Recent Publications of Interest *continued from page 2*

Stereotactic body radiotherapy for isolated para-aortic lymph node recurrence after curative resection in gastric cancer

Mi-Sook Kim, Sung Yui Yoo, Chui Koo Cho, Hyung Jun Yoo, Kwang Mo Yang, Jin Kyu Kang, Dong Han Lee, Jong Inn Lee, Ho Youn Bang, Min Suk Kim, Hae Jin Kang.

J Korean Med Sci. 2009 Jun;24(3):488-92. Epub 2009 Jun 16.

OUR SUMMARY: Metastases from gastric cancer are common and can progress rapidly; even with aggressive treatment 5-year survival rates are low. However, researchers from Korea Institute of Radiological & Medical Sciences hypothesized that there is a certain population of such patients in whom the disease follows a more indolent course, based on studies of patients with resected liver metastases. This population may benefit from SRS of isolated metastases from gastric primaries. Thus, they treated 7 such patients with the CyberKnife® System, delivering 45 to 51 Gy (median 48 Gy) in 3 fractions. The patients were followed for 14 to 33 months (median 26 months). Local control was achieved in 6 of 7 patients; 2 patients were disease-free, 3 were alive with disease, and 2 patients died of disease progression. Three-year actuarial overall survival was 43%, and disease-free survival was 29%. The authors conclude that the results support their hypothesis that an indolent subgroup with less aggressive disease progression who could benefit from the use of local treatments such as CyberKnife Radiosurgery.

Abstract Deadlines

AUA - American Urological Association	November 16, 2009
AACR - American Association for Cancer Research	December 1, 2009
AHNS -American Head and Neck Society	December 11, 2009
ASCO - American Society of Clinical Oncology	January 12, 2010

Congresses & Events

CNS - Congress of Neurological Surgeons Location: New Orleans, LA	October 24, 2009
CHEST - American College of Chest Physicians Location: San Diego, CA	October 31, 2009
ASTRO - American Society for Radiation Oncology Location: Chicago, IL	November 1, 2009
NASS - North American Spine Society Location: San Francisco, CA	November 10, 2009
RSNA - Radiological Society of North America Location: Chicago, IL	November 29, 2009

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FOCUS ON RADIOSURGERY

NEWSLETTER N°8, October 2009

ACCURAY®

A MESSAGE FROM ACCURAY

The field of extracranial radiosurgery has expanded rapidly over the past seven years, led by the innovations of the CyberKnife® Robotic Radiosurgery System. At the end of June over 70,000 patients had been treated with the CyberKnife System and one quarter of all patients treated with the CyberKnife System were treated between July 2008 and June 2009. Nearly 60% of these were extracranial treatments. Treatments of lung and prostate cancer are expanding most rapidly.

The evolution of extracranial radiosurgery has required our Research and Engineering groups, in collaboration with expert CyberKnife users, to meet several technical challenges. Fiducial tracking algorithms for early spine treatments led to algorithms for tracking fiducials for other body applications. Lung and pancreas treatments in the early part of this decade inspired the development of the Synchrony® Respiratory Tracking System so that lesions that move with respiration could be treated while patients breathed freely rather than being required to hold their breath or limiting lesion motion with abdominal compression. An ongoing movement away from fiducial tracking began with the introduction of the Xsight® Spine Tracking System, which has nearly eliminated the need for fiducials for spine treatments, and the Xsight Lung Tracking System, improvements to which are extending fiducial-free treatment to a greater number of lung cancer patients. Image-guided tracking of extensive and unpredictable movement of the prostate has always been an aspect of CyberKnife treatments that makes clinicians confident that they can safely treat prostate cancer. With the introduction of the InTempo® System we have refined our imaging procedure and reduced the image age, so that even extensive and erratic motion can be accounted for and treatments can proceed safely. The Iris™ Variable Aperture Collimator and Sequential Optimization will enhance the convenience and efficiency of treatment planning and delivery for all applications. Each of these innovations is unique to the CyberKnife System; each is designed to improve the treatment experience for clinicians and patients; and each sets the stage for continued innovation.

Building upon a tradition of technical innovation, Accuray is committed to supporting ongoing clinical development and patient access efforts that will expand the existing published body of radiosurgery evidence as well as improve access to care for patients by breaking down many of the existing financial barriers. Focusing on patients and working hand in hand with clinicians worldwide, we look forward to providing more options in the fight against cancer.

Sincerely,

Euan S. Thomson

Euan S. Thomson, Ph.D.
President and Chief Executive Officer
Accuray Incorporated

Our latest technical innovations, and the clinical benefits of our history of innovation, will be on display at ASTRO in Chicago this year (Booth #1526). Please pay us a visit.

Rotterdam Researchers Report Quality of Life is Preserved after CyberKnife® Treatment of Lung Cancer

Joost Nuyttens, M.D., Ph.D. and Noelle van der Voort van Zyp, M.D.
Department of Radiation Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands

Although surgery is still the standard of care for resectable lung cancer, many patients cannot endure the rigors of surgery. The influence of surgery on quality of life (QoL) is still controversial. Some studies report only a temporary decline in the QoL with symptom and functional scores returning to baseline at three months,[1,2] while others state that recovery is not complete.[3,4] In a prospective study of 139 patients whose lung cancer was resected,[3] in most cases by open lobectomy, numerous post-operative complications were noted, such as prolonged chest tube placement (26%), atrial arrhythmias (14%) and lobar atelectasis (11%). Over the six-month follow-up period physical, social and mental QoL deteriorated and pain persisted in many of these patients. The authors also found that patients with poor pre-operative lung function fared worse after surgery. In a more recent study,[4] an initial drop in most QoL indicators was followed by recovery over a 24-month follow-up, but physical function, pain and dyspnea remained significantly impaired. Pneumonectomy patients generally recovered less than lobectomy patients, but significant long-term impairment was observed in all patients. The authors concluded that "patients who undergo lung resection for NSCLC do not completely recover, even by 24 months after surgery."[4]

Findings such as these underscore the potential value of an effective, non-surgical approach to the treatment of lung cancer. We investigated the impact of stereotactic radiotherapy using the CyberKnife System on the QoL of patients with inoperable, early-stage, non-small cell lung cancer. The study was approved by the Medical Ethics Committee and included 39 patients with pathologically confirmed T1-2N0M0 NSCLC. QoL was assessed using the European Organization for Research and Treatment of Cancer (EORTC) questionnaire QLQ C30 and the lung cancer supplementary module LC 13. Assessments

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Accelerated Hypofractionation for Prostate Cancer

Debra Freeman, M.D.
Naples Radiation Oncology, PA / Clinical Development, Accuray Incorporated

Five years ago, fewer than 10 patients with prostate cancer had been treated with "Stereotactic Radiosurgery (SRS)" using the CyberKnife System, delivering an accelerated hypofractionated course of radiation to the prostate. Today, nearly 4,000 men with localized prostate cancer have received CyberKnife SRS, and that number is growing. As data from the early cohorts of patients mature, we are gaining a better understanding of the potential long-term benefits of this form of therapy.

The concept of accelerated hypofractionated radiation treatment (large dose per fraction with very few fractions) for prostate cancer is not unique to the CyberKnife platform. Studies from the United Kingdom[1] and the United States,[2] using conventional linear accelerators, support the potential effectiveness of hypofractionation for prostate cancer. Similarly, reports of high-dose rate brachytherapy, alone or in combination with external beam treatment, suggest an improved biochemical response and reduced toxicity compared to conventionally fractionated radiation.[3-6] The goal of these "non-conventional" therapies is to improve the therapeutic ratio for prostate cancer, meaning higher rates of tumor control with lower toxicity.

That indeed was the goal of the first prospective, Phase II study of CyberKnife SRS for low-risk prostate cancer, initiated by Christopher King, M.D. at Stanford in December 2003. Eligible patients had biopsy-confirmed prostate adenocarcinoma, no prior treatment, and low-risk features, including initial PSA < 10 ng/ml, Gleason score 3+3 or lower and clinical stage T1c or T2a/b disease. All patients received 36.25 Gy (7.25 Gy in five fractions). By May 2008, 56 patients were enrolled in the trial; 41 had minimum six months follow-up and median follow-up >24 months. The clinical results were published earlier this year in the International Journal of Radiation Oncology Biology Physics.[7] No patient experienced a biochemical failure or biopsy-confirmed recurrence. PSA nadir at 33 months median follow-up was 0.32 ng/ml. Only two patients experienced Grade 3 urinary toxicity; no patient experienced Grade 3 or 4 rectal toxicity.

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Rotterdam Researchers Report Quality of Life is Preserved after CyberKnife® Treatment of Lung Cancer

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were performed before treatment and three, six, nine and 12 months after treatment. Toxicity was evaluated using the Common Terminology Criteria for Adverse Events version 3.0. Thirty-two patients with peripheral tumors were treated with 60 Gy in 3 fractions, and seven patients with central tumors were treated with 45-50 Gy in 3-5 fractions. Most patients were medically inoperable, although six patients had refused surgery. The patients' median age was 77 years (range 55-88 years).

Emotional QoL scores increased significantly after treatment while no significant changes were observed in the other QoL scores. After a median follow-up of 17 months, toxicity was limited. No Grade 4 or 5 toxicity occurred. Grade 3 toxicity occurred in three patients and consisted of chest pain that required analgesia. Although Grade 1 and 2 fatigue or dyspnea was not uncommon, twelve patients (31%) experienced no side effects at all. The low rate of toxicity, and the non-invasive nature of the treatment, may all have contributed to the maintenance of QoL in patients treated with the CyberKnife® System. In this frail (inoperable) population, CyberKnife treatment achieved an acceptable, overall survival (62%) and excellent local control (97%) at two years and the treatment details of these results will soon be published in the International Journal of Radiation Oncology Biology Physics.[5]

This study demonstrated that the level of QoL prior to treatment was maintained after treatment with the CyberKnife System and that emotional functioning improved significantly. While the QoL was maintained in the frail population of inoperable NSCLC patients, the overall survival was acceptable, local tumor control was excellent and toxicity was low. These results are very encouraging and hopefully will contribute to the development of SRS for non-small cell lung cancer.

References

1. Win T, Sharples L, Wells FC, et al. Effect of lung cancer surgery on quality of life. Thorax 2005;60:234-238.
2. Zieren HU, Muller JM, Hamberger U, et al. Quality of life after surgical therapy of bronchogenic carcinoma. Eur J Cardiothorac Surg 1996;10:233-237.
3. Handy JR, Jr., Asaph JW, Skokan L, et al. What happens to patients undergoing lung cancer surgery? Outcomes and quality of life before and after surgery. Chest 2002;122:21-30.
4. Schulte T, Schniewind B, Dohrmann P, et al. The extent of lung parenchyma resection significantly impacts long-term quality of life in patients with non-small cell lung cancer. Chest 2009;135:322-329.
5. van der Voort van Zyp NC, Prevost JB, van der Holt B, et al. Quality of Life after stereotactic radiotherapy for stage I non-small-cell lung cancer. Int J Radiat Oncol Biol Phys In Press.

Recent Publications of Interest

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Radical CyberKnife radiosurgery with tumor tracking: an effective treatment for inoperable small peripheral stage I non-small cell lung cancer

Brian T. Collins, Saloomeh Vahdat, Kelly Erickson, Sean P. Collins, Simeng Suy, Xia Yu, Ying Zhang, Deeepa Subramaniam, Cristina A. Reichner, Ismet Sarikaya, Giuseppe Esposito, Shadi Yousefi, Carlos Jamis-Dow, Filip Banovac, Eric D. Anderson.

J Hematol Oncol. 2009 Jan 17;2:1.

OUR SUMMARY: Georgetown University researchers used the CyberKnife System to treat 20 inoperable NSCLC patients with small, peripheral Stage I tumors. They used a 5 mm margin expansion from Gross Tumor Volume (GTV) to Planning Tumor Volume (PTV) to account for microscopic disease as well as the 1.5 mm accuracy of the Synchrony® System, and made sure that the 30-Gy isodose line extended at least 1 cm outside of the GTV. Prescribed doses ranged from 42 to 60 Gy delivered in 3 fractions. Patients were followed in six-month intervals up to three years with a median follow-up of 25 months. Five patients experienced pneumothorax due to fiducial placement. There were no local, nodal or metastatic failures. Two-year Kaplan-Meier overall survival was 87%. Side effects were generally mild and transitory. "The use of hundreds of lightly weighted beams...rather than a few heavily weighted ones has prevented the infrequent but potentially severe skin injuries reported... using other radiosurgical instruments." The authors concluded that CyberKnife radiosurgery with real-time tracking is a safe and effective treatment for inoperable patients with small, peripheral Stage I NSCLC.

Nonrandom intrafraction target motion and general strategy for correction of spine stereotactic body radiotherapy

Lijun Ma, Arjun Sahgal, Sabbir Hossain, Cynthia Chuang, Martina Descovich, Kim Huang, Alex Gottschalk, David A. Larson.

Int J Radiat Oncol Biol Phys. 2009 Jul 31. [Epub ahead of print].

OUR SUMMARY: Researchers from the University of California, San Francisco (UCSF) examined the Xsight® Spine log files of target motion in 64 patients (233 treatment fractions) to assess the degree of nonrandom motion (i.e., systematic and predictable motion, such as a baseline shift). The researchers developed an analytical formula based on the frequency and distribution of nonrandom motions in different spinal regions to determine the time between images necessary to maintain at least 1-mm translational and 1˚ to 3˚ rotational accuracy. Nonrandom motion was present in every case at every spinal region without exception. Xsight Spine tracking and correction of beam aim effectively kept error due to motion within acceptable limits for spinal SRS. Although the practice of the researchers has been to image every 1 to 2 minutes, the current research showed that the time between images may safely be longer; by imaging every 5.5 min for cervical, 5.9 min for thoracic, and 7.1 min for lumbar-sacrum targets, error due to target motion may be limited to 1 mm and 1˚ at the 95% confidence level.

Early results of CyberKnife radiosurgery for arteriovenous malformations

Federico Colombo, Carlo Cavedon, Leopoldo Casentini, Paolo Francescon, Francesco Causin, and Vittore Pinna.

J Neurosurg, Epub posted April 3, 2009.

OUR SUMMARY: CyberKnife researchers in Vicenza, Italy conducted a prospective study in which 279 patients with arteriovenous malformations (AVMs) were treated with the CyberKnife System. Treatment volumes were identified on CT scans registered to 3D rotational angiography (3DRA). Critical structures near the AVM volume were contoured on functional MRI (fMRI) scans registered to the CT/3DRA study. Maximum doses of 22.5 to 30 Gy were delivered to the 65-85% isodose line, in most patients in a single fraction. The overall rate of complete obliteration based on angiography was 81.2% in patients with 36 months of follow-up, and no permanent complications were observed in any patients. The authors attributed their treatment success and safety to careful target delineation using 3DRA, non-isocentric treatment planning that yields excellent dose homogeneity, and the ability to limit dose to critical structures using fMRI.

Accelerated Hypofractionation for Prostate Cancer

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In February of 2005, Dr. Jay Friedland and I initiated a similar prospective study for low and intermediate-risk prostate cancer, treated with CyberKnife® SRS but with a slightly lower dose of 35 Gy (7.0 Gy in five fractions). By December 2006, 112 patients had participated in the study, and their outcomes were reported in this month's issue of Technology in Cancer Research and Treatment.[8] Unlike the Stanford series, 21 patients in our cohort received adjuvant hormonal therapy, and 10 had intermediate-risk features, including T2c disease, Gleason score 7 (3+4 or 4+3), and/or PSA > 10.0. At 24 months follow-up, the PSA nadir was 0.5 ng/ml. Two patients experienced rising PSA levels at 26 and 35 months following therapy, with repeat biopsies confirming residual adenocarcinoma. One patient developed metastatic disease with no evidence of local recurrence. No patient reported Grade 3 or 4 urinary toxicity. Two patients developed Grade 3 rectal toxicity (bleeding), requiring intervention. Erectile function was preserved in 81% of patients at 2 years' follow-up.

Two Accuray-sponsored, multi-institution, prospective Phase II clinical studies are currently open and are accruing patients. One study is examining a homogeneous dose distribution chaired by Bob Meier, M.D. of Seattle's Swedish Medical Center, and the other is examining a more heterogeneous dose distribution[9] chaired by Don Fuller, M.D., of CyberKnife Centers of San Diego. For further information on participation and or enrollment please email jdavis@accuray.com.

Our friends at ASTRO have acknowledged that hypofractionated SBRT for prostate cancer "has the potential to shorten overall treatment times, improving…quality of life for patients due to reduced time commitment to treatment…and may improve upon cost-effectiveness". What a privilege to be paving the way for prostate cancer patients to achieve better outcomes from treatment. Our business truly does begin with patients.

References

1. Collins CD, Lloyd-Davies RW, Swan AV. Radical external beam radiotherapy for localised carcinoma of the prostate using a hypofractionation technique. Clin Oncol (R Coll Radiol) 1991;3:127-132.
2. Madsen BL, Hsi RA, Pham HT, et al. Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results. Int J Radiat Oncol Biol Phys 2007;67:1099-1105.
3. Demanes D, Altieri G, Barnaba M, et al. High dose rate (HDR) monotherapy is equivalent to combined HDR brachytherapy and external beam radiation therapy (EBRT) for early prostate cancer. Int J Radiat Oncol Biol Phys 2006;66:S351.
4. Demanes DJ, Rodriguez RR, Schour L, et al. High-dose-rate intensity-modulated brachytherapy with external beam radiotherapy for prostate cancer: California endocurietherapy's 10-year results. Int J Radiat Oncol Biol Phys 2005;61:1306-1316.
5. Grills IS, Martinez AA, Hollander M, et al. High dose rate brachytherapy as prostate cancer monotherapy reduces toxicity compared to low dose rate palladium seeds. J Urol 2004;171:1098-1104.
6. Martinez AA, Pataki I, Edmundson G, et al. Phase II prospective study of the use of conformal high-dose-rate brachytherapy as monotherapy for the treatment of favorable stage prostate cancer: a feasibility report. Int J Radiat Oncol Biol Phys 2001;49:61-69.
7. King CR, Brooks JD, Gill H, et al. Stereotactic body radiotherapy for localized prostate cancer: interim results of a prospective phase II clinical trial. Int J Radiat Oncol Biol Phys 2009;73:1043-1048.
8. Friedland JL, Freeman DE, Masterson-McGary ME, et al. Stereotactic body radiotherapy: an emerging treatment approach for localized prostate cancer. Technol Cancer Res Treat 2009;8:387-392.
9. Fuller DB, Naitoh J, Lee C, et al. Virtual HDR℠ CyberKnife treatment for localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy and preliminary clinical observations. Int J Radiat Oncol Biol Phys 2008;70:1588-1597.

FIRST CUSTOMER INSTALLS CYBERKNIFE SYSTEM IN EXISTING RADIATION THERAPY VAULT

Installation in Existing Vault Enables Cost Savings and Speeds Deployment Time

The CyberKnife Center of Chicago at Elmhurst Memorial Hospital in Elmhurst, Ill., has installed the CyberKnife Robotic Radiosurgery System in one of the hospital's existing radiation therapy vaults. This marks the first installation of this new CyberKnife configuration option, which can save hospitals both time and money.

"We are excited about the new CyberKnife configuration and its ability to fit into an existing vault, because it requires significantly less modification and has allowed us to get the System up and running more quickly so we can begin treating patients," said Greg Spurlock, chief operating officer of US Radiosurgery, the managing partner of CyberKnife Center of Chicago.

Because radiation therapy systems are gantry-based machines, meaning they only rotate in a single rotational plane, radiation therapy vaults are typically smaller and require less shielding than a standard CyberKnife vault. Since a key factor in the CyberKnife System's precise treatment delivery is its ability to move in virtually any direction, it wasn't previously possible to install a CyberKnife System within a radiation therapy vault. Recognizing that this was an obstacle for many hospitals, Accuray used advanced optimization techniques to reconfigure a new layout that made this type of installation possible with minimal-to-no additional shielding.

The new footprint helps hospitals to save on construction and shielding costs, and enables an accelerated go-live schedule, allowing sites to start patient treatments within a significantly shorter period of time. This is particularly beneficial for sites that are interested in securing a CyberKnife System to replace an aging gantry-based radiation therapy system, but are faced with space constraints in their existing facilities or are unable to build a new facility.

The new CyberKnife configuration made this vault modification and installation possible in just five weeks," said Chris Raanes, senior vice president and chief operating officer at Accuray. "Now hospitals can go-live with their CyberKnife program very quickly and for a fraction of the cost."

With feature nearly identical to the standard CyberKnife vault layout, the gantry LINAC vault layout requires 34 percent less vault space and reduces the equipment room footprint, giving customers more flexibility in where they can place a CyberKnife System. The vault modifications at this center were done by one of Accuray's installation preferred partners, NELCO. Vendors in this program have the expertise and resources to efficiently support customers with any required construction and modifications.

Interested in contributing an article, comments or suggestions? Please email focus@accuray.com