

SPRING 2024

# ASTRO *news*

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**+ MORE**



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# ASTRO news

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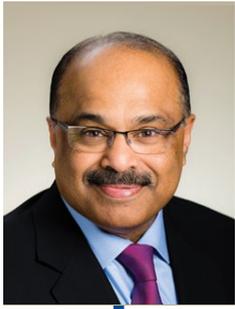
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## Radiation Oncology or Radiation Medicine?

### IN THE SPRING 2024 ISSUE OF *ASTRONEWS*

we highlight emerging and reemerging nononcological indications for therapeutic radiotherapy. The invited authors were tasked with reviewing the data that support the use of radiation therapy for these conditions, describing the biological mechanism of efficacy, and providing practical instructions on how to treat and set up a clinical program (including insurance coverage). Radiation therapy is already widely used for some nonmalignant conditions such as schwannomas, arteriovenous malformations, trigeminal neuralgia, keloids, and heterotopic ossification, for example. We chose not to discuss these more common, well-established indications.

Earlier in the history of our specialty, radiation therapy was empirically used for many more nononcological conditions, some of which were very controversial (e.g., therapeutic abortion). Drs. Roberge, Donaldson and Wallner provide a historical perspective of radiation therapy for benign disorders in their article “What Goes Around Comes Around.”

An example of a nonmalignant disorder that in the past was treated often with radiation therapy, over time fell out of use, and is now reemerging is

osteoarthritis. Drs. Kirschner and Dove discuss the data to support the efficacy of pain relief with low dose radiotherapy (3 Gy in 6 fractions; 0.5 Gy per fraction) and how to practically implement such a program in your clinic/department. Accompanying their article is a wonderful patient perspective regarding the treatment of his osteoarthritis with radiotherapy as well as an article from Dr. Koneru, with contribution from Dr. Shaffer, on his experience running one of the largest low dose radiotherapy programs for osteoarthritis in the United States. They discuss the role of radiotherapy in osteoarthritis treatment and share data on the clinic’s patient results.

Interestingly, low dose radiotherapy for osteoarthritis is more widely utilized in Europe as compared to the United States. Likewise, the treatment of other benign conditions like plantar fasciitis and hyperproliferative disorders of fascia (i.e., Dupuytren’s disease of the hands, Ledderhose disease of the feet (aka plantar fibromatosis), and Peyronie’s disease of the penis) are routinely treated with radiation outside the United States. Dr. Martin who leads a benign radiotherapy practice in Australia, reports on his extensive experience with treating plantar fasciitis. In his informative article he also

describes how Usain Bolt — Jamaican track and field star, “Fastest Man in the World” — likely had radiation therapy for plantar fasciitis and afterward went on to win another three gold medals!

Drs. Shaffer and Bajaj provide a nice overview of radiation therapy (30 Gy in 10 fractions, split course) for the prevention of progression to contraction and the need for surgery for patients with Dupuytren’s disease. The therapeutic ratio is relatively high for osteoarthritis, plantar fasciitis and Dupuytren’s disease, and the biological mechanism is modulation of inflammatory pathways.

Drs. Thomas and Bredel remind us in their functional neuro-radiosurgery article that the original intent of Swedish neurosurgeon Lars Leksell (the founder of radiosurgery) was to invent a noninvasive method to target functional brain disorders such as pain and movement disorder — not cancer. Today, radiosurgery is mainly used to treat brain malignancies and catheter-based radiofrequency ablation, implantable deep brain stimulators, and MRI-guided focused ultrasound are predominately used to treat functional disorders. However, these neurosurgical procedures can be invasive and there are several radiosurgical platforms that can deliver accurate and precise ablative therapy. Functional radiosurgery is an area of opportunity to improve patient care.

An exciting new emerging indication for radiation therapy is for cardiac radioablation for high-risk refractory ventricular tachycardia. Dr. Robinson and colleagues at Washington University have been innovators and early adopters of this treatment and provide updates and future directions. There is promising retrospective data that suggests that cardiac radioablation is more effective and is

associated with less serious adverse events (e.g., early death) as compared to invasive catheter ablation. A multicenter randomized trial has recently opened and is accruing patients (RADIATE-VT, NCT 05765175).

In a companion health policy article, Adam Greathouse (ASTRO) explains coding radiation therapy’s expanded role in nonmalignant diseases, with the reminder that reimbursement for using RT for nonmalignant conditions can be complex and vary depending on the payer, the specific condition being treated, and the prevailing coverage policies. A list of CPT codes is provided as well as very useful information on the current status of insurance coverage for radiation therapy services provided for nonmalignant conditions.

Treating nonmalignant disease in an otherwise somber cancer clinic can be both gratifying to the clinician and serve as a reprieve from the challenging work of oncology. In terms of building a practice, we have found that a satisfied patient is the best form of advertising. Many of these chronic conditions have support groups on social media where patients openly share their experience and praise the radiation oncologist who treated them. At our respective institutions/clinical practices we currently offer radiotherapy to patients with Dupuytren’s and Ledderhose disease, functional brain disorders, and are opening the randomized cardioablative radiotherapy trial for ventricular tachycardia. We are hoping to offer radiation therapy to patients with osteoarthritis and plantar fasciitis in the near future. As utilization of radiotherapy for nononcological indications expands, we may want to consider changing the name of our departments and clinics from *Radiation Oncology* to *Radiation Medicine*. 



**Dr. Mohideen welcomes letters to the editor at  
[ASTROnews@astro.org](mailto:ASTROnews@astro.org).**



## ROCR Makes Advocacy Day 2024 Unlike Any Other

**AS A SPORTS FAN**, spring training ushers in the start of the baseball season. Harry Caray once said, “It’s the fans that need spring training. You gotta get ‘em interested. Wake ‘em up and let ‘em know that their season is coming...” At ASTRO, we also have a treasured spring tradition, Advocacy Day, and I’m 100% certain that it will get our members excited about our future.

This year marks our first on the Hill advocating for the Radiation Oncology Case Rate (ROCR) program. Since its release in June 2023, momentum has been building around ROCR and its promise to stabilize payment and enhance quality — first for Medicare beneficiaries, and then ideally, to all patients. As a reminder, ROCR would change payment from per fraction to per patient, with positive inflationary updates and incentives to reduce disparities and improve quality.

Thanks to the thoughtful input from ASTRO members and radiation oncology stakeholders, ROCR is a better product today than when first released. Changes were made based upon feedback from our radiation oncology community. Our advocacy physician leaders and staff have met with more than 1,000 radiation oncologists to build awareness and get feedback. If you would like to arrange a briefing on ROCR or you’re ready to formally express support, email the ASTRO Health Policy team at [healthpolicy1@astro.org](mailto:healthpolicy1@astro.org). From small groups to big academic centers, about 50 practices have already expressed their support of ROCR, including my institution. Whether you’re a freestanding center that is suffering from the 23% drop in payments since 2013 or a hospital that’s experiencing declines in technical revenues, we appreciate your support!

I’m pleased to see how the community is rallying around ROCR as a solution to these Medicare payment declines. It was great to work with our colleagues at the American College of Radiation Oncology, American College of Radiology, and American Association for Clinical Oncology on a joint statement in January supporting radiation oncology payment reform, which showed the unity of purpose and a commitment to change.

While the support grows, ASTRO’s lobbying team is hard at work with our champions on Capitol Hill, converting ROCR’s policy language into legislation. If all

goes well, this will lead to the ROCR bill that we will ask our senators and representatives to cosponsor when we take to Capitol Hill on May 21.

Advocacy Day is always such an exhilarating event for me and those of us who participate regularly. But clearly, this year is different. ASTRO has never undertaken an advocacy initiative like ROCR before, and it will require a concerted and focused effort to navigate the challenging environment in Congress.

I’ve been asked whether ROCR has chance of passage. The answer is yes, I’m confident it will pass. ROCR puts our patients first and aligns our reimbursement with what’s best for them. But ROCR will only pass if we fight with everything we’ve got, whether that’s joining us at Advocacy Day, hosting a tour of your clinic for your member of Congress, calling or emailing Congress about ROCR, or one of any number of ways to support the eventual bill.

Supervision of radiation oncology services has generated tremendous interest and feedback in response to our February 26, 2024, letter to CMS. We believe that a return to the pre-pandemic direct supervision levels will improve quality of care and maintain patient safety. ASTRO believes that a board-certified/board-eligible radiation oncologist is the clinically appropriate individual to supervise radiation treatments. However, we recognize that some flexibility is necessary for those practices that deliver care to rural or underserved populations. Furthermore, there needs to be some allowance for clinical activities that may require a physician’s attention (inpatient care, surgical procedures, tumor boards, etc.). At Advocacy Day, we expect to continue the conversations that this topic has created.

I am looking forward to our meetings in May when we will take to the halls of Congress with fellow ASTRO advocates, from board members to residents, to make our case loud and clear for ROCR and radiation oncology. 



Go to [astro.org/AdvocacyDay](https://astro.org/AdvocacyDay) for more information on ROCR and Advocacy Day.

# SOCIETY NEWS



## Rachel Jimenez, MD, begins tenure as Editor-in-Chief of *Advances in Radiation Oncology*

**ON MARCH 1, RACHEL JIMENEZ, MD**, an associate professor of radiation oncology at Harvard Medical School and chair of quality and safety in radiation oncology at Mass General Cancer Center, began her five-year term as the new editor-in-chief of *Advances in Radiation Oncology*.

Dr. Jimenez succeeded Robert C. Miller, MD, MBA, FASTRO, who served as editor-in-chief since the journal's founding in 2015. Dr. Jimenez previously served as an associate editor of the *International Journal of Radiation Oncology • Biology • Physics* (Red Journal), ASTRO's flagship journal.

Dr. Jimenez is a nationally recognized researcher who focuses on treating patients with breast cancer and the principal investigator of several ongoing clinical trials. In addition to her clinical and research work, she specializes and volunteers extensively in medical ethics, is the former president of the Association of Directors of Radiation Oncology Programs (ADROP) and serves as faculty advisor to the Association of Residents in Radiation Oncology (ARRO).

As editor-in-chief, Dr. Jimenez said she plans to emphasize the "Advances" aspect of the journal's name by "focusing on evolving technologies in our field while

highlighting the biological advances that keep radiation oncology on the cutting edge of cancer research." She said this could include the initial reports of innovations that enhance the efficacy and safety of radiation treatments, such as radiopharmaceuticals or artificial intelligence. Dr. Jimenez also sees an opportunity to expand the journal's coverage of day-to-day advances in radiation oncology, including those pertaining to reimbursement, residency training and workforce sustainability.

ASTRO launched *Advances* to provide a forum for original research in radiation oncology that is widely accessible to providers, patients and others across the globe. As an open access journal, all articles in *Advances* are free to read. This format enabled the journal

to become a resource hub for oncologists during the COVID-19 pandemic by publishing firsthand accounts and advice from clinics in the hardest-hit areas, followed by best practices to modify treatment safely and effectively during the pandemic.

Dr. Jimenez said she plans to continue leveraging the journal's open access platform to provide timely, valuable science to the field. "We rely on scientific journals more than ever to curate the most impactful, relevant scholarship for our field," she said. 

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"We rely on scientific journals more than ever to curate the most impactful, relevant scholarship for our field."

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## *In Memoriam*

ASTRO has learned that the following members have passed away. Our thoughts go out to their family and friends.

The Radiation Oncology Institute (ROI) graciously accepts gifts in memory of or in tribute to individuals.

For more information, visit [www.roinstitute.org](http://www.roinstitute.org).

**Amber Arlington, MD, MPH**  
Bend, Oregon

**C. Norm Coleman, MD, FASTRO**  
Bethesda, Maryland

**Edith Mitchell, MD**  
Philadelphia, Pennsylvania

**John O. Praag, MD**  
Rotterdam, Netherlands

## Key member of Congress visits Templeton, California radonc clinic



*Rep. Panetta (center right) with ASTRO members Lauren Tait (far right) and Ben Wilkinson (far left), physicist Kristi Garcia (center left) and dosimetrist Michele Wolfe (center) at the Coastal Radiation Oncology site in Templeton, California.*

### ON JANUARY 26, COASTAL RADIATION ONCOLOGY

**MEDICAL GROUP** physicians Lauren Tait, MD, and Ben Wilkinson, MD, hosted a tour of their Templeton Radiation Oncology Center for U.S. House Representative Jimmy Panetta (D-CA). Rep. Panetta said he was impressed with the Templeton team after seeing firsthand how they provide cancer care services to his constituents in the rural California community.

Coastal Radiation Oncology is a 14-member physician group providing community-based radiation oncology services along the Central Coast of California between north Los Angeles up to just south of San Jose. The Templeton location is located approximately three hours south of San Francisco. Drs. Tait and Wilkinson worked with ASTRO staff to organize the tour, which also featured discussion of ASTRO's Radiation Oncology Case Rate legislative proposal.

"Thank you to ASTRO for the opportunity to meet Congressman Panetta and his team. Our staff at Templeton Radiation Oncology Center highlighted all the hard work, dedication and commitment invested into providing the highest level of care for our patients in radiation oncology. Our field is devoted to treating cancer patients with precision and compassion, and I feel that was well received by the congressman," said Dr. Tait.

Clinic tours are unmatched in their ability to educate members of Congress about the value of radiation oncology. ASTRO is encouraging clinics to start the process for scheduling tours now for the upcoming August congressional recess when members of Congress will be looking for opportunities in their states and districts to meet with constituents and learn about their issues. Keep an eye out on the ASTRO Blog for a full recap on this tour and additional details to guide you through setting up your own facility tour with your congressional representatives and reach out to [advocacy@astro.org](mailto:advocacy@astro.org) to start now. 



*Kristi Garcia describing the features of a TrueBeam including IMRT, SBRT and arc-therapy to Rep. Panetta.*

## ARRO representative approved to sit on Board in ex-officio position



2023-2024 ARRO Executive Committee

### IN JANUARY, THE ASTRO BOARD OF DIRECTORS

approved the inclusion of an ARRO ex-officio representative to the ASTRO Board. This ARRO representative will significantly enhance communication and collaborative efforts between ARRO and ASTRO leadership and advocate within ASTRO leadership on important issues impacting radiation oncology

residents. The ARRO ex-officio representative will be a current member of the ARRO Executive Committee and fully informed on all ARRO education and advocacy initiatives. The inaugural ARRO ex-officio representative will serve a one-year term beginning in June 2024 and will join ASTRO Board members at the convening of their summer meeting. 

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- Member discounts for submissions to *Advances in Radiation Oncology*, meeting registrations, courses and publications.
- Access to the ASTRO Member Directory.
- Volunteer and leadership opportunities.
- Voting rights in society elections and bylaws changes.

*\*This offer is available only if you join ASTRO before December 31, 2024.*

# WHAT GOES AROUND COMES AROUND

## Radiation Therapy of Nonmalignant Disorders



BY DAVID ROBERGE, MD, SARAH S. DONALDSON, MD, FASTRO, AND PAUL E. WALLNER, DO, FASTRO

**ARTICLES IN THIS ISSUE** of *ASTROnews* highlight some exciting new areas of radiotherapeutic intervention of benign entities and will revisit several previously treated disorders that have elicited new interest. In 1991, the first textbook compilation of the use of radiation in the management of benign disorders was published in the English language and edited by Order and Donaldson.<sup>1</sup> The index of that volume listed 72 individual benign conditions, in alphabetical order from A (abortion) to X (xanthoma), which had systematically or anecdotally been managed with radiation. Each disorder was accompanied by survey responses from 834 radiation oncologists as to whether they would or would not treat the entity. Radiation management of some of the disorders had long been abandoned, but for many others, radiation was still actively employed in their treatment. In no instance did all the respondents entirely discount the use of radiation, despite a lack of evidence regarding efficacy or long-term morbidity. For some of the disorders, clinical observations based on reasonable numbers of patients were available, but often, support for intervention was based purely on personal experience or anecdotal case reports. Clinical trials were rarely available. In almost all instances, the presumed mechanisms underlying these reported therapeutic

responses were the well-documented, but scientifically ill-defined ability of radiation to modulate localized immune response, and to reduce proliferation of many normal and pathologic cell lines. In some instances, palliation of clinical symptoms was obtained for varied intervals absent any awareness of the underlying mechanism of improvement. Understanding these potential mechanisms and observations, often associated with an absence of satisfactory alternative therapies, and a lack of adequate definition of potential long-term morbidity, made individual radiation practitioners comfortable with employing radiation for many of these benign disorders. However, the editors did caution on the importance of obtaining informed consent prior to use of radiotherapy for benign disorders. Administered doses, often calculated at skin, and fractionation and protraction schedules, were as varied as the practice patterns of the respondents, and typically employed superficial or orthovoltage beam energies. Anecdotal reports suggested that for some practices, management of benign disorders might represent up to 30% of patient volume.

By 2003, with publication of the second edition of the text, radiation oncologists had largely abandoned management of benign disorders. Superficial and orthovoltage devices so well suited to management of

*Continued on following page*

many of the benign entities had often disappeared from our clinics, and topical and systemic medications to manage many of the disorders had become available. Referrals for management of benign entities became less frequent, and radiation oncologists became more focused on the complex multidisciplinary management of cancer. The text did provide additional information on the scientific underpinnings of the interventions still seen in the clinic as well as discussion of the medico-legal implications of those interventions. When available, data was provided regarding appropriate treatment techniques for the megavoltage and 3-D planning era.

With an increased ability to deliver higher and more precisely targeted doses of ionizing radiation to better defined sites, increased interest in the radiotherapeutic management of entities such as prophylaxis of heterotopic ossification, arteriovenous malformations, and acoustic neuromas, as well as emerging indications such as brachytherapy for vascular restenosis, was codified, and to a greater degree, standardized.<sup>2</sup> Occasional presentation of keloids were managed by electrons rather than superficial x-rays. Despite scientific interest, management of benign entities waned in significance within most of our facilities.

Most recently, the third edition was released in 2023 with Dr. Roberge as the lead co-editor, replacing the deceased Stanley Order, MD, FASTRO. It introduces us to an emerging era in our understanding and management of this disparate universe of entities. The previously employed A to Z (or X) disorder indexing was replaced by topics grouped by their physiological, biological and pathological underpinnings, such as autoimmune disorders, endocrinological disorders, neurological disorders, etc. Modern treatment planning and delivery techniques are codified, and literature to justify and support interventions has expanded. Critically, short- and long-term implications of the interventions are detailed.<sup>3</sup>

The final risk/benefit ratio in the management of any individual patient is determined by the physician(s) and the patient, who must often accept some measure of uncertainty in their decision making. These decisions are especially critical when the consideration is the radiation management of a benign entity. As noted by Roberge and Donaldson,<sup>3</sup> clinicians and patients must:

- Determine the natural history of the disorder process.

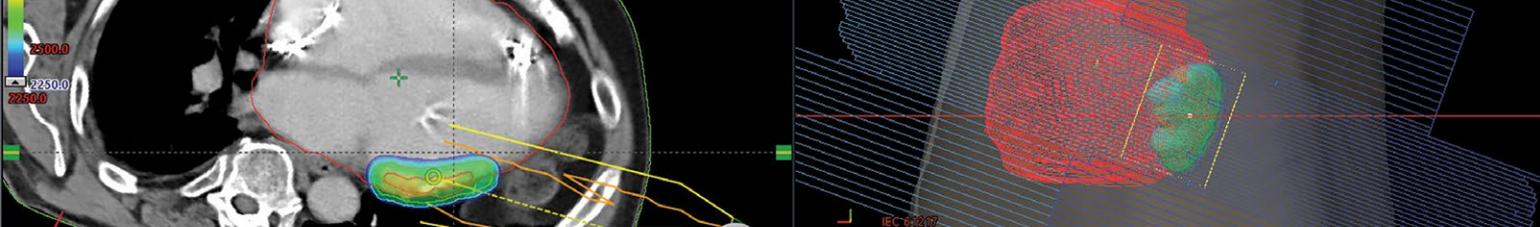
- Have a clear vision of the definition of successful treatment and ensure that the patient's expectations are in line with this definition.
- Evaluate the evidence that radiotherapy can lead to a successful outcome and when prospective comparative data is not available, be mindful of how results can be colored by biases, variability in the natural history of the disease process and the placebo effect.
- Educate oneself on the alternate treatments and their effectiveness, evidence supporting their efficacy, their associated risks and toxicities, already attempted treatments, and why other alternatives were not considered.
- Determine the potential long-term risk of radiation treatment, considering the patient age, planned total dose, fractionation, organs at risk, and any underlying co-morbidities that may increase the risk of complications.

The following articles in this issue highlight and revisit areas of radiotherapeutic intervention of benign entities. The ability of our neurology and cardiology colleagues to localize sites of neurostimulation and foci of cardiac arrhythmias coupled with our increasing ability to precisely target these sites and control for organ motion has opened new opportunities for radiation management of neurological and cardiac disorders. A deeper understanding of the basic functions of the immune system and the local and distant impact of radiation on those functions has introduced additional new therapeutic potential and prompted revisiting older, previously dismissed interventions. These new indications have the potential to advance the management of previously difficult to manage entities and to significantly alter our clinical practices. It is incumbent upon us to be open-minded and realistic to these potential benefits, and risks, for our patients' benefit. 

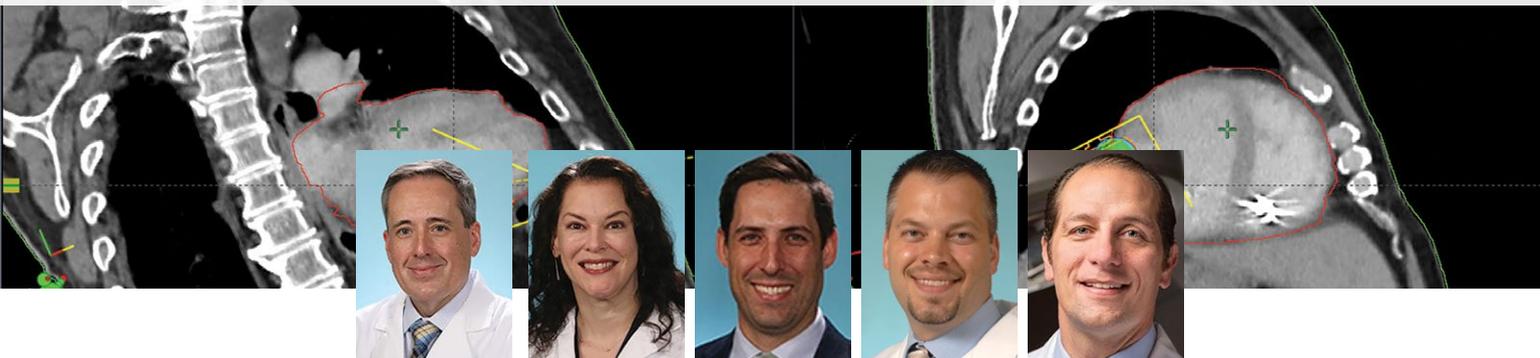
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# Cardiac Radioablation for Ventricular Tachycardia – *Updates and Future Directions*



BY CLIFFORD ROBINSON, MD; PAMELA SAMSON, MD; GEOFFREY HUGO, PHD; DAN COOPER, MD; AND PHILLIP CUCULICH, MD

**CARDIAC RADIOABLATION (CRA) IS AN SBRT TREATMENT** that has emerged as an alternative to invasive catheter ablation for high-risk refractory ventricular tachycardia (VT). Since introducing CRA in *ASTROnews* Spring 2021,<sup>1</sup> we have improved our understanding of biologic mechanisms, long-term clinical outcomes and challenges to implementation.

## Bedside back to bench

Preclinical investigations of CRA sought to recapitulate the destructive effects of catheter ablation using single doses of 15–40 Gy. A dose of 25 Gy was selected as a compromise between the late fibrosis observed in preclinical models coupled with clinical comfort level. While VT suppression by the fibrotic model was expected to take months, most patients experienced improvement in days to weeks. Therefore, fibrosis alone cannot account for the mechanism of VT suppression. Preclinical data demonstrates *improved* conduction velocity in myocardium receiving at least 15 Gy, mediated in part by increases in NaV1.5 and Cx43 expression.<sup>2</sup> Excitingly, increased conduction after radiotherapy represents a new potential mechanism for VT suppression.

## Clinical experience expands and a pivotal trial begins

Recent reports from other centers mirror our early results<sup>3,4</sup> with most (>90%) patients experiencing reduced VT burden in days to weeks. Acute serious adverse events (SAEs) have not been reported during or

immediately after CRA, though rare late (valve injury, GI injury) toxicities have been described.

Direct comparisons between CRA and repeat catheter ablation are limited and challenging due to patient selection bias. A recent matched analysis<sup>5</sup> of high-risk refractory VT patients treated with CRA versus repeat CA at our center found similar freedom from shock or VT storm (median 8.2 vs. 9.7 mo) with fewer SAEs (14% vs. 38%) and early deaths (1 vs. 5 patients) in the CRA group, suggesting that CRA may provide similar VT control rates with less toxicity.

However, rates of any VT recurrence in the years after CRA remain high. It remains unclear whether this reflects CRA efficacy or progressive cardiomyopathy. The optimal efficacy endpoint for this population — VT burden, freedom from shock, or survival — is still unclear. Therefore, we encourage centers to report all these measures.

Large scale and multi-institutional reports are ongoing. The STOPSTORM Consortium<sup>6</sup> brought together over 30 EU centers delivering CRA for VT, establishing comprehensive workflows and a large patient registry. The MUSIC Consortium<sup>7</sup> established a registry of centers using their imaging tools, including a subset for CRA. The first multicenter randomized controlled trial was recently opened (RADIATE-VT, NCT 05765175)<sup>8</sup> to evaluate the safety and efficacy of CRA versus repeat CA for patients with high-risk, refractory VT. If positive, this pivotal study could lead to a new FDA-cleared indication for radiotherapy.

*Continued on following page*

## Standardizing target selection

The target for CRA is not visible on conventional imaging but instead defined by integrating electrical and scar (echo, MRI, PET) data. One option is to co-register scar images to the simulation CT with electrical data imported as DICOM images from catheter mapping systems or manually defined by the electrophysiologist. This method enables contouring on native data, but has potential for large, compounded errors due to respiratory/cardiac motion, planar reconstructions and changes in heart volume. An alternative approach is to have each data source scored on a model (such as AHA 17-segment model) and integrate these score segments directly onto the simulation CT. This geometrically stable method avoids errors in image registration, though could lead to larger initial targets.

## Regulatory and billing issues

While radiotherapy systems have broad indications for both malignant and non-malignant conditions as part of the 510(k)-approval process, the U.S. FDA has categorized CRA as off-label use. This means any prospective evaluation of CRA must be performed as part of the FDA investigational device exception (IDE) process though patients may be treated on a case-by-case basis based on clinical need.

Submitting SBRT codes with a VT diagnosis code to insurance for off-label CRA will typically lead to denial. Centers can engage with hospital leadership to waive professional and technical fees, citing (1) intent to treat a limited number of patients, (2) limited or no net loss based on the cost of delivering SBRT relative to other reimbursable components of treatment (diagnostic imaging, electrophysiologic mapping, etc.), and (3) benefits of being an early adopter. Category III CPT codes have been developed (0745T, 0746T, and 0747T) to track utilization to provide documentation as part of future transition to Category I codes.

## Future directions

Recent years have seen an increased use of CRA for VT, but much remains to be learned, including but not limited to optimal dosing and/or fractionation, dose constraints to cardiac substructures, motion management, and the role of MR-guided radiotherapy and proton therapy.

We encourage interested individuals to take advantage of recent review articles,<sup>9,10</sup> our annual SNOSTORM meeting,<sup>11</sup> and our Center for Cardiac Radiotherapy (CNCR) website.<sup>12</sup> 

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 @SBRT\_CR

*Pamela Samson, MD, assistant professor of Radiation Oncology, Washington University in St. Louis.*

 @samsonpp

*Geoffrey Hugo, PhD, professor of Radiation Oncology and vice chair of Medical Physics, Washington University in St. Louis.*

 @gdhugo

*Dan Cooper, MD, professor of Cardiology, Washington University in St. Louis.*

 @cooper\_dh

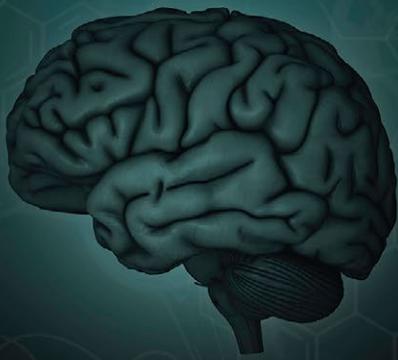
*Phillip Cuculich, MD, professor of Cardiology and Radiation Oncology and co-director of the Center for Noninvasive Cardiac Radiotherapy, Washington University in St. Louis.*

 @DoctorPhilleP

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# RADIOSURGERY FOR NONMALIGNANT INDICATIONS

## *A Functional Radiosurgery Renaissance*

BY EVAN THOMAS MD, PHD, AND MARKUS BREDEL MD, PHD

### THE HISTORY OF STEREOTACTIC RADIOSURGERY

**(SRS)** is a testament to the relentless pursuit of precision and minimal invasiveness in medical procedures. Although it has become synonymous with precision treatment of primary and secondary intracranial malignancies, it was conceived in 1951 by Swedish neurosurgeon Lars Leksell initially as a non-invasive method to target functional brain disorders such as pain and movement disorder. Leksell's vision was to create a surgical procedure that could reach any target within the brain without a scalpel, using ionizing radiation to focally lesion with sub-millimetric accuracy, areas conventionally only reachable via craniotomy. This vision became manifest originally in the form of a stereotactically mounted X-ray tube (Figure 1: A, B) but evolved into an early version of what we now recognize as the Gamma Knife platform.

Early indications for functional radiosurgery on the Gamma Knife

included not only treatment of the trigeminal nerve for classical trigeminal neuralgia, the functional disorder most radiation oncologists are most familiar with, but also:

- essential and Parkinsonian tremor (via ventral intermediate nucleus thalamotomy)
- primary and Parkinsonian dystonia (via pallidotomy)
- refractory neuropathic and stroke pain syndromes (via centromedian and contralateral thalamotomy)<sup>1</sup>

- end stage cancer pain (hypophysectomy)
- psychiatric disorders such as obsessive disorder, major depressive disorder

The noninvasiveness of radiosurgery compared with using RF catheters or other techniques for lesioning within the brain led to a surge in interest in these applications, particularly during the late 1990s and early 2000s. As deep brain stimulation became increasingly available, growth in SRS as a lesional therapy for functional indications did not keep pace with the growth of SRS for other indications, particularly benign brain tumors and brain metastases. Deep brain stimulation became the preferred interventional technique for medically refractory neurological conditions, movement disorders in particular.

Deep brain stimulation remains remarkably effective for movement disorders such as essential tremor,

Parkinson's disease and dystonia, and is still considered the gold standard procedural intervention. However, at least 40% of patients who might be candidates for deep brain stimulation based on their medical refractoriness are not eligible due to medical

comorbidity or anatomical considerations. Likely at least as many decline to undergo deep brain stimulation simply based on perception of invasiveness or desire to not bear the burden and maintenance of an implantable device. Moreover, deep brain stimulation has not been as effective as it was hoped to be for pain disorders and psychiatric conditions such as treatment refractory depression and obsessive disorder.

Then in the late 2000s, MRI guided focused ultrasound (MRgFUS) entered the scene. The

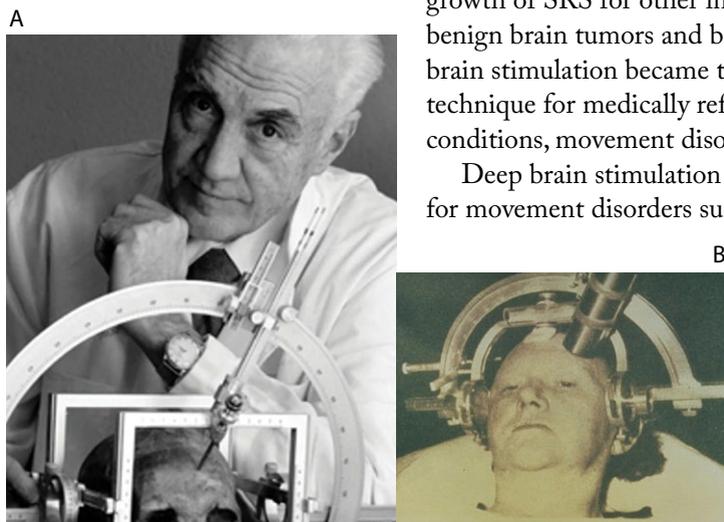
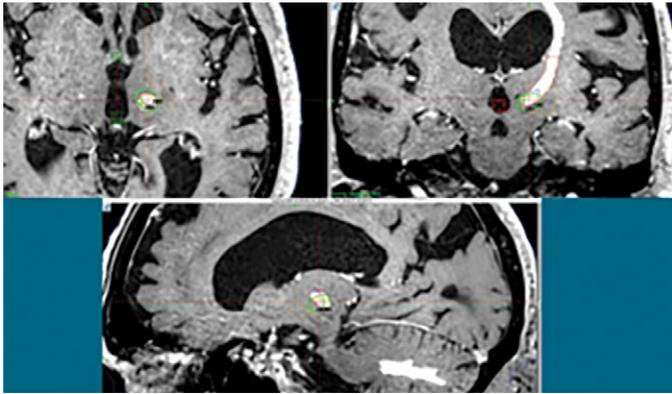


Figure 1: (left) Lars Leksell and his stereotaxy frame, and (right) a stereotactically mounted X-ray tube for the purpose of radiosurgery

*Continued on following page*



**Figure 2 - Gamma Knife Icon radiosurgical thalamotomy plan with isocenter placed on DTI-based tractographic junction of the left ventral intermediate nucleus and the left dentato-rubro thalamic tract. (Image courtesy of author.)**

treatment uses a stereotactic array of transducers whose emitted sound waves intersect in a central focal point of interference (similar to a Gamma Knife) and generate sufficient heat to produce a thermal lesion. It soon received FDA approval for treatment of essential tremor. With a few high profile publications<sup>2</sup> and aggressive direct to patient advertising, its use exploded — promising a “non-invasive” method to treat patients with essential tremor. In actuality, the treatment imposes more on the patient than expected — patients must still wear a frame, must shave their heads, and the treatment can cause severe, treatment-limiting pain due to scalp heating. Despite these considerations, the treatment remains very popular which itself is a convincing argument that there remains a very large number of patients interested in a minimally invasive lesional therapy for their medically refractory neurological disorder.

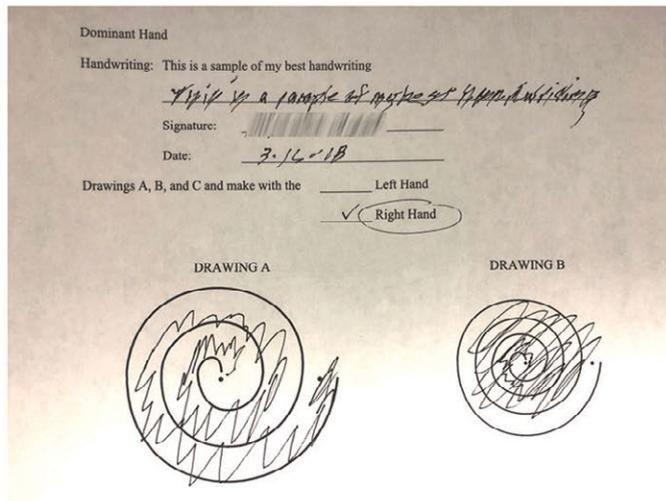
Stereotactic radiosurgery, with or without a frame, remains substantially less “invasive” than MRgFUS,

and demonstrates comparable and possibly more durable efficacy with a milder acute toxicity profile.<sup>3,4,5</sup> Improved knowledge of optimal targeting using modern tractography and connectomics is poised to improve the onset time and effectiveness of radiosurgery for tremor as well.<sup>6</sup>

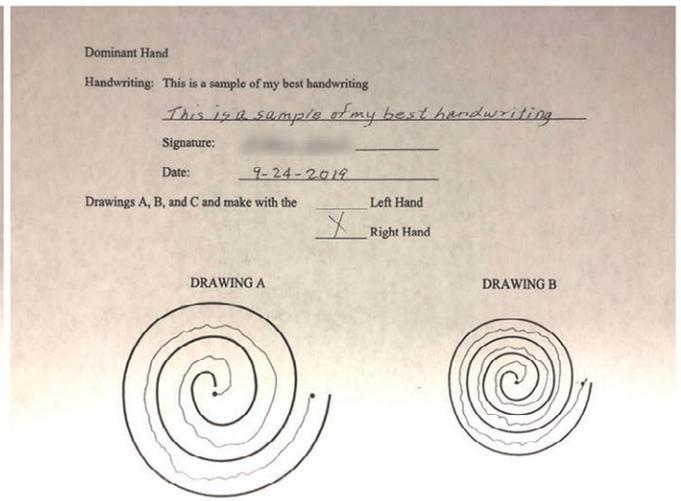
We now have four commercial platforms capable of the precision and accuracy necessary for functional radiosurgery delivery. SRS for movement disorders, trigeminal neuralgia, and epilepsy are currently explicitly delineated as medically reasonable and necessary in the CMS local coverage determination.<sup>7</sup> Other indications such as refractory psychiatric conditions are typically reimbursable with peer-to-peer review. Two vendors have received 510K approval for marketing of treatment of essential tremor (Elekta, Gamma Knife; Varian Medical Systems, TrueBeam). We lack exposure to functional radiosurgery in residency training to generate functional-trained radiation oncologists capable of building a partnership with functional neurosurgeons. Only a handful of academic programs around the United States offer enough functional radiosurgery volume that a trainee could acquire sufficient exposure upon graduation without pursuing additional training, which at present is only available on a routine basis in a single course outside the U.S. Thankfully, vendor-supported efforts are underway to develop training programs and increase access to these treatments.

Stereotactic radiosurgery is a safe, effective and time-tested treatment for refractory pain, movement disorders and psychiatric disorders. The existing patient reservoir numbers exceed that of many other radiotherapy indications. Current utilization is low, but

### Pre-SRS Thalamotomy



### Post-SRS Thalamotomy





**Figure 3 - Functional SRS Capable Platforms (top left) Elekta Esprit, (top right) Varian Edge, (bottom left) Accuray CyberKnife M6, (bottom right) Zap-X (images used with permission)**

with proper adoption and engagement, the field is uniquely poised to ride the wave that MRgFUS has created and dramatically increase our presence in this treatment space and ultimately help many patients. 



*Evan Thomas, MD, PhD, is an Assistant Professor of CNS and GU radiation oncology at Ohio State University and leader of the functional SRS division, wherein and with neurosurgical collaboration, he offers functional radiosurgery for pain, movement disorders and psychiatric conditions.*



*Markus Bredel is a Professor of CNS and breast radiation oncology as well as the Director of Functional Brain Radiosurgery, Sharon A. Spencer Distinguished Endowed Chair in Translational Radiation Oncology, and Head of Brain Tumor Research at the University of Alabama at Birmingham. He is the incoming Chairman of the Department of Radiation Oncology at the University of Miami.*

## PATIENT REFERRALS

The Ohio State University functional SRS division works in collaboration with the neurosurgical department. The referral stream is a little different than for cancers, but much like tumor boards, there are multidisciplinary conferences at many institutions for patients with neurological, pain and psychiatric disorders. Participation by a radiation oncologist is uncommon but often welcome and can be a valuable resource in management.

Many specialists remain unaware of the safe, effective and well-established role that stereotactic radiosurgery can provide. Once a successful functional SRS practice is set up, direct outreach, education and relationship building with neurology, pain and psychiatric community providers can yield referral volume as well.

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# A Pain in the Foot:

## RT as an Evidence-Based Treatment for Plantar Fasciitis



BY JARAD MARTIN, MBCHB, BSC, PHD, DMED



**IF YOU WATCHED THE DOCUMENTARY** Usain Bolt: The Fastest Man Alive, you would have registered a particularly memorable scene. In preparation for the London Olympics, the superstar sprinter is shown in a linac bunker, getting set up for treatment to his foot. Although the show doesn't elaborate the underlying diagnosis, the setup looks consistent with treatment for plantar fasciitis (PF). Also, given his treatments were supervised by Bayern Munich club doctor Hans-Wilhelm Müller-Wohlfahrt, it highlighted how widely embraced such treatments are in Germany. Ultimately he picked up another three gold medals, which is as good a testament to the efficacy of radiation therapy (RT) as any.

PF is a bane of middle age, and radiotherapy can be an effective treatment. PF affects a range of people from athletes to those on their feet all day for their occupation. It is a painful condition, and in chronic cases, it can be very difficult to manage. Low dose radiotherapy has been shown to provide superior analgesic benefit compared with a steroid injection in a randomized trial, mounting an argument for wider use in the community.<sup>1</sup>

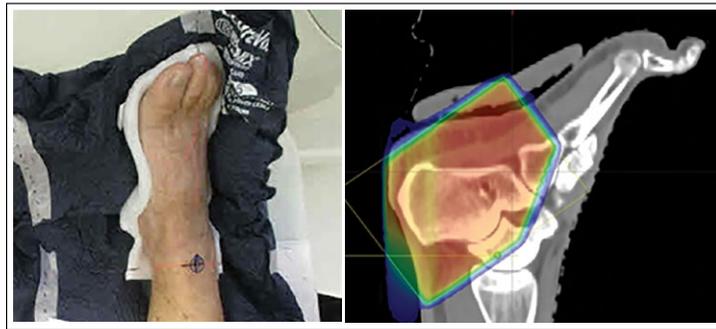
The plantar aponeurosis is susceptible to microtrauma, leading to chronic inflammation and PF. Factors such as running, obesity, occupations involving prolonged standing and poor footwear are all risk factors for this degenerative disease. The classic symptom is a sharp pain just anterior to the calcaneus.

A diagnosis is usually made clinically without a need for further investigations. If performed, an ultrasound or MRI will often show some thickening of the plantar aponeurosis. The classic finding of a calcaneal spur on plain imaging is common but has poor sensitivity or specificity for PF.

The majority of cases of PF will settle with supportive interventions such as orthotics, foot strengthening exercises and simple analgesia. Around 30% of cases persist for more than three months, at which point other interventions can be deployed. Some, such as shock wave therapy, are commonly used despite evidence from randomized trials suggesting limited efficacy.<sup>2</sup> Others, such as platelet rich perfusions, have emerging efficacy evidence but the disadvantage of being an invasive procedure.<sup>3</sup>

Low dose radiotherapy for PF takes advantage of the fact that the target cells are the monocytes driving the chronic inflammatory process, and that these tend to apoptose with low doses of radiation. By resetting this chronic inflammation, the microtraumas then have an opportunity to heal. RT has been compared with steroid injection in a randomized clinical trial (RCT) from a single Turkish hospital where 128 patients were accrued over a 13 month period.<sup>1</sup> The median changes on a 10 point visual analogue scale six months after treatment was from seven to five for the steroid group and from eight to two for the RT group, which was statistically significant ( $p < 0.001$ ).

Figure 1



Radiation doses of 6 Gy in 6 fractions delivered over two weeks are commonly deployed, although a German RCT comparing this with 3 Gy in 6 fractions found no difference in the rate of analgesic benefit leading to this lower dose now being recommended as initial treatment in international guidelines.<sup>4</sup> There is an option for repeat treatment, usually with 6 Gy in 6 fractions after 12 weeks if there has been a suboptimal benefit. Acute side effects are rare at such low doses and 70–80% of people will report some degree of pain relief.

Treatment is via a parallel opposed pair of megavoltage photon fields with 5–10mm of bolus. The field tends to include the whole calcaneus including a margin as shown in Figure 1. Patients are encouraged to continue conservative measures such as avoiding running and use of orthotics as they progress through treatment.

Among all of the potential indications of RT for benign extracranial conditions, PF occupies a relatively unique space as outlined in Table 1. Furthermore, it offers an opportunity to engage with other craft groups such as podiatrists and foot and ankle surgeons collaboratively to embrace their diagnostic and therapeutic skills, so that radiation can complement rather than compete with established practice. It is immensely satisfying to assist someone with chronic pain, as such people have often had numerous fruitless interventions, and the positive quality of life impact

from radiation is commonly rapid and sustained — a key factor to consider when your next oncology patient hobbles into clinic and admits to suffering an intractable case of PF. [A](#)

*Professor Jarad Martin, MBChB, BSc, PhD, DMed, is a radiation oncologist in Newcastle, Australia, where he also has a benign radiotherapy practice, including a combined Dupuytren's clinic he runs with local hand surgeons, and is PI on the DEPART trial of observation vs. radiotherapy both in the preventative and adjuvant settings for Dupuytren's Disease.*

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Table 1: Plantar fasciitis indications for radiation therapy treatment

|   |  |
|---|--|
| Common condition                                  | Thought at some point to affect ~10% of adults in Western countries  |
| Simple treatment                                  | Parallel opposed beams   |
| Low risks   | No acute toxicity, and very low second malignancy risk given low dose, physical location and older population affected |
| Limited efficacy of other non-invasive treatments | Wide range of approaches suggests no 'Gold Standard' definitive treatment  |
| Good level evidence to support use                | RCT showing analgesic benefit versus an active comparator  |



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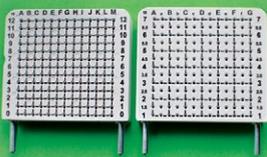
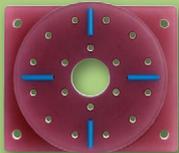
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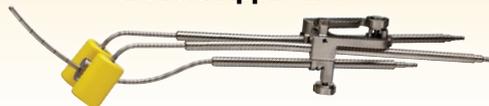
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<sup>1</sup>Communication from J. Limmer, UW Cancer Center Wausau Hospital, Wausau, Wisconsin – Dated December 14, 2000. <sup>2</sup>B.H. Heintz, R.E. Wallace & J.M. Hevezi, Med. Phys. 28(4) 671-682 (2001). <sup>3</sup>Communication from Khai Lai, Kreitton Oncology Services Shoreline, Washington – Dated March 8, 2001. <sup>4</sup>Jeff Limmer, Medical Physicist.

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# Radiotherapy for Dupuytren's Disease

BY RICHARD SHAFFER, MBBS, AND GOPAL BAJAJ, MD, MBA, FASTRO

## Introduction

Dupuytren's disease (DD) is a common benign thickening of the fascia on the palms of the hands, whose characteristic change is formation of contractures (fixed bending) of the fingers. It is part of a group of hyperproliferative disorders, including Ledderhose disease of the feet and Peyronie's disease of the penis.

## Causes (+/- epidemiology)

DD is an autosomal dominant condition with variable penetrance. Certain patients are particularly susceptible to aggressive progression and are said to have a diathesis (characterized by onset at age < 40 years, bilateral disease, disease outside palms, first degree relatives with condition). There are also non-genetic trigger factors that affect the development of this condition, for instance diabetes mellitus, manual labor, hand trauma, alcohol and smoking. DD is also associated with an increase in all-cause mortality, probably due to shared changes in the WNT signaling pathway.<sup>1</sup>

## Natural history

In the early stages of DD there is formation of nodules, cords and skin retraction. Even in the early stage there can be functional loss, which may impact dexterity and fine motor function. It has an unpredictable and variable disease course. Later stages are characterized by contracture (fixed flexion deformity) of the fingers and more pronounced functional loss (Figures 1, 2). Tubiana proposed a staging system for DD in 1999 and this was subsequently modified to regroup patients with very early contracture (Table 1).<sup>2-4</sup>

## Non-radiotherapy treatment

The advanced stages, typically where there is contracture of more than 30 degrees, with functional deficit, is dealt with by contracture release using open surgery (fasciectomy), collagenase enzyme (Xiaflex) injections or a needle aponeurotomy. Fasciectomy is probably the most effective treatment with typical contracture recurrence rates of 20% at three to five years but is also the most invasive of the treatment options. Needle aponeurotomy is much less invasive but has a high recurrence of 50-60% at three to five years.

In early stage DD, where there is either no contracture or a mild contracture, the advice until recently has been to simply observe the patient until they form a contracture, at which point it will be released using one of the aforementioned surgical methods. However, evidence shows that there is an opportunity to intervene with anti-proliferative radiotherapy to prevent symptomatic progression, contracture formation and the need for surgery.

## RT evidence

Retrospective studies have shown that radiotherapy is only effective in the early stages of the disease and is not effective where there are advanced contractures. The best trial of radiotherapy for early Dupuytren's disease was published by Seegenschmiedt et al. in 2001, and subsequently updated as a textbook chapter.<sup>2</sup> They recruited 489 patients (718 hands) to a randomized trial comparing total doses of 30 Gy in 10 fractions (two phases of 15 Gy in 5 fractions, with two months in between the phases) with 21 Gy in 7 fractions

Figure 1

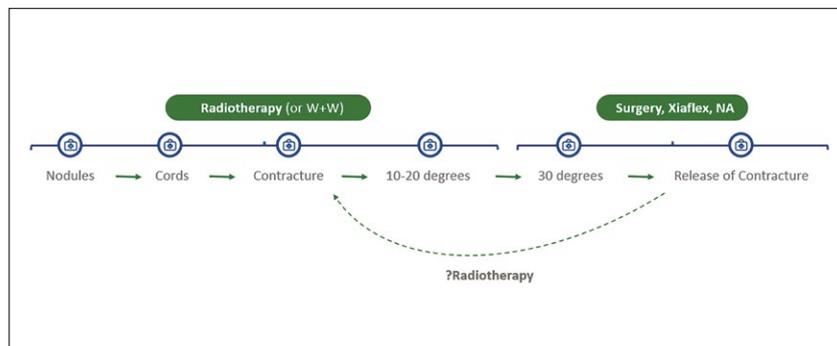


Figure 2

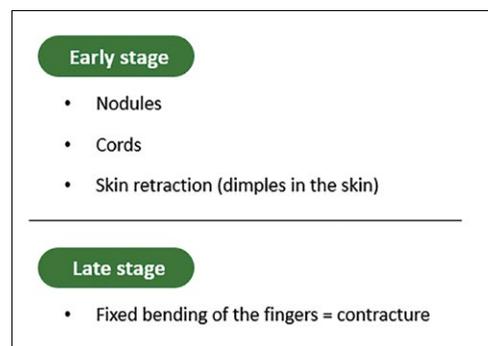


Table 1: Classification of Dupuytren's contracture according to Tubiana et al.<sup>3</sup> and modified by Keilholz and Seegenschmidt<sup>2,4</sup>

| Stage     | Clinical Symptoms                                  | Extent of Extension Deficit      |
|-----------|--|----------------------------------|
| Stage N   | Nodules, cords, skin retraction and fixation, etc. | None, i.e., no flexion deformity |
| Stage N/I | As stage N plus deformity of fingers               | 1-10°                            |
| Stage I   | As stage N plus flexion deformity of fingers       | 11-45°                           |
| Stage II  | As stage N plus flexion deformity of fingers       | 46-90°                           |
| Stage III | As stage N plus flexion deformity of fingers       | 91-135°                          |
| Stage IV  | As stage N plus flexion deformity of fingers       | >135°                            |

\*Stage N modified from Keilholz et al. (1996)

(fractions given over 2.5 weeks) for patients with early progressive disease where there is:

1. Evidence of DD (nodules, cords, skin retraction)
2. Progressive disease in the last 6-12 months
3. Either no contracture or a mild contracture of up to 20 degrees

Patients were also offered a watch and wait approach, forming a non-randomized control group of 122 patients, which were found to have very similar risk factors for progression to the treatment group. Absence of progression was superior in the 30 Gy group, compared to both the 21 Gy cohort and the control group at a median of 8.5 years of follow-up. Radiotherapy to 30 Gy conferred a three-fold reduction in the risk of progression and the need for surgery to release a contracture with radiotherapy compared with the control group (Table 2).

There is also early evidence for adjuvant RT for patients with more advanced presentations of DD after contracture release. In this setting, RT may be potentially utilized for secondary prevention of recontracture. However, these data are not mature and this approach should only be used in the context of a clinical trial or after detailed multidisciplinary discussion.

### Patient assessment

Patients should have a full history, including associated conditions, risk factors and activities requiring specialist hand function. Examination of the hands includes details of palmar and digital nodules, cords and skin retraction, Garrod's (knuckle) pads, loss of finger hyperextension or span, and measurement of finger contractures. All patients should have their feet examined for plantar fibromatosis as this is co-existent in approximately 15% of patients with DD.

It is important not to treat patients unnecessarily. For those who have early disease that only recently formed and/or is stable, a watch and wait approach can be utilized. For those with advanced disease (> 20 degrees contracture) radiotherapy is unlikely to be successful and should generally not be used.

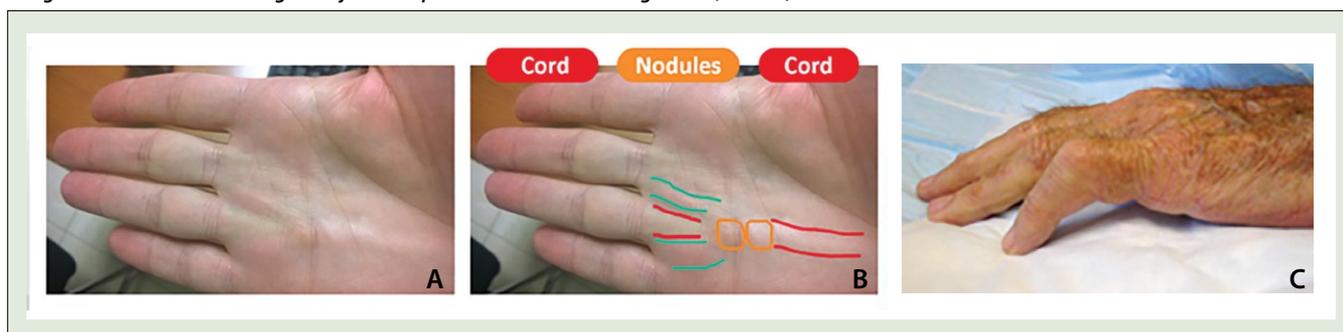
### Radiotherapy details

For those who are eligible for treatment, the radiotherapy field boundaries aim to cover the common areas that are affected by DD whilst, where possible, sparing the nail beds, the thenar and hypothenar eminences and the carpal tunnel.

The standard dose is 15 Gy in 5 fractions over one week. There is then a 10-14 week gap and a further 15 Gy in 5 fractions. Various modalities can be used, including megavoltage photons, electrons and orthovoltage (kV) treatments, although superficial modalities are preferred over megavoltage photons.

*Continued on following page*

Figures 3 A-C: Example of early stage (Tubiana N) DD (Panel A) and superimposed outline of associated cords and nodules (Panel B). Image of a contracted little finger PIP joint in a patient with Tubiana Stage II DD (Panel C).



**Table 2: Regression, progression and surgery rates for DD patients at 8.5 years follow-up**

| Stage           | Regression or Stable (%) | Progression (%) | Surgery(%) |
|-----------------|--------------------------|-----------------|------------|
| Control (n=122) | 38                       | 62              | 30         |
| 30 Gy (n=303)   | 80                       | 20              | 8          |

Due to the relatively low dose of radiotherapy used, side effects tend to be mild, with generally grade 1 skin erythema and dryness and a 20% risk of permanent grade 2 skin dryness.

There is a risk of basal cell skin cancer which is estimated at 0.1% lifetime risk for a 50-year-old. However, this risk should be carefully discussed, particularly in younger patients.

### Discussion

Moderate dose radiotherapy to 30 Gy over a split course is a well-tolerated and highly efficacious treatment for patients with early progressive DD as it reduces the chance of symptomatic progression and the formation of contractures that need invasive surgery to correct. Despite long-term compelling data showing a benefit of radiation therapy for early stage DD, adoption of this treatment approach and general awareness of the benefit of RT in early stage DD remains limited in the United States.<sup>5</sup> In contrast, RT for DD is widely utilized in Europe and other parts of the world. The basis for these differences is certainly multifactorial. Limited data, lack of training in the assessment of nonmalignant conditions, lack of capacity and variations in reimbursement are often cited. Most practicing radiation oncologists are not aware that many U.S. commercial payers support the use of radiotherapy in the treatment of DD and associated Ledderhose Disease. The author's personal experience (GKB) in treating over 600 patients with DD is that I have never experienced a denial for the treatment of this condition. Yet patients often travel far from their homes to seek out expertise for a treatment which, on most accounts, could be easily delivered at nearly any radiation oncology facility in the U.S. This disparity in access underscores a large opportunity for radiation oncologists to seek out additional training in the treatment of DD and associated conditions. 



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*Richard Shaffer, MBBS, is a specialist in radiotherapy for benign conditions and president and founder of the International Organisation for Radiotherapy for Benign Conditions.*

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## LOW DOSE RADIOTHERAPY TREATMENTS

### FOR OSTEOARTHRITIS



BY AUSTIN KIRSCHNER, MD, PHD, AND AUSTIN DOVE, MD

**LOW DOSE RADIATION THERAPY (LDRT)** has been employed for over a century to alleviate pain and improve mobility in patients with osteoarthritis (OA). Since its first documented use in 1898, LDRT for OA has been a well-accepted and utilized treatment in many countries, such as Germany where several tens of thousands of patients are treated each year.<sup>1</sup> In the U.S., the use of LDRT for OA has declined over the past few decades, but recently has had reemerging interest.

While OA is considered a “benign” disease, more than 32 million Americans suffer from it and experience considerable morbidity and associated mortality from the condition. OA is the most common type of arthritis, which results from the chronic degeneration of cartilage between bones in the joint resulting in damage to articular surfaces, bones, ligaments and surrounding structural components. OA is a clinical diagnosis for persistent usage-related joint pain, typically in patients with age greater than 45 years and morning stiffness lasting less than 30 minutes.<sup>1</sup> The pathophysiology of OA is complex with multiple inflammatory pathways interacting to increase pro-inflammatory cytokines and recruitment of proteases, which result in joint damage. The radiobiologic effect of LDRT has been shown by multiple preclinical

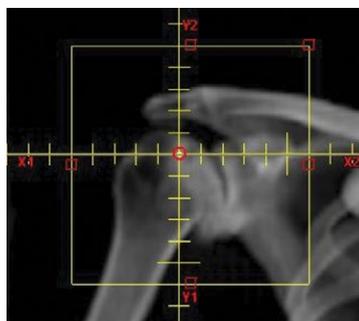
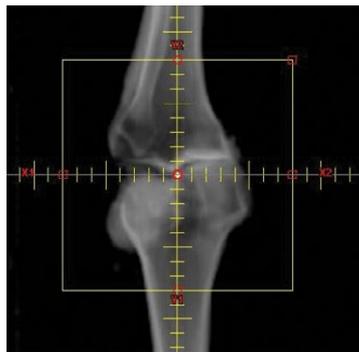
studies to modulate inflammatory pathways and cellular components to reduce pain and joint stiffness. These pathways include modulation of macrophages to anti-inflammatory M2 phenotype, reduction in the production of nitric oxide and inflammatory cytokines, and decreased transmigration of pro-inflammatory cells into the extracellular space.<sup>1</sup>

Multiple retrospective and prospective observational studies have shown significant improvement in both pain and mobility in OA patients treated with LDRT. A recently published review paper highlights numerous studies published on the benefit of LDRT.<sup>1</sup> Notable studies for OA treated with LDRT include a retrospective analysis of almost 1,000 patients with 65% having improvement in pain symptoms and a prospective study of 100 hand OA patients with 94% having pain improvement. However, efficacy of LDRT in OA has been questioned by two small randomized clinical trials that have been criticized for low patient numbers with possible underpowering and no option for reirradiation for poor responders. Nevertheless, there remains no randomized evidence for LDRT over sham RT. A large multi-institutional randomized trial of sham versus LDRT is ongoing in South Korea with anticipated completion date in 2025.<sup>2</sup>

*Continued on following page*

In clinical practice, it is crucial to correctly identify patients with OA who are most likely to benefit from LDRT treatment. Patients should have a formal diagnosis of OA before considering LDRT evaluation. Other potential causes with similar presentations should be ruled out before establishing a diagnosis of OA, such as rheumatoid arthritis, psoriatic arthritis, crystalline arthritis or avascular necrosis. Educating potential referring providers about LDRT for OA through outreach programs helps establish appropriate referrals from primary care providers, rheumatology, sports medicine, orthopedic surgery, interventional anesthesiologists and others. Additionally, many patients seen in radiation oncology clinics for other reasons may have OA and could be considered for LDRT.

During initial patient evaluations, understanding the duration and severity of symptoms as well as other attempted interventions can help determine the likely benefit from LDRT. Patients with a symptom history greater than five years or with extensive prior treatment history are less likely to benefit from LDRT. An X-ray evaluation of the affected joint can determine severity



of OA on the Kellgren and Lawrence classification (grade 0-4).<sup>3</sup> Severe OA (grade 4) is less likely to benefit from LDRT. Consideration of secondary malignancy (SM) risk should be evaluated on an individual basis, with the general recommendation of limiting offering LDRT to patients whose age is 50 years and older. However, there has not been a reported case of secondary malignancy attributed to LDRT for OA, and the risk of SM for extremity LDRT is estimated to be equivalent to the risk associated with a CT of the abdomen/pelvis.<sup>4</sup> LDRT has minimal risk of skin erythema given low dose used. No evidence suggests LDRT could negatively affect future ability to undergo joint replacement, if needed in the future.<sup>1</sup>

Regarding simulation, our institutional practice depends on the joint to be treated. A CT simulation with appropriate immobilization devices is reasonable for reproducibility, although with wider-open field design for LDRT the extreme rigor of setup can be relaxed. The recommended dose for LDRT is 3 Gy in 6 fractions (0.5 Gy per fraction), each treatment given

*Continued on next page*

## A PATIENT'S PERSPECTIVE

### AFTER SUFFERING FROM OSTEOARTHRITIS

for years, Philip Vicari, 85 years of age, had tried everything short of joint replacement to improve his condition. Despite daily use of Tylenol and Tramadol, his Visual Analogue Pain Score (VAS) remained an average of eight out of 10. After undergoing radiotherapy for an unrelated condition, Mr. Vicari became aware of low dose radiotherapy for OA. Within a few weeks after the treatment, he noticed significant improvement in both his pain and mobility.

"I began to see little things in everyday life improve — things you wouldn't think about until you can do them. After treatment, I had significantly more mobility than before. For example, I have long hair

that I have to put in a bun to keep out of my face. Prior to treatment, I couldn't lift my arms up so I would have my wife help. Now, I can do it myself again."

When asked about the procedure, he states, "The actual procedure is very simple. You get on the treatment table and lay there. You don't feel anything, no discomfort." Following treatment, he continues to stay active. "I can walk further without pain. I take less Tramadol now. I'm currently redoing my kitchen. I'm able to do much more than I could before." When asked if he would recommend the treatment, his response was simple: "I would certainly encourage others. You have nothing to lose. [You] definitely come away with more positives than before." 

on non-consecutive days two to three times per week. Prior to LDRT for OA, we recommend documentation of a visual analogue pain score (VAS) to determine severity of pain. Following treatment, we recommend obtaining additional VAS as well as a Von Pannewitz Score at six weeks to determine adequate response. If less than desired response is achieved, reirradiation could be considered with the same dose/fractionation schedule, which provides response in about 50% of patients who do not initially respond to treatment.<sup>5</sup> In summary, LDRT is a standard-of-care treatment for OA that provides good efficacy and minimal risks and should be offered in the setting of multidisciplinary care. 

*Austin Kirschner, MD, PhD, is an associate professor in the Department of Radiation Oncology at Vanderbilt University Medical Center. He is a specialist in radiotherapy for GU malignancies, lymphomas and benign disorders.*

 @AKRadDoc

*Austin Dove, MD, is one of the radiation oncology chief residents at Vanderbilt University Medical Center and will be joining Tennessee Oncology in Chattanooga, Tennessee, following completion of training.*

 @A\_Dove5

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# A 'Beacon of Hope' FOR OSTEOARTHRITIS

## *The Leonard Ferguson Cancer Center Experience*

BY BOBBY KONERU, MD, AND RICHARD SHAFFER, MBBS



**LOW DOSE RADIOTHERAPY (LDRT)** is given for osteoarthritis, tendinopathy and bursitis due to its anti-inflammatory and pain relieving properties. It typically consists of single fraction sizes of 0.5-1.0 Gy and total doses of 3-12 Gy.

It is mainly used in Central Europe, particularly in Germany. Guidelines have been developed by the German Benign Radiotherapy Group,<sup>1</sup> outlining optimal dosage and treatment protocols for osteoarthritis with LDRT. However, in North America, LDRT remains underutilized. A recent review article in the Red Journal by Dove et al.<sup>2</sup> (co-author of previous article on page 23) about radiotherapy for osteoarthritis has prompted significant interest in developing this service throughout the United States.

### **The Leonard Ferguson Cancer Center experience**

Motivated by these findings, discussions with FHN Memorial Hospital administration resulted in the establishment of a program within the Leonard Ferguson Cancer Center for LDRT, yielding remarkable symptomatic responses in the initial patients. For instance, a 68-year-old artist with hand osteoarthritis regained the ability to paint, and another patient who was painfully limping for years, was now walking pain-free after six LDRT sessions.

Encouraged by the success of our early cases, we initiated marketing efforts through print and radio advertisements, leading to a substantial increase in patient volumes. We discussed our program with local orthopedic surgeons, rheumatologists, and primary care physicians, although most of our patients were self-referred. Since 2023, our LDRT program has treated over 75 new osteoarthritis patients, addressing more than 125 joints, evolving from a curiosity-driven initiative into one of the larger LDRT programs in the country.

### **Effectiveness of LDRT for OA**

When evaluating the effectiveness of LDRT for osteoarthritis, we have found an average pain reduction from 7/10 to 3/10 (on a numerical rating scale of 0 to 10). Additionally, patients have benefited from improvements in range of motion, stiffness,

*Continued on following page*

Figure 1: Proportion of patients with a good pain response to radiotherapy for osteoarthritis

| Site           | Response Rate (weighted average) | Studies   | Patients    |
|----------------|----------------------------------|-----------|-------------|
| Hands          | 68%                              | 7         | 994         |
| Foot and Ankle | 75%                              | 2         | 262         |
| Knee           | 79%                              | 33        | 5116        |
| Hip            | 64%                              | 23        | 914         |
| <b>Total</b>   | <b>75%</b>                       | <b>65</b> | <b>7286</b> |

functional abilities, and quality of life. Various baseline factors such as symptom duration, radiological stage, age, gender, inflammatory status, radiotherapy dose parameters, total dose, timing, and number of phases are known to influence the treatment response.

Figure 1 (R Shaffer, unpublished) shows data from multiple trials, illustrating pain responses at different body sites. While the average response rate ranges from 64% to 79%, it is crucial to acknowledge the high uncertainty associated with these figures. The variability in responses may be attributed to prognostic characteristics within different patient populations studied at each anatomical site, and caution is warranted as variations may be artefactual.

### The place of radiotherapy in the osteoarthritis treatment pathway

Radiotherapy is a valuable intervention in the landscape of osteoarthritis treatment, particularly in addressing the substantial gap that exists between conservative measures and surgical options (Figure 2). Recent research highlights the limited impact of medications, underscoring the need for alternative solutions. With an overall success rate of 75% in reducing pain, radiotherapy becomes a pivotal player in filling this treatment void for patients grappling with pain and functional impairment.

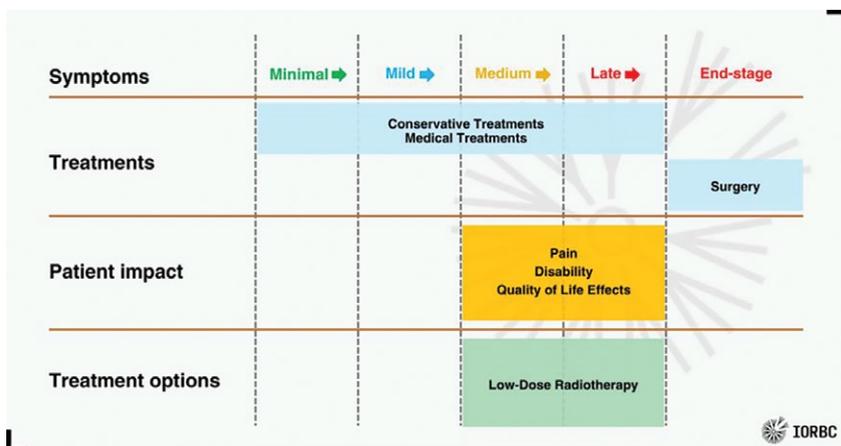
The identified gap between conservative measures and surgical interventions leaves a considerable population dealing with the impact of osteoarthritis on their daily lives. Importantly, at our clinic, we offer education in self-care, for instance, exercises and weight loss, as a crucial aspect of their overall management which is vital for all patients with this disabling condition. For individuals for whom surgery is not an option or who face prolonged waiting times due to extensive surgical queues or disease eligibility criteria, radiotherapy emerges as a viable and impactful alternative.

Radiotherapy serves as a beacon of hope for these patients, offering the prospect of pain relief, enhanced functionality, and the potential to either postpone or altogether avoid surgical procedures. We have seen this have a transformative effect on many of our patients' overall quality of life. 

*Bobby Koneru, MD, is a radiation oncologist at the Leonard Ferguson Cancer Center in Freeport, Illinois, and adjunct Assistant Professor at Loyola University Stritch School of Medicine. He is a board member of the International Organization for Radiotherapy for Benign Conditions (IORBC).*

*Richard Shaffer, MBBS, is a specialist in radiotherapy for benign conditions and president and founder of the IORBC.*

Figure 2 – Radiotherapy’s place in the landscape of osteoarthritis treatment



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# CODING RADIATION THERAPY'S EXPANDED ROLE IN NON-CANCEROUS CONDITIONS

BY ADAM GREATHOUSE, ASSISTANT DIRECTOR OF HEALTH POLICY, ASTRO

**TYPICALLY, WHEN A PATIENT HEARS** the words "radiation therapy," (RT) the immediate association is cancer, but a number of benign conditions are benefitting from it. While somewhat common in other countries, in recent years, there has been an expansion in the United States of the use of RT for nonmalignant conditions such as osteoarthritis, plantar fasciitis and Parkinson's Disease (see Table 1 for a more extensive list). For these conditions, radiation therapy is delivered in order to provide pain relief, improve function or mitigate the need for surgery. Radiation oncologists are playing a crucial role in exploring these nonmalignant RT applications, and some payers reimburse for the work involved in treating these patients.

Reimbursement for using RT for nonmalignant conditions can be complex and varies depending on the payer, the specific condition being treated, and the prevailing coverage policies. Unlike cancer treatment, where specific coding guidelines usually exist, payers often lack clear guidelines for nonmalignant applications. Radiation oncologists seeking reimbursement should be prepared to demonstrate medical necessity, which requires meticulous documentation detailing the diagnosis, rationale for using radiation therapy as the chosen treatment, and how it aligns with evidence-based practices or established protocols, if available. Additionally, confirming that alternative treatment options were explored and deemed unsuitable likely will be necessary.

The process of care for treating nonmalignant conditions is similar to RT for cancer care and can include treatment planning, simulation, device

Table 1 - Nonmalignant conditions

| Non-Malignant Condition                               |                                  |
|---|----------------------------------|
| Depression  | Keloid                           |
| Desmoid Tumors  | Ledderhose                       |
| Dupuytren's Contracture                               | OCD                              |
| Epilepsy  | Osteoarthritis                   |
| Essential Tremor                                      | Peyronie's Disease               |
| Gorham-Stout Syndrome                                 | Pigmented Villonodular Synovitis |
| Graves' Ophthalmopathy                                | Plantar Fasciitis                |
| Gynecomastia  | Pterygium                        |
| Heterotopic Ossification                              | Trigeminal Neuralgia             |
| Hypersalivation of Amyotropic Lateral Sclerosis (ALS) | Trochanteric Bursitis            |

design and construction, an isodose plan, treatment management, and physics consultation. The relevant CPT codes for these procedures are listed in the table (Table 2), but reimbursement will depend on the payer and its coverage policy. Prior to beginning any treatment for a nonmalignant condition, a patient's health insurer should be consulted.

Navigating the specific requirements and potential appeals with payers might be time consuming, but it is often the only remedy left for a patient. As RT's role in the treatment of nonmalignant conditions continues to expand and become more common, it is likely more specific payer guidelines will be created. Any questions on this front can be directed to ASTRO's Code Utilization and Application Subcommittee. [A](#)

Table 2 - CPT Codes

| CPT Code                             | Description  |
|--------------------------------------|--|
| 77263                                | Therapeutic radiology treatment planning; complex            |
| 77280                                | Therapeutic radiology simulation-aided field setting; simple |
| 77334                                | Treatment devices, design and construction; complex          |
| 77307                                | Teletherapy isodose plan; complex                            |
| 77427                                | Radiation treatment management, 5 treatments                 |
| 77336                                | Continuing medical physics consultation                      |
| 77412, G6011, G6012, G6013, or G6014 | Treatment delivery   |

\*Coverage for radiation therapy for nonmalignant conditions varies from payer to payer, and ASTRO makes no guarantee that the use of radiation therapy for the treatment of any nonmalignant disease will be reimbursed. Consult the patient's health insurance provider prior to initiating any treatment plan.

## ABR Exam and Committee Updates

### AS THE ABR ASSOCIATE EXECUTIVE DIRECTOR

for radiation oncology, I have had the opportunity to speak and publish multiple articles with the intent of demystifying the processes of item writing and exam development as well as engaging regularly with the radiation oncology community.

Previous publications have outlined how the ABR continues to review and improve every process and protocol to ensure that each exam is a fair and valid assessment. In radiation oncology, we have made many changes at the request or suggestion of the Association for Directors of Radiation Oncology Programs (ADROP) and the Association of Residents in Radiation Oncology (ARRO). The Accreditation Council for Graduate Medical Education (ACGME) publishes the required training standards for each specialty, and the ABR monitors and discusses these changes regularly.

The ABR is responsible for assessing physicians to determine if they meet the minimum standard required to gain certification. Determining exam content is the role of the volunteer committees that include program directors, department chairs and disease site experts. These committees are responsible for annually creating, reviewing, updating and redistributing the exam content, which is reflected in an exam blueprint. If a subject or treatment is no longer an important or relevant topic to study, then these volunteers will bring that information to the exam development team and the blueprint will reflect the change.

Many in our field have questioned the need for an exam to assess knowledge on physics and radiobiology. When asked, I recenter on our mission statement: “At the ABR, our mission is to certify that our diplomates demonstrate the requisite knowledge, skill and understanding of their disciplines to the benefit of patients.” While it may often be difficult to see the impact on patient care, there are fundamentals of physics and radiobiology that are interwoven into the clinic, and we are obligated to master them in order to become good clinicians. An essential responsibility

for the volunteers on the physics and radiobiology committees is to assess the subject matter and adjust the blueprint annually to maintain the validity and relevance of the exam.

As previously described, the ABR is reprioritizing exam content with a focus on clinical relevance in all qualifying exams. This includes limiting and deemphasizing questions regarding clinical trial details to those that are paradigm shifting or practice changing. To be clear, some major trials will be essential to know, but to ensure that the exams reflect these intentions, each of the committees — including physics, radiobiology, clinical, exam assembly and Angoff — welcome more volunteer participation from diplomates in all areas of practice.

The first exams to follow these guidelines have already been assembled and will be administered in 2024. It may take several years for the exams to shift, and it will be a continual goal, but the process has begun and is fully embraced. The results of each exam administration and the performance of individual items will be closely monitored to ensure the quality and reliability of the exams.

The ABR would not be successful without an amazing group of volunteers. We all give a great deal of our time to many aspects of our lives. Volunteering with the ABR offers an amazing opportunity to help shape the direction of our field and work with other wonderful professionals while ensuring that the process remains current and maintains the highest standards.

We strongly recommend that anyone interested log in to myABR and navigate to the volunteer tab to submit a volunteer application. Private practice and generalists, like myself, are encouraged to participate and appreciate the great work that is continually produced by the talented staff and volunteers for themselves. 

*Portions of this article were previously presented at ASTRO 2023 and published in The Beam Focus on RO 2023;16(5):7.*



## Improving Quality, Improving Lives

**AS WE STEP INTO A NEW YEAR**, ASTRO's APEX – Accreditation Program for Excellence® is witnessing the largest update since its inception in 2014. This year, ASTRO will unveil updated standards, a modified process and a new portal. These developments mark a significant leap forward in assuring APEX remains robust, relevant and capable of meeting the evolving needs of accreditation in radiation oncology.

### Standards

In response to the dynamic landscape, ASTRO revamped the assessment standards to reflect the latest advancements and best practices. The updated standards aim to provide a more comprehensive and precise evaluation of radiation oncology practices seeking accreditation. This includes:

- Refined evaluation criteria
- Updated Standards Guides with more detailed information and sample documents
- Enhanced assessment of specific treatment modalities, like radiopharmaceutical therapy

### Improved process

ASTRO has used the last nine years of program data to determine ways to strengthen the already effective APEX Self-Assessment and Facility Visit with new assessment sections. The updated process will support practices in continuous quality improvement and reinforce the assessment on typically low-performing

areas, allowing practices to receive additional feedback prior to the facility visit on areas that may need improvement.

### Portal

Accreditation processes are being streamlined and made more accessible through the introduction of the new portal. Like the current portal, the new portal serves as a centralized hub for all accreditation-related activities, offering an interface for both facilities and surveyors. The new platform provides new and easier access to program resources. Facilities and surveyors can review the content from the updated Standards Guide for quick reminders during the Self-Assessment and Facility Visit. Physicists also have a new high-level compendium of relevant TG and MPPG guidance.

2024 is a big year for APEX. ASTRO is proud to present these updates on the already strong APEX program to support radiation oncology practices pursuing a high standard of quality and safety. These enhancements pave the way for APEX to be a stronger, more responsive, and more effective accreditation program in the years to come.

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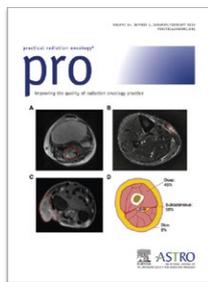
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## Stereotactic Radiosurgery and Functional Disorders: An Interview with Grace Simmons, BS; Matthew Gallitto, MD; Albert Lee, MD;

Gordon Baltuch, MD, PhD; Brett E. Youngerman, MD; and Tony J.C. Wang, MD, FASTRO

This project was conducted by clinicians and research staff in the Columbia University Irving Medical Center Department of Radiation Oncology and the Functional Neurosurgery Division of Columbia Neurosurgery.

### Can you provide a brief overview of the study and findings?

The goal of this Topic Discussion was to provide an overview of the applications of stereotactic radiosurgery (SRS) for medication-refractory functional disorders — trigeminal neuralgia, epilepsy, tremor, OCD and/or intractable pain. We reviewed the existing literature on SRS for functional conditions, summarized indications, response rates, adverse effects, and synthesized findings into suggested treatment guidelines. Overall, while the data are currently limited by small study numbers and few randomized trials, we found SRS to be a reasonable therapeutic option for well-selected patients living with medication-refractory functional disorders.

### Why did you engage in this project?

SRS is a widely known treatment modality in the context of malignant brain neoplasms, and perhaps less utilized in nononcological contexts despite studies showing efficacy for a variety of medication-refractory functional disorders. Additionally, since patients with contraindications to open surgery may benefit from SRS, it is important to have a centralized resource of evidence-based suggested dosages, constraints, patient-selection criteria and contraindications to guide treatment.

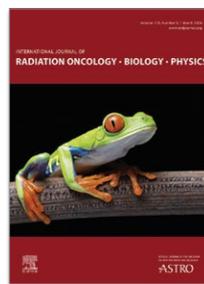
### What did you find surprising about your research?

The dearth of prospective and randomized trials and continual advances in stereotactic planning and dose delivery systems highlights functional SRS as a vibrant, new frontier. Through working on this manuscript, we became increasingly aware of the need for more longitudinal and comparative studies evaluating different SRS treatment approaches, targets and optimal patient selection criteria.

### How can this article be used to inform clinical practice?

We undertook this project to summarize and consolidate the literature regarding functional applications of SRS into treatment guidelines for clinicians. Beyond serving as a clinical management resource, we hope that this review will encourage care providers to consider if their patients may be candidates for SRS and increase the options available to those suffering from medication-refractory functional disorders.

This article is available at [https://www.practicalradonc.org/article/S1879-8500\(23\)00159-5/abstract](https://www.practicalradonc.org/article/S1879-8500(23)00159-5/abstract), as well as in the September/October 2023 issue of *Practical Radiation Oncology*.



## Radiation Therapy and Alzheimer's Disease: An Interview with David Kaul, MD

*ASTROnews* spoke with David Kaul, MD, about his recently published article in the Red Journal, "Radiation Therapy in Alzheimer's Disease: A Systematic Review." CME credit will be available for this article through the ASTRO Academy from April 15, 2024 to April 14, 2027.

## **Please summarize your research question(s) – what did you investigate and why?**

In our systematic review, we sought to compile the existing evidence on radiotherapy (RT) in Alzheimer's disease (AD), with the goal of shedding light on its feasibility, effectiveness and areas needing further research. Our investigation primarily focused on data from animal models and the few human studies available. AD is a condition with limited effective treatment options despite its growing global prevalence. We examined published data to determine whether RT could offer benefits in terms of reducing the pathological hallmarks of AD, including amyloid-beta plaques and neurofibrillary tangles, and if it could lead to cognitive improvements in patients with AD. Additionally, we aimed to elucidate potential mechanisms through which RT might exert its effects on AD pathology.

Understanding how RT interacts with the disease process, especially in animal models, is crucial for optimizing treatment strategies and considering their applicability to humans. We also sought to determine the most effective RT doses and fractionation schedules for treating AD, involving identifying dosages that provide therapeutic benefits while minimizing potential side effects. Assessing the safety profile of RT, primarily derived from animal model studies, in the context of AD was a critical part of our investigation. It's important to understand the short- and long-term effects of RT on brain health, especially given the vulnerability of the AD population, to better gauge its potential translation to human treatment protocols.

## **What were your key findings? Did anything surprise you?**

Our systematic review revealed several key findings regarding the use of RT in AD. Firstly, we found that RT, particularly at low doses, showed promise in reducing amyloid-beta plaques and neurofibrillary tangles in animal models. This suggests a potential for RT to mitigate some of the pathological features of AD, aligning with our hypothesis that RT could offer a novel approach to treatment. Secondly, evidence from animal studies indicated that RT might have a modulatory effect on the brain's immune response. This was particularly interesting as neuroinflammation is a significant component of AD pathology, and modulating this response could be key in managing the disease. Thirdly, while data on cognitive outcomes were limited and varied, some studies reported improvements in cognitive function following RT in animal models.

This indicates a potential translational value of RT for improving symptoms in AD patients, but also highlights the need for further research, especially in human subjects.

What surprised us was the consistency of the neuroprotective effects of RT across different animal models and dosing regimens. Despite the diversity in methodologies and RT protocols, the reduction in amyloid-beta plaques and the modulation of neuroinflammation were notable outcomes across several studies. This consistency adds weight to the argument for RT's potential role in AD treatment.

However, the scarcity of data from human trials was a limiting factor in our review. While the animal model studies are promising, the translation of these findings to human patients remains a significant challenge. The complexity of AD in humans, combined with the ethical and safety considerations of applying RT, means that much work is needed to determine whether these animal model findings can lead to effective treatments for AD patients.

## **What do you think patients and providers should know, at this stage, about using RT in the treatment of AD?**

At this stage, both patients and health care providers should be aware that the use of RT for AD is experimental and mainly supported by animal studies. There's limited data on the safety and effectiveness of RT for AD in humans, making it crucial to approach with caution. The mechanisms by which RT could benefit AD patients are not fully understood, emphasizing the need for further research. RT for AD is not currently an established treatment option and should not replace any existing therapies. It's essential to keep abreast of ongoing research, as future studies may provide the needed evidence to consider RT as a viable treatment.

*David Kaul, MD, is the Deputy Director of the Clinic for Radiation Oncology and Radiation Therapy at Charité – Universitätsmedizin Berlin. His expertise encompasses stereotaxy and neuro-oncology.*

The article referenced above may be found at [https://www.redjournal.org/article/S0360-3016\(23\)08172-5/fulltext](https://www.redjournal.org/article/S0360-3016(23)08172-5/fulltext), as well as in the May 2024 edition of the *International Journal of Radiation Oncology • Biology • Physics*.

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