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News Release

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Press Room in Atlanta
September 22-25
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Encouraging outcomes for pediatric brain tumor patients treated with proton therapy

Atlanta, September 22, 2013—When used to treat pediatric patients with intracranial malignant tumors, proton therapy may limit the toxicity of radiation therapy while preserving tumor control, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 55th Annual Meeting.

Typically, central nervous system malignancies are treated with surgical resection and post-operative radiation therapy. Proton therapy, an external beam radiation therapy in which protons deliver precise radiation doses to a tumor, offers significant sparing of healthy tissues outside the target region, compared to conventional photon radiotherapy. Proton therapy is frequently used to treat central nervous system malignancies in young children in order to minimize the amount of radiation exposure to their still-developing brain. Although this therapy holds great promise, to date, published clinical data are limited.

This study evaluated the largest reported group of pediatric patients treated with proton therapy—70 patients with localized ependymoma, a relatively common childhood tumor. The patients in the study ranged in age from one to 20 years and were all treated with involved-field proton radiation at the Massachusetts General Hospital in Boston from October 2000 to February

2011. Forty-six of the patients (66 percent) had a gross total resection, meaning that the tumor was completely removed; and 24 patients (34 percent) had a subtotal resection, meaning that only a portion of the tumor was removed.

Upon patient follow-up at 46 months after proton therapy treatment, the three-year local control was 83 percent; progression free survival (PFS) was 76 percent; and overall survival (OS) was 95 percent. The researchers found that subtotal resection surgery correlated with decreased PFS (54 percent) and OS (90 percent), compared to the patients who underwent complete tumor removal prior to proton therapy, who had a PFS of 88 percent and an OS of 97 percent.

In addition to survival outcomes, cognitive and endocrine outcomes were analyzed. Neuropsychological assessments were administered before and after proton therapy to measure total intelligence quotient (IQ). Scales of Independent Behavior (SIB-R), a written questionnaire that assessed functional independence, were completed by the patients' parents. Within a subset of 14 of the patients, the average IQ was 108.5 at baseline, and 111.3 after two years of follow-up. In a larger group of 28 of the patients, overall SIB-R score was 100.1 at baseline, and 100.8 after two years of follow-up. It was also noted that few patients developed evidence of growth hormone deficiency (GHD), hypothyroidism or hearing loss.

"This study represents the best available evidence on the use of proton radiotherapy in the pediatric population," said Shannon MacDonald, the principal investigator of the study, a pediatric radiation oncologist at the Massachusetts General Hospital. "Our analysis is the first to present auditory, endocrine and cognitive outcomes, the domains expected to benefit from this highly streamlined form of radiation therapy. Given the increasing numbers of proton facilities and the high cost of proton treatment, this data was urgently needed to provide evidence-based guidance on proton therapy outcomes for pediatric brain tumor patients."

The abstract, "Proton Radiation Therapy for Pediatric Central Nervous System Ependymoma: Clinical Outcomes for 70 patients," will be presented in detail at ASTRO's 55th Annual Meeting. To speak with Roshan Sethi, contact Michelle Kirkwood on September 22 - 25, 2013, in the ASTRO Press

Office at the Georgia World Congress Center in Atlanta at 404-222-5303 or 404-222-5304, or email michellek@astro.org.

ASTRO's 55th Annual Meeting, held in Atlanta, September 22-25, 2013, is the premier scientific meeting in radiation oncology and brings together more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry representatives and other health care professionals from around the world. The theme of the 2013 meeting is "Patients: Hope • Guide • Heal" and focuses on patient-centered care and the importance of the physician's role in improving patient-reported outcomes and the quality and safety of patient care. The four-day scientific meeting includes presentation of four plenary papers, 363 oral presentations, 1,460 posters and 144 digital posters in 70 educational sessions and scientific panels for 19 disease sites/tracks. Keynote and featured speakers include: William B. Munier, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality; Darrell G. Kirch, MD, president and CEO of the Association of American Medical Colleges; James Cosgrove, PhD, director of the U.S. Government Accountability Office; Otis W. Brawley, MD, chief medical officer of the American Cancer Society; and Peter Friedl, MD, PhD, of St. Radboud University Nijmegen Medical Centre at the University of Nijmegen and MD Anderson Cancer Center.

ABOUT ASTRO

ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals that specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes two medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org) and Practical Radiation Oncology (www.practicalradonc.org); developed and maintains

an extensive patient website, www.rtanswers.org; and created the Radiation Oncology Institute (www.roinstitute.org), a non-profit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

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2013 American Society for Radiation Oncology (ASTRO) 55th Annual Meeting
News Briefing, Tuesday, September 24, 2013, 2:45 p.m., Eastern time

Poster Presentation

2188 Proton Radiation Therapy for Pediatric Central Nervous System Ependymoma: Clinical Outcomes for 70 patients

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Purpose/Objective(s): The best outcomes for localized ependymoma are achieved with maximal surgical resection and radiation to the tumor bed. Minimizing unnecessary exposure to radiation is of paramount importance for these often very young children. Proton radiation spares healthy tissues outside the target region, but reports of clinical outcomes are scarce. We report survival, cognitive and endocrine outcomes for 70 patients with intracranial ependymoma.
Materials/Methods: Seventy patients with localized ependymoma treated with involved field proton radiation at the Massachusetts General Hospital between October, 2000 and February 2011 were included. Neuropsychological assessments administered before and after radiotherapy measured total intelligence quotient (IQ). Parents were given Scales of Independent Behavior (SIB-R), a written questionnaire that assessed functional independence.
Results: Median age at diagnosis was 38 months (range 3 months - 20 years). Nineteen (27%) patients had supratentorial ependymoma and 51(73%) had infratentorial ependymoma. Forty-six (66%) had a gross total resection, and 24 (34%) had a subtotal resection. Thirty seven (53%) had anaplastic histology (WHO grade III); the remainder had classic ependymoma (WHO grade II). At a median follow-up of 46 months, 3-year local control, progression free, and overall survival was 83%, 76% and 95%, respectively. Subtotal resection was significantly associated with worse progression-free survival (54% vs. 88% for GTR; p=0·001) and overall survival (90% vs. 97% for GTR; p=0·001). Anaplastic histology was observed with worse progression-free survival but did not reach statistical significance (69% vs. 83% for classic; p=0·509). In a sub-set of patients (n=14), mean IQ was 108.5 at baseline and 111.3 after mean 2.05 years of follow-up. In a larger group of patients (n=28), overall SIB-R score was 100.1 at baseline and 100.8 after 2.21 years of follow-up. Few patients developed evidence of growth hormone deficiency (GHD), hypothyroidism or hearing loss.
Conclusions: Outcomes for children treated with proton radiation compare favorably to the literature. Subtotal resection correlated with inferior outcome. The young age at diagnosis and the proximity of critical structures in patients with ependymoma make proton radiotherapy an ideal radiation modality.

Author Disclosure Block: R. Sethi: None. **B.Y. Yeap:** None. **R. Marino:** None. **K.J. Marcus:** None. **P. Caruso:** None. **M.B. Pulsifer:** None. **D. Ebb:** None. **N.J. Tarbell:** L. Stock Options; ProCure (no current value to stocks). Q. Leadership; N.T.'s spouse is on the medical advisory board. **T.I. Yock:** None. **S.M. MacDonald:** None.