Purpose/Objective(s): To resolve uncertainty about survival outcomes, we undertook a re-analysis of RTOG 9402 when the median follow-up for surviving patients was 6.9 years.

Material/Methods: The Kaplan-Meier method was used to estimate survivals and the log-rank test to compare treatments. For OS, an event was death from any cause; for PFS, it was progression or death. Cox proportional hazard models were used to estimate the hazard ratio (HR) for OS and PFS. Frequencies of pre-treatment characteristics were compared using chi-square tests.

Results: One hundred forty-seven patients were randomized to PCV+RT and 142 patients to RT. One hundred eighty-four patients (64%) have died. The unadjusted estimated 5-year OS rate is 49% for RT+PCV *vs.* 46% for RT [HR 0.83, CI (0.62, 1.10), $p = 0.1$]. Estimated OS times are 4.8 and 4.7 years, respectively. In a step-wise multivariate Cox model considering age at diagnosis, steroid use, multifocality, neurological function, KPS, type of surgery, pure *vs.* mixed histology, degree of anaplasia, treatment assignment and 1p/19q co-deletion status, the adjusted OS is prolonged by PCV+RT at diagnosis [HR 0.66, CI (0.46, 0.95), $p = 0.02$] and the risk of dying is reduced by 34% after PCV+RT. To date, 217 (75%) have progressed. The unadjusted estimated 5-year PFS rate is 37% for RT+PCV *vs.* 22% for RT [HR 0.68, 95% CI (0.52, 0.90), $p = 0.003$]. Estimated PFS times are 2.4 and 1.7 years, respectively. After adjusting for patient-specific risk factors, this significant difference persists [HR 0.57, CI (0.41, 0.79), $p = 0.0007$]. Co-deleted cases live much longer than others [median OS 8.7 years *vs.* 2.7 years, HR 0.37, CI (0.26, 0.53), $p < 0.0001$). Longer PFS with early PCV+RT is restricted to the 1p/19q subset; longer follow-up is needed to judge OS in co-deleted cases.

Conclusions: We now conclude that early aggressive treatment of patients with AO with PCV+RT may prolong OS, although the unadjusted difference in OS is not significantly different between the treatment arms. Longer OS and PFS after chemotherapy and radiotherapy appear to be exclusive to the patients with co-deleted tumors. Future studies are needed to more fully explore initial treatment strategies for patients with AO, including separate trials and different key questions for co-deleted and intact cases.

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17 Comparative Analysis of Second Malignancy Risk in Patients Treated with Proton Therapy versus Conventional Photon Therapy

C. S. Chung[1], N. Keating[2], T. Yock[3], N. Tarbell[3]

[1]Harvard Radiation Oncology Program, Boston, MA, [2]Harvard Medical School, Boston, MA, [3]Massachusetts General Hospital, Boston, MA

Background: Compared to photon radiation, proton radiation improves dose distribution to the target and decreases dose to adjacent normal tissues. The most common method of delivering proton radiation involves passive scattering. However, passive scattering produces secondary low-dose neutrons, which may induce late radiation-induced malignancies. The magnitude of second cancer risk in patients treated with proton radiation compared to photon radiation therapy has not been reported to date.

Purpose/Objective(s): To quantify the risk of a second malignancy associated with the use of proton radiation therapy compared to photon radiation therapy.

Materials/Methods: Matched retrospective cohort study of 1,450 patients treated with proton radiation therapy from 1974-2001 at the Harvard Cyclotron in Cambridge, MA, and patients treated with photon therapy in the Surveillance, Epidemiology, and End Results (SEER) cancer registry. We matched patients by age at radiation treatment, year of treatment, cancer histology, and site of treatment. We restricted the study to patients with $\geq$1 year of follow-up. The primary endpoint was the risk of a second malignancy in any site after radiation therapy.

Results: We matched 503 Harvard Cyclotron proton patients with 1591 photon patients from the SEER registry. 6.4% of proton patients (32 patients) developed a second malignancy, while 12.8% of photon patients (203 patients) developed a second malignancy. The median duration of follow-up was 7.7 years in the proton cohort and 6.1 years in the photon cohort. The median age at treatment was 56 years in the proton cohort and 59 years in the photon cohort. After adjusting for gender and the age at treatment, treatment with photon therapy was significantly associated with an increased risk of a second malignancy (Adjusted Hazard Ratio 2.73, 95% CI 1.87 to 3.98, $p < 0.0001$).

Conclusion: The results of our preliminary analysis indicate that the use of proton radiation therapy is associated with a significantly lower risk of a second malignancy compared to photon radiation therapy. Additional analyses are required, and ongoing close surveillance of these patients is necessary, given the prolonged latency period for the development of second cancers.

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18 Anti-VEGF Bevacizumab (Avastin) for Radiation Retinopathy and Optic Neuropathy

P. T. Finger

The New York Eye Cancer Center, New York, NY

Purpose/Objective(s): To report on the use of intravitreal anti-VEGF bevacizumab for radiation optic neuropathy (RON) and radiation retinopathy (RR) affecting the macula.

Materials/Methods: This study complies with the institutional review board of The New York Eye Cancer Center, the Health Insurance Portability and Accountability Act of 1996, and the tenets of the Declaration of Helsinki of 1975, as revised in 2000. Both verbal and written informed consent was obtained from all patients prior to treatment. Patients were informed that they could discontinue treatment at any time. In interventional clinical case series, 31 patients treated with plaque radiation therapy (for choroidal melanoma) developed either macular radiation retinopathy (edema, hemorrhages, capillary dropout, and intraretinal microangiopathy including neovascularization) or anterior radiation optic neuropathy (optic disc edema, hemorrhages, microangiopathy, neovascularization). Entry criteria also included a subjective or objective loss of vision. They were treated with intravitreal injections of bevacizumab (Avastin, Genentech, South San Francisco, California). Entry criteria included a subjective or objective loss of vision. Treatment involved intravitreal injection of bevacizumab (1.25 mg in 0.05 cc) every 6 to 8 weeks. Treatment was discontinued if there was no measurable response to therapy. Ophthalmic evaluations included visual acuity, ophthalmic