010 Apr 10. PMID: 20385457

Intensity Modulated Radiation Therapy (IMRT) for the Para nasal Sinus (PNS) Malignancies

- Purpose/Objective(s): Due to the difficulties of air tissue interface interactions as well as the close proximity to the optical apparatus, tumors in the PNS region treated with IMRT may have increased local failure and higher complications. The clinical outcome of patients treated with IMRT for PNS malignancies are reported.
- Materials/Methods: Between May 2001 and June 2008, 31 patients with PNS malignancies were treated with IMRT to a median dose of 60 Gy in 30 fractions. There were 13 males and 18 females, with median age 68 years. Seventeen (59%) patients had AJCC stage III/IV disease at presentation. Twenty one of 31 patients presented with clinical stage N0 neck disease. Elective nodal irradiation (ENI) is not considered due to low incidence of lymph node metastases among these patients. Histology was: 14 squamous cell, 3 adenocarcinoma, 3 adenoid cystic, 6 mucosal melanoma, 5 others. The base of skull was treated in 3 patients with perineural invasion. Median RT dose values to optic apparatus were: Optic chiasm Dmax 22 Gy (range: 1-48); right and left optic nerve Dmax were 39, 37 Gy (range: 2-62; 2-65) and right, left parotid glands were 17; 25 Gy (range: 7-30; 5-53) respectively. Clinical outcomes and toxicities were measured.
- Results: Median follow-up was 27 months (range: 4-98). The 2- and 5-year local control and overall survival rates were 89%, 82% and 75%, 66%, respectively. The 2-year locoregional control rates were 89% for stage I/II and 79% III/IV, 89% N0, 50% for N1/2, 71% squamous cell and 100% for other histologies, 100% negative margins, 78% for positive margins. There were no grade 3 or 4 ocular or salivary function related toxicities. Four patients had local recurrence, 2 residual disease, 2 regional (treated prior) and 4 distant metastases (1 squamous cell, 1 adenoid cystic ca, 2 melanomas). No marginal failures were seen.
- Conclusions: IMRT appears to be a safe and effective treatment for paranasal sinus tumors.

C. Richard, **A. Turaka**, T. Li, N. Nicolaou, E. M. Horwitz, M. N. Lango, B. Burtness, J. A. Ridge, S. J. Feigenberg. International Journal of Radiation Oncology • Biology • Physics, Vol. 78, Issue 3, S478–S479. Published in issue: November 01, 2010.

Intensity-Modulated Radiation Therapy (IMRT) in the Treatment of Oropharyngeal Carcinoma: Clinical outcomes and relation of Parotid Gland volume with Xerostomia.

- **Purpose:** To determine the pattern of failures and relation of the parotid gland (PG) volume with xerostomia in patients treated with IMRT for squamous cell cancers of the oropharynx.
- **Method and Materials:** Between January 2001- December 2006, 49 patients with oropharyngeal cancer received IMRT with curative intent at Fox Chase Cancer Center. Among these, 48 were squamous cell and 1 adenocarcinoma. The median age was 58 years (range: 41-85), 82% smokers, and 90% with stage III or IV. 85% received definitive RT (63% concurrent chemoradiotherapy, 22% RT alone) to a median dose of 70 Gy in 35 fractions and 39% (19) had neck dissection. Wilcoxon test was used to determine the correlation between PG volumes (Vmean) and Xerostomia in 28 patients and Pearson's correlation coefficient to see relation between
- the percentage weight loss with PG volume. The mean dose to PG was 26 Gy. RTOG acute toxicity scoring was used to grade Xerostomia. Patient tumor and treatment related factors, including age, T, N stage, location of primary tumor, addition of chemotherapy, and RT doses were analyzed for outcomes and toxicities.
- **Results:** The median follow up was 16 months (range: 1 – 84). The 2-year local, locoregional, distant metastases free and overall survival rates were 90%, 90%, 91% and 71% respectively with a median time to failure of 15 months. Median values for PG's were: Vmean 14 cc (5-48), 25 cc (12-77) and RT doses were 52 Gy (26-65), 25 Gy (17-32) for ipsilateral and contralateral PG's respectively. Median percent weight loss was 10% at 7th week of treatment. Only 4% patients had grade 3 xerostomia. There was no significant correlation seen for Xerostomia with percent weight loss and/or ipsilateral ($p = 0.2$) or contralateral PG volumes ($p = 0.3$).
- **Conclusion:** Use of IMRT resulted in acceptable xerostomia rates with promising locoregional control rates.

A Turaka, B Weinberg , T Li , N Nicos , B Burtness , M Lango , J Ridge , S Feigenberg. SU-GG-T-178.
http://www.aapm.org/meetings/2010am/PRAbs.asp?mid=49&aid=12605; 2010 AAPM Annual Meeting

Intensity Modulated Radiation Therapy (IMRT) for Thyroid Cancer

Abstract.

- **Objective:** To evaluate outcomes and toxicities in patients with thyroid cancer treated with intensitymodulated radiation therapy (IMRT).
- **Methods:** This was a single institution retrospective review of 10 patients with thyroid cancer treated with IMRT at Fox Chase Cancer Center between May 2001 and June 2008. The median age was 69 years. Among the 10 patients, seven had papillary carcinoma, two had T3 and 8 had T4 disease, eight had N1 disease, and two had distant metastases. Radioactive iodine was given to all patients, while the median radiotherapy (RT) dose was 60 Gy.
- **Results:** Median follow up was 28.5 months (range: 4.5-to-50.6 months). The Kaplan-Meier estimates of 3-year local control, locoregional control, and overall survival rates 90%, 90%, and 80%, respectively. Nine patients had grade 2 skin toxicity, 10 had grade 2 pharyngitis/esophagitis, 2 had grade 2 laryngitis, and 3 had grade 3 laryngitis. Few grade 2 or 3 late toxicities were observed.
- **Conclusions:** IMRT is effective in the postoperative setting for the postoperative treatment of thyroid cancer. Long-term follow-up is still needed to assess the incidence of late toxicities.

Aruna Turaka, MD, Tianyu Li, MS, Jian Q. Yu, MD, FRCPC, Nicos Nicolaou, MD, Barbara Burtness, MD, Miriam N. Lango, MD, John A. Ridge, MD, FACS., and Steven J. Feigenberg, MD. *Thyroid Science* 5(1):CLS1-8, 2010

Young age is not associated with increased local recurrence for DCIS treated by breast-conserving surgery and radiation.

BACKGROUND: We report local recurrence (LR) after breast-conserving surgery and radiation (BCS + RT) for ductal carcinoma in situ (DCIS) to determine outcomes for patients aged <or=40 years compared with older women.

METHODS:

- The study included 440 women with DCIS treated from 1978 to 2007.
- All patients received whole-breast radiotherapy with a boost in 95% of cases.
- Demographics, characteristics, surgical, and adjuvant treatments were analyzed for an effect on LR.

RESULTS:

- Median age was 56.5 years with 24 patients aged <or=40.
- Median DCIS size was 0.8 cm.
- Re-excision was required in 62% of patients, and in 75% of those aged <or=40.
- Tamoxifen was used in 22%, but only one patient aged <or=40.
- Median follow-up was 6.8 years.
- Actuarial LR was 7% (95% confidence interval of 4-11%) at 10 years and 8% (5-14%) at 15 years. There was no difference in LR by age (P = 0.76).

CONCLUSIONS:

- The long-term risk of LR after BCS + RT for DCIS is low, even in patients <or=40 years. This may be due to patient selection for small size, high utilization of re-excision, and radiation boost.
- Young age may be a smaller contributor to LR risk in DCIS than previously suggested.

Turaka A, Freedman GM, Li T, Anderson PR, Swaby R, Nicolaou N, Goldstein L, Sigurdson ER, Bleicher RJ.
J Surg Oncol. 2009 Jul 1;100(1):25-31. doi: 10.1002/jso.21284. PMID: 19373863

Hypoxic prostate/muscle PO2 ratio predicts for outcome in patients with localized prostate cancer: long-term results

PURPOSE: To correlate tumor oxygenation status with long-term biochemical outcome after prostate brachytherapy.

METHODS AND MATERIALS:

- Custom-made Eppendorf PO(2) microelectrodes were used to obtain PO(2) measurements from the prostate (P), focused on positive biopsy locations, and normal muscle tissue (M), as a control.
- A total of 11,516 measurements were obtained in 57 men with localized prostate cancer immediately before prostate brachytherapy was given.
- The Eppendorf histograms provided the median PO(2), mean PO(2), and % <5 mm Hg or <10 mm Hg. Biochemical failure (BF) was defined using both the former American Society of Therapeutic Radiation Oncology (ASTRO) (three consecutive raises) and the current Phoenix (prostate-specific antigen nadir + 2 ng/mL) definitions.
- A Cox proportional hazards regression model evaluated the influence of hypoxia using the P/M mean PO(2) ratio on BF.

RESULTS:

- With a median follow-up time of 8 years, 12 men had ASTRO BF and 8 had Phoenix BF.
- On multivariate analysis, P/M PO(2) ratio <0.10 emerged as the only significant predictor of ASTRO BF ($p = 0.043$). Hormonal therapy ($p = 0.015$) and P/M PO(2) ratio <0.10 ($p = 0.046$) emerged as the only independent predictors of the Phoenix BF.
- Kaplan-Meier freedom from BF for P/M ratio <0.10 vs. ≥0.10 at 8 years for ASTRO BF was 46% vs. 78% ($p = 0.03$) and for the Phoenix BF was 66% vs. 83% ($p = 0.02$).

CONCLUSIONS:

- Hypoxia in prostate cancer (low mean P/M PO(2) ratio) significantly predicts for poor long-term biochemical outcome, suggesting that novel hypoxic strategies should be investigated.

Turaka A, Buyyounouski MK, Hanlon AL, Horwitz EM, Greenberg RE, Movsas B.
Int J Radiat Oncol Biol Phys. 2012 Mar 1;82(3):e433-9. doi: 10.1016/j.ijrobp.2011.05.037. Epub 2011 Oct 8. PMID: 21985947

Conventional versus Hypo fractionated IMRT: Results of Late GI and GU Toxicity and Quality of Life from a Phase III Trial

- Purpose/Objective(s): To compare late gastrointestinal (GI) and genitourinary (GU) toxicity and quality of life (QOL) in men treated on a Phase III trial of hypofractionation.
- Materials/Methods: The study randomized intermediate and high-risk men to 76 Gy in 2 Gy/fx (CIMRT) vs. 70.2 Gy in 2.7 Gy/fx (HIMRT). The HIMRT arm was hypothesized to be equivalent to 84.4 Gy in 2 Gy/fx (alpha/beta = 1.5). GI and GU related QOL was assessed using the corresponding domains of the Expanded Prostate Cancer Index Composite (EPIC) questionnaire at 0, 6, 12, and 24 mos. Global QOL was assessed with the EQ5D. EPIC and EQ5D questionnaire response rates ranged from 70-80% at 0 months to 59% at 24 months. There was no difference in EPIC or EQ5D response rates between the two groups. Two sample t-tests were used to measure differences in the EQ5D, EPIC and random effect models with linear time were used to estimate the difference. Chi-square tests were used to evaluate differences in the grades of GI/GU toxicities.
- Results: One hundred fifty-threemen received CIMRT and 154 received HIMRT. Median follow-up was 55 months (range: 7.4-87.3 months). There was no difference in GI ($p = 0.13$) or GU ($p = 0.8$) EPIC domain scores between groups at baseline. Over time, GI domain scores decreased ($p = 0.01$), but the rate of change was similar between groups ($p = 0.82$). GU domain scores were stable over time ($p = 0.5$) with a similar rate of change between groups ($p = 0.6$). There was no difference in EQ5D summary scores between treatment groups at baseline ($p = 0.17$). EQ5D scores were stable over time ($p = 0.97$) with similar rates of change between groups ($p = 0.76$). At all time points, EQ5D scores correlated with EPIC GI domain scores ($p< 0.0001$ for all) and GU domain scores ($p< 0.0002$ for all). There was no statistically significant difference in grade 2+ or grade 3+, late GUor GI toxicity between the two groups.
- Conclusions: Dose escalation with HIMRT does not appear to increase the risk for GU or GI toxicity or reduce QOL, as compared to standard IMRT to 76 Gy. Global QOL was associated with GI and GU function. HIMRT is an appealing dose escalation strategy with no apparent additional toxicity. Longer follow-up is needed to fully assess the biochemical failure endpoint.

A. Turaka, F. Zhu, M. K. Buyyounouski, E. M. Horwitz, D. Watkins-Bruner, A. A. Konski, A. Pollack. Proceedings of the 52nd Annual ASTRO Meeting. International Journal of Radiation Oncology Biology Physics, Vol. 78, Issue 3, S67.

Merkel Cell Carcinoma and Sentinel Lymph Node Evaluation: Outcomes from a Single Institution

Purpose/Objective(s):

- To retrospectively examine the role of sentinel lymph node biopsy (SLNB) and further lymph node dissection (LND) in predicting outcomes in patients (pts) with Merkel cell carcinoma (MCC).

Materials/Methods: Records of 88 pts with MCC between 1990 and 2010 were reviewed.

- The primary endpoints were to evaluate loco-regional (LR) failure patterns in pts who underwent SLNB versus those who did not undergo SLNB.
- The disease-free survival (DFS), overall survival (OS) and distant metastases free survival (DMFS) were measured using Cox proportional hazards model and LR control was measured using log-rank test.

Results:

- Forty-one (46%) patients underwent SLNB.
- The two groups (SLNB vs. no SLNB) were equivalent with respect to age, tumor size, stage.
- For the SLNB pts, median age was 70 (range 38 - 99). Median follow-up was 25 months (range: 2 - 110).
- Median primary tumor (tm) size was 1.5 cm (range: 0.7 - 9.7).
- Fifteen pts had clinical Stage I disease (37%), 16 Stage II (17%), 19 with Stage III (46%).
- Pts presented most commonly with primary lesions of the head and neck (11 pts, 27%), lower and upper extremity: 27%, 39% and 3 trunk (7%).
- On pathology evaluation, 19/41 were SLN positive (46%), of which 16 underwent subsequent LND.
- Five patients with negative SLNB did not receive adjuvant radiation and 2/5 had regional recurrence.
- Six patients had local (L) failures (15%).

A. Turaka, C. T. Murphy, Z. Fang, J. M. Farma, M. N. Lango, H. Wu, P. Engstrom, N. Nicolaou, C. Perlis. Int. J. Radiation Oncology d Biology d Physics Volume 81, Number 2, Supplement, 2011: S682 .

- On univariate analysis (UA), primary tm size ($p = 0.0003$), T stage ($p = 0.04$) and number of positive LN on pathology, [pLN] ($p < 0.0001$) were found significant.
- Regional failures (RF) were noted in 12 pts (29%). On UA, age ($p < 0.0001$), tm size ($p = 0.0002$), location of primary tm ($p = 0.03$) and no of pLN+ve were significant for RF.
- In pts with negative SLNB, 5 had LR recurrence (22%), vs. 8 of 19 (42%) with a positive SLNB. Only one patient who had a negative SLNB underwent additional dissection, which was path negative.
- The 2-year LR control rates were 64% vs. 57% for pts with and without SLNB ($p = ns$).
- The 2-year DFS and OS rates were 64% and 76% vs. 56% and 64% ($p = ns$) respectively and 2-year DMFS rates were 74% vs. 81% ($p = 0.03$).
- Conclusions: Our study shows, LR control rates were better for pts with SLNB with decreased regional

Adjuvant Radiotherapy in Merkel Cell Carcinoma: A 20-year Experience at a Single Institution

Purpose/Objective(s):

- There is limited knowledge of the effects of adjuvant radiotherapy (RT) in patients with Merkel cell carcinoma. We aim to examine the role of adjuvant RT in patients with MCC.

Materials/Methods:

- Retrospective reviewe: 1990 and 2010. The primary endpoints were loco-regional (LR) failure, disease-free survival (DFS) and overall survival (OS). Survival data was analyzed using the Cox proportional hazard model, recurrence rates were analyzed using chi-square method, and the Kaplan-Meier method was used to estimate 2 and 3-year survival rates.

Results:

- A total of 88 patients with MCC were identified. The median age was 72 years (range 35 - 99). Median follow-up time was 20 months (range 1 - 190 months). There were 51 men and 37 women, 86 Caucasian. Primary tumor location was: head and neck in 37 patients (42%), 22 upper extremity (25%), 20 lower extremity (22%) and 9 trunk (10%) Thirty-one patients (35%) presented with clinically positive nodes. Resected margins were positive in 27 patients (31%). 28 patients had Stage I disease (35%), 13 Stage II (16%), 34 Stage III (43%) and 5 Stage IV (6%). Seventy-one patients (81%) were available for assessment of adjuvant therapy. 56 patients (79%) received adjuvant radiation therapy (RT). Median RT dose was 50 Gy (range 45 – 65 Gy). There were 26 total LR failures (36%), 14 in patients receiving RT (25%) vs. 12 LR failures in patients who did not receive RT (80%). For patients receiving RT, the 2-and 3-year progression-free rates were 70% and 63% vs. 35% and 34% in patients who did not receive RT ($P = 0.01$). Of the 14 failures in patients receiving RT, 3 patients had Stage I disease, 1 Stage II and 10 had Stage III. Of the 12 LR failures in patients who did not receive RT, 2 had Stage I, 3 had Stage II, 6 had Stage III disease. The use of adjuvant RT improved the risk of LR failure on univariate analysis (UA) (OR = 0.256, 95% CI 0.073 - 0.904, $P = 0.034$) and it also improved the age- and stage-adjusted LR failure risk (OR = 0.227, 95% CI 0.053 - 0.967, $P = 0.04$). The use of RT was also an independent predictor of improved LR control on multivariate analysis (MVA) (HR = 0.057, CI 0.008 - 0.407, $P<0.01$). The 2- and 3-yr OS for all patients was 84% and 72%, respectively, 2- and 3-year DFS for all patients was 76% and 60%. The use of RT did not affect DFS or OS on MVA.

Conclusions:

- We present one of the largest series on the use of adjuvant RT in the treatment of MCC. Our data for this rare and aggressive tumor demonstrates that adjuvant RT improves LR control rates. RT was an independent predictor of improved LR control after adjusting for disease stage, which suggests a LR control benefit regardless of patient stage at presentation. Collaborative multi-institution efforts would further help identify patients who would best benefit from adjuvant RT.

C. Murphy, **A. Turaka**, F. Zhu, J. Farma, M. Lango, H.Wu, P. Engstrom, T. Galloway, N. Nicolau, C. Perlis. Int. J. Radiation Oncology d Biology d Physics Volume 81, Number 2, Supplement, 2011: S686

A better prognosis for Merkel cell carcinoma of unknown primary origin.

BACKGROUND:

- There is limited evidence that Merkel cell carcinoma (MCC) arising from a nodal basin without evidence of a primary cutaneous (PC) site has better prognosis.
- We present our experience at 2 tertiary care referral centers with stage III MCC with and without a PC site.

METHODS:

- Fifty stage III MCC patients were identified between 1996 and 2011.
- Clinical data were analyzed, with primary endpoints being disease-free survival and overall survival.

RESULTS:

- Of stage III patients, 34 patients presented with a PC site and 16 patients with an unknown primary (UP) site.
- Treatment strategies varied; of patients with UP vs. PC sites, 25% vs. 44% underwent combined regional lymphadenectomy and radiation, with an additional 25% vs. 15% receiving chemotherapy.
- The median disease-free survival for a UP site was not reached vs. 15 months for a PC site (hazards ratio = .48, P = .18).
- The median overall survival for a UP site was not reached vs 21 months for a PC site (hazards ratio = .34, P = .03).
- Multivariate analysis showed that UP status was a significant factor in overall survival (P = .002).

CONCLUSIONS:

- Stage III MCC with a UP site portends a better prognosis than MCC with a PC site.

Chen KT, Papavasiliou P, Edwards K, Zhu F, Perlis C, Wu H, **Turaka A**, Berger A, Farma JM.
Am J Surg. 2013 Nov;206(5):752-7. doi: 10.1016/j.amjsurg.2013.02.005. Epub 2013 Jul 5. PMID: 23835211

Absolute lymphocyte count: a potential prognostic factor for Merkel cell carcinoma.

BACKGROUND: Absolute lymphocyte count (ALC) is a laboratory value commonly obtained during workup of patients with Merkel cell carcinoma (MCC).

OBJECTIVE: We report the prognostic impact of ALC as a surrogate of immune status in MCC.

METHODS:

- A complete blood cell count was available for 64 patients with MCC in the month before definitive surgery, chemotherapy, or radiation.
- Statistical analysis was performed with classification and regression tree analysis, log rank test, and Cox model.

RESULTS:

- Median overall survival (OS) for the cohort was 97 months.
- Median OS for patients with an ALC less than 1.1 k/mm(3) was 18.8 versus 110.1 months for those with ALC greater than or equal to 1.1 k/mm(3) (P = .002, hazard ratio 0.29).
- Multivariate analysis of OS controlling for ALC, sex, stage, adjuvant chemotherapy, hematologic malignancy, and immunosuppression demonstrated ALC as a prognostic factor (P = .03).
- Disease-free survival at 36 months for ALC less than 1.1 k/mm(3) was 26.9% versus 64.4% for those with ALC greater than or equal to 1.1 k/mm(3) (P = .01).
- ALC was not a significant predictor for disease-free survival on multivariate analysis (P = .12).

LIMITATIONS: This is a single-institution retrospective data set.

CONCLUSION: ALC is associated with OS but not disease-free survival in MCC using a threshold of less than 1.1 k/mm(3). This test may provide additional prognostic information for patients with MCC.

Johnson ME, Zhu F, Li T, Wu H, Galloway TJ, Farma JM, Perlis CS, **Turaka A.**
J Am Acad Dermatol. 2014 Jun;70(6):1028-35. doi: 10.1016/j.jaad.2014.01.890. Epub 2014 Mar 22. PMID: 24666998

Presence and Clinical Significance of Polyomavirus in Merkel Cell Carcinoma of Unknown vs. Known Primary Cutaneous Origin

- Introduction: We have previously reported that patients with Merkel cell carcioma (MCC) of unknown primary (UP) have a better prognosis compared to patients with MCC of known primary cutaneous (PC) origin. A viral cause for MCC has been suggested, as human polyomavirus (Merkel cell polyomavirus, MCPyV) has been identified in up to 80% of MCC tumors. We sought to evaluate the presence of MCPyV in nodal tissues of patients with UP vs. PC MCC, and the clinical significance.
- Methods: We selected five patients with UP MCC and six patients with PC MCC with nodal metastases in adequate formalin-fixed, paraffin-embedded (FFPE) tissue. We also identified six patients with nodal metastases from either melanoma (n=4) or breast (n=2) to serve as controls. Tissues were de-paraffanized and total nucleic acids extracted using Qiagen tissue kit. Both MCPyV and human beta-actin gene (HB-actin, control) were amplified and detected by real-time PCR. Clinical data and outcomes were compared.
- Results: HB-actin was identified in all tissue samples. None of the control tissues (melanoma or breast) stained positively for MCPyV. Three out of 6 patients with PC MCC stained positively for MCPyV, and 3 out of 5 patients with UP MCC stained positively for MCPyV. Although sample sizes were small, there did not appear to be any correlation with MCPyV positivity and location of nodal metastasis, positive lymph node ratios, recurrence-free survival or overall survival. The median age of patients who stained positively for MCPyV was significantly lower than those who did not (58 years vs. 76 years, $p<0.005$).
- Conclusion: With our preliminary data, MCPyV positivity does not appear to have an effect on survival in MCC or UP vs. PC status, and cannot be used as a mechanistic explanation for improved survival in patients with UP MCC.

K. T. Chen, J.Y. Sun, **A. Turaka**, Y. Tang, J.M. Farma, H. Wu. ASC20140090. 9th Annual Academic Surgical Congress 2014

Multidisciplinary therapy of stage IIIA non-small-cell lung cancer: long-term outcome of chemoradiation with or without surgery.

BACKGROUND:

- Stage IIIA non-small-cell lung cancer (NSCLC) is highly heterogeneous due to differences in the size of the primary tumor and the extent and location of nodal disease.
- Although the addition of surgery to chemoradiation (CRT) did not improve overall survival (OS) for stage IIIA patients in a randomized intergroup trial (INT 0139), subset analyses of the trial suggest that a trimodality approach incorporating lobectomy may be superior to bimodality therapy with chemoradiation alone.

METHODS:

- We analyzed the outcomes of patients with stage IIIA NSCLC (T3N1, T1-3N2) treated between Jan 2000 -Dec 2008.
- We compared OS for those undergoing definitive chemoradiation to those undergoing chemoradiation followed by either lobectomy or pneumonectomy.
- Demographic variables were balanced by propensity score analysis method.

RESULTS:

- In our analysis of 249 patients, the median age was 65 years, 43% were men, and 96.5% had N2 disease.
- Chemoradiation followed by lobectomy yielded superior OS compared with chemoradiation (median OS 39 months vs 22 months, P = .038 after propensity score adjustment).
- There was no significant survival benefit for pneumonectomy over CRT (median survival 28 vs 22 months, P = .534).

CONCLUSIONS:

- Our data corroborate the findings of the INT 0139 trial.
- We propose that a formal randomized trial be performed comparing chemoradiation followed by lobectomy vs definitive chemoradiation in patients with stage IIIA disease whose tumors are resectable by lobectomy.
- Our data do not support the incorporation of pneumonectomy in the management of stage IIIA patients with N2 disease.

Aggarwal C, Li L, Borghaei H, Mehra R, Somaiah N, **Turaka A**, Langer CJ, Simon GR. Cancer Control. 2014 Jan;21(1):57-62. PMID: 24357742

Tri modality Treatment (Carboplatin + Paclitaxel + Radiation Therapy and Surgery) of Locally Advanced Lung Cancer: The Fox Chase Cancer Center Experience

- Purpose/Objective(s): The goal of this analysis was to determine patterns of failure and overall survival of locally advanced non-small cell lung carcinoma (LA-NSCLC) patients (pts) treated with induction chemoradiation therapy (CRT) using Carboplatin (C), Paclitaxel (P) and radiation therapy (RT) followed by planned surgery (S).
- Materials/Methods: Between 2002 and 2008, 146 pts were treated with trimodality therapy for LA-NSCLC. To be considered a candidate, pts had either operable N2 disease or bulky hilar disease (T1 - 3, select T4, N0 - 2, Stage II-IIIA, resectable chest wall disease) after CRT. During this time course, trimodality therapy was offered on a phase II trial between 2002 and 2006 (n = 19). After the study closed due to poor accrual, additional pts were treated per this protocol (n = 43). Trimodality treatment consisted of chemotherapy administered weekly C (AUC of 2) and P (50 mg/m2) during RT, 50.4 Gy (1.8 Gy/day, 5 days/week), surgical resection and adjuvant C (AUC 6) day 1 and P 100 mg/m2/wk days 1, 8, and 15 Q 4 wks x 3. The demographic characteristics, prognostic information and treatment information between pts treated on protocol and off-protocol were compared (n = 62). The pathological response rates, rate of distant metastases (DM), progression free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier curve and Fisher's exact test for categorical variables.
- Results: Median follow-up was 35.0 months (range: 2.5 - 85.1) for the entire group. Median age was 63.5 years (41 - 78), 70% were former smokers, 26% current smokers. The median primary tumor size was 5 cm (range: 1.1 - 10), 63% had clinical N2 disease. Seventy nine percent (n = 15) of pts on protocol and 47% (n = 20) off-protocol were treated to RT dose of 50.4 Gy. R0 resection was performed in 63% (n = 12) and 98% (n = 42) of on and off-protocol pts respectively (p = 0.08). Lobectomy/ bilobectomy was performed in 53%; 35% had pneumonectomy. Pathologic CR at the primary site was noted in 20% for the total group (21% and 19% each group, p = 0.70) and in 48% at nodal sites (47% and 49%, p = 0.83). Loco-regional failures were noted in 8 pts (13%): 3 (16%) and 5 (12%) in each group (p=0.08). Five (26%) pts treated on protocol developed DM, while 11 (26%) treated off-protocol had DM. Estimated 3- year PFS were 65% and 59%, (p= 0.74); and OS rates at 3-yrs were 56% and 62% (p = 0.69) respectively.
- Conclusions: Induction CRT using Carboplatin, Paclitaxel can be incorporated into standard practice along with RT dose escalation to improve future outcomes. Based on our data, there was no difference in outcomes for Stage III NSCLC pts treated with trimodality therapy, on or off-protocol. This is likely attributable to the established, collaborative, multidisciplinary team approach in a single center.

A. Turaka, Z. Fang,W. J. Scott, P. C. Shah, R. Mehra, C. Aggarwal, H. Borghaei, E. King, S. J. Feigenberg, C. J. Langer. International Journal of Radiation Oncology Biology Physics, Vol. 81, Issue 2, S592–S593. Published in issue: October 01, 2011.

Role of Radiation Therapy for Malignant Thymoma: A Single Institution Experience

- Purpose/Objective(s): To evaluate the benefit of radiation therapy (RT) following surgery for malignant thymoma and identify risk factors that may affect treatment related outcomes.
- Materials/Methods: We conducted a retrospective review of 34 patients (pts) with malignant thymoma treated between 1995-2010 at our institution. The clinicopathological factors were reviewed for all pts including gender, WHO histology, modified Masaoka stage, presence of myasthenia gravis, size of the lesion, type and extent of surgery and margin status. Overall survival (OS), local relapse free (LRFS) and distant metastases free (DMFS) survival rates were estimated using Kaplan-Meier method. Cox's proportional hazard regression model was used to assess the relationship of OS and LRFS with the risk factors.
- Results: Six of thirty-four were Masaoka stage IA-B, 11 stage IIB (32%), four stage III and 10 stage IVA. Median age was 58 years (range: 24-79). Myasthenia gravis was seen in 5 pts. Seventeen had large tumors (> 8 cm). WHO classification: type A five, AB five, B1 and B2 four patients each, B3 in 11 and five pts had type C. R0 resection was done in 14 pts, R1 in 10 pts, R2 in 3 and no surgery (biopsy only) in seven pts. Thirteen pts had positive margins. Adjuvant RT was given to 19 pts, 4 had preoperative RT and one pt was treated with definitive concurrent chemoradiation (stage IVA). Neoadjuvant chemotherapy was given to 10 pts (5 pts had Cyclophosphamide, Adriamycin, Cisplatin [CAP]; 3 pts Cisplatin, Etoposide [EP] and 2 pts Carboplatin, Paclitaxel). Four pts received adjuvant chemotherapy (2 CAP, 1 EP and 1 pt Carboplatin, Paclitaxel). Median follow up was 56 months (range: 4.1-248). The median RT dose was 5040 cGy (range: 4500-6600) with 180-200 cGy dose per fraction in 25-35 fractions over 42 days (32-69). The 5-year OS for patients with stage I was 66.7%, stage II 90%, stage III 75% and stage IVA 41.7% (pZ 0.02). The 5 yr LRFS was 100% for stage I, 91% stage II, 100% stage III and 65.6% stage IVA (pZ 0.51). In a subset analysis for stage II pts treated with and without RT (NZ11), the 5 yr OS, LRFS and DMFS rates were 100%, 50% (pZ0.04); 100%, 50% (pZ 0.03) and 76%, 100% (pZ0.54) respectively. At last visit, 16 pts were disease free (47%), 3 pts had local recurrence (9%) and 12 developed distant metastases (35%). On Univariate analysis, OS varied with Masaoka stage (pZ0.02), WHO histology (pZ0.005) and size of the lesion (8 cm or more, pZ 0.08). None of the other factors such as gender, myasthenia gravis, type and extent of surgery and margin status had an impact on OS, LRFS or DMFS.
- Conclusions: In this analysis, high risk pts based on Masaoka stage, WHO classification and bulky tumors (> 8 cm size) benefited from radiation therapy and use of RT should be strongly considered based on the risk factors particularly for stage II pts.

A. Turaka, T. Li, W.J. Scott, H. Borghaei, P.C. Shah, M.K. Buyyounouski. DOI: http://dx.doi.org/10.1016/j.ijrobp.2012.07.1499. International Journal of Radiation Oncology Biology Physics, Vol. 84, Issue 3, S563, November 01, 2012

Twice Daily Versus Once Daily Radiation Therapy in Unselected Limited-Stage Small Cell Lung Cancer Patients: "Medicine-Based" Evidence

Purpose/Objective(s): Evidence-based medicine is rooted in evidence from high-quality Phase III randomized trials examining a highly selected patient population. Phase III evidence has demonstrated the benefit of twice daily (BID) over once daily (QD) radiation therapy (RT) for limited stage small cell lung cancer (LS-SCLC). The purpose of this study is to compare BID vs QD RT in an unselected population of consecutive LSSCLC patients to learn if BID RT is beneficial for the population at our institution.

Materials/Methods: Between 1991 and 2012, 215 patients (pts) received chemoradiation and were retrospectively reviewed. Two different RT dose patterns were used at the preference of the patient and physician but, largely driven by patient convenience. BID RT (15%) consisted of 45 Gy in 30 twice daily fractions. The median RT dose for QD RT (85%) was 52.2 Gy (range, 10.8-71). Cisplatinum chemotherapy was used in the majority (63%). Prophylactic cranial irradiation (PCI) was used in 44%, median dose 30 Gy. Local control rates (LCR) and overall survival (OS) were analyzed using Kaplan-Meier method for univariate analysis and Cox proportional hazard model for multivariate analysis (MVA). Both analysis included age, RT dose, BID RT, type of chemotherapy for LCR and additionally for OS, interval to development of brain metastases after PCI, and interval between thoracic RT and PCI, and PCI dose.

Results: Median follow-up was 18.7 months (range, 0.6-209 months). Median age was 64 years (range, 41-92 years), 34% were former smokers, 17% current smokers. The median time to local recurrence was 18 months (range, 0.3-209 months) and the median OS 19 months (range, 0.6- 209 months). The 3-year LCR was 88%. The 3 and 5-yr OS rates were 24% and 16%. Local failure was noted in 18 (8%) pts, locoregional 13 (6%), distant metastases in 136 (63%), and 75 (35%) pts developed brain metastases. The interval to development of brain metastases after PCI was 19 months (range, 4.4-203 months) and interval between thoracic RT and PCI was 118 days (range, 0-708 days). On UA, age was significant predictor for LCR (p Z 0.008). On UA, the 5-yr OS for pts treated with 45 Gy, BID was 22% vs 16% for other RT doses (6% absolute benefit, p Z 0.04). Also, the addition of PCI lead to an improvement in OS (5-yr OS: 19% vs 14%, with 5% absolute benefit; p Z 0.02). There was a trend towards improvement in OS in pts treated with Cisplatinum chemotherapy (5-yr OS: 20% vs 11%, p Z 0.07). On MVA, the only factor significant for LCR ($p < 0.04$) and OS was age ($p < 0.03$).

Conclusions: Within the limitations of the study population and the methodology of this analysis, our retrospective review is consistent with the results of Phase III evidence that BID is superior to QD RT. This "medicine-based" evidence reinforces the treatment policy at our institution, which is to favor BID RT whenever feasible.

A. Turaka, T. Li, M.J. Naik, M. Unger, E. King, P.C. Shah, W.J. Scott, H. Borghaei, and M.K. Buyyounouski, International Journal of Radiation Oncology Biology Physics, Vol. 87, Issue 2, S507–S508, Published in issue: October 01, 2013

Effectiveness and Timing of Prophylactic Cranial Irradiation (PCI) in Limited Stage Small Cell Lung Carcinoma (LS-SCLC) Patients: A Single Institution Experience

Purpose/Objective(s): PCI has shown benefit on both disease free survival and overall survival (OS) in meta-analysis of patients (pts) with LS-SCLC after complete response to chemo-radiation therapy (CT-RT). There was decrease in the incidence brain metastases (BM) after PCI (25.3% decrease at 3 years, Auperin meta-analysis, NEJM, 1999), with 5% absolute benefit on OS. We performed an exploratory analysis to evaluate the effectiveness and timing of PCI.

Materials/Methods: This is a single institution retrospective review. Between 1991 and 2012, 215 pts with LS-SCLC were treated with CT-RT. PCI was used in 44% (n Z 95) of pts after complete response to CT-RT. The median PCI dose was 30 Gy (range, 15-44 Gy), in 10 once daily fractions. BM control and overall survival (OS) were analyzed using Kaplan-Meier method for the univariate analysis (UA) and Cox proportional hazard model for multivariate analysis (MVA). Both analyses included age, RT total dose, BID RT (hyperfractionation), type of chemotherapy, interval to development of brain metastases after PCI/CTRT in non-PCI pts, interval between thoracic RT and PCI and PCI dose.

Results: Median follow-up was 19 months (range, 0.6-209 months). Median age was 64 years (range, 41-92 years). BID RT (45 Gy in 30 twice daily fractions) was given in 15% (31/215). Cisplatinum chemotherapy was used in 63% of pts. The 3-year locoregional control rate was 88%. The 3 and 5-yr OS rates were 24% and 16%. Addition of PCI lead to an improvement in OS (5-yr OS: 19% vs 14%, with 5% absolute benefit; $p < 0.02$). Seventy five (35%) pts developed brain metastases: of these, 37 after PCI and 38 pts non-PCI ($p < 0.26$). The interval to development of brain metastases was 15 months (range, 0.2-209), with a median interval of 19 months after PCI vs.13 months in non-PCI pts. The 1 and 2-yr actuarial rate of BM development was 11% vs 23% and 34% vs 40% for PCI vs non-PCI pts. The 3 and 5-year actuarial rate of BM was 45%, and 48% for all pts. Twenty percent of pts treated with PCI developed BM at 17 months vs 10 months for untreated pts. The interval between thoracic RT and PCI was 4 months (range, 0-24). The 2-yr rate of BM development was 22% for those treated early vs 46% for pts treated later than 4 months with PCI; $p < 0.04$). The 2-yr incidence of BM with PCI doses of <30 vs 30 Gy was 43% vs 29%. On MVA, PCI dose (p Z 0.008) and time to development of BM at 2 yrs ($p < 0.0001$) were significant for OS. For PCI pts, age (pZ0.009), Cisplatin based chemotherapy ($p< 0.03$) were significant for BM on MVA and there was trend towards decrease in BM with BID thoracic RT ($p < 0.08$).

Conclusions: The results of our retrospective analysis are comparable to the previously published data and support the use of PCI for pts with LSSCLC. PCI has shown benefit on OS and earlier administration led to decrease in the incidence of brain metastases.

A. Turaka, T. Li, M.J. Naik, M. Unger, E. King, P.C. Shah, W.J. Scott, H. Borghaei, and M.K. Buyyounouski. International Journal of Radiation Oncology Biology Physics, Vol. 87, Issue 2, S518. Published in issue: October 01, 2013.

Curative Radiation Therapy for Primary Ocular Lymphomas: Demonstration of Dose Response

Purpose/Objective(s):

- Orbital lymphomas (OL) are rare and account for less than 1% of all cases of Non-Hodgkin lymphoma. Radiotherapy (RT) alone provides good local control rates (97-100%) for extranodal marginal zone lymphoma (MALT) of the orbit.

Materials/Methods:

- Between 1991 and 2008, 23 patients (28 eyes, 5 bilateral, 20%) treated with local radiation therapy for orbital lymphoma were reviewed.
- Treatment consisted of 24-36 Gy, 1.5-2.5 Gy per fraction (median 30Gy in 20 fractions) of RT to the orbit using 6 MV photons (median fields: 2).
- Patient tumor and treatment related factors including age, stage, histology, and systemic evaluations, type of treatment, RT details and late side effects were analyzed for the local control rates (LC), relapse free and overall survival (OS) by number of patients and orbits independently.

Results:

- The median follow-up was 27months (range: 1-123 months). The median age was 72 years (range: 37-87), 11 were females, 12 males.
- Most common presenting symptom was proptosis (74%).
- Twenty patients had tumor in orbit only, 2 in conjunctiva only and 1 in both conjunctiva + orbit. Histology was MALT in 13 patients, and other low grade B cell NHL in 10 others.

H. Borghaei, **A. Turaka**, T. Li, M. R. Smith, R. J. Schilder, N. Nicolaou. Int. J. Radiation Oncology d Biology d Physics Volume 78, Number 3, Supplement, 2010,: S556

- The 5-year LC and OS rates were 95%,63% by patients and 96%,68% by orbits respectively.
- The 5-year LC rate at patient level for MALToma was 91% versus 100% for other NHL histologies ($p = 0.3$) and 100% for RT dose > 30 Gy versus 75% for <30 Gy ($p = 0.04$). One patient had both systemic + orbital relapse and systemic relapse was seen in two.
- The median interval to first relapse was 25 months (0.99- 122.37).
- On univariate analysis including age (< 70 versus . >70 years), stage (IAE vs. others), histology (MALT versus others), and location of tumor (orbit vs. others), there was no difference in outcomes except for RT dose (> 30Gy vs.< 30Gy) for LC ($p = 0.04$).
- 4/23 patients had three lines of improvement in Snellen's visual acuity after one year of treatment. Minimal dry eye was seen in 77% patients.
- Five patients developed cataracts. There were no late effects like corneal ulcer, papillopathy or secondary glaucoma.

Conclusions: Radiation therapy alone is the extremely effective in the curative management of primary localized orbital lymphoma. RT dose of 30 Gy provides better LC rates.

Results of Radiation Therapy for Primary Extranodal Lymphoma of the Head and Neck: A Report of Case Series

- Purpose/Objective(s): Radiation therapy is an important treatment modality for the extra-nodal lymphoma (ENL) of the head and neck. Intensity Modulated radiation therapy (IMRT) has been shown for head and neck cancers to be associated with decreased late side effects like Xerostomia compared with conventional RT techniques (Conv.RT). The purpose of the study is to determine the clinicopathological features, treatment outcomes and late toxicities in patients (pts) with ENL of head and neck treated with different RT techniques.
- Materials/Methods: Retrospective review of records from 2007-2010 identified 14 pts with ENL of the head and neck treated with. Eight were treated with IMRT and 6 with conventional RT technique. Thirteen had CD20+ non-Hodgkin lymphoma [NHL; 7 diffuse large B cell (DLBCL), 3 MALT, 3 others], and one Hodgkin's lymphoma (HL; classic). All pts underwent routine staging work-up with negative bone marrow biopsy for all. Pre and post-treatment PET scans were done in 7 pts. Initial chemotherapy (R-CHOP x 4-6 courses for DLBCL, ABVD x 4 for HL), or no chemotherapy (MALT) was followed by involved field radiation therapy (median RT dose: 36 Gy for NHL, 30 Gy HL, 150- 180 cGy per fraction in 20 fractions over 4 weeks).
- Results: The median follow up was 28 months (range: 1- 52). The median age was 60 years (range: 42-95; 7 males and 7 female). Nine had stage IEA disease, 3 had stage II and 2 stage IV. Five had oropharynx involvement, two had paranasal sinus (DLBCL) 2 nasopharynx (1 DLBCL, 1 MALT) and 1 vallecula (HL). The overall response rate after combined modality treatment was 100%. There were no FDG avid lesion noted on posttreatment PET. There were no local or neck node relapses at last follow up. The 2-year actuarial survival rate was 80%. One DLBCL patient had systemic relapse involving stomach and bilateral testes, was treated with second-line chemotherapy and radiation therapy. At the last follow up, 12/ 14 were alive. RTOG grade 2 acute skin changes were noted in 6 pts (3 by each RT technique), grade 2 mucositis in 5 pts (3 with Conv.RT) and grade 2 xerostomia in 6 pts. None of the pts developed grade 3 xerostomia (both acute and late). Late grade 2 Xerostomia was seen in 5 pts treated with Conv.RT but not with IMRT.
- Conclusions: RT following chemotherapy or used alone in ENL of head and neck was associated with local and distant disease control in the majority of patients, with a toxicity profile that appears favorable for IMRT compared with conventional radiation therapy techniques. Larger studies are required to confirm that IMRT is as effective as conventional involvedfield RT.

A. Turaka, T. Li, M.M. Millenson, and M.R. Smith; International Journal of Radiation Oncology Biology Physics, Vol. 84, Issue 3, S621 Poster Viewing Abstracts S621, November 01, 2012

Lacrimal gland lymphoma: Role of radiation therapy.

BACKGROUND: To report the clinical and treatment outcome of patients with lacrimal gland lymphoma (LGL) treated with radiation therapy (RT).

MATERIALS AND METHODS: Institutional review board approved retrospective chart review of eight patients and literature review.

RESULTS:

- The study patients included six males and two females with a mean age of 70 years (range 58-88 years).
- The mean follow-up period was 23 months (range 3-74 months).
- Four patients had mucosa-associated lymphoid tissue (50%) lymphoma and four patients had other non-Hodgkin's lymphoma variants.
- Four patients had bilateral disease (50%).
- Four patients had primary LGL (stages I-IIAE, 50%) and four had LGL as part of systemic lymphoma (stage IVAE, 50%).
- The median RT dose was 2987 cGy (range 2880-3015 cGy).
- All patients had complete response to RT with symptomatic relief.
- Minimal dry eye was seen in all patients.
- There were no late effects such as corneal ulcer, radiation retinopathy, maculopathy, papillopathy, or secondary neovascular glaucoma.

CONCLUSIONS: RT alone is an extremely effective treatment in the curative management of localized LGL and provides durable, local control of secondary LGL.

Townsend N, **Turaka A**, Smith MR. Oman J Ophthalmol. 2012 Jan;5(1):37-41. doi: 10.4103/0974-620X.94765, PMID: 22557875

Extranodal Lymphoma and Radiation Therapy: A Single Institution Experience

- Purpose/Objective(s): To analyze the outcomes and patterns of relapse of patients with extranodal lymphoma (ENL) patients treated with radiation therapy (RT) alone or combined modality treatment.
- Materials/Methods: A retrospective analysis of patients treated for extranodal lymphoma from 2000 - 2012 was performed. Inclusion criteria for this analysis included: stage, low grade, intermediate or high grade histologies, treated with curative intent. Overall survival (OS) and local control (LC) rates were analyzed via Kaplan-Meier estimation method.
- Results: We identified 45 patients who met the inclusion criteria. The median follow up was 18 months (range: 0-74). The median age at diagnosis was 68 years (range: 41-95). 89% were whites. Among these, 43 (95%) had Non-Hodgkin lymphoma and 42 patients (93%) were CD 20 positive. Twenty five patients had Stage IAE (55%) disease, 8 had stage II and 12 had stage IV disease. The most common histology was MALT (mucosa-associated lymphoid tissue): 18 patients (40%). Twenty-four patients had low grade histology (55%), 18 patients had intermediate grade (41%). Nineteen patients (42%) had head and neck ENL, while other common sites included orbit, stomach and breast (51%). Thirty one patients were treated with involved field radiation therapy (IFRT). IMRT was utilized to treat 14 (36%) patients. The median RT dose was 30 Gy. Twelve patients were treated with R-CHOP chemotherapy, R-CDOP for 3, R-CVP for 2 and single agent Rituxan for 4 patients. In the whole series the 2-year and 5-year OS rates were 79% and 63% respectively. The LC rates were 95% at both 2- and 5-years. The 2 year LC and OS rates for stage I were 92% and 79%. On univariate analysis, none of the factors including age, stage, histology, location of the ENL influenced OS or LC rates except for RT dose (vs. > 30 Gy, $p < 0.002$), use of IMRT ($p < 0.04$) on OS and use of IFRT on LC rate ($p < 0.02$). The most common pattern of failure was distant (17%), with only 2 (5%) documented in-field relapses.
- Conclusions: Radiation therapy offers excellent local control particularly for stage IAE ENL. Radiation therapy alone with involved field technique may offer a feasible and effective modality for patients who cannot tolerate more aggressive treatments. Better systemic therapy approaches are needed to reduce the distant metastatic failure rate and improve survival in extranodal lymphoma.

M.E. Gamez, T. Li, M.M. Millenson, M.R. Smith, **A. Turaka**. DOI: http://dx.doi.org/10.1016/j.ijrobp.2012.07.1656
International Journal of Radiation Oncology Biology Physics, Vol. 84, Issue 3, S620. Published in issue: November 01, 2012.

Evolving Treatment Methods in the Management of Primary Breast Lymphoma (PBL)

Role of Radiation Therapy

Although the primary goal of treatment remains ultimately curing the patient, the line between curing a patient and "do no harm" is thin.

Intensity modulated radiation therapy (IMRT) has nearly replaced conventional photon-beam radiotherapy in treating many disease sites. The primary advantage is the ability to deliver the optimal dose of radiation to the tumour site while reducing the exposure of surrounding healthy tissue. At our facility, we prefer management with IMRT in order to reduce surrounding toxicity while maintaining efficacy. In addition to radiation technique, other means of reducing radiation exposure include limiting the total dose delivered as well as modifying the radiation field.

The ideal dose of radiation in the management of these patients is contentious. Most studies historically used a wide array of doses ranging from 30 to 50 Gy. More recently, a phase III study examined the ideal radiation dose and showed no differences when patients were treated with a lower dose of radiation. Indolent NHL (Follicular and marginal zone lymphoma) patients were randomized to receive 40-45 Gy in 20-23 fractions or 24 Gy in 12 fractions, while aggressive NHL (DLBCL, as part of combined modality therapy) were randomized to receive 40-45 Gy in 20-23 fractions or 30 Gy in 15 fractions. NCCN guidelines recommend doses of 24-30 Gy (1.8-2.0 Gy per fraction over 2-3 weeks duration) to the marginal zone lymphoma (non-stomach extranodal sites) and 30-36 Gy as consolidation after chemotherapy for DLBCL. The whole breast alone is considered in the clinical target volume (CTV). Extrapolating from this data, at our institution we typically treat patients to 30-36 Gy for PBL. Over time there has been a movement to limit radiation treatment fields in order to reduce toxicity while still maintaining good outcomes. More recently, involved-field radiation therapy (IFRT) has largely replaced extended-field radiation therapy. IFRT involves radiation to the clinically involved region in addition to the adjacent nodal regions. For patients with stage I-II PBL this results in radiation to the breast as well as involved axillary lymph nodes. The use of involved-nodal radiation therapy (INRT) or treatment only to the involved pre-chemotherapy and post-chemotherapy lymph nodes is a newer concept which has demonstrated encouraging results. Multiple international trials are currently examining the role of INRT in treating lymphoma. These results will likely further modify our delineation of the treated volume.

The ideal methodology for treating PBL remains controversial. While chemotherapeutic regimens and radiation options vary by institution, it is generally agreed that combined modality therapy offers the best rates of cure. Rather than improving outcomes in these patients, over the next years the goal will be to limit toxicity while maintaining similar efficacy. These goals will likely be met when the ideal balance between chemotherapy and radiation is reached, thereby curing the patient while limiting unnecessary side effects.

Shaikh T, **Turaka A** (2013). Evolving Treatment Methods in the Management of Primary Breast Lymphoma (PBL). OMICS J Radiology 3: e122. doi:10.4172/2167-7964.1000e122

Nasopharyngeal Hodgkin lymphoma

- A 50-year-old woman presented to her primary care physician with right nasal congestion and right parotid swelling.
- Past medical history was not significant, and she was a current smoker with a 35 pack-year history. Symptoms did not respond to antibiotics or steroids, and she was referred to an otolaryngologist. Physical exam and nasal endoscopy demonstrated a swelling in the adenoid pad, more prominent on the right.
- Computed tomography (CT) scan confirmed the presence of a nasopharyngeal soft tissue density measuring 4.1 cm in diameter.
- A biopsy revealed atypical lymphoid hyperplasia. There were scattered large atypical cells with prominent nuclei positive for CD30; focally positive for CD15; and negative for CD20, CD45, CD56, and Epstein-Barr virus (EBV; LMP1). There were no clonal B cells on flow cytometry. This was felt to be suspicious for classical Hodgkin lymphoma.
- An adenoidectomy was subsequently performed.
- MRI done 3 months later, the mass had recurred, and nasal endoscopy with excision of nasopharyngeal mass was performed.
- Pathology demonstrated a nodular infiltrate of small lymphocytes with scattered classical Reed-Sternberg cells. The lymphoma cells were positive for CD15, and CD30 with a characteristic Golgi staining. They were negative for CD20, CD45, and EBV (LMP1), and no clonal *IGH* gene arrangement was identified. CD3 stain highlights background T lymphocytes. This was felt to be consistent with lymphocyte-rich classical Hodgkin lymphoma of the nasopharynx.
- Additional work-up: Bone marrow was negative for lymphoma, and PET-CT scan demonstrated fluorodeoxyglucose avidity only in the nasopharynx; standard uptake value maximum was 7.4, with no lymphadenopathy identified.
- She was therefore stage IEA. It was recommended that the patient receive 2 cycles of ABVD chemotherapy followed by a restaging PET scan. However, pulmonary function tests obtained before initiating chemotherapy demonstrated a decreased diffusing capacity, at 61% of predicted level.
- She received two cycles of doxorubicin, vinblastine, and dacarbiazine. Restaging PET scan demonstrated a complete response.
- She was then referred for radiation therapy (RT) to the primary, and received 20 Gy in 10 fractions to the nasopharynx (2 Gy per fraction, five fractions per week) of involved field RT using intensity-modulated RT. Daily cone beam CT was done for treatment verification and image guidance. The lymph nodes in the neck were not included in the treatment volume.
- She tolerated treatment well without significant toxicity.
- She was without clinical evidence of disease recurrence at the last follow-up visit, 2 months post-RT.

Johnson ME, Robu VG, **Turaka A**. J Clin Oncol. 2014 Apr 10;32(11):e40-1. doi: 10.1200/JCO.2012.48.6183. Epub 2014 Jan 21. PMID: 24449240.

Primary mucosa-associated lymphoid tissue lymphoma of the thyroid with concomitant papillary carcinoma

Objective: Papillary thyroid carcinoma combined with thyroid mucosa-associated lymphoid tissue (MALT) lymphoma is exceedingly rare and there is no standard management.

CASE REPORT: A 60-year-old woman with a long-standing history of Hashimoto's thyroiditis presented with a painless lump on her right throat of 3 months' duration. She denied any dysphagia or hoarseness, or B symptoms.

- A 2 cm right thyroid mass was palpated on examination, without any palpable neck lymph nodes bilaterally.
- A mildly enlarged (right lobe 3 .5 x 3.2 cm) and heterogeneous thyroid without any focal masses or adenopathy was noted on ultrasonography (USG) and confirmed by computed tomography (CT) scan.
- Fine needle aspiration (FNAC) was non-diagnostic, with possible lymphoproliferative disease or thyroiditis.
- She underwent a right thyroid lobectomy. Pathology showed MALT lymphoma, Hashimoto's thyroiditis and 4 mm papillary carcinoma, follicular variant, confined to the lobe. On immunohistochemical staining, cells were positive for CD20, focally positive for CD10 (cluster designation), Bcl 6 (B-cell lymphoma) and negative for Bcl 2. Atypical lymphoplasmacytic infiltrate with kappa light chain restriction consistent with extra-nodal marginal zone MALT lymphoma was noted.
- Workup for lymphoma including CT scan of the neck, chest, abdomen and pelvis, peripheral blood flow cytometry, complete blood count, comprehensive panel and lactic acid dehydrogenase was negative. Serum thyroid stimulating hormone (TSH) confirmed existing thyroiditis and staged as IEA.
- A multidisciplinary team discussion involved treating her with radiation therapy alone.
- She received 3,000 cGy in 20 fractions over 27 days, 150 cGy per fraction. Target area included right thyroid bed as well as left lobe and isthmus of the thyroid gland, and excluded neck lymph nodes. Dose was prescribed to 95% isodose line and antero–posterior portals were used.
- Mild erythema was noted over the involved field in addition to mild dysphagia secondary to esophagitis.
- Serial CT scans done every 6 months showed no evidence of disease. Predictably, thyroiditis progressively worsened with elevated TSH and dose of levothyroxine was increased. She was disease free at the last follow-up of 3 years.

Conclusion: Patients with Hashimoto's thyroiditis are prone to develop other thyroid pathology, including rare tumours such as MALT lymphoma. The differential diagnosis for a neoplasm in such patients should be wide.

Shaakir Hasan, **Aruna Turaka**. Journal of Radiotherapy in Practice / *FirstView* Article pp 1-3 Cambridge University Press 2014. DOI:http://dx.doi.org/10.1017/S1460396914000090 (About DOI), Published online: 20 February 2014.

ROLE OF RADIATION THERAPY FOR GASTRIC LYMPHOMA: A SINGLE INSTITUTION EXPERIENCE.

- **Objectives:** Extra-nodal lymphoma of the stomach is rare among all NHL's. Stage I & II marginal zone lymphoma (MALT) of the stomach is usually treated with definitive radiation therapy alone and provides high local control rates (LCR) and overall survival (OS). We reviewed the treatment results of radiation therapy (RT) for stage I and II MALT lymphoma at our institution.
- **Methods:** We performed a retrospective review of all patients diagnosed and treated for gastric lymphoma between 1999-2013. Intensity modulated radiation therapy (IMRT, VMAT) was adopted since 2010 and AP-PA, 3D-conformal radiation therapy (3D-CRT) techniques were used prior. Logistic regression was used to correlate patient and treatment factors with LCR and OS. Kaplan-Meier method was used to estimate OS and LCR.
- **Results:** Twenty five patients (pts) met the inclusion criteria. A total of 21 patients had MALT (84%), 18 (72%) had stage IE disease, 2 (8%) with IIE disease. None of the pts had B symptoms. Median age was 62 years (range: 33-85). Median follow up was 37 months (range: 1.08-158.0). Median RT dose was 30 Gy (range: 27-36). Helicobacter Pylori (H Pylori) was positive in 9 pts (39%) and a trial of antibiotics was given to 12 pts (52%) prior to RT. IMRT was used for 7 pts (18%), 10 pts (40%) were treated with 3D-CRT, 6 pts (24%) with AP-PA fields. Use of IMRT resulted in optimizing the doses to the normal critical structures particularly to the left kidney. Median survival cannot be estimated as the survival curve did not reach 50% mortality rate. The 3- and 5-year actuarial rates of LCR for all pts were 95%, 79% and OS was 90%. For stage I and II MALT, the 3- and 5-year LCR and OS rates were 100% and 94% respectively with RT alone. None of the pts had local recurrence in the stage I and II at the time of last follow up. On univariate analysis, RT technique, performance status, histology type, H Pylori status, RT dose, only PS was significant for OS ($p < 0.0001$).
- **Conclusions:** Our results correlate with the outcomes from the published data. RT alone should be the primary treatment modality for patients diagnosed with Stage I or IIE Gastric MALT.

Aruna Turaka, Tianyu Li, Talha Shaikh, Natasha Townsend, Michael Millenson. 2014 Pan Pacific Lymphoma Conference, Fairmont Orchid on the Big Island of Hawaii on July 21-25, 2014.

ROLE OF PROPHYLACTIC RADIATION THERAPY TESTICULAR LYMPHOMA: CASE SERIES.

- OBJECTIVES: Primary testicular lymphoma is a rare, aggressive form of extra-nodal NHL comprising of 0.6% of all Non Hodgkin's Lymphoma (NHL), seen in older men. The primary treatment is usually surgery with orchiectomy followed by anthracycline based chemotherapy. Prophylactic radiation therapy to the contra-lateral testis and CNS prophylaxis are usually done due to the aggressive nature and poor prognosis associated with testicular NHL.
- METHODS: We present case series of 3 testicular lymphoma patients (pts) treated with combined modality therapy in our center between 2010-2013. Clinical data and outcomes were assessed. All patients had bone marrow biopsy, CSF cytology apart from other staging work up studies.
- RESULTS: All three patients had diffuse large B cell lymphoma with 1 pt with Stage IE, 1 had stage IIIE and other presented with IVAE (bilateral, metachronous with an interval of 3 months). None of the patients had B symptoms. Bcl-6 was positive in 2 pts and Bcl-2 in 2 pts. CSF was negative for lymphoma in all. All the patients had surgery-high inguinal orchiectomy (bilateral in stage IVAE). Median age was 67 years (53-78 years). Median follow up was 31 months (range: 15-39). R-CHOP chemotherapy was given to all (6 cycles in 2 pts, 4 cycles for 1 pt). All patients received 4 doses of intrathecal-Methotrexate. Prophylactic radiation therapy to the contra-lateral testis was given to 2 pts (except for the pt with stage IVAE pt as he had bilateral orchiectomy), 30 Gy in 20 fractions using 150 cGy per fraction over 3 weeks. 16-20 Mev electron energy was chosen and the dose was prescribed to 90% isodose line and treated with an enface Electron field. Para-aortic lymph nodes were not included in the RT fields. None of the patients had any grade 2-3 RT related toxicities except for grade 1-2 skin changes over the treated region. The 2 year disease free survival and overall survival rates were 100%. All patients were alive at the time of last follow up visit without any relapse of lymphoma.
- CONCLUSIONS: Our series have shown that addition of prophylactic radiation therapy results in preventing relapses in the contra-lateral testis, correlating with the results of the other published series.

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Radiation therapy for pituitary metastasis: report of four cases

AIMS AND BACKGROUND: To report the clinical outcomes of four patients with pituitary metastases treated with radiotherapy.

METHODS: Retrospective chart review of four cases.

RESULTS:

- The mean age of the patients was 66 years; two were women and two were men.
- The mean duration of symptoms at initial presentation of the primary tumor was 2.25 months.
- The location of the primary tumor was the breast in one case and the lung in three.
- Magnetic resonance imaging of the brain revealed sellar masses in all cases.
- The mean interval between the primary tumor diagnosis and the development of pituitary metastases was 22.5 months.
- The metastases were treated with radiation therapy (palliative/stereotactic/intensity modulated) at a mean dose of 3219 cGy.
- At the last follow-up, three patients were dead and one was alive.

CONCLUSIONS:

- Treatment with three-dimensional conformal radiotherapy or stereotactic radiotherapy is a suitable non-surgical option for patients with pituitary metastases.

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