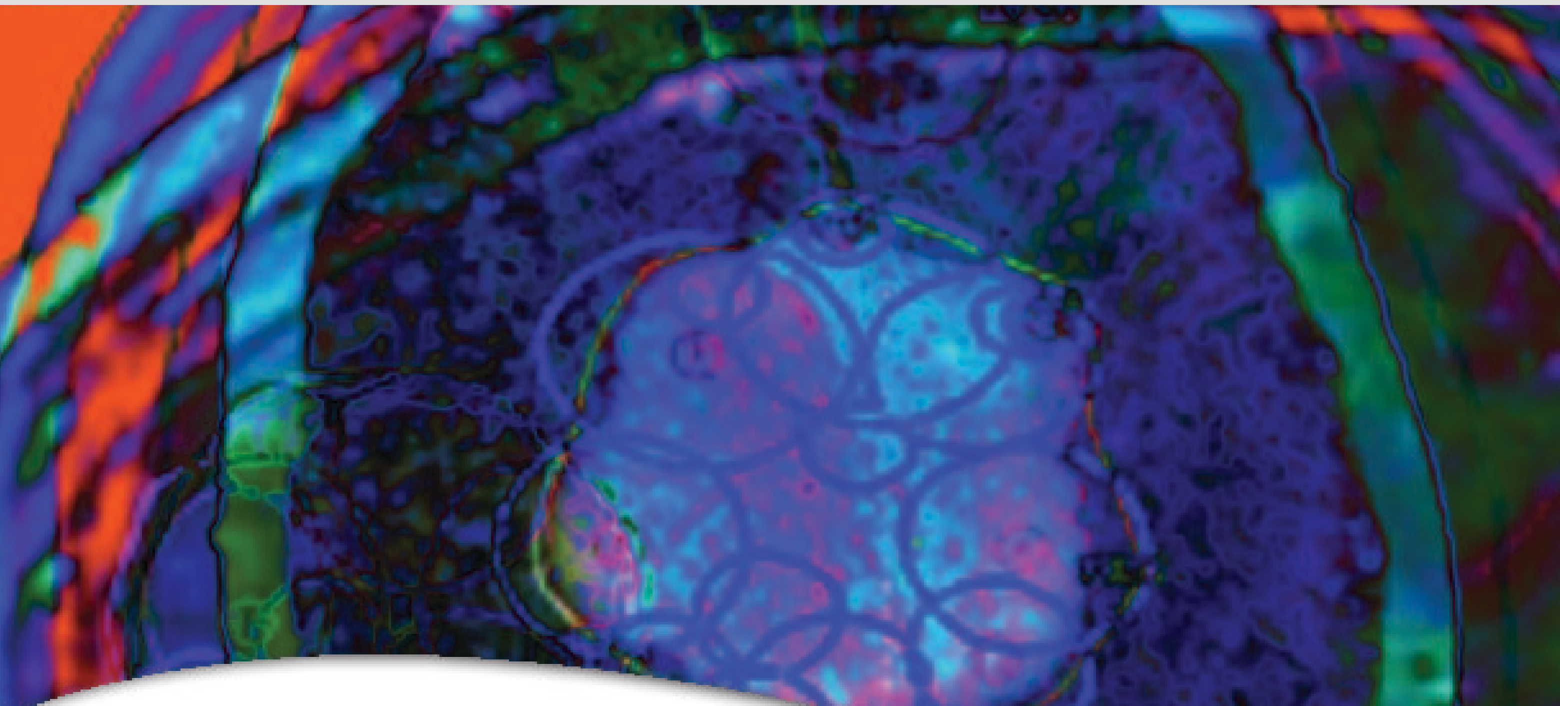
APPLIED RADIATION ONCOLOGY™

VOL 2 NO 3 SEPTEMBER 2013



CME **Stereotactic radiosurgery: The Cleveland Clinic experience and future directions using a Gamma Knife**

G Neyman, M Ouzidane, A Godley, T Djemil, and S Chao, Cleveland Clinic, Cleveland, OH

CME **Minimally invasive hysterectomy for uterine cancer: A radiation oncologist's perspective**

R Cattaneo and M Elshaikh, Henry Ford Hospital, Detroit, MI

Technology Trends: Speedy delivery makes rotational IMRT the technique of choice

C Bolan

Editorial:
Overview of Gamma Knife radiosurgery and vaginal brachytherapy

CME **Radiation Oncology Case**
Stereotactic body radiotherapy for spine metastasis

APPLIED RADIATION ONCOLOGY™

Editor-in-Chief
John Suh, MD

Publisher
Kieran N. Anderson

Associate Publisher
Cristine Funke, RT(R)

Executive Editor
Cristen Bolan

Contributing Editor
Joseph Jalkiewicz

Art Director/Production
Barbara A. Shopiro

Circulation Director
Cindy Cardinal

TEL: 908-301-1995, FAX: 908-301-1997
info@appliedradiationoncology.com
www.appliedradiationoncology.com

CIRCULATION, COVERAGE and ADVERTISING RATES: Completed details of regarding circulation, coverage, advertising rates, space sizes, and similar information are available to prospective advertisers. Closing date is 30 days preceding date of issue. Click here to view our media planner.

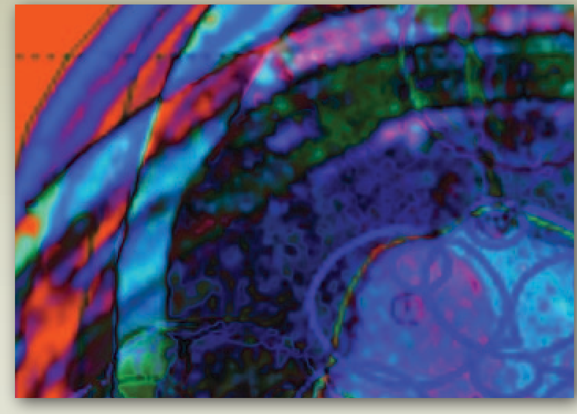
EDITORIAL CONTRIBUTIONS: *Applied Radiation Oncology* accepts clinical-review articles and cases that pertain to radiation oncology and related oncologic imaging procedures that will be of interest to radiation oncologists. Manuscripts and cases may be sent electronically to Cristen Bolan, Executive Editor for review with our Advisory Board. The opinions and recommendations expressed herein, in articles, columns and cases, are not necessarily those of the publisher. Every precaution is taken to ensure accuracy, but the publishers cannot accept responsibility for the correctness or accuracy of the information supplied or for any opinion expressed. Before using procedures or treatments discussed or suggested by authors, clinicians should evaluate their patients' conditions, compare the recommendations of other authorities, consider possible contraindications or dangers, and review applicable manufacturer's product information. Editorial closing date is the first day of the month 3 months prior to the issue date. Articles and cases should be geared to the practitioner and should reflect practical everyday clinical applications rather than research activity. Articles and cases may pertain to clinical management, administration, fiscal, technical, and medico-legal issues. Clinical review articles are also solicited by our Editorial Advisory Board. Any editorial submission should be original and unpublished, approximately 1500-2500 words and include the appropriate images, image captions and references. All submissions are to be submitted electronically by emailing a MS Word document, high resolution images, and selected DICOM image data sets to our Editor, Cristen Bolan for review and approval. Authors will be notified by email of acceptance or rejection and of any major recommended revisions. Prior to publication, a PDF of your article or case will be emailed to you for final approval. Manuscripts and case should be emailed to Cristen Bolan, at Cristen@appliedradiationoncology.com.

Anderson Publishing, Ltd
180 Glenside Avenue, Scotch Plains, NJ 07076
(908) 301-1995

Editorial Board

APPLIED RADIATION ONCOLOGY™

September 2013
Vol. 2, No. 3



DEPARTMENTS

Applied Radiation Oncology *is electronically published quarterly by Anderson Publishing, Ltd.,180 Glenside Avenue, Scotch Plains, NJ 07076. Subscription is free of charge to all medical professionals and available by clicking here. Complaints concerning non-receipt of this e-journal must be made via email to our Publisher, Kieran Anderson at kieran@appliedradiationoncology.com.*

Congratulations to our first Clinical Case Contest winner, D. Hunter Boggs, MD. As the winner, Dr. Boggs' case received the most votes from our online community and was selected by our Advisory Board as the best prepared and most interesting case submitted during August 2013. Dr. Boggs will receive an American Express gift card valued at $250. For details on how you can enter your case, click here.

Profound radiation pneumonitis preceding pathologic complete response in a patient with locally advanced nonsmall cell lung cancer

D. Hunter Boggs, MD, Steven Feigenberg, MD, and Randi Cohen, MD

CASE SUMMARY

A 79-year-old man with a remote history of smoking presented with blood-tinged sputum. After imaging/workup, he was staged with T2bN2M0 (stage IIIA) squamous-cell carcinoma of the lung and was scheduled for chemoradiotherapy (CRT) and subsequent restaging/evaluation for surgical resection. He received 6,300 cGy of external beam radiation therapy (EBRT) in 35 fractions to his left lung mass, left hilar adenopathy, and paratracheal lymphadenopathy using 6-field intensity-modulated radiation therapy (IMRT) (Table 1) with weekly carboplatin AUC 5 on days 1 and 22 and weekly docetaxel 20mg/m2. He developed mild esophagitis and RTOG grade II dermatitis as well as dose-limiting thrombocytopenia, which were managed conservatively. Rapid radiographic onset of radiation pneumonitis was noted at 5 weeks after CRT (although clinical symptoms remained mild), and surgery was postponed. After 30 days of oral prednisone (20 mg/day), the patient showed marked improvement and proceeded to surgery. Surgery was well tolerated, and analyses indicated a complete pathologic response to CRT.

Prepared by ***Dr. Boggs, Dr. Feigenberg,*** *and* ***Dr. Cohen,*** *while at University of Maryland School of Medicine, Baltimore, MA.*

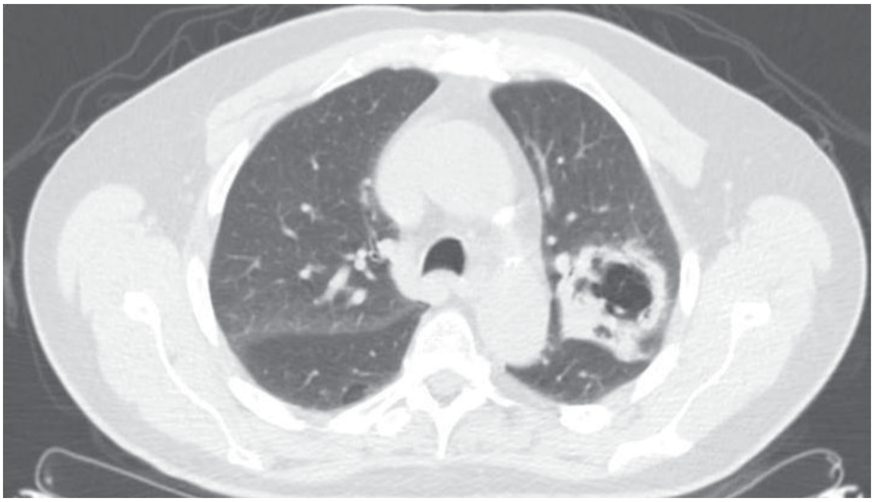


FIGURE 1. *Pretreatment PET/CT demonstrating necrotic left upper lobe nodule, with SUVmax in the primary of 14.4 and 17.3 in a left hilar node. Hypermetabolic left hilar lymph node was noted (SUVmax = 17.3) with no additional lymphadenopathy. Initial pulmonary function testing demonstrated a FEV1 of 3.11 L, FEV1/forced volume vital capacity ratio that was 95% of predicted value, and DLCO of 103% of predicted value. A subsequent chest CT showed the mass in the left-upper lobe to be encasing the posterior superior segmental bronchovascular bundle with extension to the left upper lobe pulmonary arterial bifurcation and a 3.0 × 1.8 × 1.8-cm soft-tissue prominence compatible with mediastinal lymphadenopathy.*

IMAGING FINDINGS

At presentation: At initial presentation, a chest radiography showed a 6.5-cm left upper lobe cavitary lesion. Computed tomography (CT)-guided biopsy of the mass demonstrated poorly differentiated squamous cell carcinoma with necrosis. Positron emission tomography/CT (PET/CT) showed a maximum standardized uptake value (SUVmax) of 14.4 in the primary and 17.3 in a left hilar node

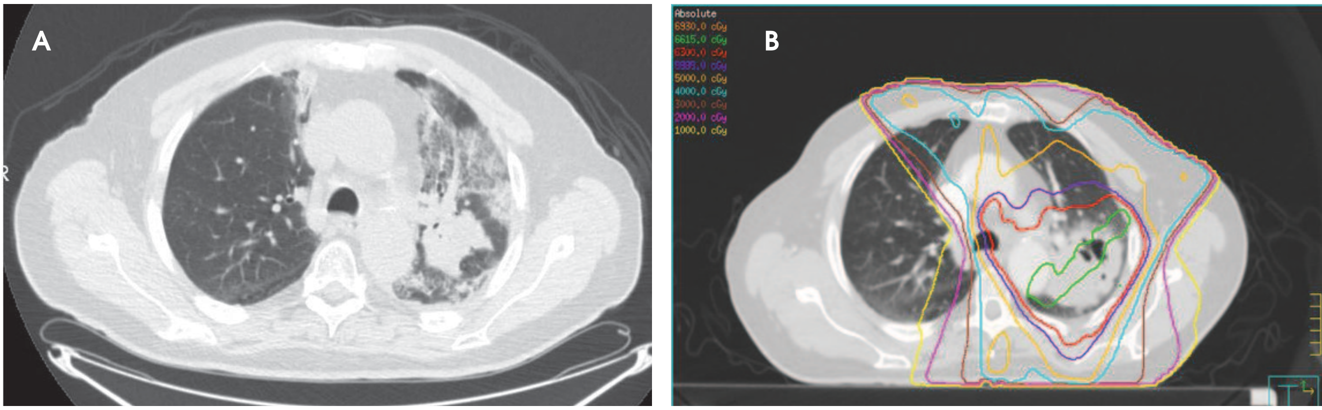


FIGURE 2. *(A) One month after CRT, pulmonary function testing showed an FEV1 of 2.82 (103% of predicted), TLC of 6.01 (85% of predicted), residual volume of 2.23 (81% of predicted), and DLCO of 14.1 (60% of predicted). Restaging PET/CT 1 week later (5 weeks post-CRT) showed diffuse consolidation throughout the left-upper lobe associated with intense tracer uptake (SUVmax range, 6.8–8.5) consistent with radiation pneumonitis. The mass contiguous to the left hilum measured ~3.6 cm, and portions of the mass were associated with very low-level 18F-FDG uptake (SUVmax = 3). A zone of pleural-based consolidation in the right lung was noted in the right midanterior chest adjacent to the mediastinal pleural surface (SUVmax = 4.9). These findings were consistent with postradiation pneumonitis.*
Figure 2. (B) Corresponding lung isodose distributions in the radiation treatment plan correspond to the pneumonitis pattern that developed. The pattern most closely corresponds with the 70% isodose line (received 43 Gray).

(Figure 1). Quantitative ventilation/perfusion scanning demonstrated a mismatch corresponding to the known tumor. Mediastinoscopy demonstrated poorly differentiated squamous-cell carcinoma in the 4L lymph node. The 4R, 7, and left mainstem bronchus biopsies were negative for metastatic disease. Other initial metastatic workup included magnetic resonance imaging (MRI) of the brain.

In evaluation for surgery: At 1 month after CRT, the patient noted a mild increase in shortness of breath with exertion (although able to perform 30 minutes of cardiovascular exercise 3-4 times/week) and a productive intermittent cough. Pulmonary function testing showed a forced expiratory volume of 2.82 (103% of predicted), total lung capacity of 6.01 (85% of predicted), residual volume of 2.23 (81% of predicted), and CO lung diffusion capacity (DLCO) of 14.1 (60% of predicted). Restaging PET/CT at 5 weeks after treatment showed diffuse consolidation throughout the left-upper lobe associated with intense tracer uptake (SUVmax range, 6.8-8.5) consistent with radiation pneumonitis (Figure 2).

Perioperative: After 30 days of oral prednisone, CT (Figure 3) showed decreases in reactive lung changes. The patient underwent a left thoracoscopy with pleural biopsies, followed by a left thoracotomy and left upper lobectomy. On operative report, an atelectatic left lung was recognized with the parenchyma of the posterior aspect of the upper lobe and the superior segment of the lower lobe appearing dark and consolidated, consistent with areas of treated disease and pneumonitis. By comparison, the anterior aspect of the upper lobe and rest of the lower lobe appeared normal. The patient subsequently underwent a staged thoracotomy and left upper lobectomy where additional reactive adhesions of the lung to the mediastinal pleura were recognized. Fibrosis was particularly intense surrounding the aortopulmonary window and the posterior aspect of the upper lobe where the gross tumor volume was located. Changes to the lung tissue extended across the posterior aspect of the fissure to the superior segment, where the radiographically identified consolidation had extended. Thoracic lymphadenectomies were then performed at levels 5 and 7 to 12. Pathology from the resected left-upper lobe showed fibrosis, coagulative necrosis, and reactive epithelial cells with no evidence of malignancy. None of these lymph node areas showed evidence of malignancy, indicating a complete pathologic response to neoadjuvant CRT.

Follow-up: At 1 month after surgery, the patient was asymptomatic with oxygen saturation of 96% of room air.

DISCUSSION

This case of radiation pneumonitis presented with minimal symptomatic change, no identifiable predictors of rapid pneumonitic response, and lung dose–volume histogram (DVH) criteria within institutionally acceptable limits.

Radiation pneumonitis is observed clinically in 10% to 20% of patients receiving concurrent CRT for locally advanced nonsmall cell lung cancer, with a much higher percentage of patients exhibiting asymptomatic radiographic changes.[1-3] Type II pneumocytes demonstrate early response to lung irradiation and endothelial damage leading to vascular congestion and capillary swelling 1 to 6 weeks

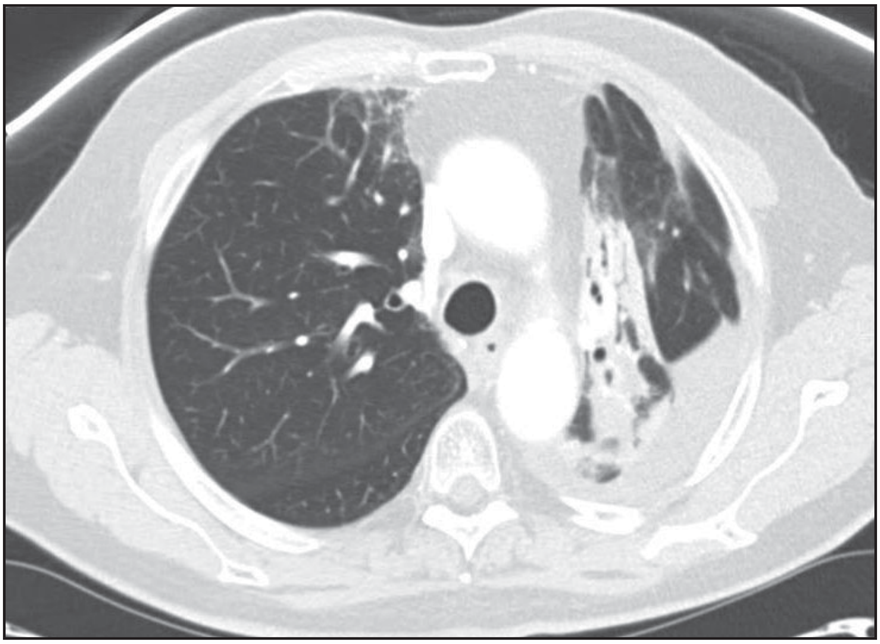


FIGURE 3. *CT acquired after 30 days of oral prednisone showed decreases in reactive lung changes. The patient proceeded to surgery. Pathology from the resected left-upper lobe showed fibrosis, coagulative necrosis, and reactive epithelial cells with no evidence of malignancy. Lymph nodes showed no evidence of malignancy, indicating a complete pathologic response to neoadjuvant RT.*

after irradiation, which can clinically manifest as a reduction in DLCO on pulmonary testing, as observed in our patient.[4] The acute phase of radiation-induced lung injury is transient and typically occurs within 4 to 12 weeks of completing therapy. Fibrosis occurs 6 to 12 months after completing RT and is caused by infiltration of fibroblasts into alveolar walls, which progresses to vascular sclerosis.[5]

Risk factors for developing clinically significant radiation pneumonitis include ECOG performance status > 1, female sex, age > 60 years, and concomitant chemotherapy.[5-8] Docetaxel administration is associated with radiation pneumonitis, and weekly schedules have been associated with higher rates of pneumonitis than have administrations every 3 weeks.[9]

Nonsmokers also have less baseline damage to their lungs prior to RT and show higher rates of pneumonitis than smokers.[10] Significant dosimetric parameters, such as V20 ≤ 25, V25 ≤ 20, V35 ≤ 15 and V50 ≤ 10, have shown to result in 2% rates of ≥ grade 3 pneumonitis and were achieved in this patient [10-12] (Table 1). Other than concomitant chemotherapy and advanced age, the patient had few risk factors that would have predicted the severity of his pneumonitic reaction.

Figure 2 demonstrates the isodose distribution in our plan and corresponding development of radiographic pneumonitis. Radiographic evidence of pneumonitis may appear at a marked geographic distance from the planning target volume and may be confused with infection or lymphangitic spread of neoplasm. When interpreting radiographic changes post-RT for purposes of restaging, it is vital for the radiation oncologist to work with the radiologist to describe the treatment plan and beam arrangements that may account for unusual areas of posttreatment change within the lung.[5] The contralateral linear consolidation pattern observed in our patient corresponds well to beam arrangements visualized during treatment planning, supporting suspicion for radiation-induced pneumonitis.

Corticosteroids are often used to improve symptomatic pneumonitis. To our knowledge, this is the first reported case in which corticosteroids were used with the primary goal of improving the patient's pulmonary function to increase eligibility for surgery.[4,13] The patient had suffered a dramatic decline in DLCO, which made him less than ideal as a surgical candidate.[14,15] A 1-month trial of oral corticosteroids resulted in radiographic and symptomatic improvement of pneumonitis, and he proceeded to surgery.

The patient experienced an atypically rapid and large-volume lung reaction at doses that do not usually produce such a response. In addition, the patient experienced a complete response to neoadjuvant CRT. Pathologic complete response rates for locally advanced lung cancer patients undergoing trimodality therapy are ~15% to 20% and result in improved overall survival when compared to incomplete responders.[15,16] The patient had no known family or personal history of syndromes associated with increased radiosensitivity; however, the marked response of both normal and neoplastic tissue to RT should be noted. The literature does not address pneumonitis as a predictor of either radiographic or pathologic response to neoadjuvant CRT.

CONCLUSION

We report a patient with locally advanced lung cancer who demonstrated an atypically rapid and dramatic lung tissue radiographic response to neoadjuvant CRT while showing only mild-to-moderate clinical manifestations of radiation pneumonitis. His functional parameters declined sufficiently that he was no longer a surgical candidate. A limited course of oral corticosteroids resulted in sufficient improvement to make him again eligible for surgery. We also observed a complete pathologic response after definitive resection, which may reflect enhanced radiosensitivity of both normal and neoplastic tissue. Radiation pneumonitis, although well documented, continues to be poorly understood and difficult to predict, but may prove useful in predicting clinical responses to neoadjuvant therapy in locally advanced lung cancer.

REFERENCES

1. Curran WJ Jr, Paulus R, Langer CJ, et al. Sequential vs concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. J Natl Cancer Inst. 2011;103:1452-1460.
2. Mehta V. Radiation pneumonitis and pulmonary fibrosis in non-small-cell lung cancer: pulmonary function, prediction,and prevention. Int J Radiat Oncol Biol Phys. 2005;63:5-24.
3. Bradley J, Graham MV, Winter K, et al. Toxicity and outcome results of RTOG 9311: a phase I-II dose escalation study using three-dimensional conformal radiotherapy in patients with inoperable non-small-cell lung carcinoma. Int J Radiat Oncol Bio. Phys. 2005;61:318-328.4. Movsas B, Raffin TA, Epstein AH, Link CJ Jr. Pulmonary radiation injury. Chest. 1997;111:1061-1076.
5. Choi YW, Munden RF, Erasmus JJ, et al. Effects of radiation therapy on the lung: radiologic appearances and differential diagnosis. RadioGraphics. 2004;24:985-998.
6. Marks L, Bentzen S, Deasy JO, et al. Radiation dose-volume effects in the lung. Int J Radiat Oncol Biol Phys. 2010;76:570-576.
7. Tsujino K, Hirota S, Endo M, et al. Predictive value of dose-volume histogram parameters for predicting radiation pneumonitis after concurrent chemoradiation for lung cancer. Int J Radiat Oncol Biol Phys. 2003;55:110-115.
8. Kim M, Lee J, Ha B, Lee R, Lee KJ, Suh H. Factors predicting radiation pneumonitis in locally advanced non-small cell lung cancer. Int J Radiat Oncol Biol Phys. 2011;29:181-190.
9. Chen YM, Shih JF, Perng RP, Tsai CM, Whang-Peng J. A randomized trial of different docetaxol schedules in non-small cell lung cancer patients who failed previous platinum-based therapy. Chest. 2006;129:1031-1038.
10. Jin H, Tucker SL, Hui HH, et al. Dose-volume thresholds and smoking status for the risk of treatment related pneumonitis in inoperable non-small cell lung cancer treated with definitive radiotherapy. Int J Radiat Oncol Bio Phys. 2009;91:427-432.
11. Rodrigues G, Lock M, D'Souza D, Yu E, Van Dyk J. Prediction of radiation pneumonitis by dose–volume histogram parameters in lung cancer—a systematic review. Radiother Oncol. 2004;71:127-138.
12. Kong F, Hayman J, Griffith K, et al. Final toxicity results of a radation-dose escalation study in patients with non-small-cell lung cancer (NSCLC): predictors of radiation pneumonitis and fibrosis. Int J Radiat Oncol Biol Phys. 2006;45:1075-1086.
13. Graham M, Purdy J, Emami B, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small-cell lung cancer (NSCLC). Int J Radiat Oncol Biol Phys. 1999;45:323-329.
14. Magaña E, Crowell R. Radiation pneumonitis successfully treated with inhaled corticosteroids. South Med J. 2003;96:521-524.
15. Albain KS, Swann RS, Rusch VW, et al. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. Lancet. 2009;374:379-386.
16. Albain K, Rusch V, Crowley J, et al. Concurrent cisplatin/etoposide plus chest radiotherapy followed by surgery for stages IIIA(N2) and TIIB non-small-cell lung cancer: mature results of Southwest Oncology Group Phase II Study 8805. J Clin Oncol. 1995;13:1880-1892.

APPLIED RADIATION ONCOLOGY® — **CLINICAL CASE CONTEST** GET PUBLISHED...WIN CASH! **VIEW GUIDELINES** *ENTER TODAY!*

On behalf the Publishers and Advisory Board of *Applied Radiation Oncology*, we are very pleased to announce our first Clinical Case Contest Winner for the month of August.

Dr. D. Hunter Boggs' Clinical Case entitled "Profound radiation pneumonitis preceding pathologic complete response in a patient with locally advanced nonsmall cell lung cancer" received the most votes from online viewers and additionally was selected by our Advisory Board as the best prepared and most interesting case submitted during the month of August. Dr. Boggs will be receiving and an American Express Gift Card valued at $250!

We urge you and your colleagues to submit your most interesting clinical cases to our monthly contest, as we will be choosing a winner each month through December. All winners will receive $250 American Express Gift Card and have their case published in *Applied Radiation Oncology*, which now reaches over 4,500 radiation oncology professionals electronically each quarter.

You may submit your case online by visiting www.appliedradiationoncology.com/contest where you can view our author guidelines.

Thank you all for your continued support of *Applied Radiation Oncology*.

Most sincerely,

Kieran N. Anderson
Publisher

CME Information

Activity description

In this issue of *Applied Radiation Oncology,* our faculty has assembled a number of articles and cases that provide practical insight on topics including new techniques in Gamma Knife stereotactic radiosurgery (SRS), robotic-assisted hysterectomies and their risks, the use of external beam radiotherapy (EBRT) for scleredema adultorum of Buschke, and stereotactic body radiotherapy for the treatment of spine metastasis.

Learning objectives

After reviewing this activity, participants will:

- Gain an awareness of the risk for vaginal-cuff dehiscence after hysterectomy and the apparent increased risk with more frequent use of robotic-assisted hysterectomy.
- Recognize the risk for vaginal-cuff dehiscence with the increased use of vaginal-cuff brachytherapy.
- Understand the development, practical use, and future of Gamma Knife radiosurgery.
- Be familiar with the clinical applications and outcomes for Gamma Knife radiosurgery.
- Understand the role of external beam radiotherapy as a treatment option for the management of scleredema adultorum of Buschke in the setting of uncontrolled type-2 diabetes mellitus.
- Comprehend the role of spine stereotactic body radiotherapy in the management of spinal metastases.

Accreditation/Designation statement

The Institute for Advanced Medical Education is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The Institute for Advanced Medical Education designates this enduring material for a maximum of *3 AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Principal faculty and their credentials

Gennady Neyman, PhD, Physicist, Department of Radiation Oncology, Cleveland Clinic, Cleveland, OH.

Mohamed A. Elshaikh, MD, Radiation Oncologist, Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI.

Ehsan H. Balagamwala, MD, Resident, Department of Radiation Oncology, Cleveland Clinic, Cleveland OH.

Abhilasha J. Patel, MD, Chief Resident and PGY-4, Department of Radiation Oncology, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Target audience

Radiation oncologists, surgical oncologists, radiologists, and oncological imaging physicians.

System requirements

In order to complete this program, you must have a computer with a recently updated browser. A printer configured to print from the browser is necessary in order to obtain a hard copy of earned certificates.

For any questions or problems concerning this program or for issues related to your CME account, please contact IAME at 802-824-4433 or info@iame.com

Instructions for participation

This activity is designed to be completed within the designated time period. To successfully earn credit, participants must complete the activity during the valid credit period. To receive *AMA PRA Category 1 Credit™*, you must receive a minimum score of 70% on the post-test.

1. Review all articles and cases that are part of this educational activity.
2. Click here to be redirected to the IAME website.
3. Log in to your IAME account or (new users) create a login. New users should purchase credits.
4. Take the CME quiz, and complete the online evaluation form.
5. Print your certificate.

CME pricing

The cost of CME credits is $50 per issue. As a special offer, you can purchase all the CME credits in every issue through the end of 2013, including our October 2012 issue for the discounted price of just $95. That's just $95 for 15 CME credits.

Estimated time for completion: 3 hours
Date of release and review: September 17, 2013
Expiration date: September 17, 2015

Disclosures

Author Toufik Djemil, PhD, serves as a teacher for Brainlab Inc. Andrew Godley, PhD, is a consultant for Elekta AB. Gennady Neyman, PhD, is a consultant for Elekta AB.

No other authors, or any individuals at IAME or *Applied Radiation Oncology* who had control over the content of this program, have any relationships with commercial supporters.

EDITORIAL

John Suh, MD, Editor in Chief

Enabling image guidance can help improve precision particularly for fractionated delivery.

Dr. Suh is the Editor-in-Chief of Applied Radiation Oncology, *and Professor and Chairman, Dept. Radiation Oncology at the Taussig Cancer Institute, Rose Ella Burkhardt Brain Tumor and Neuro-oncology Center, Cleveland Clinic, Cleveland, OH.*

Overview of Gamma Knife radiosurgery and vaginal brachytherapy

Welcome to the third quarter edition of Applied Radiation Oncology 2013! On behalf of the advisory board and publisher, we appreciate your support of this e-journal, which features two articles and two case reports. We are encouraged by the favorable feedback that we have received from our readers.

In this edition, Dr. Neyman and colleagues review the history of Gamma Knife radiosurgery and evaluate the procedure, imaging, treatment planning, quality assurance, and clinical uses of the Gamma Knife based on the Cleveland Clinic experience, which has been an active unit since January 1997. Since Dr. Lars Leksell introduced the term radiosurgery in 1951, many patients with vascular malformations, benign brain tumors, functional disorders, such as trigeminal neuralgia, and malignant brain tumors, have greatly benefited from this technology. Like many centers, the Cleveland Clinic has continuously upgraded its systems and currently uses the Perfexion model, providing greater flexibility in treating targets throughout the brain in a more efficient and effective manner. Unlike many centers, MRI and CT images are obtained for the vast majority of patients to confirm positioning and minimize spatial distortion errors of MRI scans. The authors review some of the newer developments, including collapsed-cone convolution algorithm, which more accurately calculates dose distribution in the treatment field, relocatable frame system (Extend), allowing for stereotactic radiotherapy using a vacuum-assisted bite-block device, and a cone-beam computed image-guidance system, enabling image guidance that can help improve precision particularly for fractionated delivery.

The second article from Cattaneo and Elshaikh provides a radiation oncologist's perspective on minimally invasive hysterectomy for patients with uterine cancer—the most commonly diagnosed gynecological malignancy in the United States. With the introduction of robotic-assisted laparoscopic techniques and keen interest in reducing hospital stays and potential perioperative complications associated with more traditional hysterectomy, this approach has been widely adopted. Although this approach is clearly less invasive than total abdominal hysterectomy, the vaginal-cuff dehiscence rate approaches 4.1% compared to < 1% when following a traditional hysterectomy. This coupled with the increased use of vaginal brachytherapy based on the PORTEC-2 results makes this article timely. Since vaginal-cuff dehiscence appears higher for those patients undergoing robotic-assisted laparoscopic techniques, radiation oncologists should take the necessary steps and precautions to detect and prevent vaginal-cuff dehiscence as outlined in the article, including inspection of the vaginal cylinder after completion of the procedure.

We hope you enjoy this issue of *Applied Radiation Oncology*. If you are interested in submitting an article, we would welcome your submission. We also encourage you to participate in our monthly clinical case review contest. The winning case will be published in a future issue of *Applied Radiation Oncology,* and the author will receive an American Express Gift Card in the amount of $250.

For those attending the ASTRO meeting, I hope you enjoy the meeting in Atlanta.

John Suh, MD

CME SEE PAGE 8 FOR DETAILS

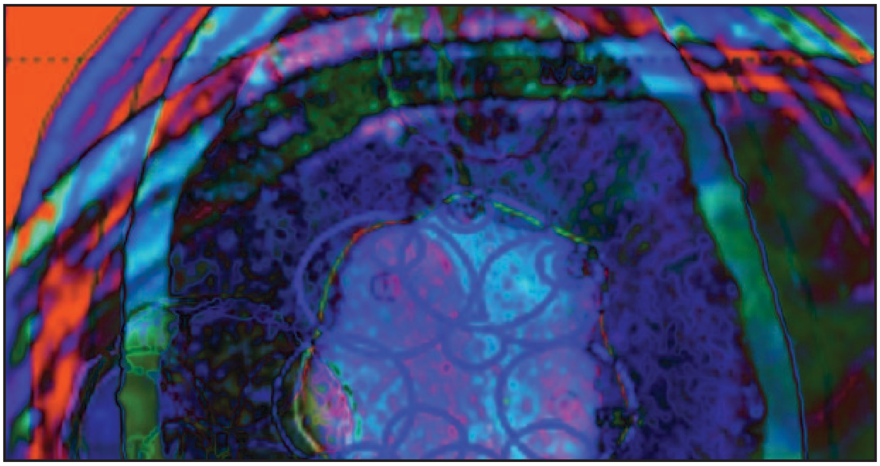
Stereotactic radiosurgery — The Cleveland Clinic experience and future directions using a Gamma Knife

Gennady Neyman, PhD, Malika Ouzidane, PhD, Andrew Godley, PhD, Toufik Djemil, PhD, and Sam Chao, MD

In 1951, Swedish neurosurgeon Dr. Lars Leksell introduced the term radiosurgery, a type of surgery where the surgeon's knife was substituted with a combination of beams of ionizing radiation.[1] In 1967, together with Dr. Larson, a physicist, Dr. Leksell created a fixed-source Cobalt-60 (Co-60) unit, Gamma Unit I, which was the first stereotactic apparatus to perform radiosurgical treatments of intracranial targets.[2] Co-60 was chosen as the radiation source because it produces a high-energy beam capable of irradiating deep-seated lesions. Gamma Unit I comprised 170 separate Co-60 beams with 3-mm-x-5-mm slit-shape collimators, and was used to irradiate brain tumors.

Quickly it became obvious that the next generation of Gamma Knife (GK) machines had to produce larger and more spherical radiation fields, which would be a better fit to the typically spherical shape of tumors. In 1975, Gamma Unit II was designed using cylindrical collimators, 4 mm to 20 mm in diameter. The Gamma Knife technology then evolved through several models. In the first model, the 201 Co-60 sources (models A and U) were arranged in a hemispherical array, and irradiation could be delivered using 4 different circular collimator sizes (4, 8, 14, and 18 mm). The drawback of those models was the time-consuming loading and reloading of the Co-60 sources. The unit was redesigned in 1988 (model B) to solve this problem. The process of manually setting the target position was also very labor intensive, so in 1999, models C and 4C, were introduced, which were capable, albeit in a limited range, of shifting the x-y-z target coordinates via an automatic positioning system (APS). However, the APS took up space and reduced the range of motion of the couch, and consequently, limited the access to certain regions of the skull.

Drs. ***Neyman, Ouzidane, Godley, Djemil,*** *and* ***Chao*** *are in the Department of Radiation Oncology, Cleveland Clinic, Cleveland, OH.*



To avoid these limitations, the Perfexion model was introduced in 2006; it is based on a single integrated collimator system of 3 different sizes (4, 8, and 16 mm) and an automated couch position. The 192 Co-60 sources of GK Perfexion are split into 8 sectors, potentially better shaping the radiation fields, as these sectors can each move independently with 3 open positions and 1 blocked position. The full automation achieved by the Perfexion GK, including both the positioning of the patient and beam shaping, greatly decreases staff workload and increases patient

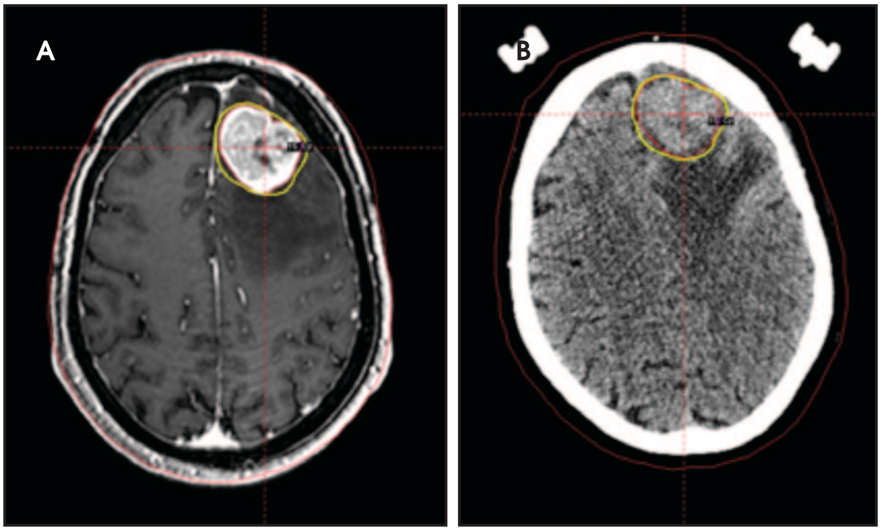


FIGURE 1. Demonstration of coregistration an MRI image on the left (A) to a CT image on the right (B).

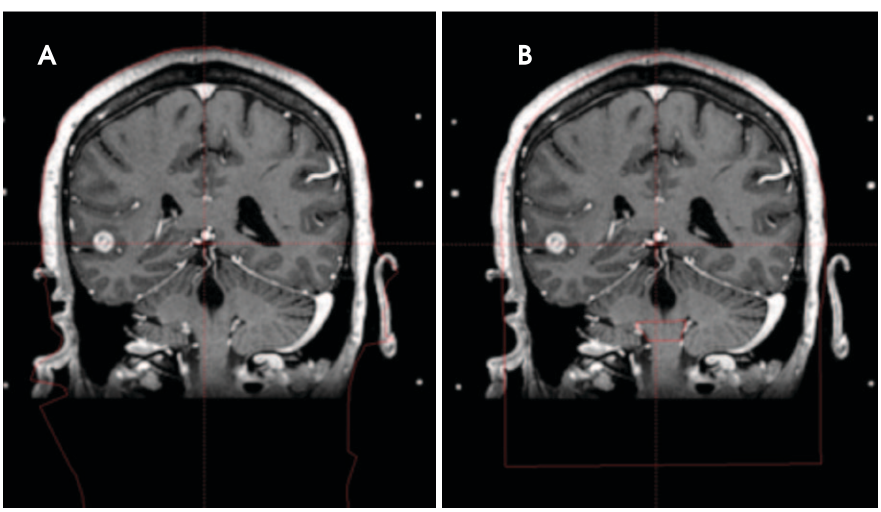


FIGURE 2. Segmentation of the skull using CT on the left (A) image and by manual measurements in the right (B) image.

throughput. The large number of noncoplanar beams, lack of a heavy gantry, short collimator-to-source distance compared to linear accelerators (linacs), and its simplicity are the inherent advantages of the GK stereotactic radiosurgery (SRS) system. It also need to be emphasized that there are some disadvantes using GK compared with the linac based radiosurgery like: the cost of the periodic re-loading of the sources (usually every 5-6 years) and it's limited use only to the cranial targets. From another side most of the linacs on the market don't have the same mechanical isocenter accuracy as GK.

GK Perfexion was installed and commissioned at the Cleveland Clinic Gamma Knife Center in July 2007.

Cleveland Clinic Gamma Knife procedure

Placement of the Leksell head ring

On the morning of the procedure, the Leksell frame is positioned on the head of the patient, usually using 4 posts/screws under local anesthesia. The Perfexion GK machine allows for central placement of the head frame, fairly independent of the tumor location. Only in 3 cases from more than 2000 patients treated at Cleveland Clinic including patients with multiple targets we were not able to treat all the targets in the same session without re-positioning of the frame. In certain cases of surgical skull defects, a slotted post is used to position the frame with only 3 posts.

MR and CT imaging

One of the most important aspects of radiosurgery is accurate imaging of the target. Both high-resolution magnetic resonance imaging (MRI) and computer tomography (CT) are typically used for GK treatment planning at Cleveland Clinic. The use of 2 independent imaging modalities confirms positioning and helps minimize errors from spatial distortions of the MRI. Additionally, angiograms are used for arteriovenous malformations (AVM) and vascular tumor radiosurgery. The dedicated radiation treatment software for Gamma Knife (Gamma Plan) allows the coregistration of preframe MRI with postframe CT with the CT fiducial device attached using the mutual information volume algorithm. Gamma Plan version 10 allows for restriction of the co-registration to the area close to the region of interest instead of the whole head. This can greatly improve the accuracy and ease of the co-registration process (Figure 1). The advantages of the co-registration technique include:

1. no distortions from the Leksell frame on MRI scans,
2. easier for patient to tolerate the MR scan without a frame on his head, and
3. decreased workload for Gamma Knife personnel on the day of treatment.

Neurosurgeons perform the co-registration at Cleveland Clinic. The Gamma Plan doesn't quantify for the user how accurate the coregistration is, so the neurosurgeons have to rely on a good

CME

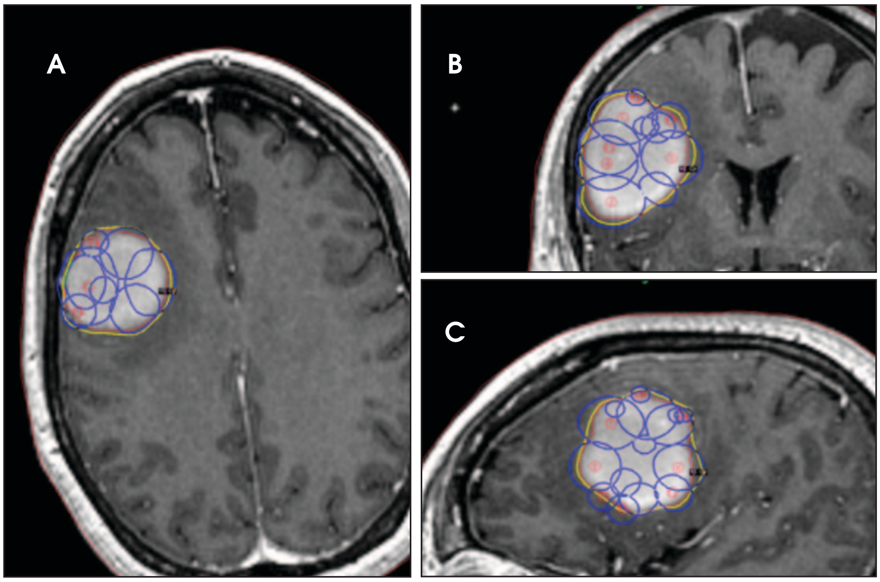


FIGURE 3. *(A, B, C) Dose distribution of metastatic tumor using inverse planning with tumor contour in red, prescription line in yellow, and individual shots in blue color*

Table 1. Daily QA of the machine

Verify presence of emergency equipment and procedures
Verify audio/visual monitoring
Verify radiation monitors (fixed and portable)
Verify source position indicator lights
Verify that interlocks and interrupts are functional
Verify timer accuracy (2%) and exposure termination
Verify that the docking device is securely mounted to the table and that the frame adapter can be correctly docked in the docking device

visual match in the vicinity of the target. With this approach the CT scanners have to go through a rigorous QA program to check for the quality of its images.

In our center, for MRI of most lesions, a 3-dimensional (3D) volume gadolinium-enhanced acquisition is used with T1 FLAIR sequence at 256 x 256 matrix, 1-mm slice thickness and no gap. CT imaging is mostly done with contrast at 512 x 512 matrix and 1 mm to 2 mm slice thickness. Angiograms, when necessary, are corrected using digital subtraction techniques.

Measurements of the skull geometry

Traditionally, the patient's skull geometry is defined by measuring the distances from the center of the frame to 24 preselected points on the skull using the skull scaling instrument. Those measurements are susceptible to human error and sometimes are not very accurate in simulating the skull, especially when the patient's skull is deformed because of the bone resection. In our center, an existing patient CT scan allows us to use a relatively new feature of the Gamma Plan—extracting the contour of the patient skull from the CT image (Figure 2).

Target localization

The MR and CT are visually compared to see if spatial distortions more than 1 mm are present in the MR images. This procedure is usually performed by a physicist with the participation of the neurosurgeon.

Target delineation

Target delineation is accomplished by a neurosurgeon. In certain cases, the targets are drawn on both MR and CT studies and compared.

Treatment planning

This is a combined effort by each member of the team consisting of the neurosurgeon, the radiation oncologist, and the physicist, to produce the best plan. The plans are compared using dose volume histograms (DVH) for the outlined targets and organs at risk (OAR). The plan is designed with the prescription to the target at 50% isodose line or higher. In certain cases the new inverse treatment planning feature of Gamma Plan version 10 is used, which can ease the job of planning, especially for the coverage of big and complicated targets (Figure 3).

From the DVH, a number of plan indices are calculated and compared between different plans:

- Conformity Index (CI) = PIV/TV, where PIV is the prescription isodose volume and TV is the target volume.
- Gradient Index (GI) = PIV0.5/PIV, where PIV0.5 is the volume getting half the prescription dose.
- Homogeneity Index (HI) = Dmax/Dmin, where Dmax and Dmin are maximum and minimum dose respectively.

The goal for the planning is to achieve 100% target coverage, or very close to that (no less than 98%). In the process of planning, the plan with the

Table 2. Outcomes from cranial SRS treated at the Cleveland Clinic

Tumor / disorder	Dose (Gy)	Local control
Meningioma	13-143	93% at 10 years[4]
Pituitary adenoma		
Nonsecretory	16	95% at 5 years[5]
Secretory	18-25	54% normalization of acromegaly[6], 34% for prolactinomas[7]
Vestibular schwannoma	12-13	91% at 5 years[8]
Arteriovenous malformation	14-27	73% obliteration rate[9]
Trigeminal neuralgia	80-90 (to 100% isodose line)	~75% at 1 year pain response[10]
Brain metastases		75%-80% at 1 year[11]
2 cm or less	20-24	
2.1 to 3 cm	18	
3.1 to 4 cm	15	

smaller CI and less dose to the critical organs is chosen. When the plan is finalized, the physicist checks the plan for target coverage, dosimetric indices, and dose distribution. Another important check is the deliverability of the treatment as planned, without risks of collisions with the machine. The physicist also makes sure the dose rate used for the calculations in the Gamma Plan is accurate by comparing it to tabulated values of decayed dose rate from initial calibration of the sources and also by running a quick calculation. Typical daily quality assurance (QA) checks on the Gamma Knife machine, which are done before treatment of the first patient of the treatment day, are presented in Table 1.

Treatment implementation

GK Perfexion usually creates just one run per patient treatment even for multiple targets. Separate runs are necessary when different gamma (neck) angles are used. Before actual treatment the radiation oncologist is checking that the frame is stable on the patient by pushing the frame up and down.

Clinical uses

The Gamma Knife can be used to treat malignant and benign tumors, vascular disorders, and functional disorders. Malignant tumors include brain metastases and recurrent malignant gliomas. Benign

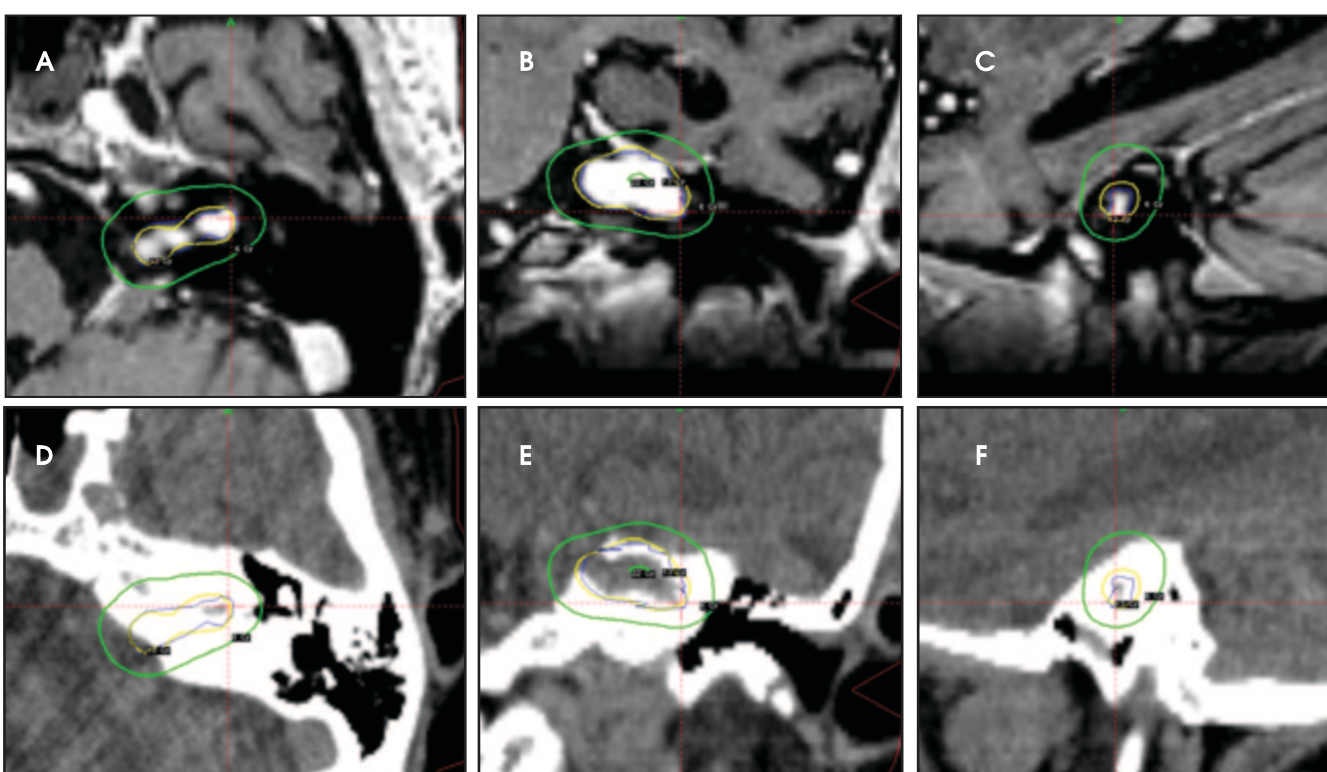


FIGURE 4. *Dose distribution for an acoustic schwannoma using CCC algorithm on MRI (A-C) upper images and CT (D-F) bottom images.*

tumors include vestibular schwannomas, meningiomas, pituitary adenomas, and glomus tumors. Vascular disorders are typically AVMs. Functional disorders include trigeminal neuralgia and Parkinson's disease. At Cleveland Clinic, the decision to treat is made by the neurosurgeon and radiation oncologist, and which is facilitated through the Tumor Board that meets twice a week. Table 2 is a summary of outcomes of the most common indications treated at the Cleveland Clinic.

Future Developments

Collapsed-cone convolution algorithm for the gamma plan

Elekta has already implemented the collapsed-cone convolution (CCC) algorithm for Gamma Plan, which requires a whole-head CT scan. The collapsed cone convolution algorithm has some advantages compared with the traditional tissue-maximum ratios algorithm (TMR) that assumes the head uniformly as water, and can achieve more accurate calculations of the dose distribution in the field of GK radiosurgery. The main advantages of CCC are: a) it more accurately models build-up effects; b) it takes head heterogeneity into account; and c) it increases tissue correction and accuracy to dose calculation for targets near air cavities and bone.

Despite those advantages, the CCC algorithm is rarely used in clinical practice because most institutions use only MRI studies for planning without CT scans. Also, the CT protocol has to be adjusted because of the particular requirements for field of view (FOV). Using our database, it was shown that the TMR algorithm systematically overestimates the actual physical dose delivered compared with recalculations of the same plans using CCC algorithm by about 6% to 8 %.[12] An example of a 2% loss of dose coverage for an acoustic schwannoma tumor, recalculated by CCC algorithm after being calculated originally by TMR algorithm, is shown in Figure 4.

A relocatable frame system for multiple-session GKRS

Gamma Knife surgery traditionally was limited to a single-session treatment with the rigid frame-based technique. It is known that certain brain tumors may have a better outcome using fractionated radiation treatments. This is typically how linear accelerator-based systems treat.[13] Elekta has released the Extend System that allows the GK Perfexion System to treat multisession GK procedures. This is a noninvasive frame that uses a vacuum-assisted bite block device positioned on a carbon-fiber frame. The reposition check tool, which consists of a Plexiglas frame and electronic measurements probes, is used to position the patient's head in the same place for each subsequent treatment. The mean intrafractional positional difference is about 0.5 mm with a standard deviation of 0.3 mm using the Extend System, when it was studied in 10 patients with 36 fractional treatments.[14]

Cone-beam computed image guidance system for GKRS

Another recent development in GK radiosurgery was described by Ruschin et al.[15] The authors integrated a custom-built cone-beam computed tomography (CBCT) installation for image guidance in GK Perfexion System. This can improve the precision of fractionated radiation treatment delivery. A kV cone beam CT system was integrated with a GK machine and consists of the 40-cm x 30-cm flat-panel x-ray detector and an x-ray tube placed on an imaging arm. The images of the phantom showed that the maximum targeting error was 0.4 mm. The system needs additional clinical evaluation before it can be fully implemented in clinical practice.

Conclusion

The Cleveland Clinic Gamma Knife procedure and clinical results are summarized in this article. The continuing developments in this field can greatly expand the possibilities of Gamma Knife radiosurgery and solve some of its previous limitations.

References

1. Leksell L. The stereotactic method and radiosurgery of the brain. *Acta Chir Scand.* 1951;102:316-319.
2. Leksell L. *Stereotaxis and radiosurgery: An operative system.* Thomas Publishers, Springfield, IL, 1971.
3. Balagamwala EH, Suh JH, Barnett GH, et al. The importance of the conformality, heterogeneity, and gradient indices in evaluating Gamma Knife radiosurgery treatment plans for intracranial meningiomas. *Int J Radiat Oncol Biol Phys.* 2012;83:1406-1413.
4. Flickinger JC, Kondziolka D, Maitz AH, Lunsford LD. Gamma knife radiosurgery of imaging-diagnosed intracranial meningioma. *Int J Radiat Oncol Biol Phys.* 2003;56:801-806.
5. Sheehan JP, Starke RM, Mathieu D, et al. Gamma Knife radiosurgery for the management of nonfunctioning pituitary adenomas: A multicenter study. *J Neurosurg.* 2013.
6. Jagannathan J, Yen CP, Pouratian N, Laws ER, Sheehan JP. Stereotactic radiosurgery for pituitary adenomas: A comprehensive review of indications, techniques and long-term results using the Gamma Knife. *J Neurooncol.* 2009; 92:345-356.
7. Sheplan Olsen LJ, Robles Irizarry L, Chao ST, et al. Radiotherapy for prolactin-secreting pituitary tumors. *Pituitary.* 2012;15:135-145.
8. Murphy ES, Barnett GH, Vogelbaum MA, et al. Long-term outcomes of Gamma Knife radiosurgery in patients with vestibular schwannomas. *J Neurosurg.* 2011;114:432-440.
9. Pollock BE, Gorman DA, Coffey RJ. Patient outcomes after arteriovenous malformation radiosurgical management: Results based on a 5- to 14-year follow-up study. *Neurosurgery.* 2003;52:1291-1296;discussion 6-7.
10. Kanner AA, Neyman G, Suh JH, Weinhous MS, Lee SY, Barnett GH. Gamma knife radiosurgery for trigeminal neuralgia: Comparing the use of a 4-mm versus concentric 4- and 8-mm collimators. *Stereotact Funct Neurosurg.* 2004;82:49-57.
11. Chao ST, Barnett GH, Vogelbaum MA, et al. Salvage stereotactic radiosurgery effectively treats recurrences from whole-brain radiation therapy. *Cancer.* 2008; 113:2198-204.
12. Neyman G, Somell B, Nordstrom H. Comparison of collapsed cone convolution with the traditional tissue maximum ratio algorithm for dose calculation in a Gamma Knife radiation treatment planning system. *Medical Physics.* 2013;40, 6:337 (AAPM annual conference proceedings, 2013, Indianapolis).
13. Tuniz F, Soltys S, Choi C, et al. Multisession Cyberknife steroatactic radiaosurgery of large, benign cranial base tumors: Preliminary study, *Nerosurgery.* 2009;65:898-907.
14. Schlesiner D, Xu Z, Taylor F, et al. Interfraction and intrafraction performance of the Gamma Knife Extend system for patient positioning and immobilization. *J Neurosurgery* (Suppl). 2012;117:217-224.
15. Ruschin M, Komljenovic P, Ansell S, et al. Cone beam computed tomography image guidance system for a dedicated intracranial radiosurgery treatment unit. *Int J Radiat Oncol Biol Phys.* 2013;85:243-250.

CME SEE PAGE 3 FOR DETAILS

Minimally invasive hysterectomy for uterine cancer: A radiation oncologist's perspective

Richard Cattaneo II, MD, and Mohamed Elshaikh, MD

Endometrial cancer is the most commonly diagnosed gynecological malignancy in the United States, with 47,130 estimated new cases in 2012.[1] Hysterectomy with bilateral salpingo-oophorectomy, with or without pelvic or para-aortic lymphadenectomy, is the standard staging procedure for patients with endometrial cancer.[2]

Traditionally, endometrial cancer has been surgically managed with laparotomy through a large vertical incision. More recently, robotic-assisted laparoscopic hysterectomy (da Vinci System, Intuitive Surgical System, Inc., Sunnyvale, CA) has been adopted for treatment of endometrial cancer in many centers all over the world. Recent studies reported a reduction in perioperative complications and shorter hospital stays with quicker recovery for laparoscopic approaches compared to total abdominal hysterectomy.[3-7]

However, with the increased use of laparoscopic, including robotic-assisted, hysterectomies, there appears to be an increased rate of vaginal-cuff dehiscence, a rare complication after hysterectomy. The rate of this complication is relatively higher after robotic-assisted hysterectomy, reaching up to 4.1%[8] compared to < 1% following total abdominal hysterectomy.[9]

Dr. Cattaneo and Dr. Elshaikh are in the Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI.

The radiation oncologist's perspective

While surgical staging alone is curative in most of the patients with early-stage endometrial carcinoma, selected patients with an adverse prognostic feature, eg, high tumor grade, deep myometrial invasion, and nonendometrioid histology, will benefit from adjuvant radiation therapy following hysterectomy. Two major prospective, randomized studies showed that adjuvant radiation treatment after hysterectomy resulted in a significant reduction in locoregional recurrence.[10-11]

The use of adjuvant vaginal-cuff brachytherapy for patients with endometrial cancer is effective in reducing vaginal-vault recurrence, which is the most common site of recurrence after hysterectomy in patients with endometrial cancer. In a prospective randomized study (PORTEC-2), vaginal-cuff brachytherapy was compared to pelvic external beam radiation treatment (EBRT) in regards to efficacy in reducing vaginal-cuff recurrence as well as health-related quality of life. The estimated 5-year rate of vaginal recurrence was only 1.8% after vaginal-cuff brachytherapy.[12]

With the increased utilization of vaginal brachytherapy as an effective adjuvant treatment following hysterectomy,[13] together with the increased utilization of minimally invasive hysterectomy for patients with endometrial cancer, we sought to discuss our perspectives in regard to the potential challenge of an increased rate of vaginal-cuff dehiscence after a robotically-assisted hysterectomy for those patients who will require adjuvant vaginal-cuff brachytherapy.

The relative increased rate of vaginal-cuff dehiscence is attributed to a variety of reasons, including the use of electrocautery for colpotomy, the suturing technique used, and the magnification view causing suture bites to

CME

FIGURE 1. A vaginal brachytherapy coronal CT image shows the vaginal cylinder projecting deep in the pelvis.

be smaller than desired. Predisposing factors for vaginal-cuff dehiscence include poor wound healing, excessive pressure at the vaginal vault, eg, sexual intercourse,[14] and vaginal instrumentation, eg, the insertion of a vaginal cylinder for vaginal brachytherapy.[15] Other proposed risk factors for vaginal-cuff dehiscence include poor surgical technique, smoking, use of the Valsalva maneuver, postoperative infection, hematoma, steroid use, connective tissue disease, vaginal trauma/rape, use of vaginal dilator, diabetes mellitus, and chronic constipation.[16-18]

While there is only one case report to date for patients with vaginal dehiscence as a result of vaginal-cuff brachytherapy, we think this complication is under reported. We have recently diagnosed a patient with vaginal-cuff dehiscence as a result of vaginal-cuff brachytherapy. A 62-year-old female underwent robotic-assisted laparoscopic hysterectomy with bilateral salpingo-oophorectomy for FIGO 2009 stage IB endometrioid adenocarcinoma, FIGO grade 1. Based on a multidisciplinary tumor conference, it was recommended to treat her with adjuvant vaginal-cuff brachytherapy. She presented for computed tomography (CT) simulation for vaginal-brachytherapy treatment planning approximately 9 weeks after her hysterectomy. During simulation, the vaginal cylinder was noted to abnormally project high into the pelvis (Figure 1). On speculum examination, there was evidence of complete vaginal-cuff dehiscence. She underwent surgical closure of the vaginal cuff on the same day.

Radiation oncologists should be aware of the very low risk of vaginal-cuff dehiscence and take steps prevent and detect the condition as early as possible. At the time of the brachytherapy simulation, it can be useful to perform careful speculum and manual examinations of the vaginal cuff for findings of vaginal-cuff dehiscence. The appropriate size of the vaginal cylinder should be selected. The location of the vaginal cylinder should be radiologically verified with each application to rule out abnormal positioning of the cylinder.

Vaginal-cuff dehiscence should be ruled out if the vaginal cylinder projects abnormally deep in the pelvis. To reduce the risk of dehiscence during insertion of the vaginal cylinder, it is helpful to avoid high pressure on the vaginal cuff. After the procedure, one should inspect the vaginal cylinder for any abnormal blood or clear vaginal fluid that could suggest dehiscence. On the other hand, this very rare complication can be prevented by initiating vaginal brachytherapy no sooner than 6 weeks after a hysterectomy to allow adequate healing time.[19] However, delaying the start of adjuvant radiation treatment > 9 weeks after a hysterectomy may be associated with increased risk of tumor recurrence.[20]

Conclusion

Vaginal-cuff dehiscence is an unusual complication of hysterectomy. With the increased use of laparoscopic, robotic-assisted approaches, there appears to be an increased rate of vaginal-cuff dehiscence. In addition, there is an increased use of adjuvant vaginal brachytherapy for treatment of endometrial cancer. Although vaginal-cuff dehiscence is still very rare after vaginal-cuff brachytherapy, patients should be counseled about this rare treatment-related complication. Early identification and urgent management of this complication is recommended.

References

1. Siegel R, Naishadham D, and Jemal A, Cancer Statistics, 2012. *CA Cancer J Clin.* 2012;62:10-29.
2. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet*. 2009;105:103.
3. Ribeiro SC, Ribeiro RM, Santos NC, et al. A randomized study of total abdominal, vaginal and laparoscopic hysterectomy. *Int J Gynaecol Obstet*. 2003;83:37-43.
4. Cho Y-H, Kim D-Y, Kim J-H, et al. Laparoscopic management of early uterine cancer: 10-year experience in Asan Medical Center. *Gynecol Oncol*. 2007;106:585-590.
5. Bell MC, Torgenson J, Seshadri-Kreaden U, et al. Comparison of outcomes and cost for endometrial cancer staging via traditional laparotomy, standard laparoscopy and robotic techniques. *Gynecol Oncol.* 2008;111:407-411.
6. Boggess JF, Gehrig PA, Cantrell L, et al. A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: Robotic assistance, laparoscopy, laparotomy. *Am J Obstet Gynecol.* 2008;199:360.
7. DeNardis SA, Holloway RW, Bigsby IV GE, et al. Robotically assisted laparoscopic hysterectomy versus total abdominal hysterectomy and lymphadenectomy for endometrial cancer. *Gynecol Oncol.* 2008;111:412-417.
8. Kho R, Akl M, Cornella J, et al. Incidence and characteristics of patients with vaginal cuff dehiscence after robotic procedures. *Obstet Gynecol*. 2009;114:231-235.
9. Croak A, Gebhart J, Klingele C, et al. Characteristics of patients with vaginal rupture and evisceration. *Obstet Gynecol.* 2004;103:572-576.
10. Creutzberg CL, van Putten WL, Koper PC Lybeert ML, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: Multicentre randomised trial. PORTEC study group. Post operative radiation therapy in endometrial carcinoma. *Lancet.* 2000;355:1404-1411.
11. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: A Gynecologic Oncology Group study. *Gynecol Oncol.* 2004;92:744-751.
12. Nout R, Smit V, Putter H, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): An open-label, non-inferiority, randomised trial. *Lancet*. 2010;375:816-823.
13. Patel M, Cote M, Ali-Fehmi R, et al. Trends in the utilization of adjuvant vaginal cuff brachytherapy and/or external beam radiation treatment in stage I and II endometrial cancer: A surveillance, epidemiology, and end-results study. *Int J Radiat Oncol Biol Phys.* 2012;83:178-184.
14. Kalu E, Fakokunde A, Evans-Jones J. Postcoital vault dehiscence and instestinal prolapse following abdominal hysterectomy. *J Obstet Gynaecol.* 2006;26:74-75.
15. Albuquerque K, Shah K and Potkul R. Vaginal cuff dehiscence after intracavitary brachytherapy for endometrial cancer. *J Contemp Brachytherapy*. 2012:111-112.
16. Agdi M, Al-Ghafri W, Antolin R, et al. Vaginal vault dehiscence after hysterectomy. *J Minim Invasive Gynecol.* 2009;16:313-317.
17. Ceccaroni M, Beretta R, Malzoni M, et al. Vaginal cuff dehiscence after hysterectomy: A multicenter retrospective study. *Eur J Obstet Gynecol Reprod Biol*. 2011;158:308-313.
18. Somkuti S, Vieta P, Daugherty J, et al. Transvaginal evisceration after hysterectomy in premenopausal women: A presentation of three cases. *Am J Obstet Gynecol*. 1994;171:567-568.
19. Kirsner R, Eaglstein W. The wound healing process. *Dermatol Clin.* 1993;11:629-640.
20. Elshaikh MA, Cattaneo II R, Jacobson G, et al. Interval between hysterectomy and start of radiation treatment is predictive of recurrence in patients with endometrial carcinoma. A single Institution experience. *Int J Radiat Oncol Biol Physics.* 2012;84(3S, supplement):S97.

TECHNOLOGY TRENDS

Speedy delivery makes rotational IMRT the technique of choice

Cristen Bolan, MS

Intensity-modulated radiation therapy (IMRT) has become the method of choice for treating complex-shaped planning target volumes (PTV).[1] During the last few years, rotational IMRT (rIMRT) techniques, such as volumetric-modulated arc therapy (VMAT) and helical tomotherapy have become widely available, delivering similar or better-quality treatments compared to conventional fixed-field IMRT (cIMRT).

Several studies have compared rIMRT techniques to helical tomotherapy and cIMRT. These comparisons focus on treatment plan quality based on satisfying target coverage while respecting defined organs-at-risk (OAR) criteria, target dose homogeneity, and treatment delivery efficiency.[1] What sets rIMRT apart from helical tomotherapy and cIMRT are the faster treatment times.

Need for speed

Radiation oncology centers worldwide have implemented the VMAT technique using the following systems, RapidArc™ and TrueBeam™ by Varian Medical (Palo Alto, CA); the VMAT™ system by Elekta (Stockholm, Sweden); or the Smart-Arc™, a module for VMAT available on the Pinnacle[3] treatment planning solution from Philips Healthcare (Andover, MA). The distinguishing feature of these rIMRT systems is the treatment delivery time, which is much faster than that of cIMRT. In VMAT delivery, both dose rate and gantry rotation speed can vary, and these additional degrees-of-freedom increase the capability of beam intensity modulation.[2]

"The advantages of reduced treatment time are a reduction in interfraction motion, improvement in patient comfort, and an increase in patient throughput," noted Jonas D. Fontenot, PhD, Adjunct Assistant Professor of Physics, Department of Physics, Mary Bird Perkins Cancer Center, Baton Rouge, LA.

The Mary Bird Perkins facility was an early adopter of Elekta's VMAT system, initiating its VMAT program in mid-2009. Today, doctors treat all of the conditions that can be treated with cIMRT, including prostate, head and neck, lung, and brain and spinal cord cancers. In the last 18 months, they have started to use VMAT for lung stereotactic body radiation therapy (SBRT).

"SBRT is a hot topic in radiation oncology right now, and we are finding a lot of applications for VMAT. It has almost completely replaced cIMRT at our center," said Fontenot.

Fontenot explains that the quality of the dose distribution that the patient receives with a VMAT plan is comparable to cIMRT. "It is not a matter of improving the dose received by the patient; however, the real benefit is the efficiency with which the treatments can be delivered. Studies from our group and others have shown that VMAT treatments can be delivered in 1/3 of the time as a cIMRT plan," he said.

"If we were treating a patient with prostate cancer with cIMRT, we would probably need to use 7 or 9 fields, and a plan like that would take approximately 9 or 10 minutes to deliver. Contrast that with VMAT, where we can deliver the same quality treatment in a single arc that takes about 1-and-a-half minutes to deliver (Figure 1). Comparatively speaking, it's quite a bit faster, which has several advantages."

The University of Alabama at Birmingham radiation oncology program, which works with Varian's RapidArc system as well as the TrueBeam platform, was looking to broaden its SBRT program and to do hypofractionated frameless stereotactic radiosurgery (SRS).

TECHNOLOGY TRENDS

FIGURE 1. *Doctors can use Elekta VMAT with complete or partial arc to reduce treatment times from 8 to 12 minutes or conventional radiation therapy to as little as 2 minutes.*

"The linacs can expand our SBRT program. They enable single and multifraction, hypofractionated frameless SRS treatments, offer better image-guidance over time, and more provide efficient treatments elsewhere in the body. We acquired the TrueBeam system for its efficient administration of SRS," explained John B. Fiveash, MD, Radiation Oncologist, Department of Radiation Oncology, Associate Professor and Vice Chairman for Academic Programs, University of Alabama at Birmingham.

Designed for image-guided radiotherapy and radiosurgery, TrueBeam is a fully-integrated system designed from the ground up to treat moving targets at higher treatment delivery speeds with a dose delivery rate of up to 2,400 monitor units per minute. The system improves precision through better synchronization between imaging, patient positioning, motion management, beam shaping, and dose delivery technologies by performing accuracy checks every 10 milliseconds throughout an entire treatment.

"The greatest savings is in higher dose-per-fraction cases," said Dr. Fiveash. As he recalls, the amount of time spent on a very-high-dose treatment for lung or liver surgery used to take 60 to 90 minutes. Today, with TrueBeam, they are scheduling high dose-per-fraction treatments in 30-minute time slots.

For some anatomical sites, quicker treatments can lead to greater accuracy as patients are more comfortable and less likely to move during the therapy. In prostate cancer, for example, gas patterns or rectal or bladder filling can move the target on the organ, and faster treatments leave less time for error caused by movement (Figure 2).

"If you have treatments lasting 10 to 12 minutes, 25% of the patients will have motion of the prostate > 3 mm. If you have a treatment that lasts a minute or two, it's about 5% or less. A quick treatment with RapidArc or flattening filter free mode (FFF), if you're doing stereotactic treatments in particular, has the advantage of accuracy," said Dr. Fiveash.

With the FFF mode, the number of beam pulses per second remains the same (360 pulses/second at the maximum dose rate); however, the absence of attenuation due to the metal filter results in higher photon dose in the central portion of the beam. This means that the same dose could be delivered up to 4 times faster for this energy.[3]

A recently published study found that the 6-MV flattening filter-free mode (6F) of the Varian TrueBeam enables faster dose delivery and shortens treatment time, which is especially beneficial for stereotactic radiosurgery.[4]

"You can combine RapidArc with FFF mode and can do beam time in < 5 minutes. For multiple targets, it's a big time saver. If you are treating multiple tumors, like metastases, it could take 2 to 4 hours on a Gamma Knife, but we can do that in 15 minutes," Dr. Fiveash indicated. "That allows you to do extremely fast treatments for SRT and SBRT, all in a conventional time slot or 2 times lots. As a result, you can treat 4 to 5 patients in an hour."

The ability to use the FFF mode on the TrueBeam system (Figure 2) is an important feature for doctors at UCSD Moores Cancer Center, La Jolla, CA. "I was excited about getting TrueBeam because of speed, the quality of the on-board imaging, and because it has the whole FFF technology," said Arno J. Mundt, MD, Professor and Chair at UCSD Moores Cancer Center, La Jolla, CA.

The actual beam-on time for treating prostate cancer has dropped to 60 seconds. "The total time at a minimum would be 3 minutes—that includes going from one fixed-beam position to the next. RapidArc is much faster compared to static IMRT, which had a beam-on time of 3 to 5 minutes. And now it's 60 seconds. It is a significant improvement in speed," pointed out Todd Pawlicki, PhD, Director of Medical Physics at UCSD. "If you have more complicated targets, for head and neck cancer and for lung, the time savings can be even greater."

As Dr. Mundt indicates, the advantages of speed correlate more to patient comfort than to better outcomes.

"Improving the delivery of treatment is not necessarily associated with better outcomes because you can spare tissues very well with conventional IMRT," he said. "However, even if you have the same sparing [of organs at risk], I would opt for the speed to make the treatment better quality. The longer a patient is on the table, the more you will have problems immobilizing the patient for accurate treatment delivery. You want to get the patient on and off the table in

TECHNOLOGY TRENDS

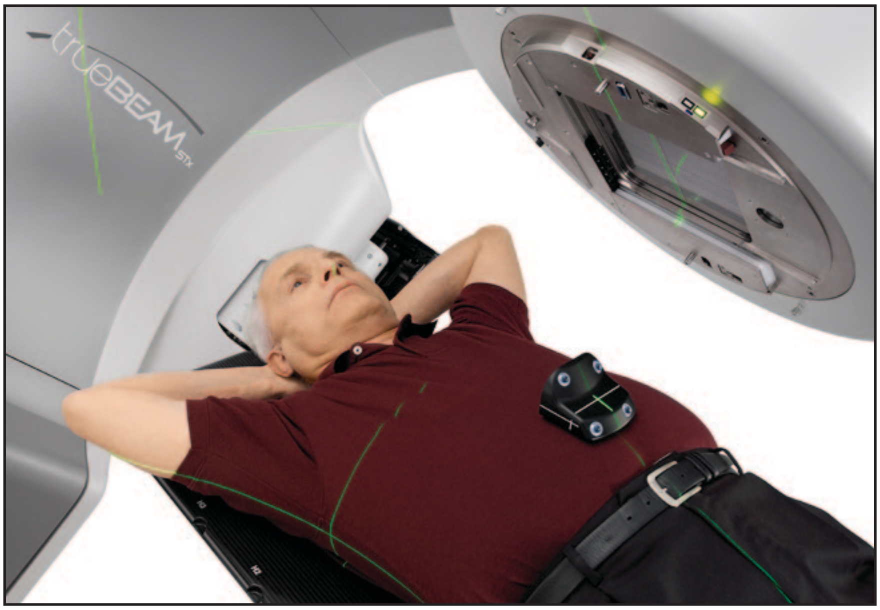


***FIGURE 2.** For lung and other tumors subject to respiratory motion, TrueBeam STx offers Gated RapidArc radiotherapy, which makes it possible to monitor the patient's breathing and compensates for movement of the tumor while the dose is being delivered in a continuous rotation of the treatment machine.*

the shortest amount of time to provide a better quality treatment."

Advantages of throughput

The shorter treatment times also improve throughput, said Dr. Mundt, adding that there are several advantages to increased throughput. First, the less time the patient is on the table, the less discomfort the patient experiences and the lower the potential for movement (Figure 2). Second, from a hospital administrative standpoint, throughput is crucial for running an effective clinic. This may in turn enable the clinic to treat more patients per day.

"When treating the majority of your patients with VMAT, there can be an increase in throughput," noted Koren Smith, MS, DABR, Medical Physicist, Johns Hopkins University School of Medicine, Department of Radiation Oncology and Molecular Radiation Sciences, where patients are treated on both Elekta's VMAT system and the TomoTherapy by Accuray Inc. (Sunnyvale, CA).

Similarly, at UCSD Moores Cancer Center, where RapidArc and TrueBeam are employed, clinicians are treating 40 to 50 patients per single linac per day. "It has significantly increased our patient throughput," said Dr. Mundt.

The role of helical tomotherapy

Helical therapy technology has been available since 1993, when Mackie et al developed a rotating fan-beam technique using a dedicated helical tomotherapy system.[5-6] Today, however, the faster delivery speeds of rIMRT systems may have outpaced the slower treatments helical tomotherapy provides.

Nonetheless, many clinicians believe the better dose distribution and quality treatment plans achieved with tomotherapy outweigh faster treatment times. "The high conformality of the radiation dose with respect to the risk to critical organs is one of the advantages of using tomotherapy. It avoids critical structures very well while hitting the target," said Dr. Matthew West, Chief Physicist at Tulsa Cancer Institute, Tulsa, OK, who has over 10 years of experience working on TomoTherapy systems.

A recently published study comparing rIMRT to cIMRT and tomotherapy, showed rIMRT and tomotherapy were both advantageous with respect to OAR sparing and treatment delivery efficiency, at the cost of higher dose delivered to normal tissues.[1]

These results align with the results found by clinicians at Johns Hopkins University School of Medicine, where approximately 20% to 25% of patients are treated on VMAT or TomoTherapy systems. "We have done planning studies on VMAT and TomoTherapy, and they are comparable. The planning objectives are met on both types of plans and while small differences can be seen, there are not major differences," said Smith.

The average 'beam on' time for VMAT when treating the prostate or pancreas, using a single-arc, and conventional fractionation, such as a 1.8Gy to 2Gy fraction size, is < 2 minutes, indicates Smith. On TomoTherapy, however, the beam-on time for a typical prostate patient is 2 to 4 minutes. Yet Smith considers the treatment times on TomoTherapy to be very reasonable.

"TomoTherapy is very effective, and it is not an outdated technology. In a lot of planning comparisons, it can deliver more homogenous dose to the target while sparing critical structures more than other types of delivery," Smith reported.

While there have been several technical advances in rIMRT systems, helical tomotherapy has recently undergone a system overhaul. In October 2012, Accuray Inc. launched its new TomoTherapy H Series, including the TomoHDA System, designed with faster planning, faster delivery, and increased quality. Some of the key features of the TomoHDA system include TomoEDGE Dynamic Jaws technology, designed to


Versa HD

TECHNOLOGY TRENDS

provide added flexibility in treatment delivery by sharpening dose fall off and accuracy.

"The advantage of TomoTherapy with respect to OAR is the high conformality, especially with TomoEdge or dynamic jaws. The efficiencies arise from the TomoTherapy process. Dose falls off much faster in a superior and inferior direction than it used to, and it also provides much tighter dose distribution," West pointed out.

Wiezorek et al also concluded that the overall treatment plan quality using tomotherapy seemed better than the other treatment planning technologies.[1]

According to the lead author of the study, Tilo Wiezorek, PhD, Department of Radiation Oncology, University of Jena, Jena, Germany, the advantage to tomotherapy is a higher degree of freedom compared to VMAT techniques or fixed-beam IMRT. However, he added, "A fixed-beam IMRT plan with a mixture of high photon energy (eg, 15MV) and lower energy (eg, 6MV) in combination with a preoptimized beam-angle setup very often offers better dose distributions for PTVs with a strong asymmetric position in the body and for high-weight patients, too. Especially for retreatments of patients with previous dose impact this offers a better choice," said Dr. Wiezorek.

Recent improvements to the TomoTherapy system may give it an edge when it comes to accuracy and even speed. New TomoEDGE Dynamic Jaws technology combined with VoLO Planning, a graphics processing unit (GPU)-based treatment planning solution, enables high-speed parallel processing for both dose calculation and optimization. VoLO leverages advanced graphics processing technology and a new calculation algorithm to significantly reduce treatment-planning times and add flexibility in developing even very complex radiation therapy plans.

"VoLO has sped up the time it takes to turn around a treatment plan," said West. "On the older system without VoLO, before we even started planning, it could take between 30 minutes and 4 hours, depending on how complicated the case was. Now with VoLO it only takes 2 minutes before we start planning."

He continued, "When you look at the efficiencies, the system is very simple. Unlike a conventional accelerator, there are no ancillary components or special modes for special types of treatments, so whether you're planning a prostate, brain, breast or stereotactic case, you plan it and treat them the same. The efficiencies come in terms of ease of workflow and safety."

"The simplified process—no machine treatment aids, no transfer of planning data—allow dosimetry to utilize the same general planning approach independent of treatment type. The therapists can focus on the patient and their setup. The treatment data isn't transferred from one computer to another, but is verified by physics prior to treatment. Ultimately, this attention to patient setup and image guidance allows clinicians to reduce treatment margins and minimize dose to critical structures," said West.

The dose factor

Since the goal of radiation therapy is to administer a therapeutic dose of radiation to a target while limiting the side effects caused by delivering the dose to surrounding tissues and vital organs, there is an ongoing pursuit in radiotherapy to achieve an optimal dose distribution.

The trend to lower radiation exposure to patients has been reinforced by industry organizations, such as MITA, The American Association of Physicists in Medicine (AAPM), the Alliance for Radiation Safety in Pediatric Imaging, and Image Wisely. Therefore, radiation dose is another important consideration when comparing rIMRT to cIMRT and helical tomotherapy.

The perceived benefit of the VMAT radiotherapy delivery technique over IMRT is a reduction in delivery time, but VMAT also uses fewer monitor units (MU), resulting in a lower patient total body dose. A study comparing the delivery efficiency and time for the IMRT and VMAT plans for a series of prostate cases found VMAT plans resulted in a statistically significant reduction in the rectal V25Gy parameter of 8.2% on average over the IMRT plans.7 These reductions in rectal dose were achieved using 18.6% fewer MU and a delivery time reduction of up to 69%.7 Therefore, in addition to speed, the lower cumulative MU of the VMAT system is important for patient safety because it reduces the overall amount of radiation.

"A secondary advantage of VMAT with respect to cIMRT is that VMAT units require less MU, which is a measure of how much radiation is produced by the accelerator. Fewer MU means lower amounts of leakage dose outside of the treatment field. The patient receives lower doses out of field, which corresponds to a theoretical reduction to treatment related cancers. It is like the ALARA principle," indicated Fontenot.

Lowering radiation to patients is not exclusive to rIMRT. Although conventional MU verification calculations are not applicable to TomoTherapy treatments,[8] Fontenot points out that helical tomotherapy delivers highly conformal dose distributions.

"Tomotherapy utilizes a similar delivery approach and delivers highly conformal dose distributions, which lets us deliver a very high dose of radiation to the target, and a very low dose of radiation to the surrounding critical structures. Tomotherapy relies on treating the tumor from several different directions, which involves irradiating larger volumes of normal tissue albeit at much lower doses," said Fontenot.

"When you're comparing VMAT and tomotherapy on the basis of low dose volumes, we've had studies indicating that there are some tradeoffs. The intermediate dose range on tomotherapy is a little better, and VMAT is a little better in the low to very-low dose range."

Fontenot says the jury is still out on which one is better at sparing normal tissue at low to intermediate doses, and how those differences translate into risks of secondary cancers.

Is it a tie?

With so many variables involved in radiation therapy, Dr. Wiezorek is reluctant to declare a winner.

"From my point of view, we cannot proclaim a principle advantage of rIMRT versus cIMRT," said Dr. Wiezorek.

While in many cases the reduced delivery times on rIMRT offer a significant advantage, this time advantage may be limited in some complex cases.

"Rotational techniques offer faster treatments for low complex targets, such as prostate cancer, or high complex and symmetrical PTVs, like head and neck with 3 dose levels. However, for high complex and symmetrical PTVs, rIMRT is faster only if TomoTherapy is used or only if a maximum of 2 arcs are used for VMAT. If some regions have to be blocked, rotational techniques do not significantly speed up the treatment," said Dr. Wiezorek.

However, with recent advances in rIMRT systems and tomotherapy technology, these techniques may soon outperform cIMRT in both speed and accuracy.

References

1. Wiezorek T, Brachwitz T, Georg D. Rotational IMRT techniques compared to fixed gantry IMRT and tomotherapy: Multi-institutional planning study for head-and-neck cases. *Radiat Oncol*. 2011;6:20.
2. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. *Med Phys*. 2008;35: 310-317.
3. Varian TrueBeam – Flattening-Filter-Free Mode. http://sudentas.com/physics/varian-truebeam/flattening-filter-free/. Accessed August 7, 2013.
4. Wang JZ, Rice R, Mundt AJ, et al. Feasibility and advantages of using flattening filter-free mode for radiosurgery of multiple brain lesions. *Pract Rad Onc*. 2012;2, e165-e171.
5. Mackie TR, Holmes T, Swerdloff S, et al. Tomotherapy: A new concept for the delivery of dynamic conformal radiotherapy. *Med Phys*. 1993;20: 1709-1719.
6. Zuang T, Huang L, Qi P, Yu J. Radiation therapy: Clinical application of volumetric modulated arc therapy. *App Rad Onc*. 2013;2.
7. Hardcastle N, Tome WA, Foo K, Et al. Comparison of prostate IMRT and VMAT biologically optimised treatment plans. *Med Dosim*. 2011;36:292-298.
8. Gibbons JP, Smith K, Cheek D, Rosen I. Independent calculation of dose from a helical TomoTherapy unit. *J App Clin Med Phys*. 2009;10:1.

CME SEE PAGE 4 FOR DETAILS

Stereotactic body radiotherapy for the treatment of spine metastasis

Ehsan H. Balagamwala, MD, Samuel T. Chao, MD, and John H. Suh, MD

CASE SUMMARY

A 56-year-old female with renal cell carcinoma (RCC) diagnosed 7 months prior to presentation was evaluated for severe left-sided back pain originating in the left anterior hip with radiation down the left leg. She reported parasthesias along with the pain, which was present at rest and worsened with movement. She denied any associated bowel or bladder dysfunction, saddle anesthesia, or gait difficulties. At presentation, she was on maintenance Sunitinib and had an increasing narcotic requirement.

IMAGING FINDINGS

Magnetic resonance imaging (MRI) with and without intravenous contrast demonstrated loss of L4 vertebral height and replacement of the L4 vertebral body with a contrast-enhancing heterogenous expansile mass, which extended into the left pedicle. Mild extraosseous epidural soft tissue as well as moderate narrowing of the L4-5 neural foramen was also noted (Figure 1).

*Prepared by **Dr. Balagamwala** while at Cleveland Clinic, Cleveland OH, and by **Dr. Choa** and **Dr. Suh** while at Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Tassig Cancer Institute, Cleveland Clinic, Cleveland OH.*

DIAGNOSIS

Spine metastasis from renal cell carcinoma

DISCUSSION

Spine is the third most frequent site of metastasis, and approximately 10% of all cancer patients develop symptomatic spinal metastasis. About 10% to 20% of patients with spine metastasis will develop spinal cord compression.[1] The majority (70%) of spinal metastases are located in the thoracic spine and approximately half of all patients have multiple spinal metastases. Patients with spine metastasis can present clinically with pain and/or neurologic dysfunction. In patients with neurologic dysfunction, it is imperative to rule out spinal cord compression. The preferred imaging modality for spine imaging is MRI, however, in patients with contraindications to MRI, a computed tomography (CT) scan or a myelogram would be acceptable. Prompt spine imaging also helps in establishing the stability of the spine.

Initial management of spinal metastasis involves the use of narcotic and non-narcotic pain medications. However, if spine instability or spinal cord compressions are present, surgical decompression and spinal stabilization are mainstays of therapy. Radiotherapy, either conventionally fractionationated external beam radiotherapy (CRT) or spine stereotactic body radiotherapy (sSBRT) can also be utilized for the treatment of spinal metastasis.

FIGURE 1. *The image shows a sagittal T2-weighted MRI sequence demonstrating a heterogenous expansile mass in the L4 vertebral body with mild epidural extension.*

One of the main goals of palliative radiotherapy to the spine is pain control.[2] For many decades, CRT has been utilized. Because the treatment field involves the spinal cord, CRT can be delivered safely up to 2 times before the risk of myelopathy outweighs the

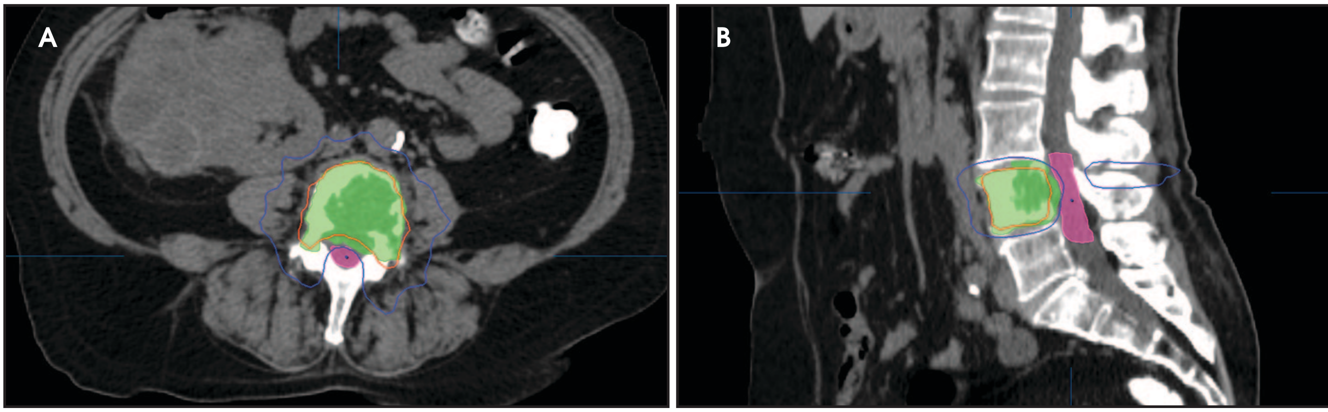


FIGURE 2. Axial (A) and sagittal (B) treatment planning CT images for sSBRT to the L4 vertebral body. The planning treatment volume (PTV) is demonstrated by the green color wash, the cauda equina by the pink color wash, the 16Gy isodose line (IDL) by the red line and the 10Gy IDL by the blue line.

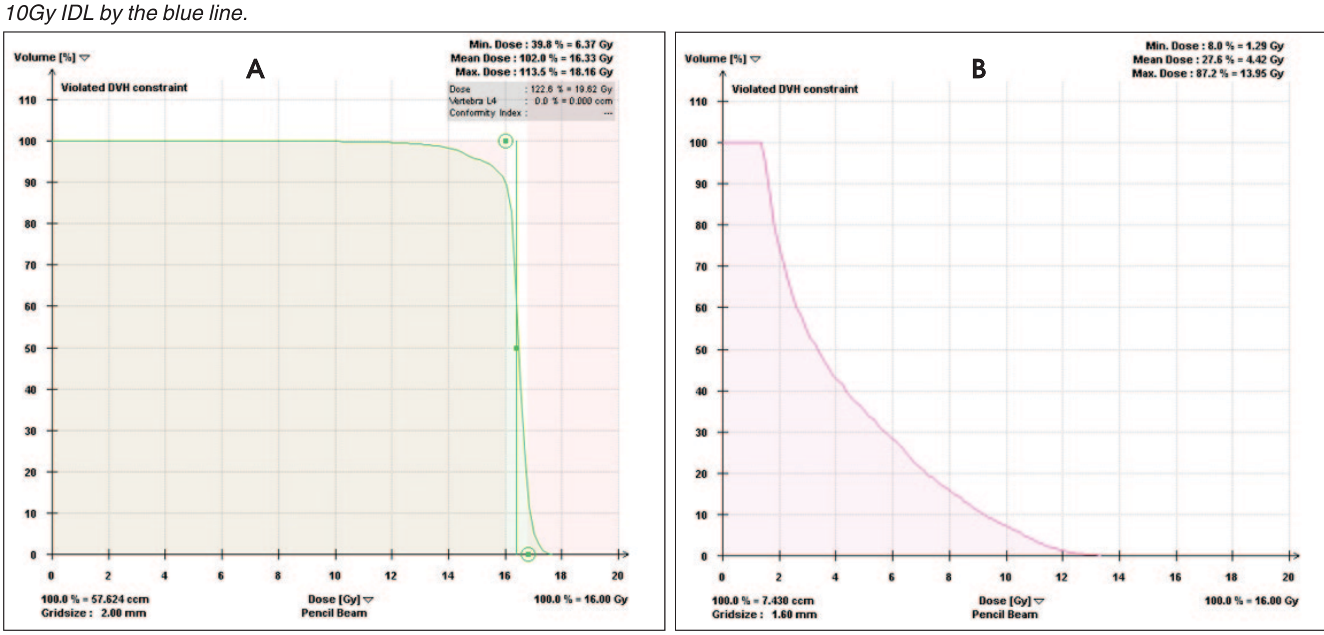


FIGURE 3. PTV (A) and cauda equina (B) dose volume histograms (DVHs) are shown. We aim to achieve ≥ 90% coverage of the PTV by the prescription dose. For the cauda equina we limit the maximum dose to < 16Gy and 10% of cauda equina receiving ≤ 12Gy.

potential benefits.[3] With the advancement of chemotherapy regimens and the development of targeted chemotherapeutics, patients with metastatic RCC have longer survival, which necessitates more durable pain control.[4] Furthermore, patients who have undergone prior CRT without significant pain relief or patients who have received prior incidental spinal radiation secondary to treatment for their primary cancer (such as lung cancer or anal cancer) are poor candidates for CRT for spinal metastasis.

Over the past 2 decades, sSBRT has been developed and refined, allowing for the delivery of high dose conformal radiotherapy to the spine, while adequately sparing the spinal cord. Importantly, sSBRT enables the delivery of a higher biologically effective dose (BED) than CRT does. Although differences in technique exist between institutions, here we will discuss the approach utilized at the Cleveland Clinic, which is congruous with the approach of the ongoing RTOG 0631 trial.[5] We refer the interested reader to a recent review for a detailed discussion of institutional differences.[6]

Most centers utilize either a single-fraction or a hypofractionated regimen. At Cleveland Clinic, most patients are treated with either 16Gy or 18Gy in 1 fraction with the higher dose reserved for radioresistant histologies. For treatment planning, we limit the spinal cord to a maximum dose < 14Gy and 10% of spinal cord receiving ≤ 10Gy and limit the cauda equina to a maximum dose < 16Gy and 10% of cauda equina receiving ≤ 12Gy (Figures 2 and 3).

With either the single fraction or hypofractionated regimens, most centers have reported local control rates ≥ 80%.[6]

Nguyen et al studied sSBRT in 48 patients with 55 RCC spinal metastases treated with either 24Gy in 1 fraction, 27Gy in 3 fractions, or 30Gy in 5 fractions and demonstrated a local control rate of 82.1% and a complete pain response of 44% and 52% at 1 month and 12 months post-sSBRT, respectively.[7] We recently reported our results for 57 patients with 88 spinal metastases from RCC and demonstrated a complete pain response of 27.1% and 63.6% at 1 month and 12 months post-sSBRT, respectively. Multivariate analysis demonstrated that multilevel disease and neural foramen involvement were associated with radiographic failure and multilevel disease and pre-existing vertebral body fracture were associated with pain failure.[8] Hunter et al recently compared the efficacy of CRT versus sSBRT for patient RCC spinal metastases. He showed that sSBRT offered more complete pain relief (33% vs 12%, p=0.01), whereas CRT offered more partial pain relief (56% vs 29%, p=0.01). A trend towards longer duration of pain relief with sSBRT was also demonstrated (4.8m vs 1.7m, p=0.05).[4] These differences may be attributable to the higher BED delivered by sSBRT compared to CRT.

The most common acute toxicities from sSBRT include fatigue (up to 40%) and gastrointestinal effects (10-20%).[9] Major long-term toxicities include the risk of developing vertebral body fractures as well as the risk of spinal cord myelopathy.

Rose et al evaluated 62 consecutive patients with 71 vertebral bodies treated with 18Gy to 24Gy in a single fraction and reported a 39% incidence of new or progressive vertebral fractures. Risk factors for fractures were location (T10 to sacrum), lytic metastasis and > 40% vertebral body involvement.[10] A multi-institutional study by Sahgal et al of 254 patients with 410 vertebral levels found a fracture incidence of 14% and identified dose per fraction (> 20Gy), preexisting vertebral fracture, lytic metastasis presence of paraspinal, and/or epidural disease and spinal deformity as risk factors for developing a vertebral fracture post-sSBRT (Sahgal et al, provisionally accepted to *Journal of Clinical Oncology).*

Risk of spinal cord myelopathy from sSBRT is estimated to be < 1%.[3] Sahgal et al performed a multi-institutional study of 5 myelopathy cases comparing it to 19 unaffected patients post-sSBRT. His analysis demonstrated that thecal-sac maximum doses of up to 10Gy in a single fraction were safe. Furthermore, using BED calculations, he demonstrated that 30 to 35 2-Gy equivalent for up to 5 fractions was also safe.[11] Aggregating all the available clinical reports of spinal-cord tolerance in the setting of sSBRT, Kirkpatrick et al concluded that 13Gy in 1 fraction or 20Gy in 3 fractions confers a spinal-cord myelopathy risk of < 1%.[3]

CONCLUSION

Spine SBRT is now a well-established technique for the treating spinal metastasis that has enhanced the treatment of patients with spine metastasis. Many studies have shown that sSBRT provides excellent local control and is safe and effective in the primary as well as salvage settings. sSBRT provides rapid and durable pain relief and can also be utilized in patients that have significant epidural disease. Currently, sSBRT remains the only effective nonsurgical option in patients previously irradiated for spinal metastases. sSBRT is not only a convenient option for patients as it can be delivered in one setting but it also has a low risk of acute and late toxicities.

REFERENCES

1. Eleraky M, Papanastassiou I, Vrionis FD. Management of metastatic spine disease. *Curr. Opin Support Palliat Care.* 2010;4:182-188.
2. Hartsell WF, Scott CB, Bruner DW, *et al.* Randomized Trial of Short- Versus Long-Course Radiotherapy for Palliation of Painful Bone Metastases. *Jnci J Natl Cancer Inst.* 2005;97:798-804.
3. Kirkpatrick JP, van der Kogel AJ, Schultheiss TE. Radiation dose-volume effects in the spinal cord. *Int J Radiat Oncol Biol Phys.* 2010;76:S42-49.
4. Hunter GK, Balagamwala EH, Koyfman SA, *et al.* The efficacy of external beam radiotherapy and stereotactic body radiotherapy for painful spinal metastases from renal cell carcinoma. *Pr Radiat Oncol.* 2012;2:e95-e100.
5. Anon. RTOG 0631 Phase II/III Spine Mets.
6. Balagamwala EH, Cherian S, Angelov L, *et al.* Stereotactic body radiotherapy for the treatment of spinal metastases. *J Radiat Oncol.* 2012;1:255-265.
7. Nguyen Q-N, Shiu AS, Rhines LD, *et al.* Management of spinal metastases from renal cell carcinoma using stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys.* 2010;76:1185-1192.
8. Balagamwala EH, Angelov L, Koyfman SA, *et al.* Single-fraction stereotactic body radiotherapy for spinal metastases from renal cell carcinoma. *J Neurosurg. Spine.* 2012;17:556-564.
9. Masucci GL, Yu E, Ma L, *et al.* Stereotactic body radiotherapy is an effective treatment in reirradiating spinal metastases: current status and practical considerations for safe practice. *Expert Rev Anticancer Ther.* 2011;11:1923-1933.
10. Rose PS, Laufer I, Boland PJ, *et al.* Risk of fracture after single fraction image-guided intensity-modulated radiation therapy to spinal metastases. *J Clin Oncol Off J Am Soc Clin Oncol.* 2009;27:5075-5079.
11. Sahgal A, Ma L, Gibbs I, *et al.* Spinal cord tolerance for stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys.* 2010;77:548-553.

CME SEE PAGE 4 FOR DETAILS

The treatment of scleredema with repeat radiation

Abhilasha J. Patel, MD, Shefali Gajjar, BS, Jordan Abel, MD, and Sandra Hatch, MD

CASE SUMMARY

A 50-year-old man with a history of poorly controlled type 2 diabetes mellitus presented to the Texas Department of Corrections Dermatology clinic in 2004 with an 8-year history of worsening neck and upper-back skin thickening associated with pain, difficulty in turning his head, and pruritus over the involved skin. He was subsequently diagnosed with scleredema adultorum of Buschke associated with poor control of his diabetes based on clinical presentation and skin biopsy results from the back.

He was initially treated with topical treatments, but they failed and the patient was referred for external beam radiation. He received multiple rounds of radiation treatments from 2004 to 2009 due to the progressive nature of his disease in the setting of poorly controlled diabetes with varied response to treatment. A patchwork of radiation fields were used to prevent significant overlap when needed (Table 1). The patient tolerated treatments well, but did receive antihistamines for pruritus and aloe vera cream for skin erythema. Following his final round of treatment in 2009, the patient had excellent pain relief. His skin was less indurated and more elastic. He continues to use topical body lotion for postradiation changes and Benadryl for occasional pruritis. He has not required any further treatment and most likely will not receive additional radiation to previously treated areas based on the cumulative dose received.

*Prepared by **Dr. Patel, Dr. Abel,** and **Dr. Hatch** while at the University of Texas Health Science Center at San Antonio, San Antonio, TX, and by **Ms. Gajjar** while at the University of Texas Medical Branch, Galveston, TX.*

DIAGNOSIS

Scleredema adultorum of Buschke associated with poor control of diabetes

DISCUSSION

Scleredema adultorum of Buschke is a skin condition that can occur in the setting of different medical aliments, but most commonly in poorly controlled diabetes mellitus. Its prevalence in diabetic patients has been reported up to 14%.[1] It typically presents as diffuse, nonpitting, indurated skin with possible erythema and pain and is most commonly located in the posterior neck, scalp, and upper back. On histology, there is increased mucin deposition and widening of the collagen bundles in the reticular dermis.[2,3] Treatment consists of multiple modalities, including topical cyclosporine, penicillin, methotrexate, psoralen, and UV-A (PUVA) and radiation therapy; however, no single treatment has proven to be effective in the majority of patients for a prolonged period of time.[4]

Radiation therapy has a variable history in the treatment of scleredema. Angeli Besson et al reported a case of scleredema treated with 20Gy in 10 fractions using electron beam therapy.[5] Although a complete recovery was not accomplished, the patient had improved functional use of his legs and back and was able to stop systemic corticosteroid treatment. Tamburin et al used the same treatment schedule in a patient with scleredema associated with Type 1 diabetes mellitus.[6] The patient received a total of 20Gy electron beam radiation therapy (EBRT) after failing initial treatment with corticosteroids. Following treatment with EBRT, the patient had both symptomatic relief and clinical regression, and remained disease free at time of publication. Lee et al provided further evidence for the use of EBRT.[3] Two patients were

Table 1. Treatment course with external beam radiation

	Pretreatment symptoms	Post-treatment symptoms	Dose	Fields	Energy	Prescription
2004	Limited ROM, pain, thickening/itching	Less indurated/more elastic/better pain	20Gy (2Gy/fx)	Back/neck en face	9 MeV	1.5-cm depth
2007	Pain/tightness	Mild relief	21.6Gy (1.8Gy/fx) with 1 cm bolus	Back/neck en face	9 MeV	90% isodose line
2008	Pruritis/pain	Mild relief	20Gy (2Gy/fx) with 1 cm bolus	Neck/shoulders conformal	6 MV	Per plan
2009	Limited ROM/pain	Excellent pain relief	20Gy (1.25Gy/fx) with 1 cm bolus	Back/neck conformal	6 MV	Per plan

treated. One received 24Gy in 2Gy per fraction and the other received 20Gy in 2Gy per fraction. They reported symptomatic and clinical improvement but not complete remission of disease. No major complications were reported. Tobler et al reported a case of scleredema in a diabetic patient.[7] A total dose of 20Gy in 2Gy fractions was delivered via 12 MeV electrons. At 7 months, the patient had diminished skin thickening and maintained the improvement in range of motion. Bowen et al were among the first to report the effects of retreatment with radiation.[8] Three patients were treated with 2 courses of either electrons or mixed photon/electron radiation. All 3 patients experienced improvement in shoulder abduction from pretreatment baseline. The patients treated with electrons experienced minimal side effects. However, the patient treated with mixed photon therapy developed sore throat, nausea, fatigue, and headache during treatment. This suggests the possibility that photon therapy may not be equivocal to electron therapy, as more side effects were noted with photons versus electron treatments. Konemann et al treated a diabetic patient with electrons twice in 6 months .[9] A total of 20Gy in 2Gy fractions was delivered via 9 MeV electrons. The patient reported symptomatic improvement after the first treatment, but no clinical improvement was observed. The second course of treatment provided both symptomatic and clinical results.

CONCLUSION

These reports identify inconsistencies with the effectiveness of radiation to provide complete remission of disease in scleredema adultorum. However, they also show that symptomatic relief and some clinical response can occur for patients, even if only briefly. Treatment of scleredema with radiation has become the treatment of last resort for patients who do not respond to other treatments. Large radiation fields are used to cover affected areas. A tissue-equivalent bolus material is placed over the skin to bring dose to the surface and provide better coverage. The treatments are painless and last a few minutes. Benign skin pathology usually requires lower radiation dosages and shorter treatment courses than does malignancy, which reduces the risk of side effects. There are limitations when using EBRT to treat scleredema. Patients usually have to be retreated after symptoms recur. This increases the risk for radiation-induced side effects, which may occur acutely or years later. Some of the cutaneous complications with radiation used to treat other disorders are radiation-induced cancer, radiation dermatitis, acne, infections, and dyskeratosis.[10] Because of the acute and late side effects of radiation, regular follow-up during and after treatment is required. The long-term effects of retreatment with EBRT have yet to be studied in scleredema. Nonetheless, radiation is an effective treatment option with regard to symptom improvement and quality of life.

REFERENCES

1. Satter MA, Diab S, Sugathan TN, Sivanandasingham P, Fenech FF. Scleroedema diabeticorum: A minor but often unrecognized complication of diabetes mellitus. *Diabet Med*. 1998;5:465-468.
2. Beers WH, Ince A, Moore TL. Scleredema adultorum of Buschke: A case report and review of the literature. *Semin Arthritis Rheum*. 2006;35:355-359.
3. Lee MW, Choi JH, Sung KJ, Moon KC, Koh JK. Electron-beam therapy in patients with scleredema. *Acta Derm Venereol*. 2000;80:307-308.
4. Meguerditchian C, Jacquet P, Beliard S, et al. Scleredema adultorum of Buschke: An under-recognized skin complication of diabetes. *Diabetes Metab*. 2006;32 (5 Pt 1):481-484.
5. Angeli-Besson C, Koeppel MC, Jacquet P, Andrac L, Sayag J. Electron-beam therapy in scleredema adultorum with associated monoclonal hypergammaglobulinaemia. *Br J Dermatol*.1994;130:394-397.
6. Tamburin LM, Pena JR, Meredith R, Soong VY. Scleredema of Buschke successfully treated with electron beam therapy. Arch Dermatol. 1998;134: 419-422.
7. Tobler M, Leavitt DD, Gibbs FA Jr. Dosimetric evaluation of a specialized radiotherapy treatment technique for scleredema. *Med Dosim*. 2000;24:215-218.
8. Bowen AR, Smith L, Zone JJ. Scleredema adultorum of Buschke treated with radiation. *Arch Dermatol*. 2003;139:780-784.
9. Konemann S, Hesselmann S, Bolling T, et al. Radiotherapy of benign diseases – scleredema adultorum Buschke. *Strahlentherapie und Onkologie*. 2004;180:811-814.
10. Carrotte-Lefebvre I, Delaporte E, Mirabel X, Piette F. Radiation-induced skin reactions (except malignant tumors). *Bull Cancer*. 2003;4:319-325.