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Image-guided intensity modulated radiation therapy (IG-IMRT) reduces bowel side effects in cervical cancer patients

San Antonio, October 19, 2015— For cervical cancer patients undergoing postsurgical radiation therapy, image-guided intensity-modulated radiation therapy (IG-IMRT) resulted in a 14 percent reduction in moderate-to-severe bowel side effects when compared to conventional three-dimensional conformal radiation therapy (3-D CRT), according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

Post-operative pelvic radiation therapy is the current standard of care for many patients with cervical cancer, yet may affect surrounding organs and tissue and be associated with long-term gastrointestinal side effects. IG-IMRT uses technology to manipulate beams of radiation to conform to the shape of a tumor, thus allowing clinicians to limit exposure to surrounding tissue.

The phase III randomized clinical trial, conducted at Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Tata Memorial Centre in Mumbai, India, included 240 patients,
ages 18 and over who were undergoing adjuvant chemoradiation therapy (combined chemotherapy and radiation therapy) and had no pre-existing bowel disease or injury. This planned interim analysis of the study assessed 117 of the patients who had completed an average of 20-months follow-up (range: two to 46 months). Patients were categorized into two groups: 56 patients received 3-D CRT and 61 patients received IG-IMRT. Patient groups were randomized and had similar treatment histories, with 41.3 percent (23 patients) of the 3-D CRT group having radical hysterectomies and 43.5 percent (27 patients) of the IG-IMRT group having radical hysterectomies. Additionally, 91.8 percent (51 patients) of the 3-D CRT group had chemoradiation therapy, with 85.5 percent (52 patients) of the IG-IMRT group undergoing chemoradiation therapy. RT included 50 Gy, administered over 25 treatments in a five-week timeframe. CRT patients received Cisplatin (40 mg/m2) congruently. This was followed by two fractions of brachytherapy (cylinder based intravaginal brachytherapy) of 6 Gy each.

Patients randomized to the 3-D CRT group received treatment on a linear accelerator, and the IG-IMRT patients received treatment using Tomotherapy. Strict constraints were applied in the administration of the IG-IMRT to ensure that no more than 200 cc and 100 cc of small bowel received 15 and 40 Gy respectively.

At each follow-up visit, patients’ bowel side effects were recorded by clinicians using 11 symptom scales of Common Toxicity Criteria for Adverse Events (CTCAE version 3.0). In the 3-D CRT group, 58.9 percent (33 patients) experienced ≥2 acute bowel toxicity (indicating moderate to severe diarrhea, vomiting, nausea, lower abdominal distension or pain) compared to 54 percent (33 patients) in the IG-IMRT group (p=0.59). The reported late grade ≥2 bowel toxicity was 25 percent (14 patients) in the 3-D CRT group and 11.4 percent (7 patients) in the IG-IMRT group (p=0.13); and the late grade ≥3 bowel toxicity (indicating severe diarrhea, lower abdominal pain, subacute intestinal obstruction requiring medical or surgical intervention, bowel perforation or death) was 17.6 percent (10 patients) in the 3-D CRT group and 3.2 percent (2 patients) in the IG-IMRT group (p=0.02). Further, research indicated that neither the surgery type nor the administration of CRT had an impact on bowel side effects.
“These initial results of this interim analysis are encouraging and trend toward possibly a clinically important reduction in moderate-to-severe bowel side effects with the use of IG-IMRT, however at interim analysis the results are statistically nonsignificant,” said Supriya Chopra, MD, lead study author and associate professor of radiation oncology at ACTREC, Tata Memorial Centre in Mumbai, India. “While we evaluated patients with cervical cancer in this trial, a significant proportion of patients with other cancers undergo postoperative pelvic radiation worldwide. Therefore, the results of this trial could impact the choice of future radiation delivery technique for various pelvic malignancies.”

The abstract, “Phase III RCT of Postoperative Adjuvant Conventional Radiation (3DCRT) Versus IGIMRT for Reducing Late Bowel Toxicity in Cervical Cancer (PARCER) (NCT01279135/CTRI2012/120349): Results of Interim Analyses” will be presented in detail at the Plenary Session at ASTRO’s 57th Annual Meeting at 2:15 p.m. Central time on Monday, October 19, 2015.

To speak with Dr. Chopra, please call Nancy Mayes from October 18–21, 2015 in the ASTRO Press Office at the Henry B. González Convention Center, San Antonio, at 210-258-8104 or 210-258-8105, or email press@astro.org.

ASTRO’s 57th Annual Meeting, being held at the Henry B. González Convention Center in San Antonio, October 18-21, 2015, is the nation’s premier scientific meeting in radiation oncology. The 2015 Annual Meeting is expected to attract 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. Led by ASTRO President Bruce D. Minsky, MD, FASTRO, a radiation oncologist specializing in gastrointestinal cancers, Professor of Radiation Oncology, and the Frank T. McGraw Memorial Chair at The University of Texas MD Anderson Cancer Center, Houston, the theme of the 2015 Meeting is “Technology Meets Patient Care.” Dr. Minsky’s Presidential Symposium, “Multidisciplinary Management of Esophageal and Rectal Cancers,” will feature Leonard L. Gunderson, MD, MS, FASTRO, and Joel E. Tepper, MD,
FASTRO, to highlight imaging, staging, genomics and data mining approaches, as well as the latest advances in esophageal and colorectal cancer treatment. ASTRO’s four-day scientific meeting includes presentation of more than 2,100 abstracts: five plenary papers, 351 oral presentations, 1,609 posters and 171 digital posters in more than 53 educational sessions and 26 scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including cancer biology in radiation oncology, the essential roles of a physician, and patient safety: Arul Chinnaian, MD, PhD, Professor and Director, Michigan Center for Translational Pathology; Francisco G. Cigarroa, MD, Past President and Chancellor, University of Texas; and Gerald B. Hickson, MD, Senior Vice President and Assistant Vice Chancellor, Vanderbilt University Medical 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 who 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 three medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org), and Advances in Radiation Oncology (www.advancesradonc.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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Phase III RCT of Postoperative Adjuvant Conventional Radiation (3DCRT) Versus IGIMRT for Reducing Late Bowel Toxicity in Cervical Cancer (PARCER) (NCT01279135/CTRI2012/120349): Results of Interim Analyses

Author Block: S. Chopra1, R. Engineer2, U. M. Mahantshetty2, T. Dora1, S. Kannan1, R. Phurailatpam3, S. N. Paul1, J. Swamidis1, J. Ghosh1, S. Gupta1, T. Shylasree2, A. Maheshwari2, R. Kerkar2, and S. K. Shrivastava2;1ACTREC, Tata Memorial Centre, Navi Mumbai, India, 2Tata Memorial Centre, Parel, Mumbai, India

Purpose/Objective(s): Phase III randomized study of three dimensional conformal radiation (3DCRT) vs. image guided radiation therapy (IGIMRT) was initiated in 2011 with a primary aim to demonstrate reduction in grade ≥2 late bowel toxicity in patients undergoing adjuvant chemoradiation for cervical cancer.

Materials/Methods: Patients >18 years undergoing adjuvant (chemo) radiation (CRT) with no preexisting bowel morbidity were eligible. The study design included permuted block stratified randomization according to type of hysterectomy (Wertheim’s hysterectomy (WH) or simple hysterectomy) and use of chemotherapy (CRT vs RT alone). CRT included 50 Gy/25# 5 weeks +/- weekly cisplatin (40 mg/m2). This was followed by 2 # brachytherapy of 6 Gy each. Those randomized to 3DCRT and IMRT arm received treatment on linear accelerator and Tomotherapy respectively. Strict constraints were applied in IMRT arm to ensure that no more than 200 cc and 100 cc of small bowel received 15 and 40 Gy respectively. At each follow up toxicity was captured using Common Toxicity Criteria for Adverse Event version 3.0. Patients were censored at recurrence or at initiation of salvage treatment. On follow up worst grade of bowel toxicity was considered for statistical analysis.

The trial is designed to detect a 13% difference (from 18% to 5%) with an α of 0.05 and β of 0.80. A total of 240 patients will be required. An interim analysis was planned when 50% (120/240) of the patients completed a median follow up of 18 months. Chi square test was used to demonstrate incidence of toxicity between the two arms. At interim analysis p<0.025 will be required to reject null hypothesis.

Results: A total of 120 patients completed a median follow up of 20 months (2-46). Of these 58 were randomized to 3DCRT and 62 to IGIMRT arm. In 3DCRT and IMRT arm 41.3% and 43.5% underwent WH and 91.8% and 85.5% received CRT. Three patients withdrew consent after randomization (2:3DCRT; 1=IMRT) and did not receive any treatment. There was 1 protocol deviation each in 3DCRT and IMRT arm. A total of 56/58 and 61/62 patients were evaluable for toxicity in each arm. Overall 33/56 (58.9%) and 33/61(54%) patients experienced grade ≥2 acute bowel toxicity in 3DCRT and IMRT arm (p=0.59). The late grade ≥2 bowel toxicity was 25% and 11.4% (p=0.13) and late grade ≥3 toxicity was 17.6% and 3.2% (p=0.02) in 3DCRT and IMRT arm respectively. No difference in primary endpoint was observed with type of surgery or use of CRT.

Conclusion: There is no difference in late grade ≥2 late bowel toxicity with the use of IG-IMRT. However significant reduction is observed in incidence of late grade ≥3 toxicity with use of IG-IMRT. Final analyses will be conducted after completion of accrual and median follow up of 3 years.

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