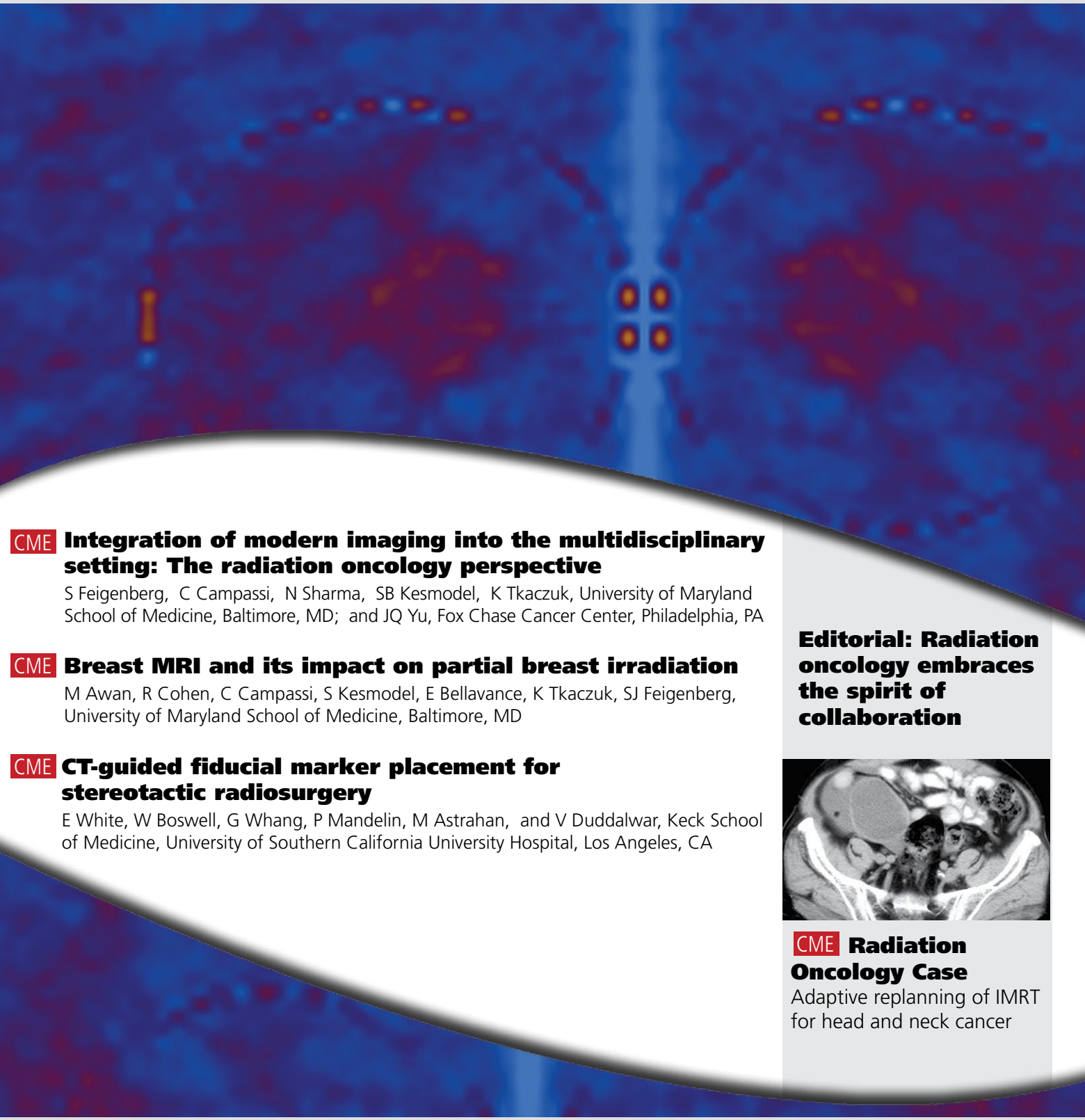
APPLIED RADIATION ONCOLOGY™
OCTOBER 2012



CME **Integration of modern imaging into the multidisciplinary setting: The radiation oncology perspective**

S Feigenberg, C Campassi, N Sharma, SB Kesmodel, K Tkaczuk, University of Maryland School of Medicine, Baltimore, MD; and JQ Yu, Fox Chase Cancer Center, Philadelphia, PA

CME **Breast MRI and its impact on partial breast irradiation**

M Awan, R Cohen, C Campassi, S Kesmodel, E Bellavance, K Tkaczuk, SJ Feigenberg, University of Maryland School of Medicine, Baltimore, MD

CME **CT-guided fiducial marker placement for stereotactic radiosurgery**

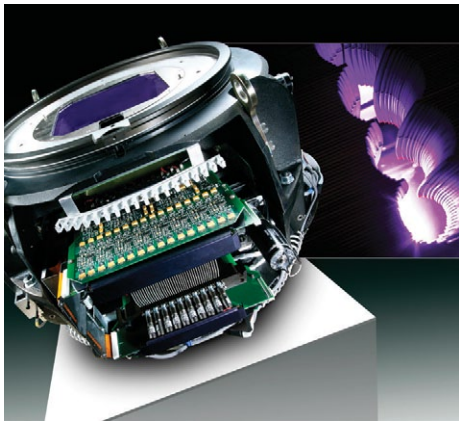
E White, W Boswell, G Whang, P Mandelin, M Astrahan, and V Duddalwar, Keck School of Medicine, University of Southern California University Hospital, Los Angeles, CA

Editorial: Radiation oncology embraces the spirit of collaboration

CME **Radiation Oncology Case**

Adaptive replanning of IMRT for head and neck cancer

...twice the leaves at twice the speed



Agility is not licensed for sale in all markets. Please contact your local Elekta representative for details.

With Agility™, it's reality.

As the ultimate device for advancing modern radiotherapy, Elekta's Agility MLC precisely sculpts radiation with 160 high-resolution leaves across a 40 cm x 40 cm field. Capable of managing the broadest spectrum of therapies, Agility also boasts ultra-fast leaf movements with extraordinarily low leakage to maximize the potential for advanced techniques such as SRS, SRT and VMAT.

4513 371 0993 03:12

Human care makes the future possible.
More at elekta.com/imagine

ELEKTA

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.

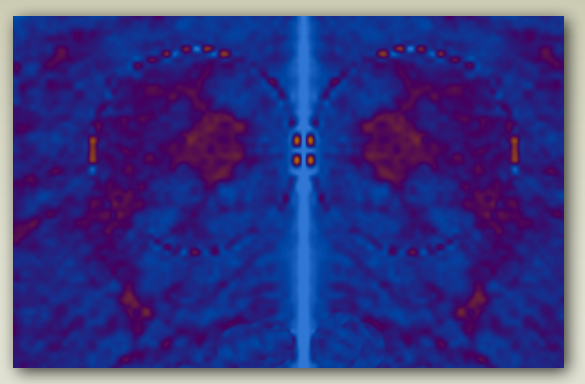
EDITORIAL CONTRIBUTIONS: *Applied Radiation Oncology* accepts clinical-review articles and cases that pertain to radiation oncology and related oncologic imaging procedures that will be of interest to radiation oncologists. Manuscripts and cases may be sent electronically to Cristen Bolan, Executive 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™

October 2012
Vol. 1, No. 1



DEPARTMENTS

Applied Radiation Oncology *is electronically published on a quarterly basis by Anderson Publishing, Ltd., at 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.*

Access medical images the easier way.

itMD

www.itMD.net | info@itMD.net

We're an easy to use online software provider that eliminates the need for medical CDs. Access one convenient location where all your patients' images can be viewed, shared and downloaded, no matter where they come from. You and your staff can eliminate the costly and inefficient handling of medical CDs when patients come for their visit or when they see other specialists.

Aggregation

Studies sent to you directly online. Patients or staff can upload studies on CDs remotely. No need to handle another CD, all of your images are in one convenient place.

Easy To Use

Integrated and intuitive FDA-approved universal viewer. Your studies are instantly accessible, all in one single location and one simple login and password.

Share

Instead of delivery or handling physical media, you can instantly share your images and reports from our online database. Also, automate downloads into your own PACS.

Collaboration

Communicate with other specialists in real time. Greatly improve patient satisfaction by displaying their images and reports on an iPad or computer during their visit.

No need to learn and figure out multiple, confusing viewers for every different CD.
No need to remember multiple usernames and passwords for each place you send your patients to get images from.

itMD | Powering collaborative medicine.

EDITORIAL

John Suh, MD, Editor in Chief

Peer-to-peer collaboration is one of the most effective tools for developing your skills and knowledge as a medical practitioner.

Radiation oncology embraces the spirit of collaboration

The ultimate goal of the radiation oncologist is to diagnose, treat, and support patients coping with malignancies. The challenge is to manage the vast complexities of oncological care.

As the Editor-in-Chief of *Applied Radiation Oncology*, with 20 years of experience as a radiation oncologist, I know that peer-to-peer collaboration is one of the most effective tools for developing your skills and knowledge as a medical practitioner. That is why I am proud to announce the debut of *Applied Radiation Oncology* on October 1, 2012. *Applied Radiation Oncology* is a quarterly physician-authored e-journal, featuring practical and actionable information for radiation oncologists striving to enhance the efficiency and quality of radiotherapy.

Applied Radiation Oncology provides an online platform where peers convene in a collegial manner to contribute review articles and clinical cases, providing practical solutions to the challenges often encountered in the clinical setting. The e-journal focuses on imaging, contouring, target delineation, treatment planning, patient immobilization, organ tracking, safety and quality, and other timely topics essential to the discipline.

Applied Radiation Oncology is also a key resource for easily and conveniently acquiring Continuing Medical Education (CME) credits online. The CME learning objectives are designed to offer useful information that is immediately translatable to your clinical practice today.

As radiation oncologists increasingly embrace a multidisciplinary approach to care, consulting with radiologists, medical oncologists, surgeons and the medical physicists,[1] *Applied Radiation Oncology* will provide unique insights into effective strategies for cross-specialty care.

I look forward to receiving feedback and collaborating with you in the collegial spirit embodied by *Applied Radiation Oncology,* in a continued effort to augment the level of expertise in our specialty—in hopes of delivering better patient outcomes.

Sincerely,

John Suh, MD, FASTRO, FACR
Chairman of the Department of Radiation Oncology
Associate Director of the Gamma Knife Center at
the Brain Tumor and Neuro-Oncology Center
Cleveland Clinic
Cleveland, OH

References

1. Emiliani E. Continuing medical education in radiation oncology. *Tumori.* 1998;84:96-100.

CME Information

Activity Description

In this issue of *Applied Radiation Oncology* our faculty has assembled a number of articles and cases that we feel provide practical insight to radiation oncology professionals on topics including partial breast irradiation, modern imaging techniques, fiducial marker placement, IMRT for head and neck cancer, and distinguishing radiation necrosis from tumor progression.

Breast MRI scans help physicians determine which patients are best suited for accelerated partial breast irradiation (APBI). The authors of **Breast MRI and its impact on partial breast irradiation** demonstrate how MRI is advantageous for selecting patients for preoperative radiotherapy and for APBI treatment planning. The authors also evaluate how MRI improves diagnostic accuracy of conventional imaging to select potential candidates for neoadjuvant radiotherapy.

In the article, **Integration of modern imaging into the multidisciplinary setting: The radiation oncology perspective,** the authors illustrate how a multidisciplinary approach to cancer care improves efficiency in work-ups and decision-making to optimize patient outcomes. This article provides examples of cancer care specialists collaborating to more effectively manage lung, breast, and liver cancer in patients. The accurate placement of fiducial markers in patients is critical to the success of image-guided radiation therapy.

The article, **CT-guided fiducial marker placement for stereotactic radiosurgery** provides the essentials of how stereotactic radiosurgery (SRS) systems utilize fiducial markers, a step-by-step guide on how to perform the procedure, a review of potential complications, and what to do when they occur.

In the case, **Adaptive replanning of IMRT for head and neck cancer: A case report of replanning in a middle-aged patient with squamous cell carcinoma of the tonsil,** the authors emphasize the importance of adjusting treatment plans to track anatomical changes. By combining the adaptive radiotherapy intensity-modulated radiation therapy (ART IMRT) plan with the original IMRT plan, clinicians can recontour the organs at risk (OAR) and reduce toxicity in the patient. After a patient receives stereotactic radiosurgery (SRS), the noninvasive and accurate diagnosis of radiation necrosis versus tumor progression is important, yet the clinical course of each can differ widely.

In the case, **Wanted: Dead or alive? Distinguishing radiation necrosis from tumor progression after stereotactic radiosurgery,** the authors provide recommendations for accurately diagnosing this syndrome, thereby permitting selection of the most appropriate treatment.

Learning Objectives

- How MRI improves preoperative loco-regional staging of breast cancer.
- Why MRI is more accurate than CT in APBI planning.
- How multidisciplinary cancer care fosters more efficient work-ups and decision making to improve survival rates.
- How to effectively share and review information across specialties.
- How to identify anatomical changes in the organs at risk (OAR).
- How to compare and register initially planned and re-planned images.
- How to distinguish between radiation necrosis versus tumor progression, and mixed radiation necrosis and tumor progression, post-stereotactic radiosurgery (SRS).
- An understanding of how different imaging techniques present varying diagnoses for radiation necrosis.

Target Audience

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

Estimated time for completion:	Three (3) hours
Date of release:	October 15, 2012
Expiration date:	October 14, 2014

Accreditation

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the Institute for Advanced Medical Education (IAME).

IAME is accredited by the ACCME to provide continuing medical education for physicians. IAME designates this activity for a maximum of three (3) AMA/PRA Category 1 CME Credits.™ Physicians should only claim credit commensurate with the extent of their participation.

Disclosures

None of the authors, or any individual at IAME who had control over the content of this program, has any relationships with commercial supporters.

Instructions For Participation

1. Review all articles and cases that are part of this educational activity
2. Click here to be redirected to our CME provider's website
3. Purchase your CME credits
4. Complete the online evaluation form
5. Print your certificate

CME Pricing

The cost of CME credits is $50 per issue. As an inaugural offer you can purchase all the CME credits in every issue through the end of 2013 for the discounted price of just $95. That's just $95 for 15 CME credits.

CME SEE PAGE 5 FOR DETAILS

Breast MRI and its impact on partial breast irradiation

Mussadiq Awan, MD, Randi Cohen MD, MS, Cristina Campassi, MD, Susan Kesmodel, MD, Emily Bellavance, MD, Katherine Tkaczuk, MD, and Steven J. Feigenberg, MD

For women with early stage breast cancer, breast conserving surgery (BCS) followed by postoperative whole-breast irradiation (WBI) is associated with 85% to 95% long-term local control and is equivalent to a mastectomy in survival.[1-4] The combination of BCS and adjuvant radiation is termed breast conservation therapy (BCT). The rationale for using WBI is to decrease local recurrence by eliminating potential small foci of tumors in the surgical bed or elsewhere in the breast. As 75% to 90% of recurrences occur at or near the surgical bed,[5,6] an additional boost of radiation is delivered to the surgical bed following a moderate dose of WBI.

In the United States, WBI is typically delivered over 6 to 6 ½ weeks, 5 days per week. The time commitment for adjuvant radiation can be difficult for many women, particularly if they are not in close proximity to a radiation facility. This limited access to radiation facilities is one of the primary reasons why patients do not receive radiotherapy following BCS. Investigators have evaluated methods to shorten (ie, accelerate) therapy to increase the use of radiotherapy. The most common approach used to shorten therapy is accelerated partial breast irradiation (APBI). This approach delivers radiation only to the surgical bed, deliberately avoiding the rest of the breast. This drastically but safely shortens treatment from 6 weeks to 1 week or less.

APBI can be delivered via several different methods and is outside the scope of this article. The major risk of this approach is the small but real risk of a tumor recurrence 2 cm and further from the surgical bed. This concept is currently being tested nationally and internationally, with the largest protocol nearing completion through the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39. This study rapidly accrued patients in the most favorable population. Subsequently, the eligibility criteria were modified, and the study is currently open only to the high-risk population (ER-negative tumors, 1 to 3 involved lymph nodes, or young patients).

In 2009, based on published prospective and retrospective experiences, the American Society for Radiation Oncology (ASTRO) published consensus guidelines identifying patients that are "suitable," "cautionary," or "unsuitable" for APBI.[7] A number of clinical and pathologic criteria were determined to be "suitable," including patients aged ≥60, clinical unifocality with total tumor extent <2.0 cm (by mammography and ultrasound exams), tumor pathology of invasive ductal carcinoma or other favorable subtypes, and no lymph node or lymphovascular space involvement. All of the literature to date had been based on mammograms with or without an ultrasound.

Breast MRI has the highest sensitivity for detection of breast cancer (>90%). While mammography remains the gold standard for screening, breast MRI has been shown to identify mammographically and clinically occult breast cancer in certain subsets of patients. As a result, since 2007 the American Cancer Society has recommended breast MRI in combination with mammography for screening women who have a 20% to ≥25% lifetime risk of breast cancer.[8] In a newly diagnosed breast cancer patient, breast MRI has been shown to assess tumor size more accurately than mammography and breast ultrasound. Additionally, breast MRI has shown higher sensitivity

***Dr. Awan** is a Resident, and **Dr. Cohen** is an Assistant Professor, Department of Radiation Oncology; **Dr. Campassi** is an Assistant Professor, Department of Radiology; **Dr. Kesmodel** is an Assistant Professor of Surgery, and **Dr. Bellavance** is an Assistant Professor of Surgery, Department of Surgical Oncology; **Dr. Tkaczuk** is a Professor and Director of the Breast Evaluation and Treatment Program, Department of Medical Oncology; and **Dr. Feigenberg** is an Associate Professor/Director of Clinical Research, Department of Radiation Oncology, University of Maryland School of Medicine, Baltimore, MD.*

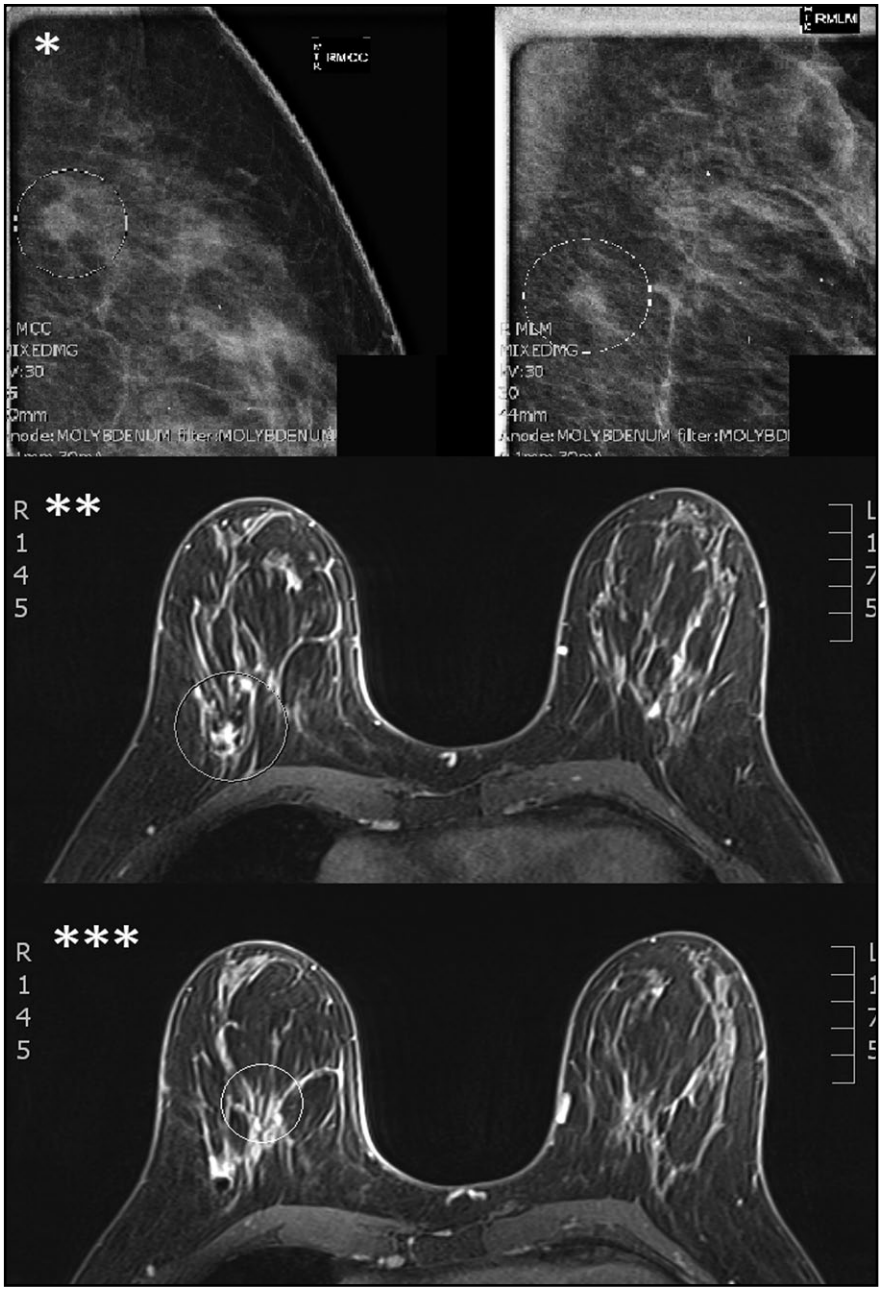


FIGURE 1. *(*) Craniocaudal and medial lateral oblique mammographic views of the right breast demonstrating the index lesion of invasive ductal carcinoma in a patient who was clinically a candidate for APBI. (**) Breast MR image demonstrating the index lesion measuring approximately 1.4 cm in greatest dimension and showing an additional area of total enhancement measuring about 2.5 cm. (***) A breast MR image demonstrates an additional focus of cancer 5 mm in greatest dimension and 2.5 cm anteromedial to the biopsy-proven cancer.*

than conventional imaging for detection of multicentric and multifocal disease in the ipsilateral breast and in synchronous contralateral breast cancer. Additional multifocal or multicentric cancer is found by breast MRI in the same breast in 11% to 34% of women with unicentric breast cancer on conventional imaging,[9,10] while synchronous contralateral breast cancer is found by MRI in 3% to 9% of patients.[11] Even with all this supportive data, the role of breast MRI remains controversial as MRI has not been shown to reduce the re-excision rate or decrease local recurrences. One reason for this lack of benefit is the use of WBI, which is used to treat subclinical disease in the breast. With the advent of APBI, MRI may have a more significant impact as APBI deliberately avoids these uninvolved portions of the breast. This article seeks to review the literature related to the utility of MRI in the subset of patients considering treatment with APBI.

The role of MRI in selecting candidates for APBI

Recently a number of studies have evaluated the ability of preoperative MRI to select patients for APBI. Godinez et al[12] reviewed 79 patients who underwent preoperative bilateral breast MRI and were eligible for APBI. Patients were determined eligible preoperatively if they had lymph node negative, biopsy proven, unifocal invasive ductal carcinoma (IDC, 67 patients) and/or ductal carcinoma in situ (DCIS, 12 patients) ≤3.0 cm in greatest dimension by mammogram and ultrasound. The patients ranged in age from 29 to 75 years (mean 48). MRI identified a total of 80 additional lesions in the ipsilateral breast with 34 lesions in a different quadrant than the index cancer. Thirty (38%) of the 79 patients were found to have additional biopsy-proven malignant tumors, of whom 8 had malignant foci outside of the quadrant in which the indexed lesion resided. Ultimately, only 62% of patients were considered appropriate for APBI.

An important critique of this study is the inclusion of a significant portion of young women and those considered high-risk due to a significant family history, a relative with the BRCA mutation, or a personal history of a BRCA mutation. Twenty-eight (35%) of the

CME

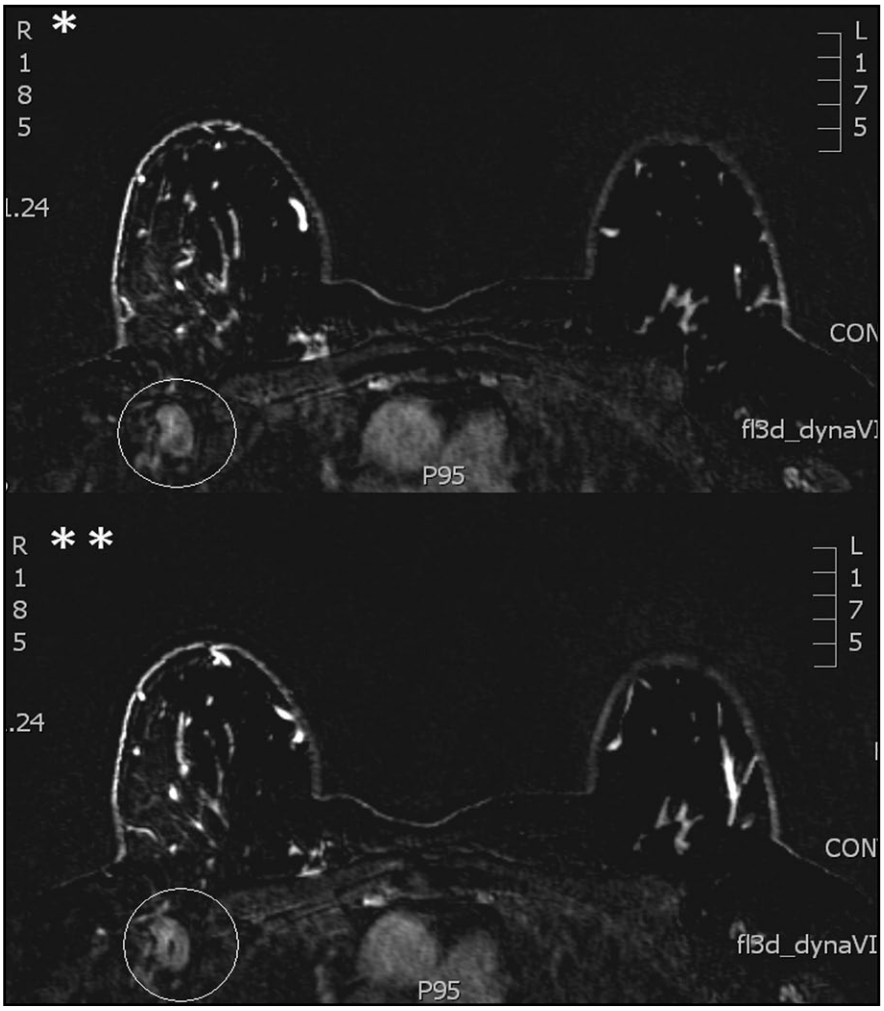


FIGURE 2. *Both images depicting a single asterisk (*) and 2 asterisks (**) demonstrate an abnormal lymph node measuring approximately 2.3 cm in greatest dimension with attributes of cortical thickening and compression of fatty hilum in a candidate for APBI without clinical adenopathy.*

79 patients were <40 years old, and half were found to have additional malignant foci. Twenty-nine (37%) patients were considered high risk, and 41% had an additional malignant focus. It is unknown how many of these patients had the BRCA mutation. Per ASTRO guidelines, age <50 years or the presence of a BRCA mutation would make a patient "unsuitable" for APBI.

Tendulkar et al[13] published a retrospective review of 260 patients who met criteria for the NSABP B-39/RTOG 0413 study, which are largely similar to the criteria that Godinez used. A significant difference in selection criteria was that invasive lobular carcinomas were included and 0 to 3 positive lymph nodes on final pathology were allowed in the Tendulkar study. All 260 patients had a bilateral breast MRI prior to surgery. Twenty-five percent of patients were <50 years old. There were 35 (13%) patients with ipsilateral suspicious findings by MRI, only 11 (4.2%) of which were proven to have multifocal/multicentric involvement. Thus, there was a 68.7% false positive rate. The median distance from the index lesion was 3 cm. There were 16 (6.0%) contralateral suspicious findings by MRI, 4 (1.5%) of which were biopsy-proven synchronous contralateral disease for a 75% false-positive rate. The authors notably report that multifocal ipsilateral invasive lobular carcinoma (ILC) was found in 3 of 17 (18%) cases, "significantly higher than that found in the aggregate of non-ILC histologies (3%, p = 0.04)." Current ASTRO recommendations for selection of candidates for APBI exclude the presence of ILC in consideration of this high rate of multifocality. Notably, Tendulkar et al did not find women younger than 50 to be at higher risk of synchronous lesions.

Most recently, Kuhr et al[14] published a similar retrospective study of 113 patients with the exact criteria that Godinez used for selecting potential candidates for APBI. In 10 of 113 patients, MRI detected a total of 11 additional foci (7 ipsilateral, 4 contralateral), which were all found to be biopsy-proven cancers. Overall, MRI led to the detection of new ipsilateral and contralateral foci in 6.2% and 3.5%, respectively, of the patients initially considered candidates for APBI.

Compared to the Godinez study, in both the Tendulkar and Kuhr studies there was a far lower rate of detection of ipsilateral disease (38% versus 4% and 6.2%). There was also a smaller number of abnormal ipsilateral lesions on MRI in both the Tendulkar and Kuhr studies compared to the Godinez studies, despite the much larger patient population (35 lesions in 260 patients and 7 lesions in 113 patients versus 80 lesions in 79 patients). Both the Godinez and Kuhr studies utilized 1.5 Tesla magnets, while Tendulkar used a 1.0 Tesla magnet. Although the differences observed in these studies may also be due to different patient populations, the discordance in the studies between the number of additional abnormal lesions identified in the Godinez study is significant and there does not appear to be a clear explanation for this. A recent meta-analysis demonstrated that MRI had a 67% positive predictive value for

ipsilateral disease and 37% for contralateral disease.[15]

Schmitz et al[16] prospectively reviewed 62 women with pre-operative MRI imaging followed by wide local excision and histopathological correlation. There was excellent correlation between the index tumor and MRI-visible lesions with a mean size difference of 1.3 mm. However, subclinical disease a distance of 1 cm or more from the MRI-identified tumor was identified in 52% of specimens, and subclinical disease a distance of 2 cm or more from the MRI identified tumor was identified in 25% of specimens.

MRI leads to the detection of a significant number of ipsilateral lesions in 4% to 38% of patients who are otherwise candidates for APBI (Figure 1). Whether these lesions would develop into clinically significant breast cancers is unclear. Depending on the technique and extent of wide excision, some of these lesions may have been excised, and it is unclear whether APBI fields would cover these lesions. Additional data correlating imaging and pathology needs to be obtained in order to ensure an adequate margin of radiation treatment. It is in this area that further study needs to be done in regard to the utility of MRI in selecting patients for APBI.

The role of MRI in APBI planning

Previous data have suggested that computed tomography (CT) planning for APBI is suboptimal as it is often difficult to identify the lumpectomy site on CT imaging.[17] One group found that MRI of the breast in the supine position yields a smaller, more accurately defined lumpectomy cavity with less interobserver variability than CT.[18] However, Giezen et al[19] found that the MRI did not add additional information to the surgical cavity delineation if the visualization score[20] was low. Classically, WBI is performed in the supine position; however, with improved immobilization investigators can take advantage of the prone position, which displaces the surgical cavity away from various critical structures,[21-23] making it easier to safely deliver the doses of radiation needed for APBI.

Ahn et al[24] demonstrated the feasibility of using MRI guidance for planning of APBI in the prone position. Simulating 2 volunteers in both the supine (with both body and surface coils) and prone positions (with breast coils) demonstrated a clear superiority of the prone position by (1) reducing the signal-to-noise ratio (SNR), (2) reducing the deformation of the breast, and (3) reducing respiratory motion. The group also reported on the reproducibility of the setup.

Jozsef et al[25] at New York University utilized cone-beam CT prior to performing APBI on 70 prone patients. They found the positioning to be reproducible with mean shifts of <0.2 cm in any direction.

MRI planning for APBI is both logistically feasible and reproducible and provides some clear advantages over CT planning particularly in visualization of the lumpectomy cavity. However, due to poor spatial resolution, CT is also needed to plan for accurate dose calculation and, subsequently, MRI and CT images will need to be fused. On-board imaging will require radiographic or CT anatomy to verify the treatment position. These uncertainties will need to be reduced further prior to the increased utilization of MRI.

The role of MRI in selecting patients for neoadjuvant radiation therapy to the breast

An interesting finding from NSABP B-39 has been that 3-dimensional conformal radiotherapy (3D-CRT), which treats the largest volume and has the shortest history of any technique, is by far the most commonly utilized delivery method utilized on this trial, encompassing >70% of the patients on the APBI arm. We suspect its popularity is related to the completely noninvasive nature of the approach compared to the 2 invasive brachytherapy approaches.

At the University of Maryland, we have previously investigated the potential benefits of delivering APBI using 3D-CRT in the preoperative setting and demonstrated that the radiated volumes are significantly smaller compared to those in the postoperative setting, increasing the number of patients eligible for partial breast radiation via this approach. In addition, the dose to all normal structures was also significantly reduced using preoperative APBI.[26] This theoretical advantage could lead to improved cosmetic outcomes and decreased long-term toxicity, which has been seen in up to 10% of patients treated with 3D-CRT. Based on these advantages, we opened a feasibility study utilizing preoperative APBI-3D-CRT.

To be eligible for such treatment, patients not only have to meet the APBI criteria, but the risk of multifocal disease and nodal disease also needs to be excluded. To select potential candidates for neoadjuvant radiotherapy, MRI improves diagnostic accuracy of conventional imaging. As mentioned earlier, MRI finds ipsilateral mammographically-occult disease in 4% to 38% of patients who would otherwise be candidates for APBI. Further, breast MRI used with conventional imaging can also exclude axillary disease in all breast cancer patients with an estimated specificity of between 93% and 100% (Figure 2).[27-29] Unfortunately, the sensitivity for staging the axilla is low. Thus, a woman with a clinical lymph node negative exam with an otherwise early stage cancer who underwent a breast MRI that is negative for additional foci of disease or for whom any additional MRI foci were demonstrated to be benign would be an ideal candidate for neoadjuvant radiotherapy.

MRI may also play a role in evaluating response to therapy similar to that seen following neoadjuvant chemotherapy. Based on the initial 12 patients treated with neoadjuvant APBI at UMMS, 25% had a complete pathologic

CME

response (pCR), which may increase with further escalation in dose, although developing noninvasive predictors of pCR is imperative before nonsurgical approaches can be considered. Functional MRI techniques can determine differences in vascular, biophysical, and biochemical responses in tumors versus the normal tissue.

Dynamic contrast-enhanced MRI[30] is used to characterize vascular information in tumors based on the onset and rate of contrast enhancement to differentiate malignant from normal tissues. Diffusion-weighted MRI[30-32] is used as a biophysical imaging marker to extract differences in the microenvironment between malignant and normal tissue based on the differences in rate of cellular growth, which is characterized using the diffusion coefficient of water. MR spectroscopy[33-35] is used to measure the levels of different metabolites, such as choline, creatine, and lactate, in tissue, evidencing biochemical changes that occur in the tumor. Taken together, these 3 methods are likely to improve sensitivity and specificity in predicting treatment response, although further prospective data are warranted.

Conclusion

MRI improves preoperative locoregional staging of breast cancer, which should translate into reducing the risk of occult multicentric disease in the breast. In addition, MRI adds another advantage for selecting patients for preoperative radiotherapy by accurately staging the axilla.

References

1. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N. Engl. J. Med.* 2002;347:1227-1232.
2. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N. Engl. J. Med.* 2002;347:1233-1241.
3. Fisher B, Dignam J, Wolmark N, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-17. *J. Clin. Oncol.* 1998;16:441-452.
4. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European organization for research and treatment of cancer 10801 trial. *J Natl Cancer Inst* 2000;92:1143-1150.
5. Beitsch PD, Shaitelman SF, Vicini FA. Accelerated partial breast irradiation. *J Surg Oncol.* 2011;103:362-368.
6. McCormick B. Partial breast radiation for early-stage breast cancer. *Curr Opin Obstet Gynecol.* 2012;24:31-37.
7. Smith BD, Arthur DW, Buchholz TA, et al. Accelerated partial breast irradiation consensus statement from The American Society for Radiation Oncology (ASTRO). *Int J Radiat Oncol Biol. Phys.* 2009;74:987-1001.
8. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin.* 2007;57:75-89.
9. Liberman, L, Morris EA, Dershaw DD, et al. MR imaging of the ipsilateral breast in women with percutaneously proven breast cancer. *AJR Am J Roentgenol.* 2003;180:901-910.
10. Morrow M, Freedman G. A clinical oncology perspective on the use of breast MR. *Magn Reson Imaging Clin N Am.* 2006;14:363-378.
11. Lehman, CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *N Engl J Med.* 2007;356:1295-1303.
12. Godinez J, Gombos EC, Chikarmane SA, et al. Breast MRI in the evaluation of eligibility for accelerated partial breast irradiation. *AJR Am J Roentgenol.* 2008;191:272-277.
13. Tendulkar RD, Chellman-Jeffers M, Rybicki LA, et al. Preoperative breast magnetic resonance imaging in early breast cancer: Implications for partial breast irradiation. *Cancer.* 2009;115:1621-1630.
14. Kuhr M, Wolfgarten M, Stolzle M, et al. Potential impact of preoperative magnetic resonance imaging of the breast on patient selection for accelerated partial breast irradiation. *Int J Radiat Oncol Biol Phys.* 2011;81:541-546.
15. Plana, MN, Carreira C, Muriel A, et al. Magnetic resonance imaging in the preoperative assessment of patients with primary breast cancer: systematic review of diagnostic accuracy and meta-analysis. *Eur Radiol.* 2012;22:26-38.
16. Schmitz AC, van den Bosch MA, Loo CE, et al. Precise correlation between MRI and histopathology - exploring treatment margins for MRI-guided localized breast cancer therapy. *Radiother Oncol.* 2010;97:225-232.
17. Petersen RP, Truong PT, Kader HA, et al. Target volume delineation for partial breast radiotherapy planning: clinical characteristics associated with low interobserver concordance. *Int J Radiat Oncol Biol. Phys.* 2007;69:41-48.
18. Jolicoeur M, Racine ML, Trop I, et al. Localization of the surgical bed using supine magnetic resonance and computed tomography scan fusion for planification of breast interstitial brachytherapy. *Radiother Oncol.* 2011;100:480-484.
19. Giezen M, Kouwenhoven E, Scholten AN, et al. MRI- versus CT-based volume delineation of lumpectomy cavity in supine position in breast-conserving therapy: An exploratory study. *Int J Radiat Oncol Biol Phys.* 2012;82:1332-1340.
20. Smitt MC, Birdwell RL, Goffinet DR. Breast electron boost planning: Comparison of CT and US. *Radiology.* 2001;219:203-206.
21.Formenti SC, Truong MT, Goldberg JD, et al. Prone accelerated partial breast irradiation after breast-conserving surgery: Preliminary clinical results and dose-volume histogram analysis. *Int J Radiat Oncol Biol Phys.* 2004;60:493-504.
22. Jozsef G, Luxton G, Formenti SC. Application of radiosurgery principles to a target in the breast: A dosimetric study. *Med Phys.* 2000:27:1005-1010.
23. Merchant TE, McCormick B. Prone position breast irradiation. *Int J Radiat Oncol Biol Phys.* 1994:30:197-203.
24. Ahn KH, Hargreaves BA, Alley MT, et al. MRI guidance for accelerated partial breast irradiation in prone position: imaging protocol design and evaluation. *Int J Radiat Oncol Biol Phys.* 2009;75:285-293.
25. Jozsef G, DeWyngaert JK, Becker SJ, et al. Prospective study of cone-beam computed tomography image-guided radiotherapy for prone accelerated partial breast irradiation. *Int J Radiat Oncol Biol Phys.* 2011;81:568-574.
26.Nichols EM, Dhople AA, Mohiuddin MM, et al. Comparative analysis of the post-lumpectomy target volume versus the use of pre-lumpectomy tumor volume for early-stage breast cancer: Implications for the future. *Int J Radiat Oncol Biol Phys.* 2010;77:197-202.
27. Garcia Fernández A, Fraile M, Giménez N, et al. Use of axillary ultrasound, ultrasound-fine needle aspiration biopsy and magnetic resonance imaging in the preoperative triage of breast cancer patients considered for sentinel node biopsy. *Ultrasound Med Biol.* 2011;37:16-22.
28. Kvistad KA, Rydland J, Smethurst HB, et al. Axillary lymph node metastases in breast cancer: Preoperative detection with dynamic contrast-enhanced MRI. *Eur Radiol.* 2000;10:1464-1471.
29. Yoshimura G, Sakurai T, Oura S, et al. Evaluation of axillary lymph node status in breast cancer with MRI. *Breast Cancer.* 1999;6:249-258.
30. Fangberget A, Nilsen LB, Hole KH, et al. Neoadjuvant chemotherapy in breast cancer-response evaluation and prediction of response to treatment using dynamic contrast-enhanced and diffusion-weighted MR imaging. *Eur Radiol.* 2011;21:1188-1199.
31. Park SH, Moon WK, Cho, N, et al. Diffusion-weighted MR imaging: Pretreatment prediction of response to neoadjuvant chemotherapy in patients with breast cancer. *Radiology.* 2010;257:56-63.
32. Nilsen LB, Fangberget A, Geier, O, et al. Diffusion-weighted magnetic resonance imaging for pretreatment prediction and monitoring of treatment response of patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy. *Acta Oncol.* 2010;49:354-360.
33. O'Flynn EA, Desouza NM. Functional magnetic resonance: Biomarkers of response in breast cancer. *Breast Cancer Res.*2011;13:204.
34. Tozaki M, Oyama Y, Fukuma E. Preliminary study of early response to neoadjuvant chemotherapy after the first cycle in breast cancer: Comparison of 1H magnetic resonance spectroscopy with diffusion magnetic resonance imaging. *Jpn J Radiol.* 2010;28:101-109.
35. Meisamy S, Bolon PJ, Baker EH, et al. Neoadjuvant chemotherapy of locally advanced breast cancer: Predicting response with in vivo (1)H MR spectroscopy—a pilot study at 4 T. *Radiology.* 2004;233:424-431.

SEE PAGE 5 FOR DETAILS CME

CT-guided fiducial marker placement for stereotactic radiosurgery

Eric White, MD, William Boswell, MD, Gilbert Whang, MD, Paul Mandelin, DO, and Vinay Duddalwar MBBS

Image-guided radiation therapy (IGRT) utilizes real-time imaging to deliver more precise radiation therapy with respect to tumors. The development of highly conformal radiation therapy techniques places more stringent requirements on the accuracy of beam targeting.

In practice, large uncertainties exist in tumor volume delineation and in target localization due to physiologic organ motion. IGRT uses orthogonal x-rays to visualize radiopaque fiducial markers implanted within and adjacent to the tumor for real-time tracking during the entire treatment cycle.[1] Stereotactic radiosurgery (SRS), which is delivered in a single fraction, and stereotactic radiotherapy (SRT), which is delivered in up to 5 fractions, using the Cyberknife robotic system were developed at Stanford University and approved by the U.S. Food & Drug Administration in 2001. A robot (Figure 1) delivers highly focused 6MV photon radiation from a single, highly collimated beam from hundreds of angles. Figures 1 and 2 demonstrate the many components of the radiotherapy system within the vault room, where the patient is treated.

Dr. White *is an Assistant Professor of Radiology, Director of Musculoskeletal Radiology, Department of Radiology;* ***Dr. Boswell*** *is a Professor of Radiology and Urology and Associate Chairman, Department of Radiology;* ***Dr. Whang*** *is an Assistant Professor of Clinical Radiology and Medical Director of Imaging, Department of Radiology; and* ***Dr. Duddalwar*** *is an Assistant Professor of Radiology, Department of Radiology, at the Keck School of Medicine, University of Southern California University Hospital, Los Angeles, CA.*

Dr. Mandelin *is a Resident, Department of Radiation Oncology, Keck School of Medicine, University of Southern California University Hospital, Los Angeles, CA.*

The system continuously synchronizes beam delivery to the motion of the tumor, allowing significant dose reduction in treatment margins while eliminating the need for breath holding. The patient wears a special vest that has light-emitting diodes that track the tumor according to the patient's respiration or other movements. This movement is detected by the ceiling-mounted camera array. This information is displayed on a computer monitor, where a breathing model is made, which can make adjustments in radiation delivery in real time, including predicting tumor location.

The system has interchangeable collimators with sizes from 5 to 60 mm and utilizes its noncoplanar beam arrangement to deliver submillimeter accuracy. Real-time kV imaging is obtained using either bony landmark reference points (eg, 6-dimensional skull base tracking or spine tracking) or implanted radiographic fiducial markers (eg, gold seeds or coils). Figure 3 demonstrates how digitally reconstructed radiographs are obtained, and compares how the fiducial markers appear on the planning computed tomography (CT) system (synthetic images) with how the markers appear during live imaging (camera images). The combined images, called overlays, help to verify patient positioning and track patient motion.

Fiducial placement may appear adequate to the radiologist in that they are near the lesion, providing the system with the spatial information it needs to accurately deliver radiation. However, what may appear as adequate on CT images to a radiologist may not be acceptable because fiducial tracking is obtained using orthogonal radiographs, from which digitally reconstructed radiographs are made.[2] This may result in overlapping markers which will not be usable. This phenomenon is demonstrated in Figures 4 and 5, showing a diagrammatic representation of a liver tumor and fiducial markers.

Fiducial placement guidelines

Ideally, one fiducial should be centered in the treatment volume (within the center of the lesion).

CME

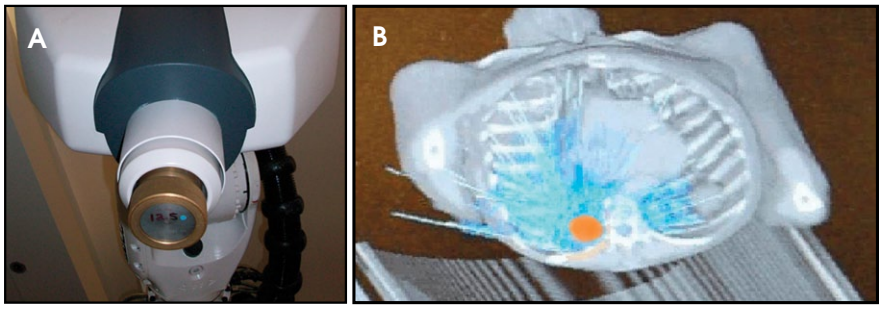


FIGURE 1. *(A) A robot delivers focused radiation from a single, highly collimated beam (shown here with a 12.5-mm collimator). (B) A 3-dimensional cutaway image of a completed therapy plan shows hundreds of individual beams (blue) focused on the target tumor (orange).*

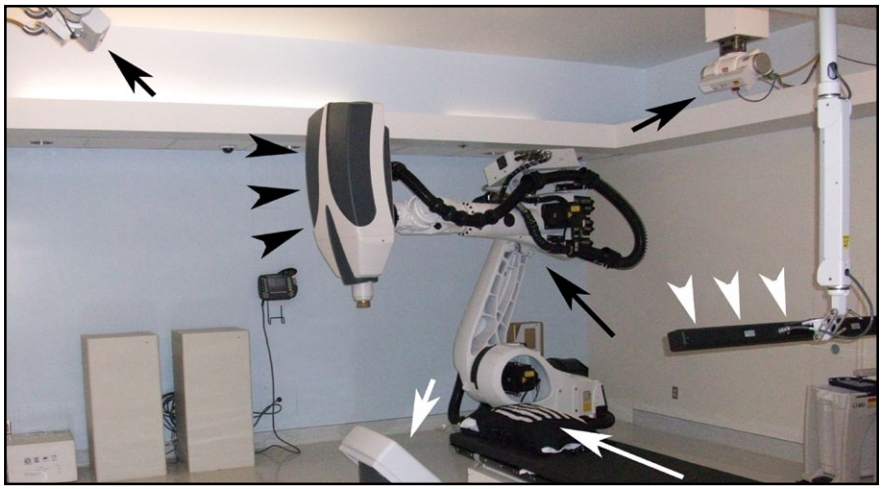


FIGURE 2. *A 6-MV linear accelerator (black arrowheads) is mounted on a robotic arm (long black arrow). Diagnostic (kv) x-ray tubes (short, black arrows) are mounted on the ceiling directed toward 2 flat-panel digital imagers (short, white arrow). The patient wears a special vest (long, white arrow) that allows detection of patient motion by the nearby camera array (white arrowheads).*

Additional fiducials should be centered around the tumor volume (bracketing the lesion superiorly, inferiorly, medially, and laterally). Optimally, the markers should be placed in different planes in the x-, y-, and z-axes (Figure 6).[3-5]

Fiducials should not be placed in the same plane (eg, the same axial-CT image plane), in such a way that they form about a 45-degree angle with the horizon (Figure 7). No fiducial should be >5 cm or >6 cm away from the lesion. There should be a minimum of 1.5 cm between fiducial markers. At least 15-degree angulation should be present between any 3 fiducials (Figure 8).[3-5] A minimum of 3 fiducials are needed to define a plane, which is necessary for the system to be able to localize treatment in space. More fiducial markers are preferred — 5 or 6 are usually placed at the authors' institution because some markers may be unusable due to overlap or marker migration.

Methods

At the authors' institution, a 16-gauge Hawkins needle available in 5-, 10-, or 15-cm lengths is used (Figure 9). This needle has an inner pencil-point stylet, which has a white knob and a blue blunt-tip stylet that is used

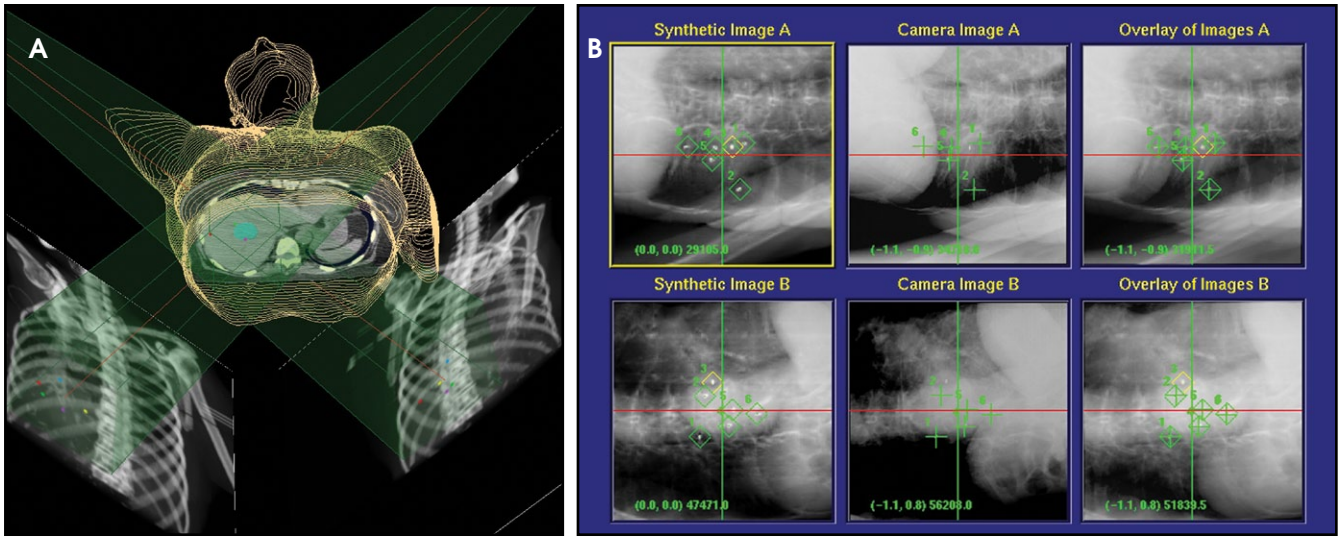


FIGURE 3. *(A) Digitally reconstructed radiographs are obtained. As shown in B, the images obtained from the planning CT (synthetic images) are compared with the images obtained during live imaging (camera images) resulting in overlay images.*

CME

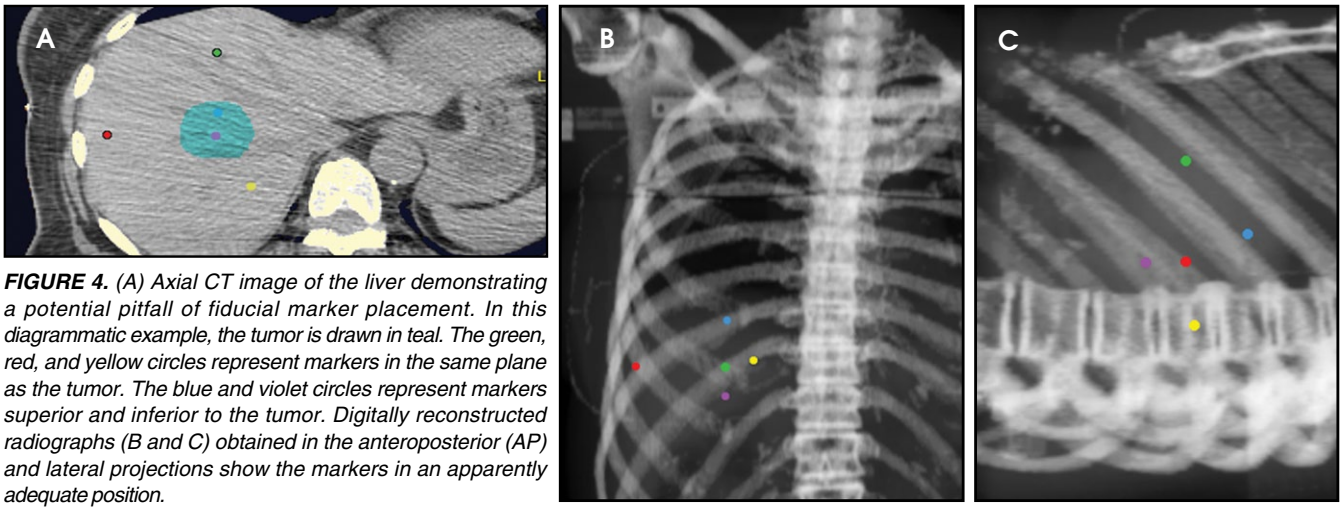


FIGURE 4. *(A) Axial CT image of the liver demonstrating a potential pitfall of fiducial marker placement. In this diagrammatic example, the tumor is drawn in teal. The green, red, and yellow circles represent markers in the same plane as the tumor. The blue and violet circles represent markers superior and inferior to the tumor. Digitally reconstructed radiographs (B and C) obtained in the anteroposterior (AP) and lateral projections show the markers in an apparently adequate position.*

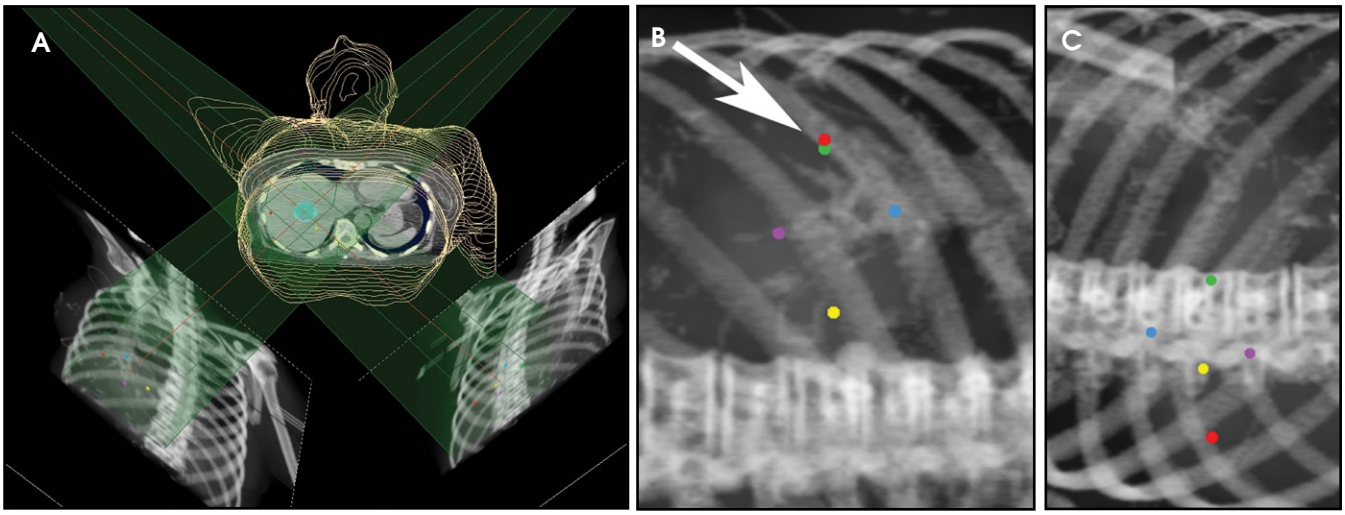


FIGURE 5. *(A) Live orthogonal imaging only utilizes oblique images (rather than AP and lateral). When oblique images of same patient are viewed (B), there is overlap of the red and green markers on the LAO view. This results in neither marker being usable, reducing the effective number of usable fiducials from 5 to 3 (C). The minimum number of fiducial markers required to define a treatment volume is 3.*

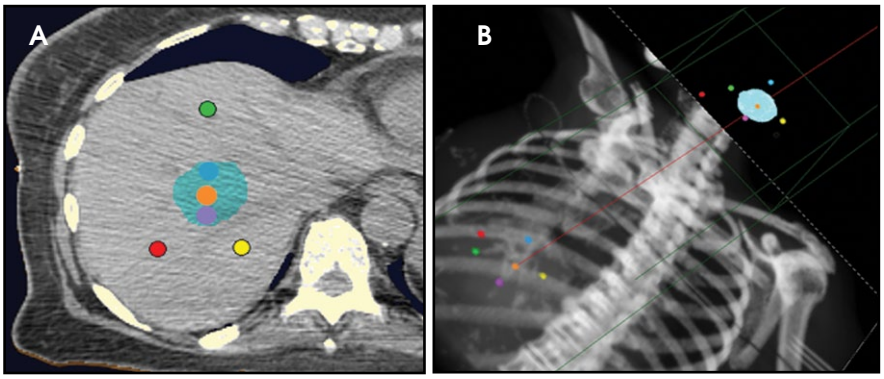


FIGURE 6. *Axial CT and corresponding digitally reconstructed radiograph show optimal fiducial marker placement. The tumor is drawn in teal. All markers are in different planes along the z-axis (the patient's head-to-toe axis). (A) The orange circle represents a marker in the center of the tumor. (B) The blue, yellow, red, green, and violet circles represent markers bracketing the lesion superiorly, medially, laterally, and inferiorly.*

to advance the fiducial marker into the tissues. This needle allows more than 1 marker to be placed after puncturing the skin just 1 time by repositioning the angle of the needle between fiducial placements.

Fiducials are small gold markers that are implanted into the soft tissues or within the lesion. They provide spatial information for the system to accurately guide radiation delivery. Gold is denser than surgical clips and appears unique on imaging with characteristic streak artifacts. Fiducials are typically required for tumors in the chest, abdomen, pelvis, or other soft tissues.

CME

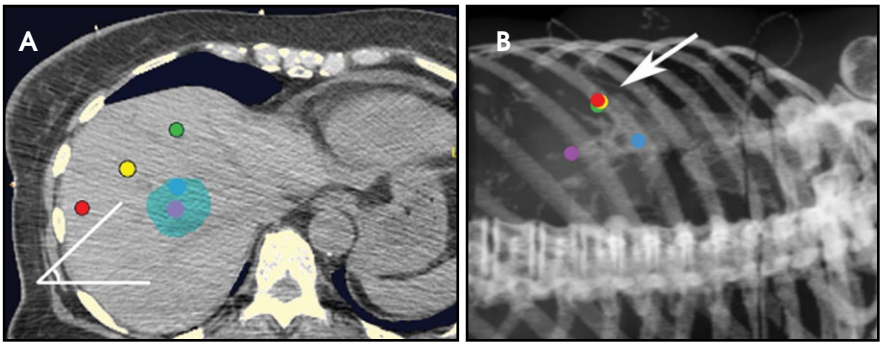


FIGURE 7. *Axial CT and corresponding digitally reconstructed radiograph demonstrate suboptimal placement of markers. (A) The blue and violet markers bracket the tumor (teal) adequately (superiorly and inferiorly). However, the green, yellow, and red markers are all in the same axial plane, and are aligned approximately 45 degrees to the horizon (B). This results in overlap on oblique imaging.*

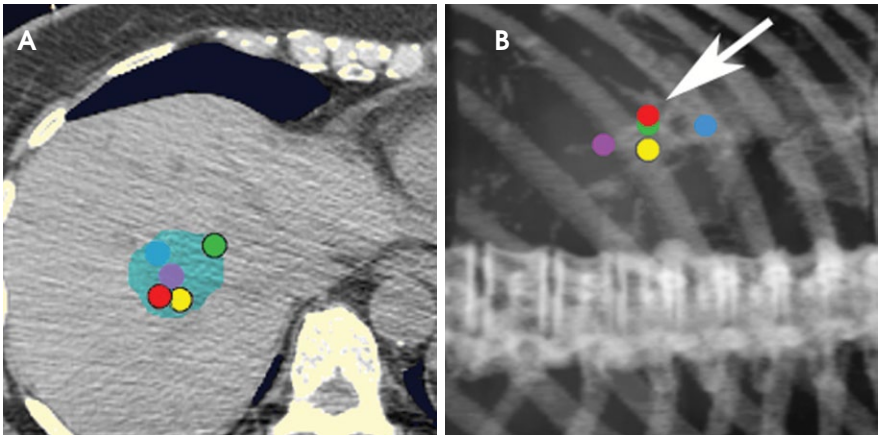
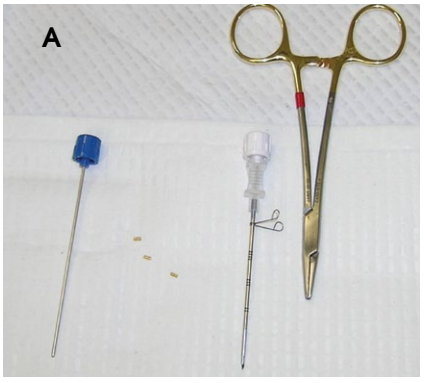


FIGURE 8. *Axial CT (A) and corresponding digitally reconstructed radiograph (B) show suboptimal placement of fiducial markers resulting in overlap. The green, red, and yellow markers are in the same axial plane and the angle formed by the 3 is <15 degrees. Also, the red and yellow markers are <1.5 cm apart.*



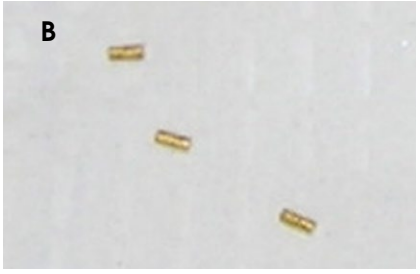
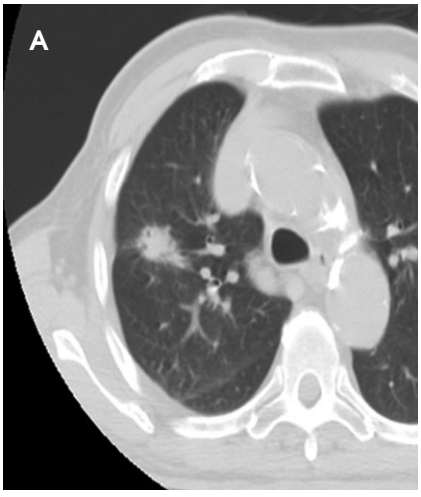
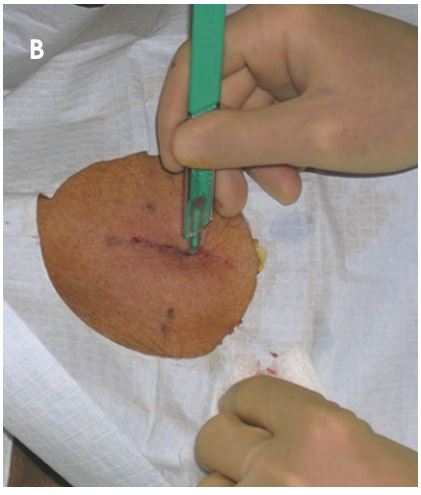


FIGURE 9. *In addition to a basic biopsy tray (A), a 16-Hawkins needle, gold-seed fiducial markers (close up view in B), and a sterile Kelly clamp are utilized.*

They may not be required for lesions near the spine, as the spine provides spatial localization. Fiducials are not required for intracranial lesions.

For the procedure, a basic biopsy tray is used with a 16-gauge Hawkins needle, 0.8 x 5-mm gold seed fiducial markers, and a Kelly clamp (Figure 9). Before the procedure, the patient's previous CT is reviewed. The patient is placed in the appropriate position (ie, supine or prone) and initial images





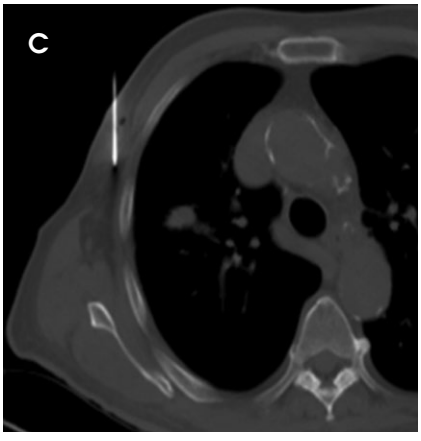


FIGURE 10. *An initial CT image shows a lung lesion (A). The site is marked on the patient's skin, and 1% lidocaine is administered for local anesthesia. A nick is made in the patient's skin (B). The Hawkins needle is placed (with the inner pencil-point stylet) and CT images are obtained (C).*

CME

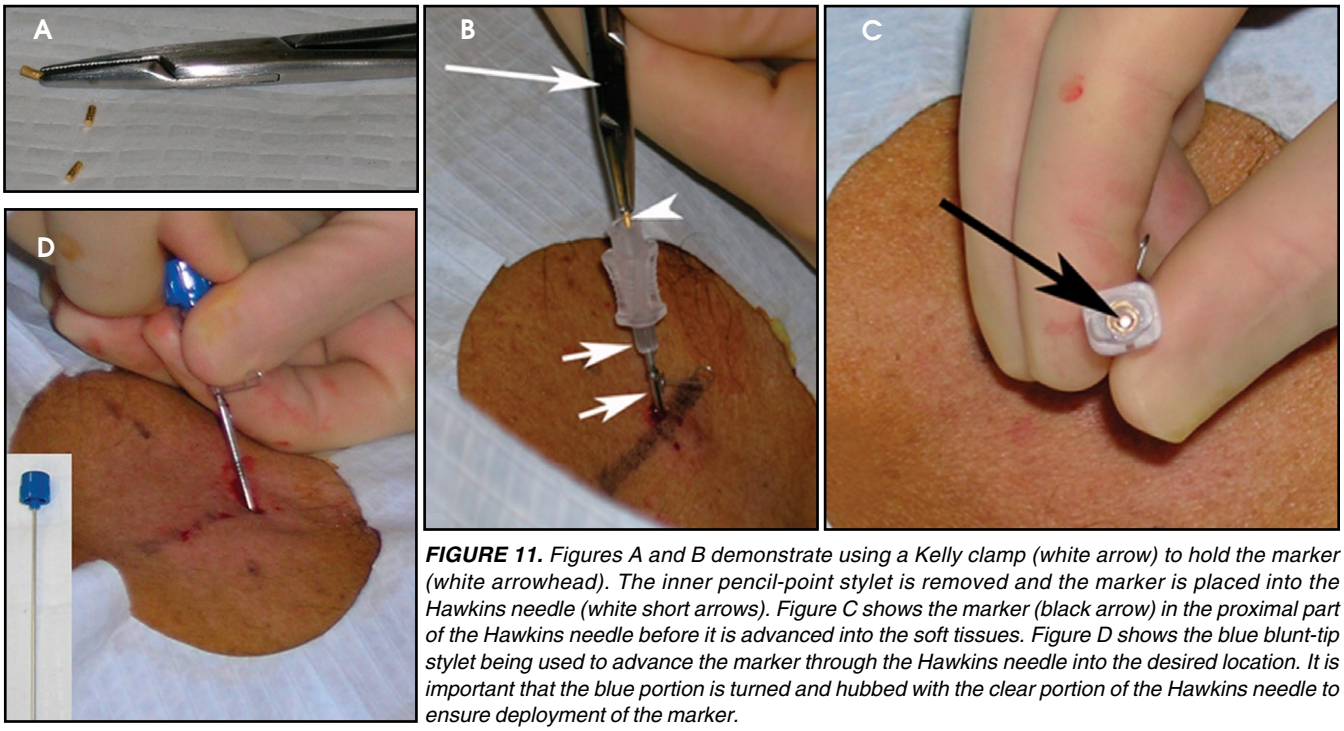


FIGURE 11. *Figures A and B demonstrate using a Kelly clamp (white arrow) to hold the marker (white arrowhead). The inner pencil-point stylet is removed and the marker is placed into the Hawkins needle (white short arrows). Figure C shows the marker (black arrow) in the proximal part of the Hawkins needle before it is advanced into the soft tissues. Figure D shows the blue blunt-tip stylet being used to advance the marker through the Hawkins needle into the desired location. It is important that the blue portion is turned and hubbed with the clear portion of the Hawkins needle to ensure deployment of the marker.*

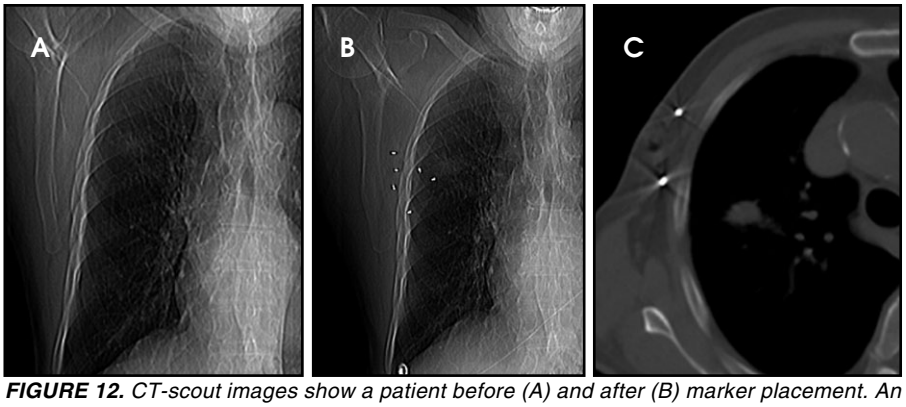


FIGURE 12. *CT-scout images show a patient before (A) and after (B) marker placement. An axial CT image (C) shows markers in the chest wall.*

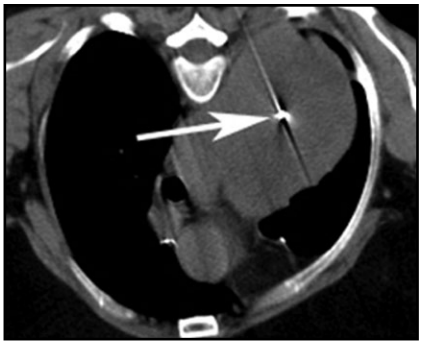


FIGURE 13. *An axial CT image (in the prone position) shows a marker (arrow) placed within the center of a lung mass.*

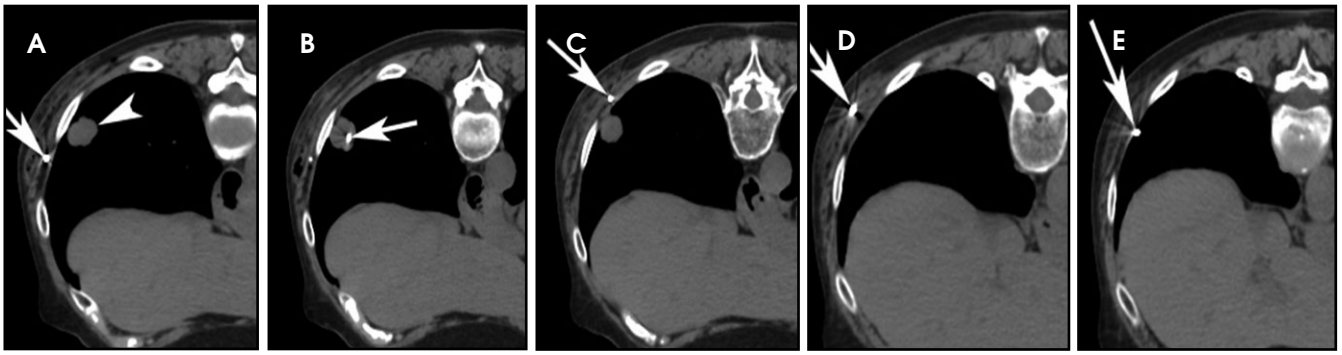


FIGURE 14. *This is an example of proper marker placement. Figures A through E are axial CT images, which are in order superiorly to inferiorly. Five fiducial markers (arrows) have been placed for a lung lesion (arrowhead). One fiducial marker is within the lung lesion, and the others are within the chest wall (extrapleural). Note how the markers are all in different locations with respect to the z-axis (the patient's head-to-toe axis).*

CME

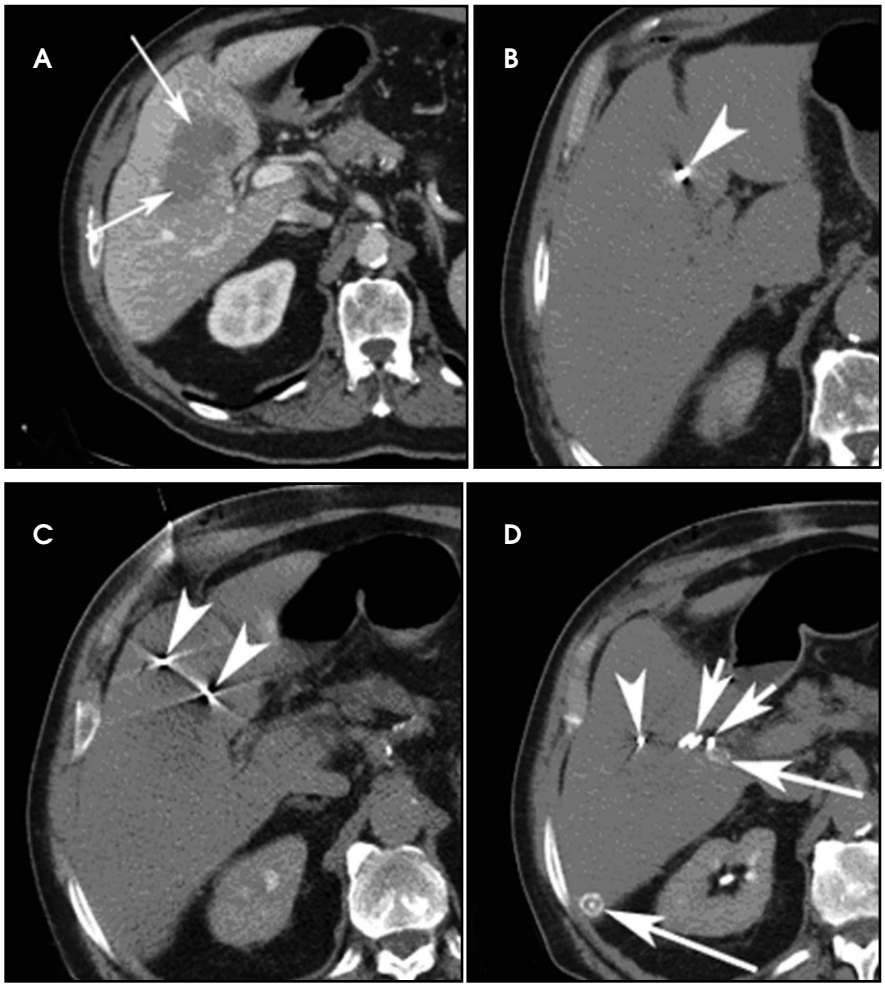


FIGURE 15. *(A) An axial CT image with contrast in the portal venous phase demonstrates a hypodense mass (long, white arrows) in the area of the gallbladder fossa in this patient with known gallbladder carcinoma. Figures B, C, and D demonstrate 4 markers (white arrowheads) within the lesion, as well as bracketing the superior and inferior aspects of the lesion. The patient could not tolerate lying on his back long enough for additional markers to be placed. The white arrows indicate clips in the gallbladder fossa. The long white arrows in D represent calcified gallstones which are loose in the peritoneal cavity.*

are obtained. The patient is prepped and draped in the usual sterile fashion. For local anesthesia, 1% lidocaine is utilized. A small nick is made in the patient's skin (Figure 10). The Hawkins needle with the pencil-point stylet in place is advanced to the desired location and confirmed by CT. Kelly clamps are used to grip the fiducial marker. It is easier to drop the marker into the Hawkins needle if the orientation of the marker is angled slightly with respect to the Kelly clamp (Figure 11). Figures 10 through 12 show a patient with poor pulmonary function tests in whom fiducial markers were placed in the chest wall to avoid a possible pneumothorax.

The pencil-point stylet is removed from the Hawkins needle. Using the Kelly clamp the fiducial marker is positioned and released into the Hawkins needle. Figure 11 shows the above steps with the fiducial marker within the proximal part of the Hawkins needle. The blue blunt-tip stylet is then placed into the Hawkins needle. This pushes the marker to the tip of the

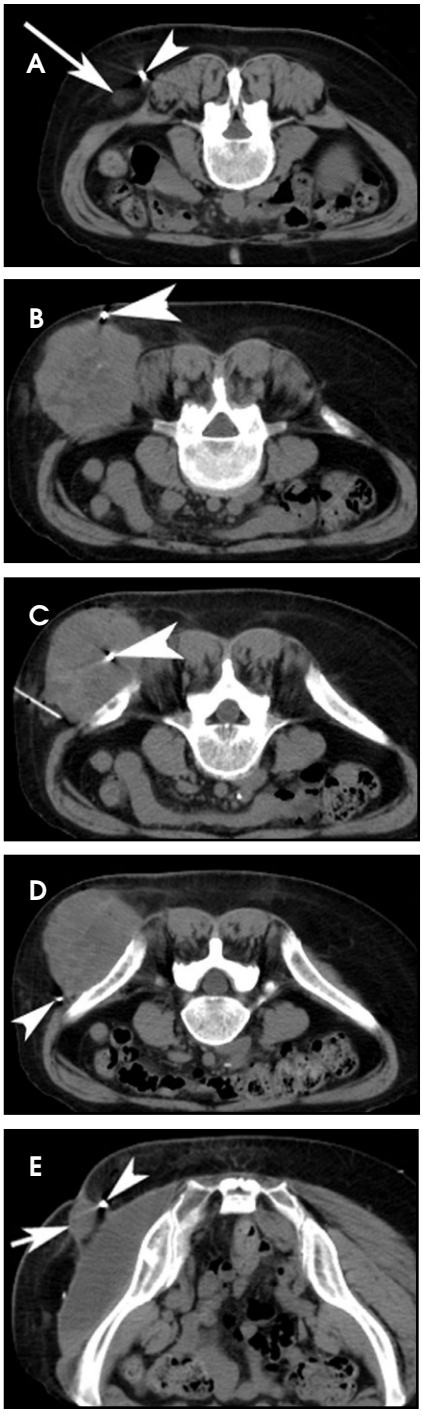


FIGURE 16. *(A to E) Axial CT images from superior to inferior, demonstrate 5 fiducial markers (arrowheads) within the center of the lesion (as seen in image C) as well as bracketing the lesion. The long and short arrows show the superior and inferior aspects of the lesion respectively. There is a seroma adjacent to the iliac bone in Figure E.*

CME

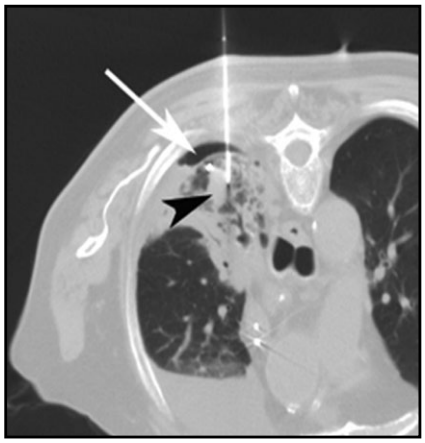


FIGURE 17. *During placement of fiducial markers into and adjacent to the right upper lobe lesion (arrowhead), a small focal pneumothorax (arrow) developed. This was followed with a chest radiograph showing pneumothorax resolution.*

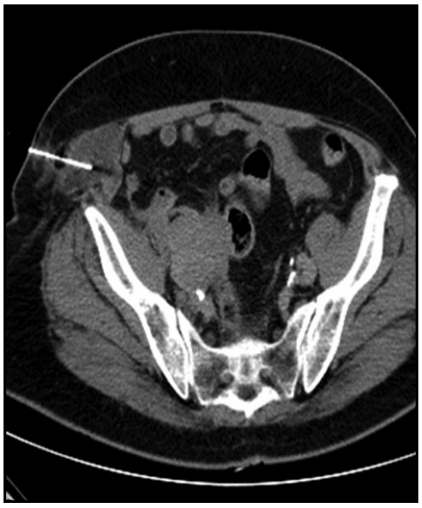


FIGURE 18. *There is a hematoma of the abdominal wall musculature adjacent to the tip of the Hawkins needle.*

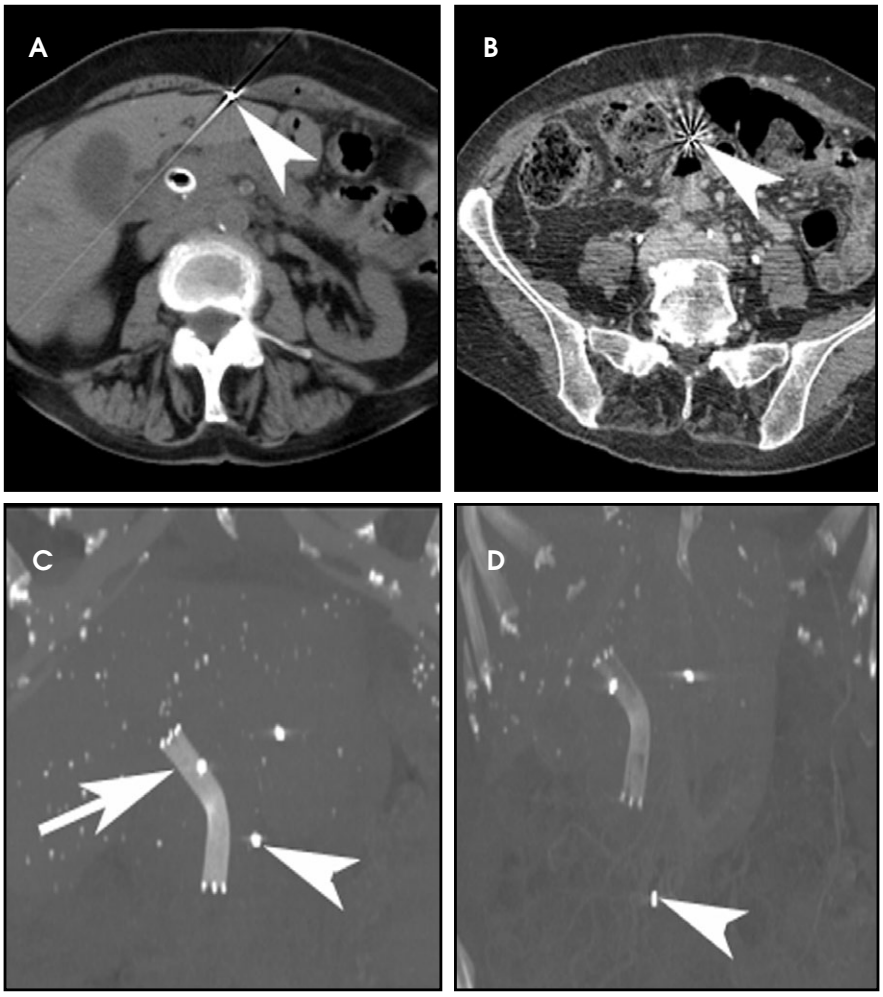


FIGURE 19. *This shows fiducial-marker migration. An axial CT image (A) and corresponding coronal maximum intensity projection (MIP) image (B) show marker location at the time of placement. An axial CT image (C) and corresponding coronal MIP image (D) 8 days later, at the time of the planning CT, show a change in position of the inferior-most marker (arrowheads). The patient has a common bile duct stent (arrow).*

needle. To ensure that the marker exits the needle, the blue blunt-tip stylet should be advanced completely by twisting the luer lock components of the stylet and Hawkins needle until the knob is flush with the needle hub. The needle can be removed at this point, or the pencil-point stylet can be replaced and the needle can be repositioned for additional marker placement. When fiducial marker placement is complete, CT images are obtained showing the location of the markers (Figure 12).

Ideally, 5 or 6 markers should be placed. It is important that they are in different planes along the x-, *y*- and z-axes. If possible, it is optimal to place a marker in the center of the lesion (Figure 13), and then place the other markers around (bracketing) the lesion, so that the isocenter of the markers is the center of the lesion. Sometimes it is not possible, as in the patient presented in Figures 10 through 12, to place a marker in the lesion center, but placing them within 5 cm will still facilitate treatment. Markers placed more than 7 cm from the lesion will likely not be usable. The system uses a small field of view (20 cm). Examples of fiducial placement in the chest, abdomen, and pelvis are shown in Figures 14 through 16.

Monitoring and safety

Patients who have fiducials placed in organs (eg, the liver) are typically observed for 2 hours after the procedure. Patients who have fiducials placed only in the soft tissues (eg, the chest wall) are observed for 1 hour. After this time patients are typically discharged. Patients typically wait 7 to 10 days to allow for "scarring in" of

CME

the fiducial markers before returning for the planning CT. Once the planning CT is performed, the radiation oncologists develop their treatment plan. If fiducial markers migrate between planning and treatment, they will not be usable unless the patient is scanned again and the treatment plan revised.

Complications

In addition to the usual small risks of bleeding and infection with interventional procedures, potential complications include development of a pneumothorax, lidocaine-related patient confusion, and fiducial-marker migration after placement. If a small pneumothorax occurs (Figure 17), the patient can be followed with radiographs to verify resolution. If a clinically significant pneumothorax occurs, a pigtail catheter can be placed. Another possible complication is development of an intramuscular hematoma. Figure 18 shows a hematoma of the abdominal wall musculature (compared to the normal contralateral side). These hematomas typically resolve without intervention. The hematoma can be followed clinically or by CT if necessary.

Fiducial-marker migration describes a change in position of markers either between placement and the therapy-planning CT scan or between the planning CT and actual treatment delivery. An example of marker migration is illustrated in Figure 19. This may also occur when markers are placed in the pleural space,[3] or in an intravascular location, such as an artery, although this is uncommon.[4] Placement of markers in an extrapleural location in the chest wall can help avoid migration. Lidocaine-related patient confusion is another potential complication. It has been our experience that some patients who have received >30 cc of lidocaine can become confused. In most patients, <30 cc is adequate to control patient discomfort.

Conclusion

Stereotactic radiosurgery is an increasingly utilized treatment method. It is important for radiologists performing CT-guided placement of fiducial markers to be able to do so safely and accurately. This article provides the essentials of how the system utilizes fiducial markers, a step-by-step guide on how to perform the procedure, a review of potential complications and what to do when they occur.

References

1. Kothary N, Dieterich S, Louie JD, et al. Percutaneous implantation of fiducial markers for imaging-guided radiation therapy. *AJR Am J Roentgenol.* 2009;192:1090-1096.
2. Saw CB, Chen H, Wagner H Jr. Implementation of fiducial-based image registration in the Cyberknife robotic system. *Med Dosim.* 2008;33:156-160.
3. Kee ST. Fiducial placement to facilitate the treatment of lung lesions with the Cyberknife system. Accuray Incorporated. 2005. *eradiology.* bidmc.harvard.edu/LearningLab/respiratory/Singal.pdf. Accessed on March 30, 2011.
4. Kee ST. Fiducial placement to facilitate the treatment of pancreas and liver lesions with the Cyberknife system. *Accuray Incorporated.* 2005. eradiology.bidmc.harvard.edu/LearningLab/respiratory/Singal.pdf. Accessed on March 30, 2011.
5. Sotiropoulou E, Stathochristopoulou I, Stathopoulos K, et al. CT-guided fiducial placement for Cyberknife stereotactic radiosurgery: An initial experience. *Cardiovasc Intervent Radiol.* 2010;33:586-589.

CME SEE PAGE 5 FOR DETAILS

Integration of modern imaging into the multidisciplinary setting: The radiation oncology perspective

Steven Feigenberg, MD, Christina Campassi, MD, Navesh Sharma, DO, PhD, Susan B. Kesmodel, MD, Katherine Tkaczuk, MD, and Jian Q. Yu, MD, FRCPC

A multidisciplinary approach to cancer diagnosis and treatment is vital to optimize care for the cancer patient. Multidisciplinary cancer management requires coordination among many different specialities involved in cancer care of an individual patient. Participants in this care include physicians from diverse oncology specialties, including surgical oncology, medical oncology, radiation oncology, pathology, radiology, nuclear medicine, genetic counseling, and depending on the tumor type, may also include various others from internal medicine and palliative care. In addition to physicians, there are nurses, nurse practitioners, physician assistants, and oncological nurse specialists that are involved in care, including patient navigators, clinic and research coordinators, and data managers as well as patient advocates and social workers.

Dr. Feigenberg *is an Associate Professor/Director of Clinical Research, Department of Radiation Oncology;* ***Dr. Campassi*** *is an Assistant Professor, Department of Radiology;* ***Dr. Sharma*** *is an Assistant Professor, Department of Radiation Oncology, University of Maryland School of Medicine;* ***Dr. Kesmodel*** *is an Assistant Professor of Surgery, Division of Surgical Oncology, Department of Surgery, Department of Surgical Oncology; and* ***Dr. Tkaczuk*** *is a Professor and Director of the Breast Evaluation and Treatment Program, Department of Medical Oncology, University of Maryland School of Medicine, Baltimore, MD.* ***Dr. Yu*** *is the Chief of Nuclear Medicine/PET, and Associate Professor of Diagnostic Imaging, Fox Chase Cancer Center, Philadelphia, PA.*

Benefits in care are multifactorial, arising from improvements in communication between disciplines leading to more efficient work-ups and decision making, which translates into improved outcomes for patients. To appreciate this point, several investigators have demonstrated that cancer care in a multidisciplinary setting is an independent predictor of improved outcomes. For example, Birchall[1] et al reported on patients with head and neck cancer in England before and after a report by the Calman-Hine Expert Advisory Group on Cancer,[2] recommending that designated cancer units and multidisciplinary care be established. They observed that patients receiving treatment in such a setting had an improved 2-year survival. Similarly, Junor[3] et al showed, in patients with ovarian cancer, that the multidisciplinary setting was an independent predictor for improved 5-year survival (65% versus 81%) compared to treatment outside this setting. Patients with Hodgkin's disease who were treated in a Surveillance, Epidemiology and End Results Program region were found to have 1.5 times higher cancer mortality as compared to patients treated at a Centralized Cancer Center, independent of age or stage of disease, suggesting that the process and quality of care was improved at the Centralized Cancer Centers.[4] These benefits are so convincing that the Commission on Cancer and the American College of Surgeons both require multidisciplinary conferences for the accreditation of health centers delivering multidisciplinary cancer care.[5-8]

One of the major benefits of multidisciplinary care is information sharing between various physicians where literature that is unique to their specialties and perspectives can be discussed, improving clinical care overall. In addition, centralized review of the pertinent patient-specific information, covering medical history, family history, physical exam findings, imaging studies, pathology results, while all cancer care specialists are present in the same conference room, is invaluable to the management of cancer patients and helps with

CME

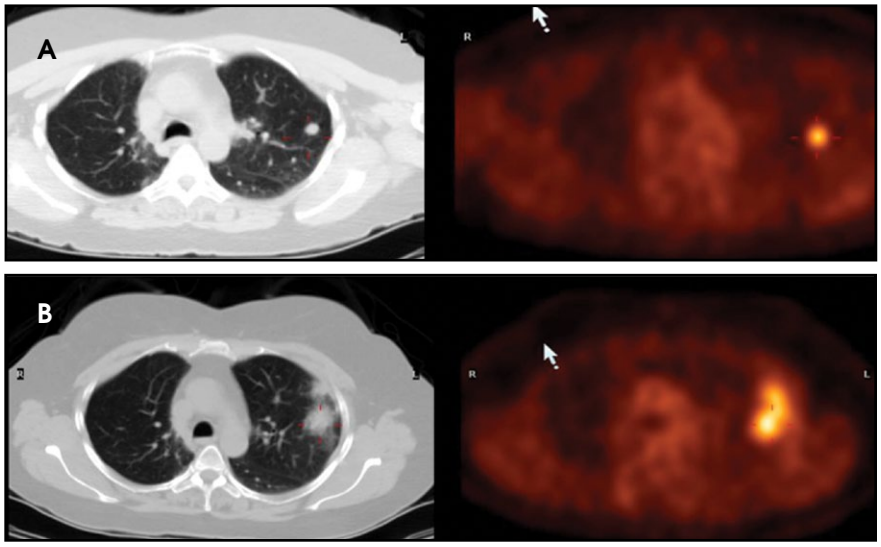


FIGURE 1. *CT and fused PET/CT images (A) pre-SBRT and (B) 3 months post-SBRT. Left upper-lobe lesion appears as patchy consolidation with some surrounding ground-glass opacities, which conformed to the intermediate dose of SBRT.*

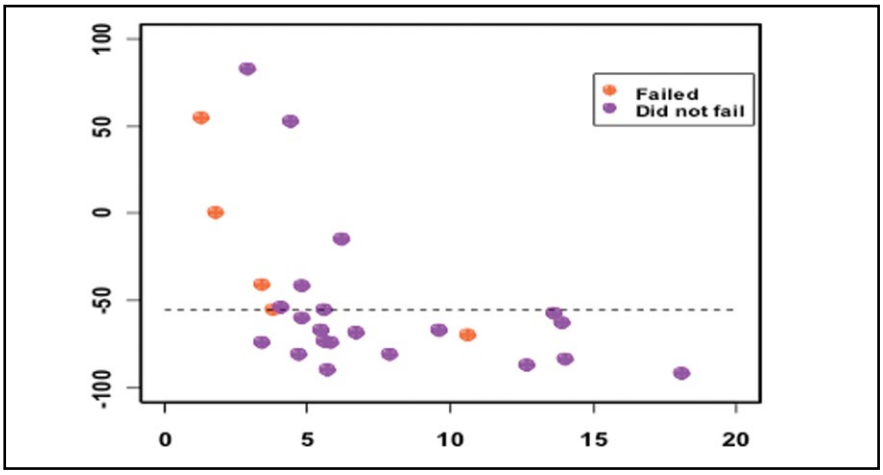


FIGURE 4. *This figure illustrates the response of therapy following SBRT (1 – (3-month post SBRT SUV max /pre SBRT SUV max)) on the y axis compared to the pre-SBRT max SUV. A drop of the 3-month-post-SBRT PET of 55% is the most important predictor of local control.*

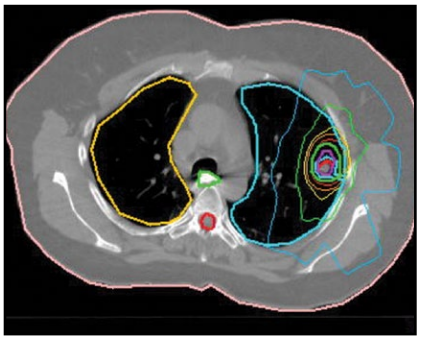


FIGURE 2. *This patient was treated with 5 nonopposing coplanar beams with isodose lines representing 20%, 50%, 90%, 100%, and 105% of the prescription dose.*

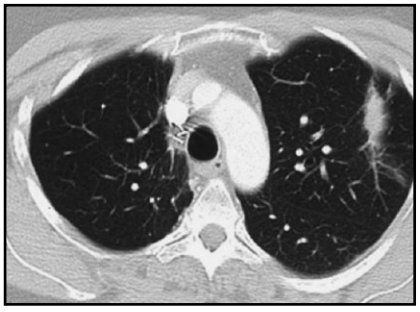


FIGURE 3. *Starting 9 months after radiotherapy, the patchy radiation changes seen 3 months following SBRT became more opaque and stretched in the direction of the dose fall-off as seen in Figure 2 and have remained stable for 5 years following SBRT (radiation fibrosis).*

immediate formulation of the recommendations for further management. Data suggest that multidisciplinary clinics are not just valuable for the participating physicians but also for their medical students, residents, and fellows who learn the value of a collaborative approach to management of complicated cases. The following cases illustrate how a multidisciplinary approach improves care with an emphasis on the impact of diagnostic radiology on cancer care.[9]

Case 1: Lung cancer

Ten years ago, there was no published prospective literature on ablative doses of radiation therapy for lung cancer (see below). Therefore, 2 of the authors of the current manuscript, Drs. Feigenberg and Yu, developed and opened a phase I dose escalation study[10] testing this novel technique, which had previously been successful in the management of inoperable brain tumors. As part of this study, the use of fluoro-deoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) was incorporated into the treatment paradigm for patients with curable disease, with the specific purpose to use PET as a potential early biomarker for treatment response similar to what others had published in the setting of locally advanced disease.[11] As is often the case in phase I studies, this patient's situation created a clinical dilemma.

The patient was a young woman with lung cancer. Her first follow-up CT scan following trimodality therapy showed a new spiculated mass that was biopsied and demonstrated a second primary nonsmall cell lung cancer. She had just recovered from a lobectomy and did not feel she could undergo

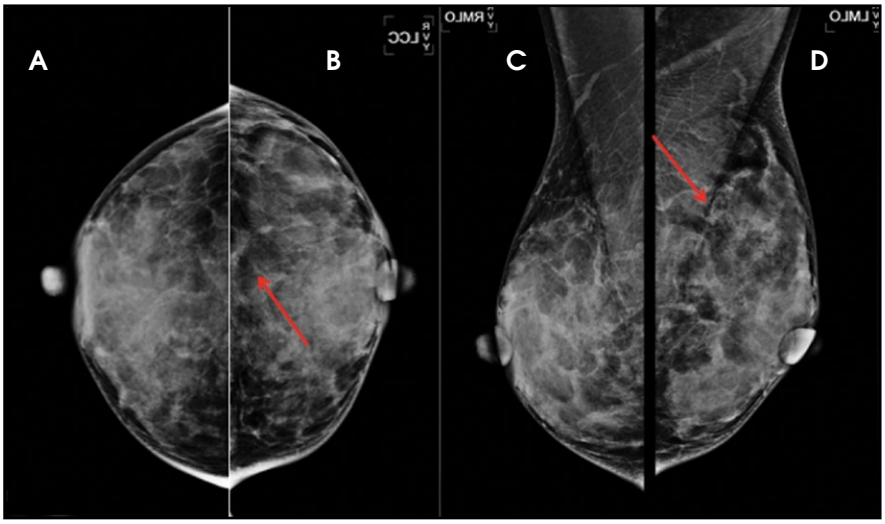


FIGURE 5. *40-year-old woman presenting for baseline screening mammogram. No family history of breast cancer or other risk factors for breast cancer. (A and B) Mammographic craniocaudal and (C and D) medio-lateral-oblique projections demonstrate extremely dense breasts with bilateral scattered and grouping calcifications with asymmetric distribution. The calcifications are more numerous in the left upper-outer quadrant and at 12 o'clock position in the left breast (B and D with arrow). No discrete mass or adenopathy is identified. BIRADS assessment category 0: additional magnification views of left breast recommended.*

further surgery. She was offered a novel treatment using stereotactic body radiotherapy (SBRT) on a phase I protocol as an alternative to a 7-week course of conventionally fractionated radiotherapy, which was the standard treatment at that time. She tolerated the SBRT treatment uneventfully, feeling well with no symptoms, and returned for her first post-therapy PET scan 3 months later as per the study protocol. At that time, images were not available in clinic, but the report was. The report read, "When compared to the last study dated 6/7/04, there has been a marked interval increase in the size of the previously noted left-upper lobe pulmonary nodule as well as increased intensity of FDG uptake in the area. The nodule has markedly increased in size and now extends out towards the pleural surface. The previous maximum standard uptake value (SUV) of 4.4 has increased to 6.7. This suggests that there has been no significant response to radiation therapy with progression of tumor growth."

As this was a medically operable patient, it was vital to review her images to determine further management. Her case was presented in conference, and it became glaringly obvious that the imaging findings were not as suspicious as the report indicated. Figure 1 demonstrates CT lung windows and the corresponding FDG PET prior to and 3 months' post-SBRT. Radiographic changes appeared as patchy consolidation with some surrounding ground-glass opacities as opposed to a solid mass-like lesion.

Dr. Feigenberg discussed the "new" treatment technique with his colleagues and demonstrated the differences in how the radiation dose could be delivered using many unique nonopposing coplanar and noncoplanar beams (Figure 2). This approach can cause a difference in the appearance of radiation pneumonitis that will more precisely conform to the tumor and will not have straight edges, typically seen using 2 opposing beams as was the standard approach.

Based on this factor, it was believed this abnormal PET finding was caused by an asymptomatic pneumonitis. It was recommended that surveillance be continued as opposed to any further intervention. Over time, the radiographically abnormal region became linear and denser, stretching in the direction of the radiation dose fall-off. This dense consolidation has remained stable for 5 years (Figure 2). This initial interaction led to several meaningful peer-reviewed presentations[10, 12, 13] and publications describing the importance of pre-SBRT PET values, post-SBRT PET values, and changes in PET values over the course of therapy (Figure 3). These findings are critical as this novel therapeutic radiation approach is currently challenging the paradigm of surgery[14] as standard of care for early stage lung cancer. This was the first data to illuminate concern of false positive results caused by radiation pneumonitis as well as the predictive value of a drop of the maximum SUV of 50%, required to ensure long-term local control.

Patient case 2: Breast cancer

Our multidisciplinary (multiD) Breast Cancer (BC) conference is held weekly before the multidisciplinary clinic and includes participants from all specialties involved in management. All newly diagnosed BC cases are presented, and pathology and imaging findings are discussed initially followed by preliminary workup and treatment recommendations. Patients are then seen on the same day in the multidisciplinary clinic held immediately after the conference by the 3 primary cancer specialists—surgical oncology, medical oncology, and radiation oncology. The recommendations are then made same day; the benefit of seeing newly diagnosed BC patients on the same day of the multiD conference is that the team can rapidly implement recommendations for further work-up if deemed necessary. In addition, the group can still consider the case or review the medical history and clinical findings given mutual accessibility at the same location.

CME

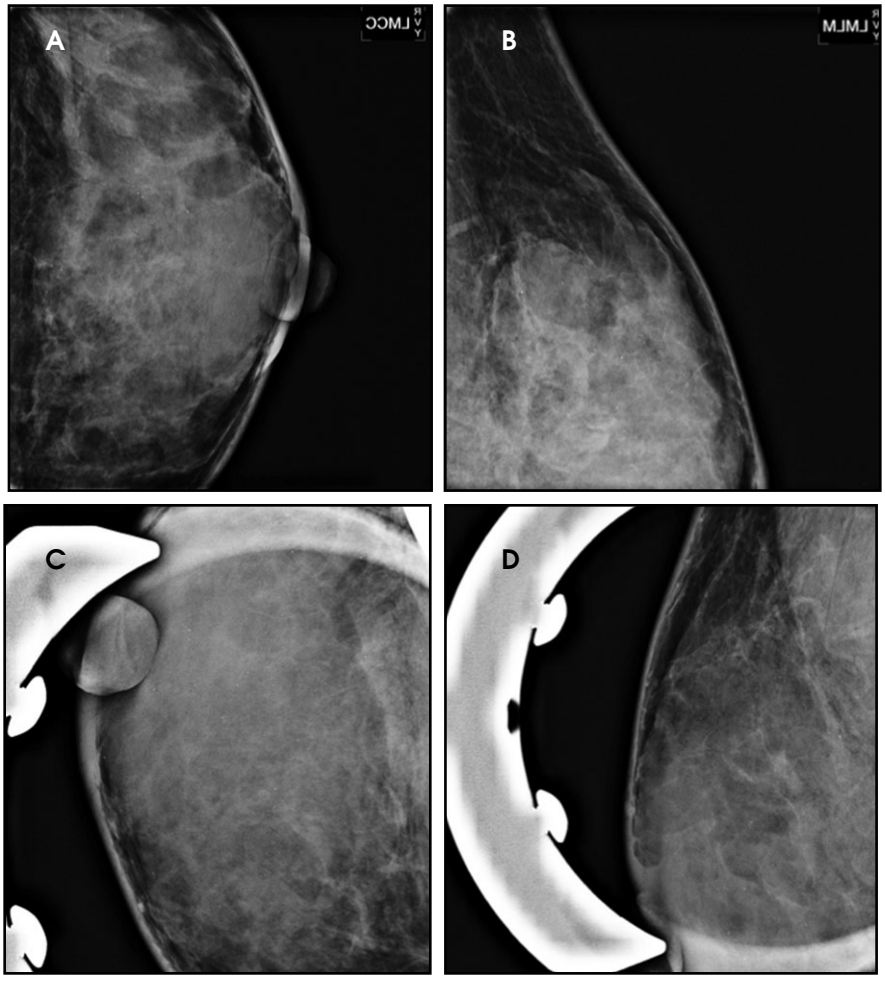


FIGURE 6. *Diagnostic mammogram: (A) Global magnification cranio-caudal and (B) latero-medial views of the upper outer left breast show multiple clusters of coarse heterogeneous, punctate, and amorphous calcifications. (C) Global magnification cranio-caudal and (D) latero-medial views of the right breast demonstrate diffuse scattered and grouped coarse, punctate and amorphous calcifications with no evidence of suspicious calcifications. BIRADS assessment Category 4: Suspicious finding. Stereotactic guided biopsy of the left breast recommended. Six-month follow-up of right breast calcifications recommended.*

The additional benefit to the patients is that they are seen by the 3 primary cancer specialists on one day and do not have to make several trips to be re-evaluated. Often patients are not aware that the management of BC may require treatments after surgery with radiation to the breast, hormonal therapy, and/or chemotherapy. These basic concepts of management of early-stage BC can also be introduced to the patients during their first visit to the multiD clinic.

The following case demonstrates many interactions between disciplines that are vital to patient care. A 40-year-old woman, with no known risk factors for breast cancer, presented for a baseline mammogram. This mammogram showed dense breasts with bilateral scattered and grouped calcifications with an asymmetric distribution, more numerous in the upper outer quadrant (Figure 5). The test was interpreted as incomplete, requiring additional evaluation with dedicated magnification views. When the patient returned for the additional diagnostic work-up, the morphology of the left breast calcifications was found to be suspicious, while the right breast calcifications were categorized as probably benign (Figure 6). Of note was that the breast thickness under mammographic compression was only 2.5 cm, usually a limiting factor to performing a needle biopsy under stereotactic guidance. The radiologist informed the patient of the results and need for biopsy. The patient was referred to the multidisciplinary breast clinic for further evaluation and discussion of treatment options.

Her case was presented to the multidisciplinary panel (breast imaging, breast surgery, medical oncology, radiation oncology, and breast pathology). Based on the imaging findings, the options of stereotactic-guided core and excisional biopsy were discussed. The patient elected to undergo a stereotactic-guided approach with the pathology demonstrating extensive atypical ductal hyperplasia. The case was discussed again in the multidisciplinary conference. Due to the presence of extremely dense breast tissue,[15, 16] an independent risk factor for breast cancer on mammogram, the patient's young age, and the newly diagnosed high-risk lesion, a breast MRI with gadolinium was recommended.

MRI demonstrated a 1-cm highly suspicious spiculated mass at the 12 o'clock position of the left breast and markedly asymmetric background parenchymal enhancement of the left breast compared to the right. Additionally, a nonspecific 1-cm left axillary node was also noted on MRI (Figure 7). The breast MRI was interpreted as suspicious. An ultrasound of the breast and the axilla confirmed the presence of 2 breast tissue abnormalities at 12 o'clock, believed to be highly suspicious for malignancy (Figure 8). The axillary node had a nonspecific appearance on ultrasound. The patient underwent biopsy of both masses and an ultrasound-guided fine-needle aspiration of the left axillary node. The larger 9-mm mass was an invasive ductal carcinoma, the smaller 8-mm mass was

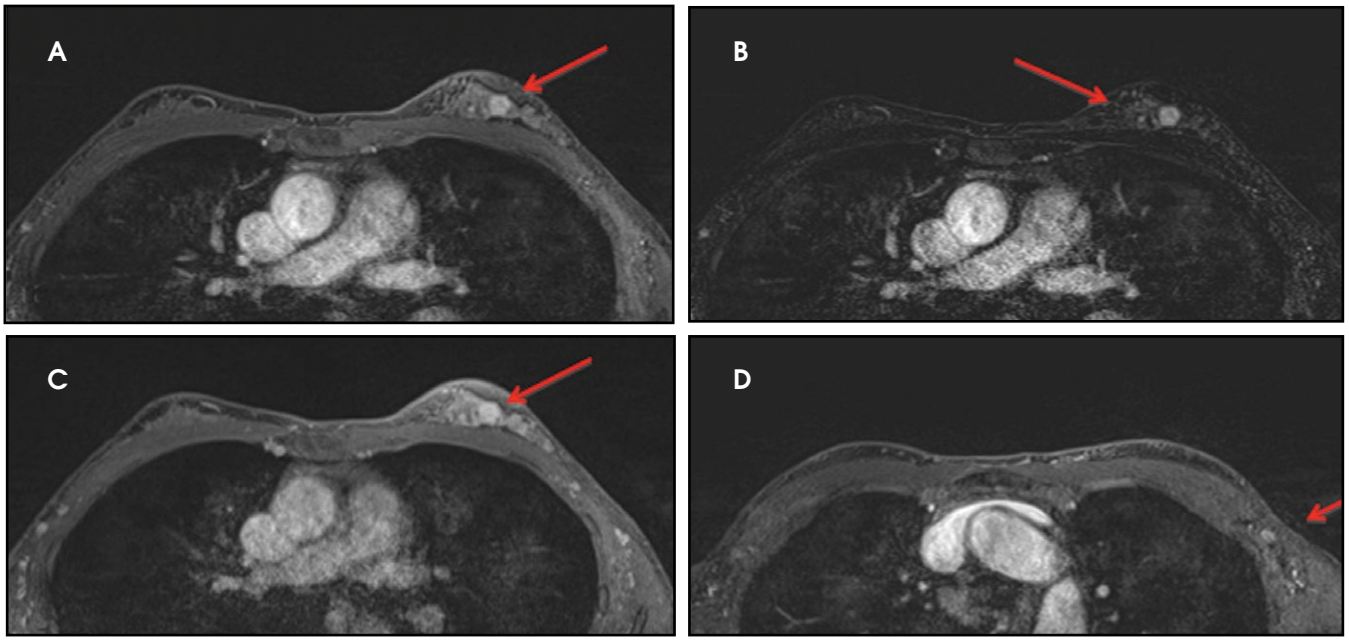


FIGURE 7. *Bilateral breast MRI: Preoperative breast MRI is requested by the surgeon as the patient is high risk due to extremely dense breasts and atypical ductal hyperplasia on core needle biopsy. (A) Axial fat-suppressed T1W and (B) corresponding subtracted image of the dynamic series is shown at first time point obtained 30 sec after injection of gadolinium based contrast. (C) High resolution axial T1W fat-suppressed image of the same image is shown 180 sec after injection of contrast. (D) Axial T1W fat-suppressed image of the axillary region is shown at the first time point. The background parenchymal enhancement is markedly asymmetric, being minimal on the right and moderate on the left (B with arrow). A highly suspicious 1-cm spiculated enhancing mass is noted at 12 o'clock position in the left breast (A with arrow) with no associated enhancement of the pectoral muscle or chest wall to suggest invasion. Correlation with mammogram (Figures 5A and 5B) demonstrates that this mass is in the vicinity of a cluster of suspicious calcifications noted on mammography. The mass demonstrates initial rapid enhancement and subsequent plateau enhancement (A and C). One left axillary lymph node demonstrates a mildly thickened cortex (D with arrow). No abnormal enhancement of the right breast or additional focal abnormal enhancement of the left breast or right axillary or internal mammary chain adenopathy is noted. BIRADS Assessment Category 5: Highly suspicious for malignancy. Recommendation: Left breast and axillary ultrasound and imaging-guided biopsy of the highly suspicious left breast mass.*

ductal carcinoma in situ, and the lymph node was positive for metastasis.

The patient was brought back to the multidisciplinary conference for a third time, where it was determined that the patient was not a good candidate for breast conservation due to the small size of her breast and a challenge for follow up due to diffuse calcifications and multifocal disease. Further discussion of the literature ensued regarding the possible need for radiotherapy and the role of a lymph node dissection.[17, 18] Delayed breast reconstruction[19, 20] was recommended to decrease the risks of loss of the implant due to encapsulation as compared to patients who undergo immediate reconstruction. Lastly, the role of axillary dissection was discussed. The recently conducted MRI evaluated the role of axillary dissection following positive sentinel lymph node biopsy[17]. The data were convincing that outcomes are not compromised by withholding dissection, although patients received radiotherapy to the whole breast, which indirectly also treats the majority of the axilla. [21, 22] In this case, since the patient was not going to receive radiotherapy following her mastectomy, an axillary dissection was recommended.

Patient case 3: Hepatocellular carcinoma

This case illustrates another example of how multiple disciplines were able to work together to convert an "incurable patient" to a "potentially curable patient." Orthotopic liver transplant (OLT)[23] is the only realistic curative treatment for patients with chronic hepatitis who are found to have hepatocellular carcinoma (HCC).

In May 2010, a 56-year-old man was diagnosed with HCC in the setting of chronic hepatitis C infection. At an outside institution, the patient was thought to have a solitary 4-cm ill-defined posterior lesion in the left lobe of the liver amenable to OLT. His alpha fetoprotein (AFP) level at presentation was 1500 ng/ml. While a transplant evaluation was being pursued, chemoembolization was performed twice in order to downstage the patient, producing a drop in AFP level to117 ng/ml, but the level rose to 566 ng/ml within 3 weeks. After transfer to the authors' institution, MRI with contrast demonstrated a cirrhotic liver with

CME

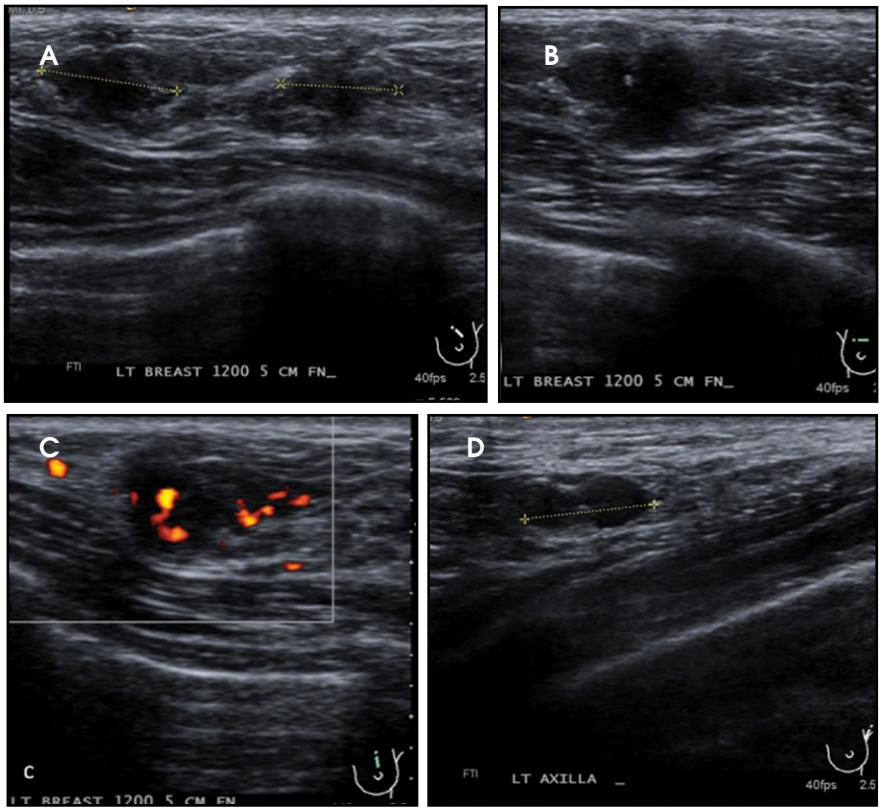


FIGURE 8. *Left breast and left axillary ultrasound. (A) Two contiguous similarly hypoechoic irregular solid masses are noted at 12 o'clock (calipers). Each mass is subcentimeter, measuring 9mm and 8mm. (B) The dominant 9-mm mass corresponds to the highly suspicious mass seen on MRI (Figures 7A - C) and (C) demonstrates significant vascularity. The second similar smaller 8-mm mass corresponds to confluent enhancing foci on MRI. (D) Ultrasound of the left axilla demonstrates the 9-mm lymph node with thickened cortex noted on MRI and is categorized as suspicious. Overall, the BIRADS assessment is confirmed as category 5, highly suspicious for malignancy. Recommendation: Ultrasound-guided core-needle biopsy of both masses and ultrasound-guided fine-needle aspiration of the left axillary lymph node.*

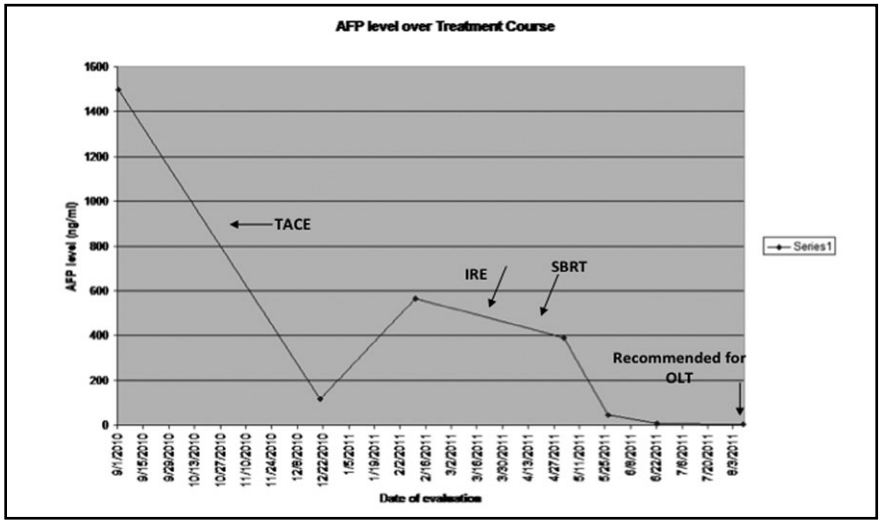


FIGURE 10. *AFP level with critical treatment milestones.*

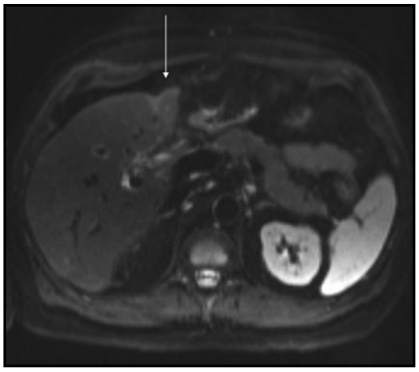


FIGURE 9. *First post-IRE/SBRT MRI scan demonstrating left lobe atrophy (arrow).*

multifocal enhancing masses in hepatic segment IV consistent with persistent HCC. In addition, there was a suggestion of tumor invasion and thrombosis of the left portal vein excluding him from OLT. Due to his overall excellent performance status, his case was discussed at the multidisciplinary hepatobiliary tumor board and "spirited" discussions among the present medical, surgical, radiation oncologists, interventional and diagnostic radiologists ensued. Due to the size of the lesion, all single-modality therapies were thought to have poor local control potential so a combination therapy was considered as the best method to potentially eradicate the large residual tumor. This approach entailed targeting the tumor through a combination of irreversible electroporation (IRE)[22, 23] performed by interventional radiology, followed by SBRT[24, 25] performed by radiation oncology. The rationale for this approach was to get a direct tumoricidal effect through IRE[24, 25] initially, and to then cover the core and periphery (including the portal vein component) of the ablated region with high-dose SBRT.[26, 27]

The patient underwent CT-guided IRE on 3/22/2011 and tolerated his treatment well. Subsequently, the patient underwent 4-dimensional simulation (to account for tumor movement with the respiratory cycle) and a 5-fraction treatment of 6 Gy each was delivered to a large portion of the left lobe.

The total dose of 30 Gy was administered over a 9-day period ending on 4/20/11, also tolerated well by the patient. A repeat MRI on 5/16/2011 demonstrated interval atrophy of the left lobe (Figure 9) with no residual enhancement and consistent with tumor regression/resolution. AFP levels (measured in ng/ml) continued to drop to 390.8 on 5/2/11, 44.7 on 5/26/11, 6.6 on 6/22/11, and 4.8 on 8/8/11 (Figure 10).

Restaging PET and bone scans along with subsequent MRI studies continued to demonstrate no further abnormal activity compatible with disease recurrence. The patient was again presented to the multidisciplinary hepatobiliary tumor board in September. Given the dramatic decline in AFP levels without evidence of recurrent or metastatic HCC, the patient was reconsidered for OLT and was subsequently placed back on the active transplant list.

References

1. Birchall M, Bailey D King P. Effect of process standards on survival of patients with head and neck cancer in the south and west of England. *Br J Cancer.* 2004;91:1477-1481.
2. Calman K, Hine D. A policy framework for commissioning cancer services: A report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. UK Department of Health http://www.dh.gov.uk/assetRoot/04/01/43/66/04014366.pdf
3. Junor EJ, Hole DJ, Gillis CR. Management of ovarian cancer: Referral to a multidisciplinary team matters. *Br J Cancer.* 1994;70:363-370.
4. Davis S, Dahlberg S, Myers MH, et al. Hodgkin's disease in the United States: A comparison of patient characteristics and survival in the Centralized Cancer Patient Data System and the Surveillance, Epidemiology, and End Results Program. *J Natl Cancer Inst. 1987;*78:471-478.
5. Nyquist JG, Radecki SE, Gates JD, Abrahamson S. An educational intervention to improve hospital tumor conferences. *J Cancer Educ.* 1995;1:71-77.
6. Nyquist JG, Gates JD, Radecki SE, Abrahamson S. Improving the educational process of cancer case conferences. *Acad Med.* 1992;67:S1-3.
7. Nyquist JG, Gates JD, Radecki SE, Abrahamson S. Investigation into the educational process of cancer case conferences. *Acad Med.* 1990; 65:S35-36.
8. Petty JK, Vetto JT. Beyond doughnuts: Tumor board recommendations influence patient care. *J Cancer Educ.* 2002;17:97-100.
9. Macaskill EJ, Thrush S, Walker EM, Dixon JM. Surgeons' views on multi-disciplinary breast meetings. *Eur J Cancer.* 2006;42:905-908.
10. Cohen RJ, Sharma N K, Yu JQ, et al. A phase I radiation dose escalation trial of stereotactic body radiotherapy for malignant lung tumors. *J Biomed Sci Eng.* 2010;3:351-358.
11. Hicks R J, Kalff V, MacManus MP, et al. The utility of (18)F-FDG PET for suspected recurrent non-small cell lung cancer after potentially curative therapy: Impact on management and prognostic stratification. *J Nucl Med.* 2001 42:1605-1613.
12. Sharma NK, Ruth K, Konski AA, et al. Low morbidity and excellent local control using image guided stereotactic body radiotherapy (IGSBRT) for lung tumors. *Int J. Radiat Oncol Bio Phys.* 2008;72:S454.
13. Husain ZA, Sharma NK, Hanlon AL, et al. Low pretreatment PET SUV predicts for increased local failure following stereotactic body radiation therapy for lung cancer. *Int J. Radiat Oncol Bio Phys.* 2010;78:S525.
14.Timmerman R D. Surgery versus stereotactic body radiation therapy for early-stage lung cancer: Who's down for the count? *J Clin Oncol.* 2010;28:907-909.
15. Sardanelli F, Giuseppetti GM, Panizza P, et al. Sensitivity of MRI versus mammography for detecting foci of multifocal, multicentric breast cancer in fatty and dense breasts using the whole-breast pathologic examination as a gold standard. *AJR Am J Roentgenol.* 2004;183:1149-1157.
16. Biglia N, Bounous VE, Martincich L, et al. Role of MRI (magnetic resonance imaging) versus conventional imaging for breast cancer presurgical staging in young women or with dense breast. *Eur J Surg Oncol. 2001;*37:199-204.
17. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: The American College of Surgeons Oncology Group Z0011 randomized trial. *Ann Surg.* 2010;252: 426-432.
18. D'Angelo-Donovan DD, Dickson-Witmer D, Petrelli NJ. Sentinel lymph node biopsy in breast cancer: A history and current clinical recommendations. *Surg Oncol.* 2012 epub ahead of print.
19. Lee BT, A Adesiyun T, Colakoglu S, et al. Postmastectomy radiation therapy and breast reconstruction: An analysis of complications and patient satisfaction. *Ann Plast Surg.* 2010; 64:679-683.
20. Christante D, Pommier SJ, Diggs BS, et al. Using complications associated with postmastectomy radiation and immediate breast reconstruction to improve surgical decision making. *Arch Surg.* 2010;145:873-878.
21. Haffy BG, Hunt KK, Harris JR, Bucholz TA. Positive sentinel nodes without axillary dissection: Implications for the radiation oncologist. *J Clin Oncol.* 2011;29:4479-4481.
22. SchlembachPJ, Buchholz TA, Ross MI, et al. Relationship of the sentinel and axillary level I-II lymph nodes to tangential fields used in breast irradiation. *Int J Radiat Oncol Biol Phys.* 2001;51:671-678.
23. Schwartz, M. E. Primary hepatocellular carcinoma: Transplant versus resection. *Semin Liver Dis.* 1994;14:135-139.
24. Guo Y, Zhang Y, Klein R, et al. Irreversible electroporation therapy in the liver: Longitudinal efficacy studies in a rat model of hepatocellular carcinoma. *Cancer Res.* 2010; 70:1555-1563.
25. Pech M, Janitzky A, Wendler JJ, et al. Irreversible electroporation of renal cell carcinoma: A first-in-man phase I clinical study. *Cardiovasc Intervent Radiol.* 2011;34:132-138.
26. Lo SS, Dawson LA, Kim EY, et al. Stereotactic body radiation therapy for hepatocellular carcinoma. *Discov Med.* 2010;9:404-410.
27. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. *J Clin Oncol.* 2008;26:657-664.

CME SEE PAGE 5 FOR DETAILS

Wanted: Dead or alive? Distinguishing radiation necrosis from tumor progression after stereotactic radiosurgery

Abigail L. Stockham, MD, Samuel T. Chao, MD, and John H. Suh, MD

CASE SUMMARY

A 41-year-old woman with a history of melanoma 8 years prior to presenting was diagnosed with a right frontal brain metastasis measuring 1.0 × 1.0 × 0.9 cm (Figure 1). She underwent whole-brain radiotherapy to 37.5 Gy in 15 fractions followed by Gamma Knife stereotactic radiosurgery (SRS) (Figure 2).

The lesion initially regressed, reaching its minimum size 7 months after SRS (Figure 3). Routine imaging at 10 months following SRS demonstrated enlarged contrast enhancement at the treatment site with extension into the left frontal lobe (Figure 4). Despite 2 courses of dexamethasone over 8 months, the lesion enlarged to more than twice its original size (Figure 5). Fluorodeoxyglucose positron emission tomography (FDG-PET), diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC), and perfusion imaging were obtained (Figure 5). The patient was never symptomatic.

Resection of the lesion for diagnosis and management was performed 18 months after SRS. The patient is currently without evidence of active disease 43 months after initial SRS.

Dr. Stockham *is a Resident in the Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic;* ***Dr. Chao*** *is Assistant Professor of Radiation Oncology, The Rose Ella Burkhardt Brain Tumor Neuro-oncology Center, Cleveland Clinic; and* ***Dr. Suh*** *is Professor and Chairman of Radiation Oncology and Associate Director of Gamma Knife Radiosurgery, The Rose Ella Burkhardt Brain Tumor Neuro-oncology Center, Cleveland Clinic, Cleveland, OH.*

IMAGING FINDINGS

Initial axial T1 contrast-enhanced magnetic resonance imaging (MRI) of the brain demonstrated a 1-cm right frontal lesion (Figure 1) consistent with brain metastasis. At 10 months post-SRS, axial T1 contrast-enhanced MRI showed punctate enhancement, suggesting excellent response to treatment (Figure 3). One month later, axial T1 contrast-enhanced MRI demonstrated interval enlargement of the enhancing area (Figure 4). At 16 months post-SRS, axial T1 contrast-enhanced MRI demonstrated an increase in the size of the treated lesion to more than twice the pretreatment area (Figure 5). Additional imaging was obtained to distinguish radiation necrosis from tumor recurrence. Advanced imaging techniques included relative cerebral blood volume MRI (rCBV) and DWI with associated ADC, which showed no decrease in diffusion (Figure 5). Metabolic imaging with FDG-PET demonstrated focal photopenia with decreased FDG uptake in the anterior right frontal lobe consistent with radiation changes (Figure 5).

DIAGNOSIS

Differential diagnosis included radiation necrosis, tumor progression, or mixed radiation necrosis and tumor progression. Histopathology at the time of resection demonstrated radiation necrosis with no evidence of recurrent tumor (Figure 6).

DISCUSSION

Each year, approximately 170,000 cancer patients develop brain metastases.[1] The current paradigm for treatment of brain metastases often includes SRS, particularly for patients with 3 or fewer lesions all <4 cm, with good performance status.[2] The most serious side effect of SRS is radiation necrosis. Asymptomatic radiation necrosis occurs in an unknown number of patients, but some reports suggest that up to 50% of patients demonstrate radiographic changes consistent with radiation necrosis. Clinical, or symptomatic, radiation necrosis may occur in up to 14% of patients.[3] The duration and severity of symptoms associated with radiation

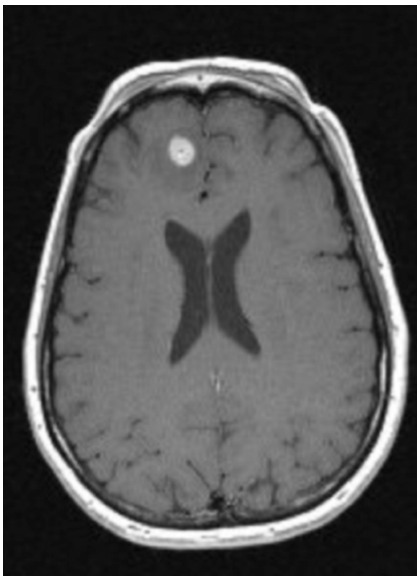


FIGURE 1. *Axial T1 contrast-enhanced MRI demonstrating a single 1-cm ring-enhancing metastasis in the right frontal lobe.*

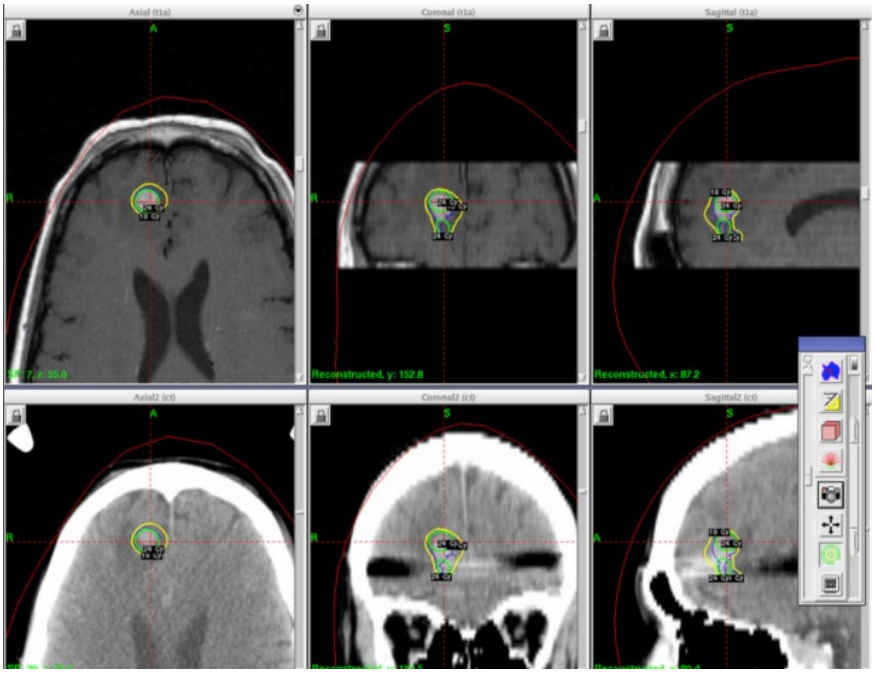


FIGURE 2. *SRS treatment plan for 18 Gy prescribed to the 53% isodose line, which covered 100% of the target. The plan utilized 6 shots using 8-mm and 4-mm helmets, with some of the sectors blocked. Target volume was 1 cm^3. The maximum dose was 34.7 Gy, maximum diameter was 2.4 cm, heterogeneity index (maximum dose/peripheral dose) was 1.928, and conformity index (prescription isodose volume/target volume) was 2.200.*

necrosis vary from a stable, asymptomatic clinical picture of limited duration to a rapidly progressive, lethal course.

The gold standard for diagnosing radiation necrosis is histopathology. To provide an accurate, noninvasive way to distinguish radiation necrosis from tumor progression, standard series MRI scans have been evaluated using characteristic imaging findings, such as "T1/T2 mismatch," or the ratio of the area of a discreet nodule on T2-weighted axial MRI to the area of a discreet nodule on T1 contrast-enhanced axial MRI, with mixed results.[4-6]

Advanced imaging techniques with DWI with ADC mapping, single photon emission computed tomography (SPECT), MR spectroscopy, PET with FDG and other novel radiotracers, and perfusion imaging (perfusion CT and perfusion MRI) have varying degrees of sensitivity and specificity for radiation necrosis and tumor recurrence (Table 1).[6-10] Standard series

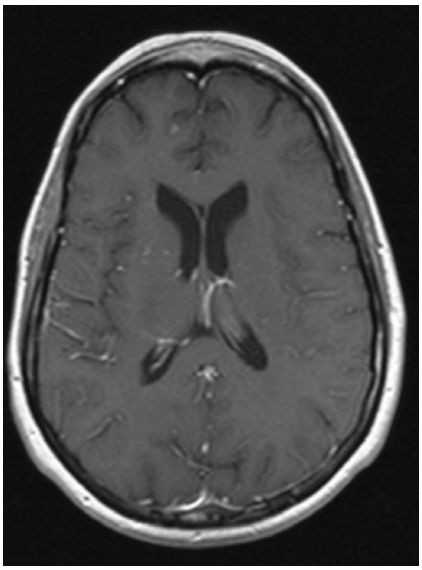


FIGURE 3*. At 10-months, post-SRS the treated right frontal lobe lesion is seen as an area of punctate enhancement in the right frontal lobe.*

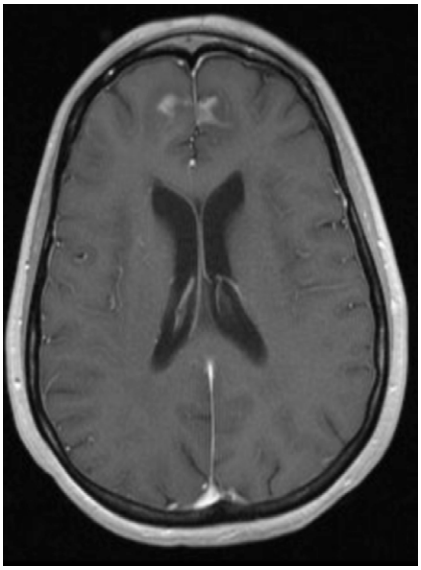


FIGURE 4. *Routine imaging at 11-months post-SRS demonstrated wispy enhancement on this axial T1 contrast-enhanced axial MRI. The patient was started on dexamethasone.*

CME

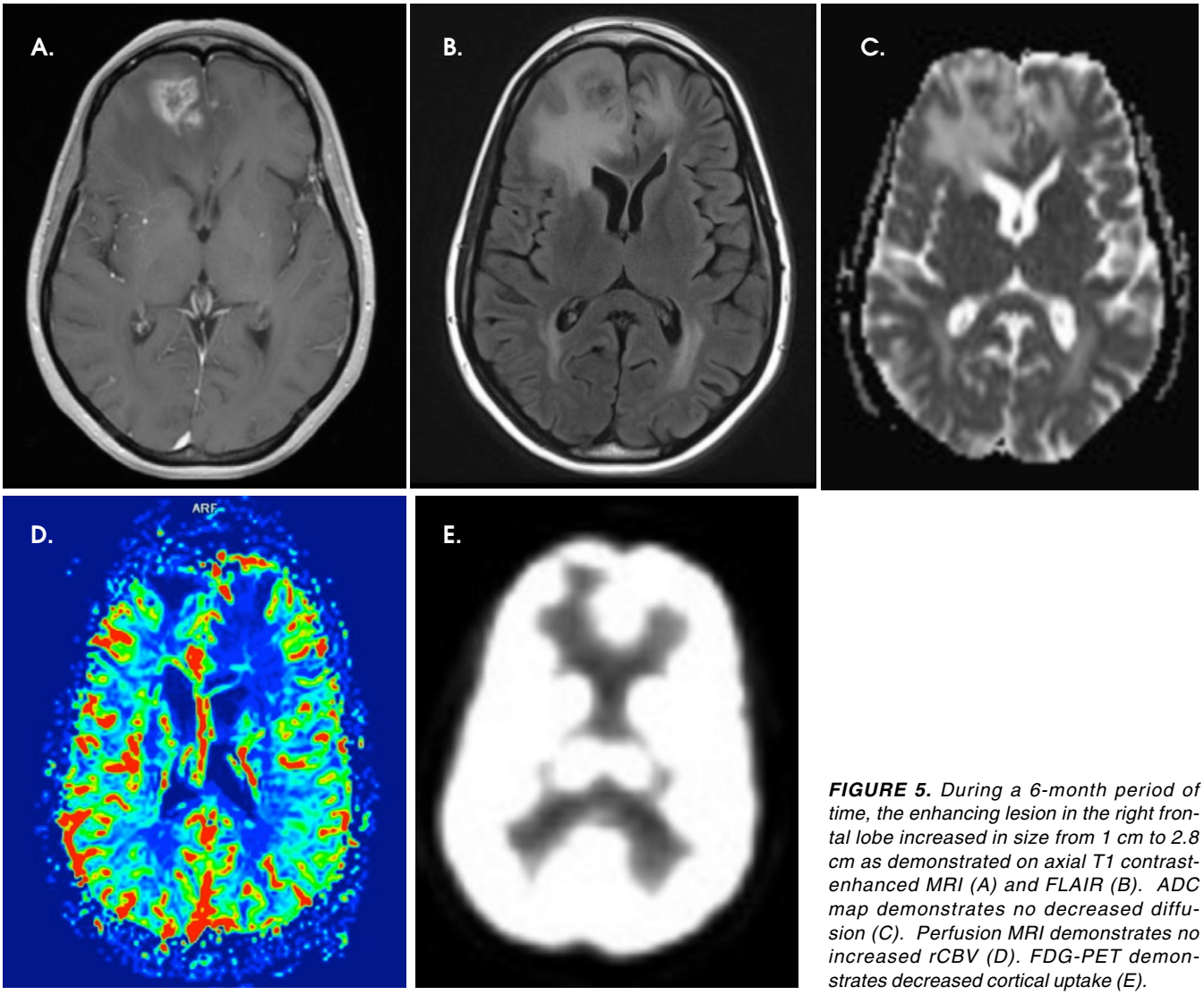


FIGURE 5. *During a 6-month period of time, the enhancing lesion in the right frontal lobe increased in size from 1 cm to 2.8 cm as demonstrated on axial T1 contrast-enhanced MRI (A) and FLAIR (B). ADC map demonstrates no decreased diffusion (C). Perfusion MRI demonstrates no increased rCBV (D). FDG-PET demonstrates decreased cortical uptake (E).*

MRI with perfusion imaging and metabolic imaging with PET are relatively widely available and have relatively high sensitivity and specificity for radiation necrosis and tumor progression. In a small series, multi-voxel MR spectroscopy has demonstrated excellent sensitivity and specificity for tumor recurrence.[3-10]

In our case, the patient was asymptomatic despite an enlarging mass in the context of no increase in rCBV, no decrease in ADC, and a decrease in uptake on PET—all supportive of a diagnosis of radiation necrosis. Histopathology confirmed the suspected diagnosis.

Many times, a patient's radiologic workup will contain some series supportive of radiation necrosis while others support tumor recurrence. Physicians often obtain serial images and consider administering an empiric trial of steroids, as in our case, which may help determine whether the lesion represents radiation necrosis or tumor recurrence. This methodology requires repeated imaging without a defined endpoint.

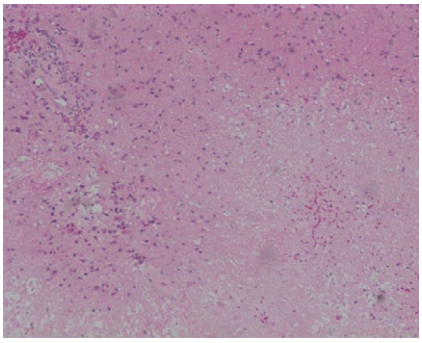


FIGURE 6. *Histopathology demonstrating coagulative necrosis (lower right corner), sclerotic vasculature, and reactive gliosis. No evidence of tumor recurrence was appreciated.*

Table 1. Sensitivity and specificity of imaging modalities utilized in the diagnosis of radiation necrosis and tumor recurrence following SRS for brain metastases

Study	Modality	Necrosis			Recurrence		
		Lesion Quotient	Sensitivity	Specificity	Lesion Quotient	Sensitivity	Specificity
Kano[4]	MRI		84%	91%			
Dequesada[3]	MRI						
		T2/T1 <0.3	80%	96%			
					T2/T1 > 0.6	15%	100%
Stockham[5]	MRI						
		T2/T1 <0.3	8%	91%			
					T2/T1 > 0.6	59%	41%
Chernov[6]	MRS					100%	100%
Chao[7]	FDG-PET (MRI) co-registration					86%	80%
Barajas[8]	PSR Perfusion MRI		96%	100%			
Vidiri[9]	Perfusion CT		72%-86%	100%			
Matsunaga[10]	SPECT				82.8%	83.7%	

MRS = magnetic resonance spectroscopy, FDG-PET = fluorodeoxyglucose positron emission tomography, Met = methionine, PSR = percent signal recovery (associated with perfusion MRI), SPECT = single photon emission computed tomography.

Noninvasive, accurate diagnosis of radiation necrosis versus tumor progression is important, as the clinical course of each can differ widely. In the SRS era, a high index of suspicion for post-SRS radiation necrosis and applying appropriate advanced imaging modalities will aid practitioners in diagnosing radiation necrosis or tumor recurrence, thereby permitting selection of the most appropriate treatment.

REFERENCES

1. Suh J. Stereotactic radiosurgery for the management of brain metastases. *N Engl J Med.* 2010;362:1119-1127.
2. Blonigen BJ, Steinmetz RD, Levin L, et al. Irradiated volume as a predictor of brain radionecrosis after linear accelerator stereotactic radiosurgery. Int. *J. Radiation Oncology Biol. Phys.* 2010;77: 996-1001.
3. Dequesada IM, Quisling RG, Yachnis A, Friedman WA. Can standard magnetic resonance imaging reliably distinguish recurrent tumor from radiation necrosis after radiosurgery for brain metastases? A radiographic-pathological study. *Neurosurgery.* 2008;63:898-903.
4. Kano H, Kondziolka D, Lobato-Polo J, et al. T1/T2 matching to differentiate tumor growth from radiation effects after stereotactic radiosurgery. *Neurosurgery.* 2010;66:486-491.
5. Stockham AL, Tievsky AL, Koyfman SA, et al. Conventional MRI does not reliably distinguish radiation necrosis from tumor recurrence after stereotactic radiosurgery. *J Neurooncol.* 2012;109;149-158.
6. Chernov M, Hayashi M, Izawa M, et al. Differentiation of the radiation-induced necrosis and tumor recurrence after Gamma Knife radiosurgery for brain metastases: Importance of multi-voxel proton MRS. *Minim Invas Neurosurg.* 2005;48:228-234.
7. Chao ST, Suh JH, Raja S, et al. The sensitivity and specificity of FDG PET in distinguishing current brain tumor from radionecrosis in patients treated with stereotactic radiosurgery. *Int J Cancer.* 2001;96:191-197.
8. Barajas RF, Chang JS, Sneed PK, et al. Distinguishing recurrent intra-axial metastatic tumor from radiation necrosis following gamma knife radiosurgery using dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. *AJNR Am J Neuroradiol.* 2009;30: 367-372.
9. Vidiri A, Guerrisi A, Pinzi V, et al. Perfusion computed tomography (PCT) adopting different perfusion metrics: Recurrence of brain metastasis or radiation necrosis? *Eur J Radiol.* 2012;81:1246-1252.
10. Matsunaga S, Shuto T, Takase H, et al. Semiquantitative analysis using thallium-201 SPECT for differential diagnosis between tumor recurrence and radiation necrosis after Gamma Knife surgery for malignant brain tumors. *Int J Radiat Oncol Biol Phys.* 2012;Apr 27. [Epub ahead of print].

RADIATION ONCOLOGY CASE

CME SEE PAGE 5 FOR DETAILS

Adaptive replanning of IMRT for head and neck cancer: A case report of replanning in a middle-aged patient with squamous cell carcinoma of the tonsil

Michael Bishop and John Greskovich, Jr, MD

CASE SUMMARY

A 39-year-old male presented with a right-sided neck mass and sore throat. The patient was placed on antibiotics initially with no resolution in symptoms. The neck mass continued to enlarge and the patient was noted to have erythema of the right tonsil. Fine-needle aspiration of the right neck mass demonstrated atypical cells, prompting an examination under anesthesia and right-sided simple tonsillectomy for further evaluation. Pathology from the excised tonsil demonstrated a moderate to poorly differentiated, human papillomavirus (HPV)-positive, p16-positive, squamous cell carcinoma. The patient was referred to radiation oncology for definitive treatment of tonsillar bed and neck disease.

IMAGING FINDINGS

Computed tomography (CT) imaging of the neck with contrast demonstrated a 3.0-cm × 1.3-cm × 2.3-cm right level IIA, cystic nodal mass, and 2 adjoining, enlarged right level IIB lymph nodes measuring 1.4 cm × 1.6 cm and 1.2 cm × 0.9 cm. 18F-2-fluoro-2-deoxyglucose positron emission tomography/computed tomography (FDG PET/CT) imaging revealed symmetric FDG uptake within the bilateral tonsillar fossae along with FDG-avid left level IIA nodes, 1.0 × 1.4 cm (SUVmax of 3.7) and 1.3× 1.4 cm (SUVmax of 3.8), right level II-V cystic node 4.3 × 4.2 × 3.4 cm (SUVmax 28.3) and right level IV node 1.0 × 1.2 cm (SUVmax of 4.3). No evidence of distant metastases was observed. On a clinical neck examination, an 8 × 7-cm right level II-V neck mass was noted, with no additional palpable nodes. Tumor staging for this patient was T1N3M0 or AJCC stage grouping, IVB.

***Mr. Bishop**, is a senior medical student at the Medical College of Georgia, School of Medicine, at Georgia Health Sciences University, Augusta, GA; and **Dr. Greskovich** is a Radiation Oncologist, Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH.*

DIAGNOSIS

HPV-positive squamous cell carcinoma of the right tonsil

TREATMENT SUMMARY

A 7-field, step-and-shoot, intensity-modulated radiation therapy (IMRT) technique was utilized, treating to a dose of 72 Gy in 40 fractions at 1.8 Gy per fraction over 8 treatment weeks with concurrent cisplatin and 5-FU chemotherapy given in-house on weeks 1 and 4 of IMRT. Daily image-guided radiation therapy (IGRT) with cone-beam CT imaging (CBCT) ensured setup accuracy. Treatment planning margins included a 3-mm expansion from gross tumor volume (GTV) to clinical target volume (CTV-72), and a 3-mm additional expansion of CTV-72 to PTV-72 for both the initial plan and adaptive replan, making total expansion of 6 mm from GTV to PTV-72.

An adaptive radiation therapy (ART) planning CT scan in the treatment position occurred at fraction number 20 of 40, with implementation of the adapted IMRT plan starting on fraction 21. There was no interruption or delay in the patient's course of radiation during the ART replanning process.

During ART planning, CT imaging demonstrated significant anatomical and geometric changes compared to the initial pretreatment CT simulation images. Overlay of initial treatment contours and dose onto the mid-treatment CT using a rigid registration algorithm (MIM® Software) demonstrated significant anatomical shift in organs at risk (OAR) with associated changes in predicted delivered dose (Figure 1). Automated deformable image registration software using mutual information (MIM® Software) was used to aid in recontouring the

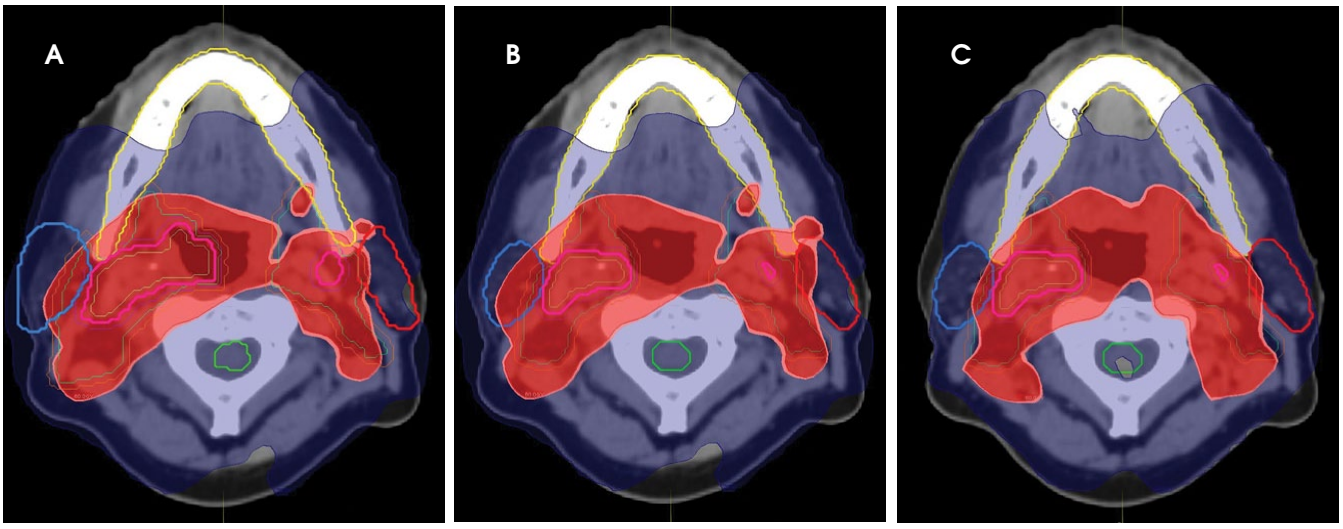
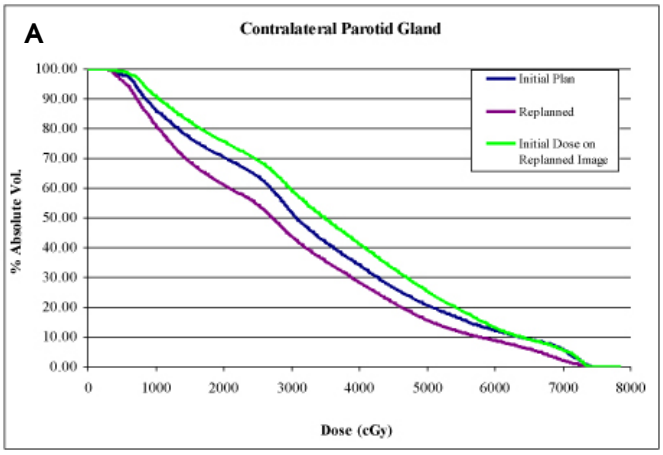
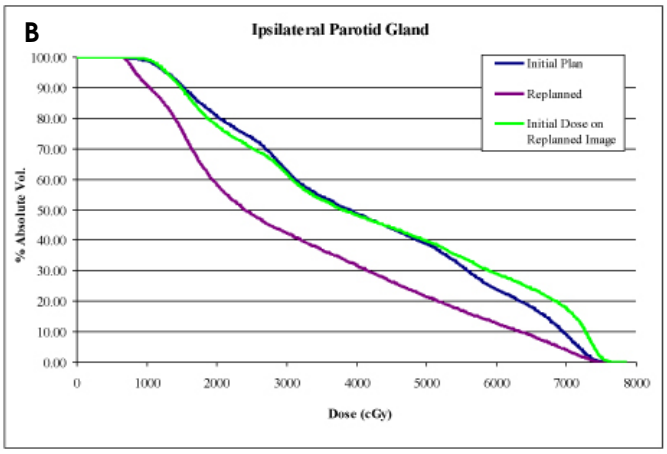


FIGURE 1. *All figures contain the mid-treatment CT image obtained following fraction 20/40. (A) Initial ROI contours and dosimetry overlay the mid-treatment CT image. (B) Initial dosimetry overlies the newly re-contoured ROIs on the mid-treatment CT image. (C) Replanned ROI contours and dosimetry overlay the mid-treatment CT image.*





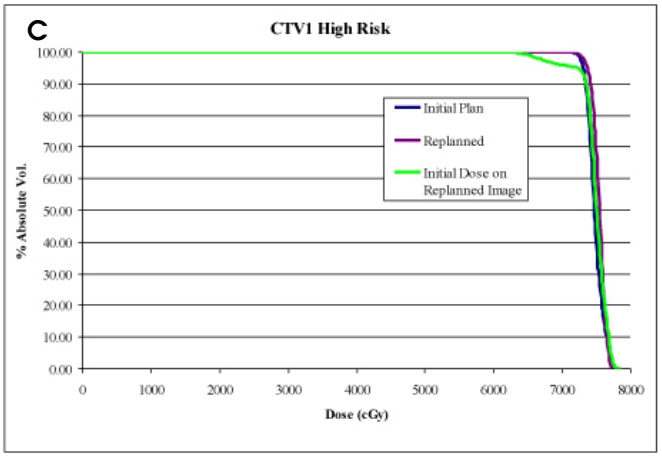


FIGURE 2. *The dose-volume histograms (DVH) from the initial plan, replan, and transferred initial plan dose onto replanned image and contours are shown in (A) contralateral parotid gland, (B) ipsilateral parotid gland, and (C) CTV1 high-risk graphs.*

OARs, CTV, and planning-target volumes (PTV) onto the mid-treatment CT scan images (Figure1). Final analysis and comparison of the original IMRT and new, ART IMRT plans demonstrated a significant improvement in delivered dose to the OARs, CTVs, and PTVs (Figure 1).

DISCUSSION

Innovative techniques in radiation oncology have greatly reduced patient toxicity while maintaining, or in some cases improving, outcomes such as local-regional control and overall

survival. IMRT has been shown to reduce overall toxicity compared to 3-dimensional radiation therapy (3DRT) in head and neck cancer.[1] Additional refinement of IMRT resulted from adaptive replanning to further reduce toxicity related to anatomical change and increased dosing to OARs. Anatomical change during treatment can result in dosimetric variations to OARs and target volumes that can be greatly improved with adaptive replanning.[2] Anatomical changes have been correlated with pretreatment nodal disease >4 cm, with the greatest change occurring in the first half of treatment.[3] Our patient was determined to be at risk for significant anatomical change based upon the extent of nodal disease and predicted therapeutic response to chemoradiation. He was scheduled upfront, prior to the start of IMRT, for an ART, mid-treatment CT scan. New ROI contours were generated by MIM software using automated deformable image registration of the initial region of interest (ROI) contours onto the mid-treatment CT followed by physician review and editing prior to ART planning.[4] Significant anatomical change affecting delivered dose to OARs was observed. Overall, ART planning improved the patient's therapeutic ratio by significantly reducing the maximum and mean doses to a number of OARs (Figure 2), preventing under dosing to $CTV_{high\ dose}$ (Figure 2), and by delivering dose more conformally to CTV and PTV. ART planning has been shown to have beneficial effects on reducing chronic radiation-induced toxicity, while maintaining comparable local-regional control and survival outcomes.[5] Our patient continues to be disease free 2 years post-ART planning with only mild, chronic radiation toxicity.

CONCLUSION

Our patient presented with HPV-positive, p16-positive, squamous cell carcinoma of the right tonsil with significant bulky nodal disease, placing him at risk for considerable anatomical and geometric changes during a course of definitive IMRT with concurrent cisplatin, 5-FU chemotherapy. If not accounted for, anatomical changes can result in overdosing of OARs and under-dosing of CTV or PTV target volumes, which may result in worse outcomes. The patient underwent ART planning at mid-treatment to account for the associated anatomical change. ART planning based upon mid-treatment CT imaging improved this patient's therapeutic ratio by reducing delivered dose to OARs while ensuring conformal dose coverage of CTV and PTV target volumes. The patient continues to be disease free 2 years post-ART planning with minimal long-term toxicity.

REFERENCES

1. Nutting CM, Morden JP, Harrington KJ, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): A phase-3 multicentre randomized controlled trial. *Lancet Oncol.* 2011;12:127-136.
2. Ahn PH, Chen CC, Ahn AI, et al. Adaptive planning in intensity-modulated radiation therapy for head and neck cancers: Single-institution experience and clinical implications. *Int J Radiat Oncol Biol Phys.* 2011;80:677-685.
3. Barker JL, Garden AS, Ang KK, et al. Quantification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT/Linear accelerator system. *Int J Radiat Oncol Biol Phys.* 2004;59:960-970.
4. Tsuji SY, Hwang A, Weinberg V, et al. Dosimetric evaluation of automatic segmentation for adaptive IMRT for head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2010;77:707-714.
5. Schwartz DL, Garden AS, Thoma J, et al. Adaptive radiotherapy for head-and-neck cancer: Initial clinical outcomes from a prospective trial. *Int J Radiat Oncol Biol Phys.* 2012;83:986-993.

TECHNOLOGY TRENDS

SRS, SBRT deliver promising results

Cristen Bolan

External beam radiation therapy has yielded promising results and improved patient outcomes in recent years, yet its accuracy and safety remain areas of concern. Side effects of radiation treatment include problems that occur as a result of the treatment itself as well as from damage to healthy cells in the treatment area.[1]

However, with improvements in radiation therapy delivery and planning, cancer patients today have more "targeted" treatment options, notably stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT).[2] Using SRS and SBRT techniques, high doses can be given in one to 5 fractions with acceptable toxicities to organs at risk.[2] In most cases, patients can resume all of their normal activities within 1 or 2 days.[3] This has led to widespread adoption of SRS and SBRT, and approximately 400 facilities are equipped to perform SRS and SBRT in the United States (U.S.).[3]

Promising results

Lung cancer is one of the deadliest and most common causes of cancer death in men and women in the U.S.[3] Although lobectomy is the standard treatment and offers the best chance of curing early-stage non-small cell lung cancer (NSCLC), a significant proportion of patients in the U.S. aging population are not surgical candidates at diagnosis.[4] In recent studies, SBRT has demonstrated excellent local control and cause-specific survival with minimal toxicity in early-stage NSCLC.[5] SBRT is considered a curative alternative to surgery not only for elderly patients with severe lung disease, but also for patients with severe heart disease, patients in poor health,[6] and patients with early-stage but inoperable NSCLC tumors.[7]

In a recent study[8] of SBRT of spinal cord lesions, a cohort of 500 cases of spinal metastases underwent radiosurgery. Long-term tumor control was demonstrated in 90% of lesions treated with radiosurgery as the primary modality, and in 88% of lesions treated for radiographic tumor progression. Long-term pain improvement occurred in 290 of 336 cases (86%). Twenty-seven of 32 cases (84%) with a progressive neurologic deficit before treatment experienced at least some clinical improvement.

These are just some of the many successful outcomes achieved with SRS and SBRT treatments, as there are many other treatment sites, such as primary and metastatic tumors to the liver, kidney, pancreas and prostate.[8]

Time and comfort contribute to accuracy

Two factors contribute to more accurate delivery of ionizing radiation: faster treatment times and patient comfort.

"We believe faster treatment in prostate cancer and patient comfort contribute to accuracy," John B. Fiveash, MD, Radiation Oncologist, Department of Radiation Oncology, Associate Professor and Vice Chairman for Academic Programs, University of Alabama at Birmingham, "With faster treatment… patients are more comfortable and less likely to move during the therapy."

In many cases, movement is a function of time. In prostate cancer, gas patterns or rectal or bladder filling can move the target, and a quicker treatment is more likely to be associated with more accurate treatment. The Assessing the Impact of Margin Reduction (AIM) study showed that prostate cancer patients treated with reduced margins and tumor tracking had lower radiotherapy-related morbidity than their counterparts treated with conventional margins.[9]

Study subjects received radiation treatment with the Calypso Beacon System, implantable electromagnetic transponders that are placed in or around a tumor and tracked continuously during external beam radiation therapy.

"The Calypso Beacon studies look at prostate studies as a function of time, and if you have look at motions over 3 mm, with 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 2, it's about 5% or less," indicated Dr. Fiveash. "A quick treatment with RapidArc or flattening filter free mode (FFF), if you're

CANCER DIVIDES. WE UNITE.

At Varian, we believe that one of the most powerful tools to battle cancer is collaboration. Let us partner with you as we deploy the newest oncology innovations in products, software and services. Together, we can draw on our collective energy to fight cancer and build a better future.

See us at ASTRO 2012, booth #5019. To learn more, visit varian.com/oncology.

VARIAN
medical systems
A partner for life

TECHNOLOGY TRENDS

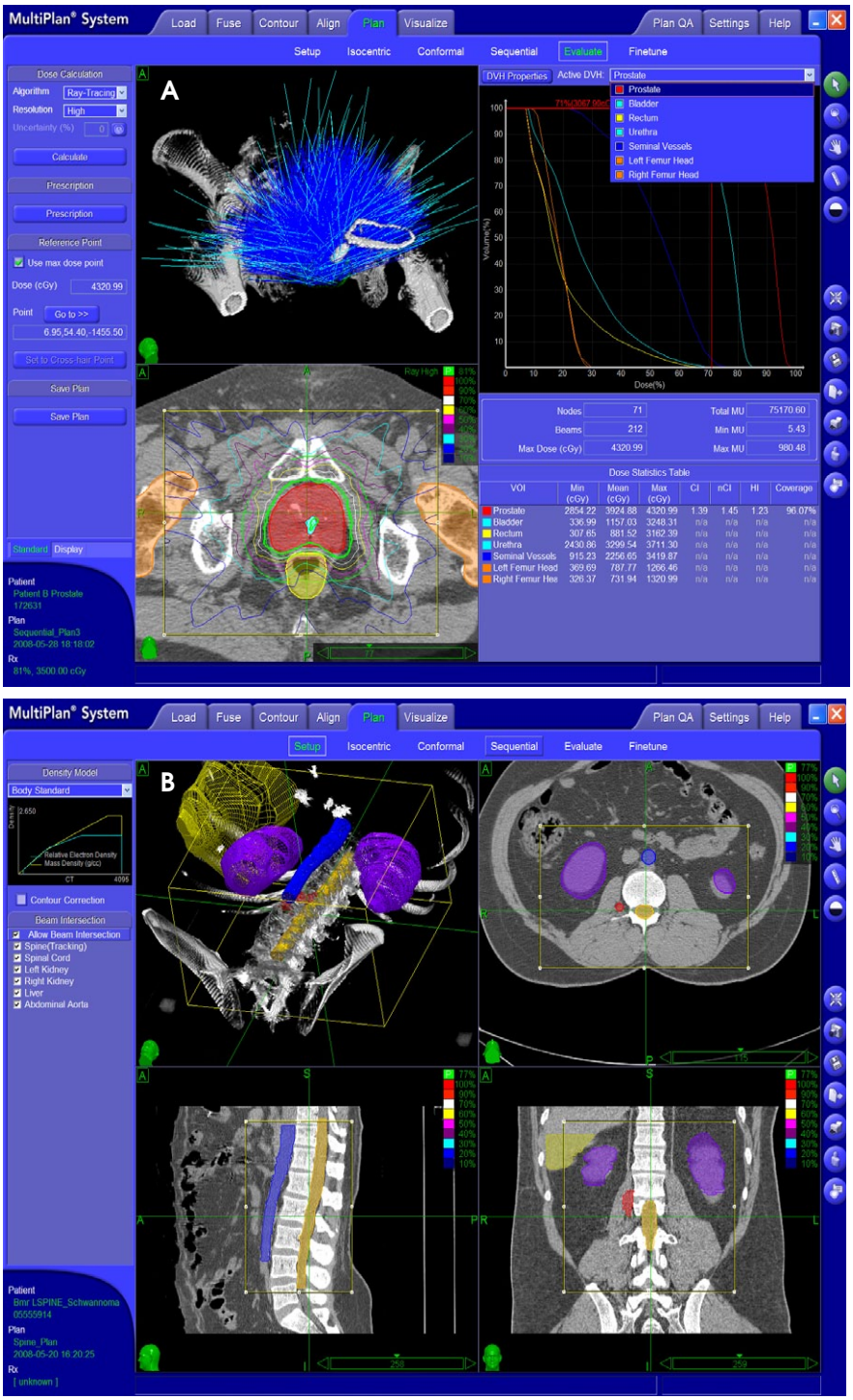


FIGURE 1. *The MultiPlan Treatment Planning System for Cyberknife is designed specifically for radiosurgery, allowing for the simple and efficient creation of even the most complex treatment plans. (A) shows a treatment plan for the prostate and (B) shows structure delineation.*

doing stereotactic treatments, in particular, has an advantage for accuracy, or you need a way to do real-time monitoring, such as with Calypso."

When the radiation oncology department at the University of Alabama at Birmingham opened a new radiotherapy facility, the primary goal was to broaden and grow its SBRT program and to do hypofractionated frameless SRS treatments with single and multifraction. The physicians also wanted better image-guidance for more efficient treatments elsewhere in the body. Already equipped with a TomoTherapy system, recently acquired by Accuray Inc., a Gamma Knife (Elekta AB), and a RapidArc system by Varian Medical Systems (Varian), the department selected Varian's TrueBeam system.

"We chose TrueBeam for frameless SRS treatment, for its more efficient administration of body radiosurgery, and to have better integration of the image guidance systems," said Dr. Fiveash.

TrueBeam rotates around the patient and can deliver radiation from multiple angles, while the operator uses advanced imaging techniques to control the beam shape and strength, and it synchronizes the beam delivery with a patient's breathing pattern. TrueBeam also features a high-intensity mode, which can deliver dose up to 4 times faster than conventional linear accelerators.

"The greatest time savings is in higher dose-per-fraction cases, which is why we wanted TrueBeam," said Dr. Fiveash. "We used to schedule patients for lung or liver surgery in 60- to 90-minute time slots to deliver a very-high-dose treatment. Now, we are scheduling 30-minute time slots, and that's a resource advantage for the machine, for the physician, and it's much more comfortable for the patient."

"We also save a lot of time for brain treatments," he added. "We are treating patients in just over 10 minutes for

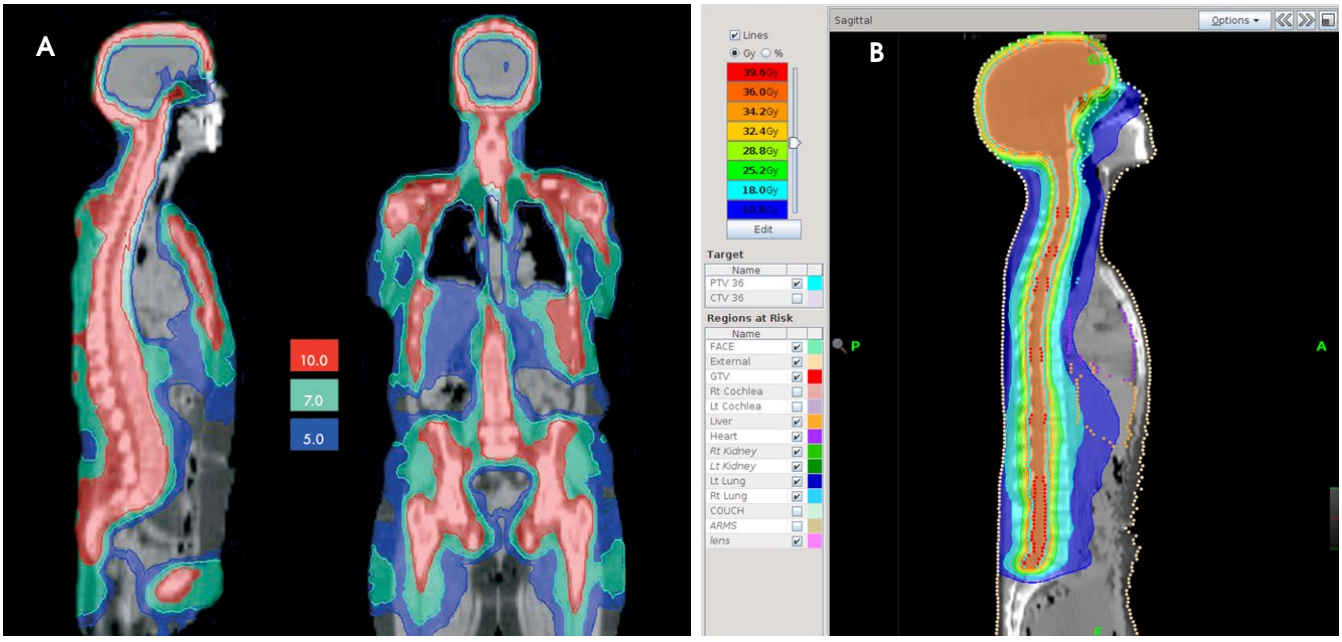


***FIGURE 2**. A treatment plan for total marrow irradiation (A) and for the cranio-spinal region (B) on Cyberknife.*

single-fractionated or hypofractionated SNS treatments, which is much quicker than other delivery devices. You can combine RapidArc with flattening filter free mode (FFF) or High Intensity Mode and do beam time in <5 min. 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, and we can do that in 15 min—there is more patient comfort and time advantages."

While time is important, it isn't everything. Frameless systems provide for greater patient comfort. "The Gamma Knife is especially effective for treating multiple metastases, such as 3 or more lesions in the brain, said Sandra S. Vermeulen, MD, a radiation oncologist at Swedish Cancer Institute in Seattle, WA. "We treat multiple lesions in the brain better with Gamma Knife than Cyberknife because it has a faster platform and better limits scatter radiation to other parts of the brain. But if you have 1 to 3 lesions, we can use the Cyberknife (a frameless radiosurgery system). Many patients don't want a frame-based system because it's uncomfortable."

The system has several distinct advantages over frame-based systems, including improved patient comfort, increased treatment degrees of freedom, and the potential to target extracranial lesions more easily.[10]

Contouring cuts treatment times

A recent advance in beam-shaping technology has led to the reduction in beam delivery time by as much as 41%. The newly released Agility is a 160-leaf, multi-leaf collimator (MLC) developed by Elekta for its Volumetric Modulated Arc Therapy (VMAT) system. The new MLC uses twice the number of leaves found on many standard MLC's, and is designed to sculpt delivered radiation to the distinctive contours of the tumor while reducing the risk of exposure to healthy normal tissues. On the VMAT, single or multiple radiation beams sweep in one or more uninterrupted arcs around the patient, reducing treatment times significantly.

By combining accelerated beam shaping and beam delivery, doctors at The James Cook University Hospital in Middlesbrough, England (UK), were able to cut 57 sec off the beam delivery time when treating a 61-year-old male with prostate cancer. The patient received his first treatment fraction, a single, 200-degree VMAT arc, in just 83 sec. In comparison, a 3-field, 3-dimensional (3D) conformal treatment would have taken 140 sec. This demonstrated a 40.7% reduction in beam delivery time with Agility/VMAT.

"The treatment speed not only reduces the likelihood that the patient will move and that the internal organs will shift position, but it also contributes to faster patient throughput, which is key. With Agility and VMAT, we expect to be able to treat 5 patients per hour," said Christopher Walker, Head of Radiotherapy Physics at The James Cook University Hospital.

Respiratory motion

One of the biggest challenges in radiotherapy is breathing, which causes the lungs, liver, prostate, and other organs to move during beam time.

One of the primary reasons for using SRS is to minimize radiation-induced normal tissue damage.[11] SRS and

TECHNOLOGY TRENDS

SBRT use image-guided radiation therapy (IGRT), which relies on medical imaging to confirm the location of a tumor during the delivery of radiation to improve the precision and accuracy of the treatment.[12]

At Swedish Cancer Institute in Seattle WA, doctors have Accuray's CyberKnife VSI, the Gamma Knife, and TomoTherapy system to treat prostate, lung and breast cancer, and colorectal carcinoma and melanoma.

Since Cyberknife uses individually targeted "pencil-beams" instead of arcs, the treatment isodose contour takes shape without using individual isocenters, and theoretically could be planned to exclude critical structures entirely.[10]

"You can fractionate with the Cyberknife platform because it is not a frame-based system," said Dr. Vermeulen. "If you have a tumor encompassing a sensitive location like near the eye, the optic nerves or chiasm, you can't treat it on Gamma Knife, but you can on Cyberknife because you can fractionate the dose to protect surrounding sensitive tissues."

Working with the CyberKnife is the Synchrony Respiratory Tracking System, which enables the radiation beam to track tumor movement in real time and allows patients to breathe normally during treatment. The patient wears the Synchrony vest, and the robot correlates chest motion and breathing patterns with the tumor position.

"The more accurate you can be, the higher the the dose can be delivered, which translates into higher tumor control rates," noted Dr. Vermeulen. "With conventional radiation, lung cancer local control rates are 60% to 70% and higher doses would damage adjacent normal tissue. However, with the targeting precision of Cyberknife we can now deliver 30% higher doses." She added, "This results in 90% local control for lung cancer, which is a phenomenal achievement."

Another breakthrough doctors at Swedish Cancer Institute are witnessing is in early-stage prostate cancer. These doctors started the radioactive seed implant program nearly 20 years ago, and today they are using Cyberknife to treat these patients with higher radiobiologic doses and seeing even fewer side effects than with seed implants.

Dr. Vermeulen said she is now working with Cyberknife to re-treat patients with metastatic disease of the spine, who had undergone conventional radiation and no longer had control of spinal metastases. "We could never do that before. This eliminates the crippling sides effects of the recurrent disease," she said.

Another valuable tool in the hospital's armamentarium is the TomoTherapy System, which uses helical, continuous, 360-degree delivery of IMRT. Tens of thousands of narrow beamlets are used, all of which are targeted directly at the tumor and individually optimized to contribute to the total tumor dose. By delivering beamlets from more angles than any other form of IMRT, the TomoTherapy System provides precise conformal radiotherapy. The advantage with TomoTherapy is that you can treat a larger area.

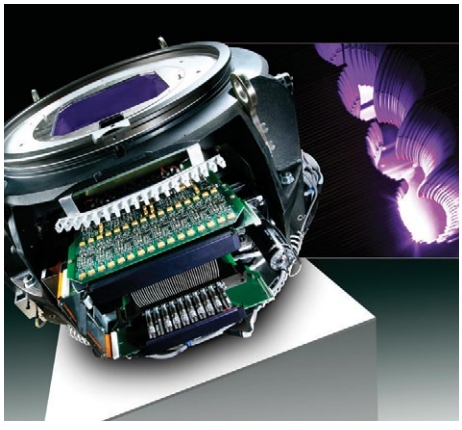
"If you have disease that has metastasized into the lymph nodes, you need to treat a quadrant or lymph node chain, the TomoTherapy application is exquisite," Dr. Vermeulen said. "Tumors which seed the spine like high-grade ependymomas and medullobalstoma require craniospinal irradiation. Where conventional radiation would have to include a significant amount of adjacent normal tissue leading to unwanted side effects, TomoTherapy can restrict the radiation to the craniospinal contents like protons can without the excessive cost to the consumer."

In the next issue of Applied Radiation Oncology, *Tech Trends will feature "Where protons meet photons," an in-depth evaluation of the pros and cons of proton and photon radiation therapy.*

REFERENCES

1. Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT). Radiologyinfo.org. http://www.radiologyinfo.org/en/info.cfm?pg=stereotactic. Accessed September 20.
2. Zeng M, Han LF. Stereotactic radiosurgery: A "targeted" therapy for cancer management. *Chin J Cancer.* 2012. doi: 10.5732/cjc.012.10011. Epub ahead of print.
3. Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT). Radiologyinfo.org. http://www.radiologyinfo.org/en/info.cfm?pg=stereotactic. Accessed September 20, 2012.
4. Koyi H, Hillerdal G. Screening for lung cancer can save lives, according to US study. Too early for mass screening—but refer smokers to CT on broad indications. *Lakartidningen.* 2012;109:208-209.
5. Taremi M, Hope A, Dahele M, et al. Stereotactic body radiotherapy for medically inoperable lung cancer: Prospective, single-center study of 108 consecutive patients. *Int J Radiat Oncol Biol Phys.* 2012; 82:967-973. Epub 2011 Mar 4.
6. Stereotactic body radiosurgery lung cancer surgery alternative. Cancer treatment group. http://www.cancertreatmentgroup.com/lung_cancer_treatment/lungstereotactic.shtml. Accessed September 20.
7. Timmerman RD, Paulus R, Galvin J. Stereotactic body radiation therapy for medically inoperable early-stage lung cancer patients: Analysis of RTOG 0236. *Int J Radiat Oncol Biol Phys.* 2009;75:S3. Supp.
8. Daly ME, Gibbs IC. Spinal radiosurgery: Delayed radiation-induced myelopathy. *Tumors of the Central Nervous System.* 2012;6:135-140.
9. Sandler HM, Liu PY, Dunn RL, et al. Reduction in patient-reported acute morbidity in prostate cancer patients treated with 81-Gy intensity-modulated radiotherapy using reduced planning target volume margins and electromagnetic tracking: Assessing the impact of margin reduction study. *Urology.* 2010 May;75:1004-1008. Epub 2010 Feb 13.
10. McVicker JH. Stereotactic radiosurgery for the spine. The Colorado Neurological Institute. http://www.thecni.org/reviews/12-1-p22-mcvicker.htm. 2001;12:1. Accessed September 21, 2012.
11. Kirkpatrick JP, Marks LB, Mayo CS, et al. Normal tissue tolerance. Estimating normal tissue toxicity in radiosurgery of the CNS: Application and limitations of QUANTEC. *J Radiosurg SBRT.* 2011;1:95-107.
12. Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT). Radiologyinfo.org. http://www.radiologyinfo.org/en/info.cfm?pg=stereotactic. Accessed September 20.
13. Hoppe B, Henderson R, Mendenhall WM, et al. Proton therapy for prostate cancer. *Oncology.* 2011;25:644-650, 652. Review.

...twice the leaves at twice the speed



Agility is not licensed for sale in all markets. Please contact your local Elekta representative for details.

With Agility™, it's reality.

As the ultimate device for advancing modern radiotherapy, Elekta's Agility MLC precisely sculpts radiation with 160 high-resolution leaves across a 40 cm x 40 cm field. Capable of managing the broadest spectrum of therapies, Agility also boasts ultra-fast leaf movements with extraordinarily low leakage to maximize the potential for advanced techniques such as SRS, SRT and VMAT.

4513 371 0993 03:12

Human care makes the future possible.
More at elekta.com/imagine

ELEKTA

CANCER DIVIDES. WE UNITE.

At Varian, we believe that one of the most powerful tools to battle cancer is collaboration. Let us partner with you as we deploy the newest oncology innovations in products, software and services. Together, we can draw on our collective energy to fight cancer and build a better future.

See us at ASTRO 2012, booth #5019. To learn more, visit varian.com/oncology.

VARIAN
medical systems
A partner for life