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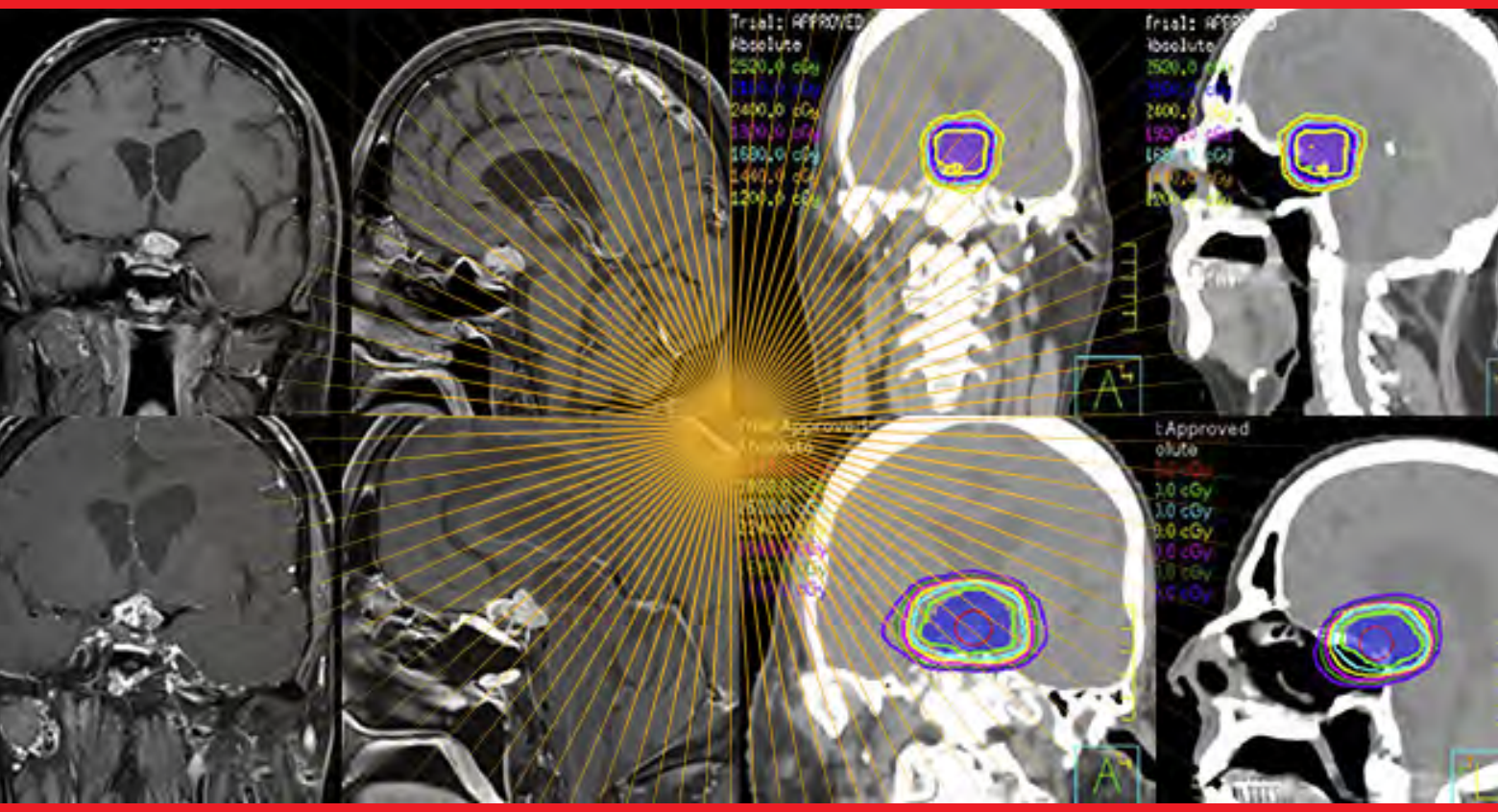

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Procedural Competency in Brachytherapy: Stepping Beyond Case Minimums

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Reconsidering, Revisiting, Refining, and Rethinking Radiation

John H. Suh, MD, FASTRO, FACR

Spring serves as a timely and welcomed reminder of a season marked by renewal and growth. As the temperature rises and once dormant plants and animals appear, this season serves as a metaphor to reconsider, revisit, refine, and rethink our current thoughts so we improve outcomes, explore novel approaches, and provide a better framework to train the next generation of radiation oncologists.

The articles in this issue of *Applied Radiation Oncology* mirror this seasonal shift by reminding us that unexpected outcomes can occur, rare diseases can be managed with radiation therapy (RT), functional radiation medicine is effective, rectal dose reduction can be achieved, and case numbers may not be the best measure of competency.

In the case report, "Unexpected Complete Response to Palliative Radiation Therapy in Non–Small Cell Lung Cancer," a patient with stage 3B non–small cell lung cancer (NSCLC) experiences an unexpected, complete response after receiving a short course of palliative RT intended primarily for symptom relief. While a single case cannot redefine standards, it invites us to reconsider assumptions about dose–response relationships and the biologic impact of hypofractionation in NSCLC.

Another case report, "Successful Re-Irradiation of Multiple Recurrent Lymphocytic Hypophysitis," highlights the successful use of reirradiation in a patient with multiple recurrent lymphocytic hypophysitis, a rare autoimmune condition with limited evidence to guide management. The findings suggest reirradiation may be a safe and effective short-term option in select refractory cases, though longer follow-up is needed to assess durability.

The review article, "Radiation Therapy for Dupuytren Disease: A Systematic Review of Clinical Outcomes and Adverse Effects," synthesizes the outcomes from 20 studies evaluating the use of RT in the management of this benign but functionally significant condition. With nearly three-quarters of patients experiencing symptom regression or stabilization, the data suggest that, when used in the early stages, RT may offer a well-tolerated, noninvasive option to slow progression in Dupuytren disease. The review is an example of the promise of functional radiation medicine, which expands the use of RT to include non-oncologic conditions such as Dupuytren.

The research feature, "Rectal Dosimetry of Different Rectal Displacement Devices for Prostate External Beam Radiation Therapy: A Multi-Institutional Retrospective Cohort Study," explores toxicity mitigation in prostate cancer treatment. In a multi-institutional cohort of 283 patients, Harkness and colleagues compare rectal dose reduction achieved with polyethylene glycol gel and inflatable balloon displacement devices. Both approaches were effective, with the inflatable balloon demonstrating greater dose-sparing across measured parameters.

In this month's Resident Voice editorial, Fara Dayani challenges us to look beyond standard measures—specifically, procedural minimums—as an assessment of residents' skill in performing brachytherapy procedures. Structured, competency-based training frameworks, she asserts, are essential for assessing readiness and building confidence in radiation oncology.

May these articles inspire new ways of seeing what may already be within reach—whether reconsidering fractionation in NSCLC, revisiting radiation for benign disease, refining dose-sparing techniques, or rethinking how we train the next generation of radiation oncologists.

On behalf of the advisory board and publisher, we truly appreciate your continued support of this e-journal and thank you for being part of the *Applied Radiation Oncology* community!

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REVIEW

Radiation Therapy for Dupuytren Disease: A Systematic Review of Clinical Outcomes and Adverse Effects

Hana Dorsey, BS; Leslie Chang, MD*

Abstract

Dupuytren disease (DD) is a fibroproliferative disorder of the palmar fascia. The main cause of DD is unknown, and traditional treatment has favored surgical intervention, though recurrence rates remain high. Radiation therapy (RT) offers a potential, noninvasive treatment alternative for DD. In this systematic review, 20 studies evaluating the benefit of RT were reviewed, with specific attention to toxicity and functional outcomes. The most frequently prescribed dose is 30 Gy using a split-course technique. The majority of participating patients were in the early stages of the disease, with an average of 74.5% of patients experiencing symptom regression as the most common outcome following RT treatment across all studies. Toxicity after RT was often observed as erythema, dryness, or atrophy of skin. Data on long-term toxicity and efficacy remain limited. In summary, available data suggest that RT is well tolerated and efficacious in preventing contracture in DD, particularly in early stage disease with nodules and <10° of contracture. However, its wide clinical adoption is limited by the methodological weaknesses of available data, and additional prospective studies are needed.

Keywords: Dupuytren, palmar, radiation, irradiation, fibroproliferative disorder

Introduction

Dupuytren disease (DD), a benign fibroproliferative disorder, affects an estimated 12% to 29% of individuals aged 55 to 75 years in Western countries.[1] It is more common and severe in men around the age of 50, with women typically developing a severe onset later on in life.

DD presents initially in a singular hand, with 80% of affected individuals eventually having features of DD in both hands.[2] Symptoms of fibrosis can occur in any location but are most common in the middle of the palm, progressing to the 4th and 5th fingers. Once one or more nodules form in the palm, they are subsequently followed by cords that develop into the distinctive digital contractures.[3] About 25% of people with DD experience discomfort or pain, with inflammation, tenderness, burning, or itching often associated with affected joints and areas of skin.[2]

The main cause of DD is not yet known. However, the development of fibrosis is associated with inflammation, and several proinflammatory cytokines have been associated with DD, including the elevated expression of TGF-β1, α-SMA, and canonical Wnt signaling.[4] DD is also associated with environmental factors such as smoking, alcohol consumption, aging, trauma, and repetitive use of the hand in various physical occupations.[3,5,6] There is ongoing evaluation of genetic risk factors, with a recent meta-analysis of 6 genome-wide association studies identifying approximately 85 single-nucleotide polymorphisms in 56 loci, implicating the hedgehog and Notch signaling pathways in DD disease etiology.[7] DD is associated with other disorders of the connective tissue, including Garrod pads, Ledderhose

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disease (plantar fibromatosis), and Peyronie disease in males.[2]

The early stages of this disease, characterized by nodule formation without contracture, currently lack standardized clinical criteria or treatment options. Surgical intervention, the mainstay of DD treatment, is considered when the patient's finger has lost 30° of metacarpophalangeal or interphalangeal extension of the joint.[8] Surgery is not typically advocated for early stages of the disease unless it is accompanied by persistent pain or discomfort, as the early proliferative stage with high cellularity has been associated with higher rates of recurrence.[9] Other treatment options range from minimally invasive to extensive surgical approaches. Collagenase clostridium histolyticum (Xiaflex) offers a nonoperative option through the enzymatic weakening of the cord. However, as a nonspecific collagenase, its mechanism can affect adjacent collagen-containing tissues and contribute to local adverse effects. Steroid injections such as triamcinolone acetonide are injected directly into nodules.[10] Percutaneous needle aponeurotomy (needling) involves mechanical separation of the pathologic cords using a fine needle, allowing digital extension without incision. Surgical options include fasciectomy, which entails partial or complete removal of the fibrotic tissue. While complete fasciectomy is associated with lower long-term recurrence compared with partial fasciectomy, this benefit is often outweighed by substantially greater acute morbidity and late complications.

Recurrence rates also differ based on treatment modality. When treated with needling, the 5-year recurrence rate of DD is reported to be 65%. Recurrence rate is 75% with collagenase injections and 10% to 75% for treatment with fasciectomy. More invasive surgery is thought to increase the risk of acute and late toxicity.[11] Furthermore, disease reactivation can occur following invasive interventions, such as collagenase injection, fasciotomy, and fasciectomy, contributing to the challenge of durable disease control.

In European countries such as Germany, radiation therapy (RT) is considered a preferred treatment option for patients with earlier stages of DD not meeting the criteria for surgical interventions. This approach has been attracting attention from the United States through the use of social media.[12] Recent emerging studies, including DEPART, a randomized controlled trial, have begun to evaluate the potential benefit of RT in the management of early stage DD.[13] However, the majority of available evidence assessing outcomes in patients receiving RT for DD consists of retrospective analyses and single-institution prospective studies. Controversy exists regarding the field design and standard of approach for these studies, including the treatment area, dose, and fractionation recommended for the course of treatment. Although various RT techniques have been described, split-course RT is a commonly reported strategy; however, considerable variation in dose and fractionation exists across studies. This systematic review evaluated the use of RT in DD, in an effort to provide an updated evidence base for this technique in DD treatment.

Methods

Using a method of screening based on Participants, Intervention, Comparison, Outcomes, and Study design, 4808 articles were initially considered for eligibility of analysis via search engines PubMed and Google Scholar throughout September 6, 2025, to November 6, 2025. This was performed using the free-text phrase *Dupuytren's Contracture Radiation Therapy*, entered as a single search string without conjunctions. Additional records were then identified through backward citation chaining from key studies and reviews, independently screened, and assessed against this review's prespecified criteria.

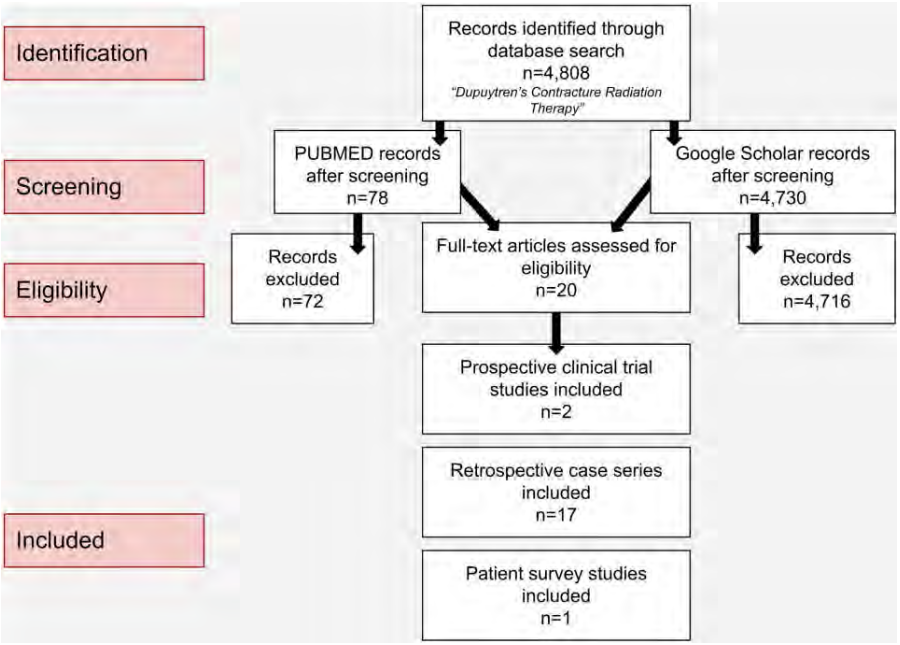
Eligibility Criteria and Study Selection

Studies were included if they evaluated the use of RT for treating DD in human subjects. Inclusion criteria consisted of clear physician or patient-reported treatment outcomes, including disease progression and deterioration, adverse effects, and the need for salvage procedures. Randomized and nonrandomized controlled clinical trials, prospective and retrospective case series, case studies, and conference abstracts were eligible for inclusion. No restrictions were applied to the language and publication year of studies. Conversely, exclusion criteria consisted of studies focusing solely on surgical interventions (such as fasciectomy) without any use of RT, as well as studies with inadequate specificity regarding RT usage. All identified records (n = 4808) underwent title and abstract screening, which eliminated 4788 records due to either irrelevance or lack of specificity on RT techniques. Ultimately, 20 studies met all criteria for inclusion (**Figure 1**).

Risk-of-Bias Assessment

Approximately 85% of the qualifying studies were retrospective with limited follow-up (FU) and limited description of FU assessment, increasing susceptibility to selection and recall bias and therefore limiting the ability to draw causal inferences. Furthermore, inconsistent and unspecified FU timing across studies limited comparability and increased the chance of selective reporting bias, specifically toward any studies with one inferred FU event. Both of the prospective studies were conducted by the same research group in Germany with a focus on the effectiveness of RT for early stage DD. The large number of retrospective case studies included introduces a higher risk of bias, given the less structured methodologies inherent to retrospective study designs. Adverse events such as erythema or dryness were well reported in most studies; however, minimal discussion was given in relation to long-term risks. Reliance on only 2

Figure 1. Flow diagram of study selection process for the review on *Dupuytren's Contracture Radiation Therapy*. A total of 4808 records were identified through database searches (78 from PubMed and 4730 from Google Scholar). After screening, 20 full-text articles were assessed for eligibility. Of these, 2 prospective clinical trial studies, 17 retrospective case series, and 1 patient survey study met the inclusion criteria and were included in the final review.



primary search engines could also have led to the omission of studies not indexed in these databases.

Results

A total of 4808 records were identified through the utilization of research database screenings. Of those, 20 studies met the inclusion criteria and were included in the final analysis: 2 prospective clinical studies,[14,15] 17 retrospective cohort/case series studies,[16-32] and 1 cross-sectional patient-reported survey study.[33] Among the 17 retrospective studies, 2 were written by the same author.[21,22] Among all included studies, 6 were in German[16,24,26,29-31] and 1 in Italian.[20] When needed, an image-capturing feature of Google Translate (Google LLC, Mountain View, CA) was used to extract the necessary data from photocopied versions of the documents. Data were compiled with all included studies and respective reported outcomes (**Table 1**).

Treatment Protocols

Each of the 20 studies varied in their RT technique, dose, approach with adjuvant therapy, FU time/frequency, duration, and outcomes. Disease progression and regression were highly inconsistent. Many reports did not specify the criteria used to classify clinical disease improvement or progression, with several studies omitting quantitative measures entirely. A wide variety of disease stages were included; however, a majority of patients were characterized as early stage DD, typically regarded as stages 0 to 1. A majority (68%) of patients among all studies were listed to either be in the early stages of DD to the study's discretion or less than or equal to stage 1 in the respective classification spectra. Several disease classification spectra were utilized (**Table 2**), including that of Tubiana et al (1966) with modifications,[14-16,18,19,23,25,33] as well as Shaw (1951),[21,22] Iselin (1967),[20,26,29,31] and Millesi (1980s).[24] There were 5 studies with unknown staging systems.[17,27,28,30,32] Several different RT modalities were used, including electrons, superficial orthovoltage or radium moulage, external beam RT, and brachytherapy. Regardless of the disease stage, most studies used doses commonly up to 30 Gy or 3000 r, and different fractionation schedules ranged from 9 to 42 Gy in total dose across studies. No dosimetric analysis was reported in the retrospective studies to confirm dose distribution. The FU period ranged from 0.9 months to 19 years. Due to the varying medians and reporting format of FU periods within the studies, a pooled mean was difficult to obtain. However, a majority of studies (60%) explicitly reported waiting at least 1 year post treatment for initial FU.

Outcomes of Radiation

When evaluating the outcomes of all qualifying studies, 13 out of the 20 (65%) reported the regression of patient symptoms as the most frequent outcome. The percentage of patients with this outcome ranged from 45% to 100%. with a mean of 74.5%.[14,17,19-24,27,28,30,32] The Schuster et al study was omitted from this mean calculation due to patient outcome being subjective, with unclear FU duration in survey modality. Regardless, the results obtained post treatment from the Schuster patient survey showed 70% to 81% symptomatic improvement.[33] The Seegenschmiedt et al 2012 study did not report total regression outcomes, but focused instead on the disease progression for patients undergoing RT. In the results, the control group reported clinical evidence of progression in 52% of patients, compared with 22% in the cohort of patients receiving 21 Gy, and 16% in the cohort of patients receiving 30 Gy. There was no statistically significant difference in disease progression based on the dose of RT used (21 Gy vs 30 Gy). However, disease progression increased among untreated control patients compared with irradiated patients ($P < .001$).[15] 5 studies reported a lack of disease progression in radiated patients as the most common outcome.[16,18,25,26,29] Only one study found

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Table 1. Summary of Radiation Therapy Studies for Dupuytren Disease

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
Prospective clinical studies														
Seegenschmiedt et al [14]	198 (95 at 30 Gy; 103 at 21 Gy)	Randomized clinical study (preliminary results)	Tubiana et al stage ≤ II	5 × 3 Gy over 2 series 8 wk apart vs 7 × 3 Gy in one series	30 Gy (95 hands), 30 Gy (95 hands)	History of treatment with local excision/ partial fasciectomy (25), steroid injection (6), NSAIDs (13), vitamin E (25), other drugs (15), unspecified (12)	>1 y in all patients	Assessed at 3 and 12 mo	Compared photocopied imaging before and after treatment. Progression defined by patient subjective response and physician evaluation of nodules and cord.	Total: 54.5%, 30 Gy: 55.8%, 21 Gy: 53.4%	Total: 37.4%, 30 Gy: 36.8%, 21 Gy: 37.9%	Total: 8.1% 30 Gy: 7.4% 21 Gy: 8.7%	Surgery: 4	Redness/dryness sites n: 76 (38%), extensive erythema in sites n: 12 (6%), dry desquamation n: 10, moist desquamation n: 3, pronounced swelling n: 3, chronic side effects n: 26 at 3 mo. FU, n: 9 (5%) at 12 mo. FU, alteration of heat and pain sensation n: 8.
Seegenschmiedt et al [15]	863 (293 at 21 Gy; 404 at 30 Gy); 166 control	Nonrandomized control trial	(1) 21 Gy/30 Gy: N: 195/199 N/I: 50/53 I: 43/47 II-IV: 5/4	5 × 3 Gy over 2 series 10-12 wk apart; or 7 × 3 Gy in one series; or none at all (control)	30 Gy vs 21 Gy	History of treatment with local excision/ partial fasciectomy (65), steroid injection (36), NSAIDs (28), vitamin E (45), other drugs (14), unspecified (16)	Median 104 mo, range 61-163 mo	The clinical evaluation (treatment side effect and efficacy) was performed at 3 and 12 moand at last FU after RT	Compared photocopied imaging before and after treatment. Progression defined by patient subjective response and physician evaluation of nodules and cord.	Not reported	Not reported	21 Gy/30 Gy/ control N: 7/3.5/34 N/I: 42/30/67 I: 58/49/87.5 II-IV: 80/75/100 Total: 22/16/52	Surgery 21 Gy: 12% 30 Gy: 8% Control: 30% Salvage RT 21 Gy: 5.5% 30 Gy: 6% Control: 20%	Redness/dryness cases n:151 (25%) extensive erythema/ moist desquamation/ pronounced local swelling cases n:16 (2%), chronic side effects at last FU in 83 sites (14%).
Retrospective case series														
Finney [21]	25	Case series	(2) Stage 1: 3 Stage 2: 4 Stage 3: 18	3000 r Ra-Moulage	3000 r	None	2-10 y	Not directly stated	Subjective improvement of softening nodules. Objective increase in movement was	Overall: 75% Stage 1: 100% Stage 2: 75% Stage 3: 72%	Overall: 25% Stage 1: 0% Stage 2: 25% Stage 3: 28%	None	Unknown	Skin dryness, occasional slight erythema.

Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
									used. No cases were reported of worsening contracture.					
Finney[22]	43: 25 gamma radiation (presented in 1953 article); 18 × RT	Case series	(**2**) In X-RT group: Stage 1: 3 Stage 2: 0 Stage 3: 13 Stage 4: 2	1-3 × 1000 r Ra-Moulage	1500-3000 r	None	>18 mo	Not directly stated	Regression was defined as a lessening of the feeling of tightness in the palm and fingers.	X-RT group only: 77.8% Stage 1: 100% Stage 2: n/a Stage 3: 76.9% Stage 4: 50.0%	X-RT group only: 22.2% Stage 1: 0 Stage 2: n/a Stage 3: 23.1% Stage 4: 50.0%	None	Unknown	Skin dryness, immediate paraesthesia.
Wasserburger[30]	146 patients	Case series	(*) I: 69 II: 46 III: 31	1-3 × 1.000 r , Ra-Moulage	1.000-3.000 rad	None	2-19 y	Not directly stated	The success is defined as restorative full extension and full abilities of the fingers with no more detectable fixed skin areas.	Overall: 69.8% I: 89.8% II: 56.5% III: 32.2%	Unknown	Unknown	Surgical intervention: 8	Not reported.
Corsi[20]	13	Case series	(**3**) All in the early stages of the disease	600-800 r of penetrating RT cycle then 2200-2500 r of plesiotherapy	Variable	Vitamin E	6 mo to 3 y	Not directly stated Multiple FUs advised for some patients	Subjective increased elasticity, smoother skin, and decreased nodules. Improved extension of the 3-4 metacarpals was also assessed as a measurement of improvement.	77%	23%	0	Surgical referral: 1	Cutaneous criteria reactions in some, also epidermolysis in some instances. The epidermolysis quickly resolved soon after.
Lukacs et al [28]	36	Case series	(*) Stage 1: 32 Stage 2: 4	(4 Gy twice a week) repeated every 2 mo	24-40 Gy	None	≤5 y	Not directly stated	Regression was defined as a definite softening of nodular lesions and improvement	Stage 1: 81% , Stage 2: 75% , Total: 81%	Stage 1: 19% Stage 2: 25% Total: 19%	None	Surgical referral: 3	Not reported.

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Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
									of contractures of the palms.					
Vogt/Hoschau [29]	109 patients	Case series	(3)I: 98 II: 4 III/IV: 7	(2 × 4 Gy) × 4 every 2 mo	32 Gy	None	>3 y	Not directly stated	No disease progression is considered a success. Initial symptoms of pain, redness, nodule formation, increased thickness, and stretching limitation were evaluated for inclusion.	1:21% II: 25% III/IV: - Total: 20%	1:74% II: 50% III/V: 86% Total: 74%	1: 4% II: 25% III/IV: 14% Total: 6%	Unknown	Not reported.
Koehler [26]	33	Case series	(3) All stage I	10 × 2 Gy 3-5 times a week (2.0 single dose daily or 3 times up to total dose of about 20 Gy)	20 Gy	None	1-3 y	Not directly stated	Progression was defined as an increase in hardening/ contractures. Improvements were subjective visual results and patient reports.	Total: 21%	Total: 61%	Total: 18%	Surgical intervention: 3 Salvage RT: 3	Not reported.
Herbst/Regler [24]	33 patients (46 hands)	Case series	(4) N: 16 I: 30 II: 3 III: 1 IV: 1 (mainly treated early stages from some patients	3-14 × 3 Gy (< 42 Gy)	9-42 Gy TD	None	>1.5 y	Not directly stated	Imaging evaluation of nodules and cords.	39/46 (85%)	6/46 (13%) findings/ symptoms remained unchanged without demonstrable progression up until time of result evaluation	(1/46) 2%	Surgery (one stage IV case due to therapy not being followed)	RT dermatitis n: 13 patients (39%). Some cases observed acute dermatitis with skin redness/ subcutaneous emphysema.

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Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
			being excluded due to extended contracture and developed recurrence noted)											
Weinzierl et al [31]	34 patients	Case series	(3) All stage I	5 × 3 Gy, 6 wk apart	15-33 Gy	None	Mean 7 y	Not directly stated	Iselin grading, decreased extension, thickening and hardening of nodules/cords.	9%	41%	50%	Surgery: 4	Skin dryness/ occasional scaling of volar skin n: 32% patients.
Keilholz et al [25]	142 (57 with >5-year FU)	Case series	(1) Total/5 year N: 82/28 N/I: 17/10 I: 30/17 II: 12/1 III: 1/1	5 × 3 Gy over 2 series 6 wk apart	30 Gy	None	Median 6 y, range 1-12 y	Not directly stated	In addition to patient-reported outcomes, functional changes and flexion deformity of fingers were measured using a protractor. The size of nodules and cords was directly measured and their consistency palpated.	3 mo: 7% N: 2% N/I: 29% I: 10% II/III: 0% 5 year: 11%	3 mo: 92% N: 98% N/I: 71% I: 83% II/III: 100% 5 year: 67%	3 mo: 1% N: 0% N/I: 0% I: 6.7% II/III: 0% 5 year: 23%	Surgery: 6 None in 5-yr f/u group	Acute mild skin reactions/ erythema/dry desquamation with burning and itching n: 61 (43%), radiodermatitis/ edema n: 14 cases (10%). Other complaints were dry skin, mild skin atrophy, slight fibrosis, and occasional telangiectasia.
Adamietz et al [16]	176	Case series	(1) 0: 5 N: 76 N/I: 15 I: 65 II: 12	5 × 3 Gy over 2 series 6-8 wk apart	30 Gy	None	Median 10 y, range 7-18 y	Not directly stated	Tubiana stage, size, and appearance of nodules and cords.	N: 15% I: 6% II: 0% III: 0% Total: 10%	N: 66% I: 29% II: 17% III: 0% Total: 49%	(in + out of field) N: 19% I: 65% II: 83% III: 100%	Surgery: 4 Salvage RT: 10	Anhidrosis/strong scaling n: 44 hands (25%), skin atrophy n: 15 palmar areas (8.5%).

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Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
			III: 3									Total: 41%		
Betz et al [18]	208	Case series	(1) N: 115 N/I: 33 I: 50 II: 7 III: 2 IV: 1	5 × 3 Gy over 2 series 6-8 wk apart	30 Gy	Prior treatments with recurrence leading to RTX referral: Surgery (8), steroid injection (1)	Median 13 y, range 2-25 y	Not directly stated	The size and number of nodules or cords were directly measured and their consistency palpated.	N: 6% N/I: 30% I: 6% II: 0% III: 0% IV: 0% Total: 10%	N: 81% N/I: 40% I: 32% II: 14% III: 0% IV: 0% Total: 59%	(in + out of field) N: 13% N/I: 30% I: 62% II: 86% III: 100% IV: 100% Total: 31%	Surgery (39 patients, 42 cases)	Minor long-term radiogenic skin/ subcutaneous changes n: 66 cases (32%), dry skin/desquamation n: 47 cases (23%), erythema n: 5 (2%), skin atrophy n: 14 cases (7%).
Grenfell/Borg [23]	4	Case series	(1) N: 2, I: 2	5 × 3 Gy over 2 series 6 wk apart	30 Gy	None	Median 35 mo, range 34-42 mo	Not directly stated	Objective reduction in size of the target lesion(s) or subjective improvement in pain or discomfort.	100%	Not reported	Not reported	Not reported	Mild local erythema and edema, minimal fatigue.
Zirbs et al [32]	297	Retrospective patient survey case series	(*) Symptom duration: < 20 mo: 56 > 20 mo: 61	2 × 4 Gy over 4 wk, with 8 wk apart between treatments	32 Gy	Prior treatment with surgery (18), needle fasciotomy (8), local steroid (3), oral vitamins (1), homeopathic cream and massage (1), shock-wave therapy (1), magnetic field therapy (1), NSAIDs (1), hand gymnastics (1), other injections (1)	Median 40 mo, range 6-115 mo	Not directly stated	Patients measured with a visual analog scale.	45% by patient report, 21.6% of nodules regressed (92/426 nodules)	35% by patient report	-	Not reported	Dryness n: 82 patients (39.8%), erythema n: 42 patients (20.4%), desquamation n: 8 patients (3.8%), chronic side effects (more than 4 weeks) n: 71 (34%).
Banks et al [17]	10 patients, 8 hands irradiated (11	Case series	(*) Not reported	5-6 × 3 Gy over 2 series 3 mo apart	30-36 Gy	None	Mean 12.1 mo, range 0.9-30.5 mo	Not directly stated	Reduction in pain or deformity of lesions.	71% (but not distinguished from plantar lesions)	24% (but not distinguished from plantar lesions)	5% (but not distinguished from plantar lesions)	Not during study period	Not reported.

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Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
	feet also irradiated)													
Latusek et al [27]	117 patients (number of hands unknown)	Case series	(*) "In the early stages of DD" 61.5 % had contractures	7 × 3 Gy in one series	21 Gy	Prior treatment with laser therapy (1%), surgery (13%), ultrasound (1%), local steroid injection (1%)	Mean 4.8 (SD ±6.11) mo, range 1-34 mo	Not directly stated	Improvement defined as a decrease in the size of nodules, reduction of contracture, or the improvement of manual function.	57.50%	35%	7.50%	Not mentioned	No skin problems n: 87.5% subjects, palmar dryness n: 2.5%, erythema n: 7.5%, superficial epidermal exfoliation n: 2.5%.
Ciernik et al [19]	5	Case series	(1) I: 2 III: 1 IV: 2	Anhidrosis n: 44 hands (25%), skin atrophy n: 15 palmar areas (8.5%)	20 Gy	Palmar aponeurectomy	Mean 14.1 mo, range 6-30 mo	Annual FUs	Joint extension 6 mo after RT	100%	0	0	Not during study period	Not reported.
Patient survey studies														
Schuster et al [33]	51 sites in the hand (15 sites in the foot)	Retrospective patient survey case series	(1) N or N/I	7 × 3 Gy in one series or 5 × 3 Gy over 2 series 6-8 wk apart	21 Gy or 30 Gy	Prior treatment with surgery (4), steroid injections (2)	Median 31 mo, range 1-61 mo	Not directly stated	Progression was defined as new or worsening clinical disease (eg, nodule growth, cord development, contracture) or worsening symptoms (pain, itching/burning, or pressure) as described by patients.	Symptomatic improvement 70-81% pain/ itching/ burning, 95% pressure, 64% mobility, overall 93% some symptomatic benefit	-	In-field: 30% In-field after re-irRT: 21%	Surgery: 2 Collagenase: 1 Needle aponeurotomy: 2 Re-irRT: 4 Massage: 1	Acute toxicity n: 13 patients (39%), dryness/ erythema/dry desquamation/ edema/tenderness n: 89 sites, late toxicities n: 10 patients (30%).
Future prospective trials														

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Table 1. continued

STUDY	TOTAL COHORT (HANDS)	ARTICLE TYPE	DISEASE STAGE CLASS	RADIATION THERAPY REGIMEN	DOSE	ADJUNCT THERAPIES	FOLLOW-UP	NUMBER OF FOLLOW-UP APPOINTMENTS	DEFINITION OF OBSERVED PROGRESSION /METHOD OF OUTCOMES	REGRESSED OUTCOMES	STABLE OUTCOMES	PROGRESSED OUTCOMES	SALVAGE PROCEDURES	SIDE EFFECTS
DEPART Trial, Burgess et al (2018-not specified)[34]	60 patients	Prospective randomized clinical trials	**2 Arms:** **Arm1: < 10° contracture** **Arm2: (*)** Not reported	10 × 3 Gy over 2 series 4-12 wk apart	30 Gy	Patients with planned LF, PNF, or CI of flexion contracture(s) were eligible for the adjuvant component	Minimum 5 y	Independently reviewed at 6 mo, 12 mo, annually up to 60 mo and then biannually up to 104 mo	QuickDASH, URAM, and a VAS for pain. CTCAE v4.03 toxicity recording.	Improved 36 mo metrics: QuickDASH: 17.83 Obs vs 10.93 LDRT (*P* = .013) URAM: 4.8 Obs vs 3.1 LDRT (*P* = .056) VAS: 2.1 Obs vs 1.0 LDRT (*P* = .001) Long-term data not yet published	Not yet published	Not yet published	Not yet published.	Acute toxicity n: 39 patients (65%), dermatitis RT n: 14 patients (23%), reduced sweating n: 12 patients (20%), pruritus/skin pain n: 4 (6.7%) Reduced sweating, although mild, tended to persist.
University of Minnesota Trial (2019-2026)[35]	50 patients	Prospective observational pilot study	(*) Not reported	5 daily treatments of 300 cGy × 10 for a total of 3000 cGy over 2 series 6-8 wk apart	30 Gy	Limited fasciectomy, PNA, and CCH injection	2 y	6 wk after completion of all RT and 1 and 2 y after	Using the 5-item Southampton Dupuytren's Scoring System questionnaire. Scores range from 0 (no problem) to 4 (severe problem), with total scores ranging from a sum of 0 to 20. High scores indicate greater impairment due to the disease.	Not yet published	Not yet published	Not yet published	Not yet published.	Not yet published.

*Classification systems used in the studies: (1) Tubiana et al classification or a modified version thereof, (2) modification of the Shaw et al (1951) classification system, (3) Iselin classification system, (4) Millesi staging system, and * staging system unknown or not defined.*

CCH, collagenase clostridium histolyticum; CI, collagenase injections; DD, Dupuytren disease; FU, follow-up; LF, limited fasciectomy; PNF, percutaneous needle fasciotomy; QuickDASH, Quick Disabilities of Arm, Shoulder and Hand; r, Roentgen; RT, radiation therapy; SD, single dose; TD, total dose; URAM, Unité Rhumatologique des Affections de la Main; VAS, visual analog scale; x-RT, medium-voltage x-ray therapy.

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Table 2. Classification Systems for Dupuytren Disease

	CLASSIFICATION SYSTEMS			
	(**1**) Tubiana (1966) with modifications	(**2**) Shaw (1951)	(**3**) Iselin (1967)	(**4**) Millesi (1980s)
Grade/ stage	N: Nodules, cords, or skin retraction in palmar fascia without finger contracture	1a: Nodule in palmar fascia but not including the skin without finger contracture 1b: Nodule in the skin but not involving the palmar fascia and no finger contracture	0: Small subcutaneous nodules without contracture	Grade 0: No contracture; normal extension
	*N/I: Nodules, cords, or skin retraction with extension deficit of 1˚ to 5˚	2: Nodule in fascia involving skin without finger contracture	1: Nodules or cords in palm or up to proximal phalanx with MCPJ contracture	Grade I: MCP or PIP joint contracture ≤45°
	I: Nodules, cords, or skin retraction with extension deficit of 6˚ to 45˚	3: Nodule in fascia involving skin with finger contracture	2: Nodules or cords extend up to the middle phalanx with MCPJ and PIPJ contracture	Grade II: Contracture > 45° but ≤90°
	II: Nodules, cords, or skin retraction with extension deficit of 46-90˚	4: All 3 prior stages with secondary changes to tendons/ joints	3: Nodules or cords extend to the distal phalanx and contracture involving all 3 phalanges	Grade III: Contracture > 90°
	III: Nodules, cords, or skin retraction with extension deficit of 91-135˚		4: Severe contracture of the PIPJ resulting in hyperextension at the DIPJ (boutonniere deformity)	Grade IV: Severe deformity and contracture of multiple fingers, functional impairment
	IV: Nodules, cords, or skin retraction with extension deficit > 135˚			

Keilholz et al modified the Tubiana classification system to include an N/I intermediate stage with contracture from 1° to 5°.

DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint.

significant progression of disease after RT following an initial FU examination 7 years after RT.[31]

The criteria for establishing disease regression, stability, or progression varied from study to study. Most studies characterized improvement as some form of relief from symptoms, such as the decrease of nodules or cords, reduction of pain or deformity, increased joint extension, and smoothness of the skin. Additionally, the percentage of irradiated patients reported to need subsequent surgical intervention post-therapy ranged from 2% to 20%.[14-16,18,24-26,30,31,33] A need for surgical referral was reported in 2 of the 20 studies,[20,28] and 8 were not reported during the study period.[17,19,21-23,27,29,32]

Adverse Events

When analyzing adverse effects and toxicities from RT, common outcomes included skin redness, erythema, dryness, desquamation, and atrophy.[14,15,18,21,23-25,27,31-33] The ongoing DEPART trial has provided new prospective data on the toxicity and persistent effects of RT. A total of 404 hands—202 randomized to observation, and 202 to low-dose RT (LDRT)—were followed for a median period of 36 months. On FU, 162 hands experienced at least one toxicity, with the vast majority (96.6%) noted as grade 1. No grade 3 events were observed. Furthermore, of the 14 grade 2 toxicities, only one (reduced sweating) persisted up to 24 months following treatment.[13] Quality-of-life outcomes using the Quick Disabilities of Arm, Shoulder, and Hand measure demonstrated improvement in the LDRT arm (10.9 vs 17.8 $P = .013$). Future results will provide a more comprehensive assessment of longer-term disease control and toxicity.

Discussion

In this systematic review, we analyzed 20 studies consisting of prospective, retrospective, and cross-sectional survey studies evaluating the effects of using RT for DD. Although different staging systems were used depending on the study's design, a majority (68%) of treated patients were reported to either be in the early stages of DD (to the study's discretion) or ≤ stage 1 in the respective classification system. Overall, 65% of patients in the 20 studies reported the regression of symptoms as the most common outcome. It is hypothesized there is a therapeutic window for RT in patients with early stage DD, as early stage patients have decreased progression (Tubiana stage N/I progression after

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RT was 30% compared with 75% in stage 2-4).[14] As RT preferentially affects rapidly proliferating tissues, RT would be more efficacious in the early disease state of high cellularity and mitosis than in later-stage disease characterized by low cellularity and high collagen concentration. Among the 13 studies deemed successful, 2 reported a 100% regression outcome.[19,23] Both studies comparatively share a smaller cohort size of ≤5 irradiated hands, but Ciernik's 2021 study included a wider array of disease stages in its patient demographics (**Table 1**).[19] Despite the overwhelming unanimity of results, the study's small cohort sizes limit the ability to draw widespread conclusions.

Only one study reported disease progression as the most common outcome following RT. In the retrospective analysis by Weinzierl et al, nearly all irradiated hands demonstrated progression as their primary outcome during long-term FU, which the authors attributed to the approximate 7-year period in which patients were not monitored between completion of RT and the first FU assessment. Importantly, the observed pattern and rate of progression did not differ meaningfully from the natural history of early DD, suggesting that RT in this cohort did not alter long-term disease behavior.[31]

It is important to recognize that not all patients with early stage DD experience progression when left untreated. A meaningful proportion can remain clinically stable for years. As the Seegenschmiedt cohort demonstrates, approximately 50% of untreated patients were reported to show no progression of symptoms during extended FU.[15] Given this variability, RT should not be considered for patients with stable and asymptomatic disease. Instead, it is best to make treatment decisions based on documented, active disease progression characterized by clinical criteria and worsening changes in hand grip strength, finger span or finger-raise measurements, or contracture deformity.[36] This will ensure that RT is only offered when biologically and clinically justified.

Chronic side effects were less commonly reported with a calculated average of 22.8% in patients, falling between an encompassing range of 13% to 30% experiencing persistent changes after treatment. Common long-term effects consisted of symptoms such as altered heat sensation, pain, or other acute effects. The timing for FU evaluation of chronic symptoms varied or was not explicitly stated. In the UK, the National Institute for Health and Care Excellence cautions there is limited evidence for the safety of RT in patients with early DD, with a discussion of theoretical risk on the development of RT-induced cancer in the long-term effects.[37] However, no cases of long-term cancer caused from RT of DD have been reported.

A high risk of bias presents an additional challenge when interpreting the results.[8] In the 2 prospective clinical studies conducted by the same author, methods and outcomes were reported comprehensively, in contrast to the majority of retrospective studies, which frequently lacked methodological detail and specificity.[14,15] Patient-reported outcome measures were often subjective and dependent on individual patient perception, rendering them more susceptible to response bias.[33] Furthermore, substantial heterogeneity was observed across the included studies with respect to patient demographics, treatment parameters, adjunctive therapies, study endpoints, and FU duration. Consequently, drawing precise conclusions from the currently available published data remains challenging.

Several prospective studies on RT in DD are underway. The ongoing DEPART randomized clinical trial will provide prospective randomized data on RT efficacy both as definitive treatment and as adjuvant treatment after needle aponeurotomy. It will also explore the adverse effects of DD following RT as described previously.[34] Furthermore, the University of Minnesota's ongoing Post-contracture Release RT for DD study has been evaluating efficacy for postoperative RT through an observational prospective pilot study format (NCT04122313).[35] Similarly, the Dartmouth-Hitchcock Medical Center has an ongoing study evaluating RT for Dupuytren's Contracture Following Non-Surgical Release (NCT06330545).[38]

Taken together, the available evidence across studies and existing trials suggests that RT may be most beneficial in earlier, proliferative stages of DD, when nodules are active, but contractures are minimal (< 10 degrees). RT should be recommended when there is documented active progression in patients, ideally captured using standardized clinical criteria (changes in hand grip strength, finger span or finger-raise measurements, or contracture deformity). If RT is used, current data support moderate-dose regimens (30 Gy in 10) fractions in a split-course modality (6-12 weeks break between 5 fraction courses) or 21 Gy in 7 fractions without break. A split-course approach is thought to best balance both risk and therapeutic effects. Patients who are unable to receive the split course regimen could be considered for the 21 Gy in a 7 fractions regimen, although there is a slightly increased risk of contracture progression.[15] Treatment planning should include fields delineated based on the fascial thickening seen on CT planning and palpation of nodules/cords plus margins.[36]

Using CT-based planning techniques, prospective studies and practice guidelines recommend the application of bolus and coverage of the involved palmar fascia with the >90% isodose line.[13,36] However, the evidence base remains limited by unspecified outcome measures and inconsistent reporting of progression, regression, and long-term control. To improve the field, future prospective, standardized trials are needed, using uniform definitions of disease activity, consistent functional

outcome measures, and detailed long-term FU to determine whether RT alters the natural history of early DD. The development of core outcome sets and universal consensus based on clinically meaningful endpoints will be essential for future progress.

Conclusion

In summary, the use of early stage RT as a noninvasive method to treat DD holds promising potential as an alternative to invasive surgery. However, debates over the variability of study design, FU duration, and outcome reports limit the strength of existing evidence in current literature. To better assess long-term efficacy for prophylactic therapy and treatment, future studies should adopt a standardized protocol, consisting of larger and controlled patient populations, to produce consistent and high-quality results. The future of these results will be essential to guide the next steps in clinical decision-making.

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RESEARCH ARTICLE

Rectal Dosimetry of Different Rectal Displacement Devices for Prostate External Beam Radiation Therapy: A Multi-Institutional Retrospective Cohort Study

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Abstract

Purpose Multiple rectal displacement device (RDD) technologies are in use or under development for the reduction of rectal toxicity in prostate cancer. In this multi-institutional retrospective cohort study, we compare the rectal dose-sparing capabilities of 2 types of RDD: polyethylene glycol (PEG) gel and inflatable balloon (IB).

Materials and Methods Dose-volume parameters of D0.1cc, D1cc, and D2cc to the rectum were used as endpoints for late rectal toxicity. All dosimetry values were converted to equivalent dose in 2 Gy fractions with α/β of 3 to better compare patients receiving differing treatment fractionation schedules.

Results Dosimetric data were analyzed for 283 patients. Of those patients, 99 received a PEG implant, 92 received an IB implant, and 92 received neither implant. Both RDD types (PEG and IB) reduced the dose to the rectum for all dose-volume parameters (D0.1cc, D1cc, D2cc) compared to the control cohort. The IB implant yielded a dose reduction of 10% compared to control patients for D0.1cc, a reduction of 17% for D1cc, and a reduction of 21% for D2cc. The PEG implant resulted in a dose reduction of 2% compared to control patients for D0.1cc, a reduction of 7% for D1cc, and a reduction of 11% for D2cc. Compared to the PEG implant, the IB implant reduced the dose by 8% for D0.1cc, by 11% for D1cc, and by 12% for D2cc.

Conclusions The use of both PEG and IB spacers significantly reduces dose to the rectum. The IB spacer provides a greater reduction in dose than the PEG spacer.

Keywords: prostate, cancer, spacer, polyethylene glycol gel, inflatable balloon, PEG, IB, implant, radiation therapy

Introduction

According to the American Cancer Society, approximately 1 in 8 men are diagnosed with prostate cancer in their lifetime, with incidence increasing with age.[1] With an estimated 1.2 million cases reported in 2018, prostate cancer is the second-most common neoplasm worldwide, second to lung cancer.[1] In the United States, the overall survival rate as judged by Surveillance, Epidemiology and End Results (SEER) data for all stages is generally good, about 98% at 5 years.[2] The disease is reportedly responsible for

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Data sharing statement: Data are available upon reasonable request. Research data (consisting of deidentified patient data) are stored in an institutional repository and will be shared upon request to Michael Kos, mkos321@gmail.com. Reuse is not permitted. Statistical analysis plans are available upon request.
Disclosures: Harkness, Field, Zhang, and Vale report no conflicts of interest. Costa and Kos report serving as principal investigators and clinical proctors and being paid for each procedure and clinical training during the trial.

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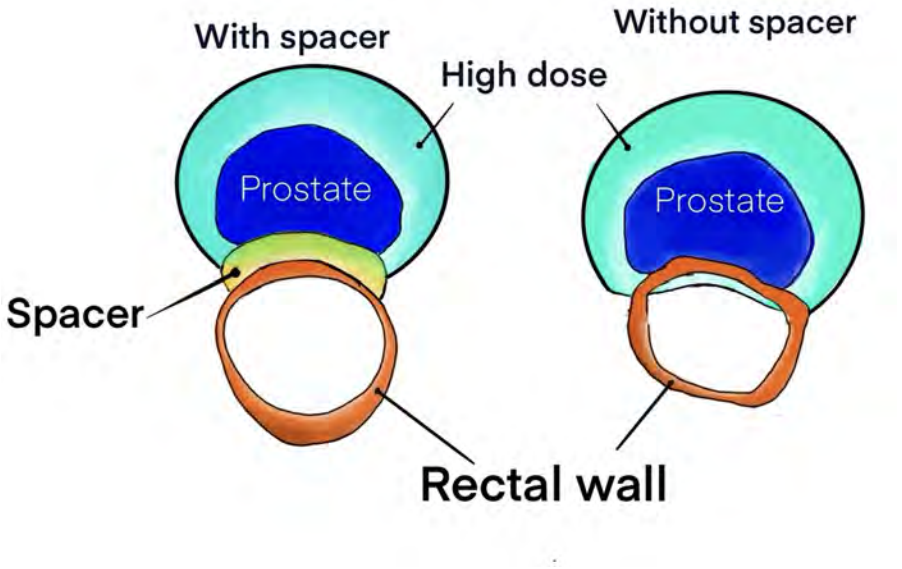
Figure 1. Depiction of the change in received dose to the rectal wall due to ideal polyethylene glycol gel (PEG) spacer placement. PEG is implanted into the perirectal space and creates over 1 cm of space between the prostate and rectal wall.



34,500 deaths annually in the United States, or 5.5% of US cancer deaths vs 6.7% worldwide cancer deaths.[1]

Treatment of localized disease generally consists of surgery or radiation, with advanced treatment comprising hormonal therapy, chemotherapy, and radiation. Quality of life (QOL) varies by stage and treatment, but most men experience a lower QOL due to worsening genitourinary function; that is, urinary incontinence and erectile dysfunction.[3,4]

Radiation therapy (RT) is a primary treatment modality for prostate cancer; dose escalation improves local control but is limited by the potential for complications in nearby organs at risk. RT may produce more favorable genitourinary outcomes compared to surgical options, but bowel complications such as increased urgency and/or frequency, diarrhea, and rectal bleeding are much more frequent.[3-5] These complications usually improve within 6 months to a year of treatment initiation, according to prior studies, but they are associated with higher incidences of long-term gastrointestinal issues.[4,5] Rectal bleeding is a common side effect of prostate RT.[6,7] If prevented or minimized, this can greatly improve QOL in the short and long term. Attenuating the radiation dosage to the rectum has been shown to reduce side effects associated with excess radiation and has been made possible by recent advances in target localization technology.[5] Radiation dose to the rectum can be reduced by physically displacing the rectum from high-dose regions and optimizing dose distributions to reduce rectal dose-volume histogram (DVH) endpoints.[8] See **Figure 1** for an example of how a PEG spacer displaces the rectum. Various rectal displacement devices (RDDs) are used to increase the space between the rectum and prostate. The 2 main types are polyethylene glycol (PEG) gel and an inflatable balloon (IB) placed between the prostate and rectum. PEG (Boston Scientific, USA) polymerizes to form a semi-solid gel. The BioProtect Balloon System (BioProtect, Israel) uses a balloon inflated with sterile water. Both technologies have been shown to reduce rectal dose.[9-12]

Rectal implants continue to reduce late QOL impacts of prostate RT at 3 years post-treatment (9.2% vs 2.0% incidence of grades > 1 for control and spacer, respectively, and 5.7% vs 0% for grades > 2).[13] Another device that has entered the market inserts a hyaluronic acid gel that has been shown effective in a randomized controlled trial.[14]

In this study, we analyzed the dose-sparing capabilities of 2 types of RDD: PEG implants and IB implants. By measuring the received dose to the rectal wall for both implant-treated patients and control patients, we present the mean received dose and dose reduction for both implants. We compare PEG and IB implants and discuss relevant clinical differences between the 2 modalities.

Materials and Methods

Patient Selection

Patients with early-/intermediate-stage prostate cancer undergoing external RT treatment between 2013 and 2020 with a spacer were enrolled in a 2-institution, retrospective cohort study. Patients who had previously undergone RT, prostatectomy, or pelvic lymph node radiation were excluded. Seminal vesicle involvement was not an exclusion factor. Controls received no RDD and were selected from consecutive cases in the same time frame when spacer modalities were not as readily available. Many of the IB patient data were collected from an international center owing to the IB's approval for use in the European Union (EU) as opposed to its pending approval in the United States.

A total of 283 patients, mean age 73 years (range 50-90 years), were analyzed. A total of 99 US patients were implanted with PEG, 92 patients (17 US patients, 75 EU patients) were implanted with IB, and 92 US patients were not implanted with either rectal spacer.

As shown in **Table 1**, the patient groups demonstrated no significant differences with respect to age, mean

Table 1. Patient Information Mean and Standard Deviation

	TOTAL	PEG	IB	CONTROL	*P* VALUE
Demographic data					
Age at treatment (years)	73.2±6.6	72.1±5.8	73.7±7.0	73.8±7.0	.13
Prostate volume (cc)	75.2±32.4	65.8±27.9	94.7±33.9	65.9±26.4	<.001
Rectum volume (cc)	68.5±26.0	60.7±22.0	74.5±26.3	70.8±28.0	.15
Treatment data					
Prescribed dose (Gy)	77.6±5.4	75.4±5.5	77.1±6.2	80.3±2.7	.39
Number of fractions	39.1±7.5	36.4±8.5	37.2±6.5	43.9±4.2	<.001
Dose/fraction (Gy)	2.0±0.3	2.2±0.4	2.1±0.3	1.8±0.2	<.001

Abbreviations: IB, inflatable balloon; PEG, polyethylene glycol.

Table 2. Mean and Standard Deviation of Rectal Dose-Volume Histogram Parameters by Spacer Type

DOSE-VOLUME HISTOGRAM PARAMETER	IB	PEG	CONTROL	*P* VALUE
D0.1cc (Gy)	71.7±8.1	78.1±3.5	80.4±1.2	<.001
D1cc (Gy)	65.2±9.5	73.7±6.0	79.5±2.1	<.001
D2cc (Gy)	61.2±9.9	69.9±7.1	78.7±2.7	<.001

Abbreviations: IB, inflatable balloon; PEG, polyethylene glycol.

prescribed dose, and mean rectal volume, with standard error reported for all mean values. Patient demographic and fractionation data were tested for statistical significance using the Kruskal-Wallis test.

Data Collection

In all cases, CT scans were collected from patients after spacer placement and before treatment. Radiation exposure to the rectum was calculated based on previously recorded volumetric and dosimetry data for all patients. Control patients consisted of those treated prior to common use of PEG, with data collected in the same fashion. The primary endpoints were rectal dosimetry in D0.1cc, D1cc, and D2cc, where D0.1cc refers to the dose given to the hottest 0.1 cc of the rectum.

Treatment Planning

Target volume margins were defined with planning target volume (PTV) expansions of 5 mm applied in all directions from the clinical target volume (CTV) except posteriorly, where a reduced 3 mm margin was implemented for the boost phase to minimize rectal dose exposure.

Fiducial marker systems differed between institutions: electromagnetic transponders (Calypso) were used at the US center; radiopaque gold seed markers were employed at the EU center. These differences in marker composition did impact target treatment planning. The PTV to CTV expansions were different for US vs international patients. For international patients, the expansion was 5 mm in the X, Y, and Z axes. For US patients, the expansion was 3.0 mm posteriorly for the initial volumes and then 3.0 mm in the X, Y, and Z axes for the boost component. Given that the majority of gel implants were in the United States, this strongly favored the gel implant dosimetry.

Equivalent Dose in 2 Gy Fractions

See **Table 1** for prescribed dose and fractionation schemes. To compare patients with different treatment fractionation schemes, all received doses were converted to equivalent dose in 2 Gy fractions (EQD2) using the following formula:

$$\mathrm{EQD}_2 = D \times \frac{d + \alpha/\beta}{2 + \alpha/\beta}$$

where D is the total prescribed dose in Gy and d is the dose per fraction in Gy.[15] For this study, an α/β of 3 was used for late rectal toxicity endpoints.[16]

Statistical and Data Analysis

All statistical analyses were conducted in Python 3.10 using SciPy and pandas libraries. Prior to comparative analysis, normality of dosimetric data was assessed using Shapiro-Wilk and Jarque-Bera tests for all DVH parameters across treatment groups. For D0.1cc and D1cc, all groups showed deviation from normality ($P < .05$); for D2cc, 1 of 3 groups approximated normality. Levene test was used to assess homogeneity of variance across groups, revealing variance heterogeneity across all DVH parameters (all $P < .05$).

Given the non-normal distributions and variance heterogeneity, nonparametric methods were employed for robust inference. Kruskal-Wallis *H*-tests were used for omnibus testing of group differences across all DVH parameters, followed by Mann-Whitney *U* tests for post hoc pairwise comparisons with Bonferroni correction (α = .0167) to control family-wise error rate across 3 pairwise comparisons.[17]

The percent difference between cohort groups was calculated using the symmetric formula:

$$\%\ \text{Difference} = \frac{a - b}{(a + b)/2} \times 100$$

Results

For each patient, D0.1cc, D1cc, and D2cc were collected and analyzed, with all doses converted to EQD2. See **Table 2** for analyzed dosimetry data for all patient groups.

Kruskal-Wallis tests revealed highly significant differences among treatment

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Figure 2. Comparison of rectal dose-volume histogram (DVH) parameters (D0.1cc, D1cc, D2cc) among inflatable balloon (IB), polyethylene glycol (PEG), and control groups. Boxplots display equivalent dose in 2 Gy fractions (EQD2) (Gy, $\alpha/\beta = 3$) with significance levels from post hoc pairwise tests (***$P < .001$).

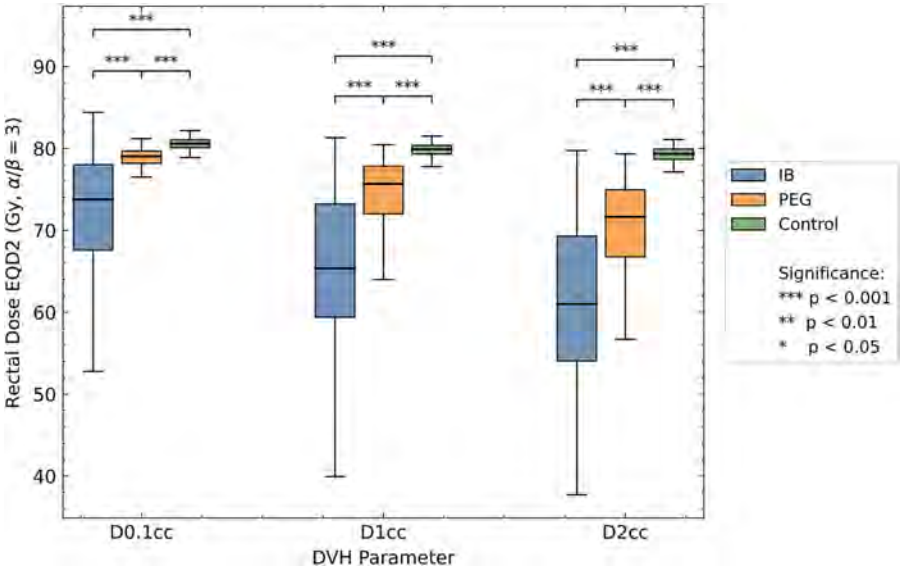
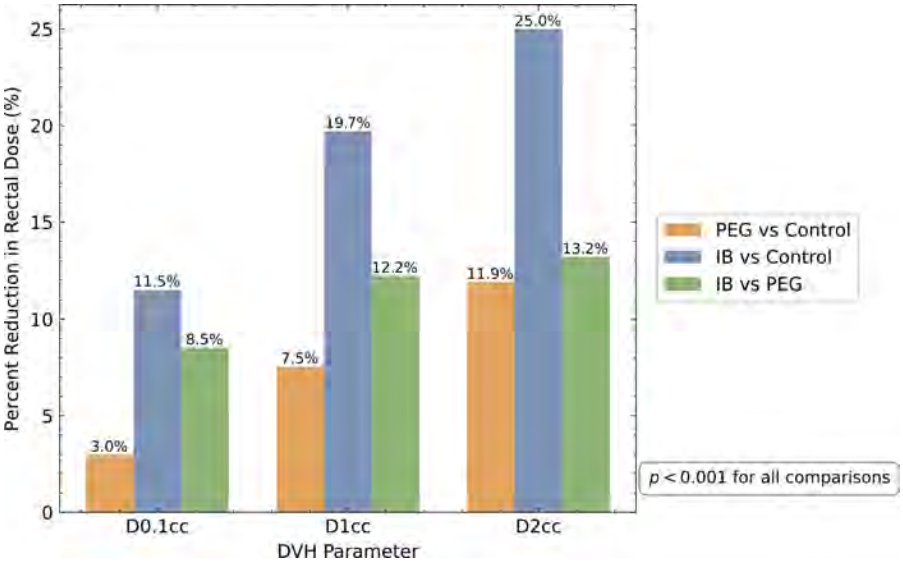


Figure 3. Dose reduction in absolute percent difference for inflatable balloon (IB) and polyethylene glycol (PEG). Absolute percent difference was calculated between each spacer type and the control arm, as well as between the IB and PEG rectal displacement device. All doses were converted to equivalent dose in 2 Gy fractions with $\alpha/\beta = 3$. DVH, dose-volume histogram.



groups across all DVH parameters (all $P < .001$), with large effect sizes (η^2H range: 0.68-0.72, all indicating large effects per conventional thresholds). All pairwise effect sizes indicated large effects (Cohen $d = 1.01$-1.07; threshold for large effects $d > 0.8$).

See **Figure 2** for a comparison of rectal DVH data from all groups. See **Figure 3** for percent difference data between cohorts. For the IB implant, we found a mean received D0.1cc of 71.7 Gy (SD = 8.1 Gy) and dose reduction of 11.5% compared to the control cohort ($P < .001$), and dose reduction of 8.5% compared to patients receiving the PEG implant ($P < .001$). We found a mean received D1cc of 65.2 Gy (SD = 9.5 Gy) and dose reduction of 19.7% compared to control patients ($P < .001$), and dose reduction of 12.2% compared to patients receiving the PEG implant ($P < .001$). We found a mean received D2cc of 61.2 Gy (SD = 9.9 Gy) and dose reduction of 25% compared to the control cohort ($P < .001$), and dose reduction of 13.2% compared to patients receiving the PEG implant ($P < .001$).

For the PEG implant, we found a mean received D0.1cc of 78.1 Gy (SD = 3.5 Gy) and dose reduction of 3% compared to the control cohort ($P < .001$). We found a mean received D1cc of 73.7 Gy (SD = 6.0 Gy) and dose reduction of 7.5% compared to the control cohort ($P < .001$). We found a mean received D2cc of 69.9 Gy (SD = 7.1 Gy) and dose reduction of 11.9% compared to the control cohort ($P < .001$).

Discussion

This multi-institutional retrospective cohort study compared rectal dose-sparing capabilities of 2 RDD technologies in 283 patients undergoing prostate external beam RT. Our findings demonstrate that PEG gel and IB implants significantly reduce radiation dose to the rectum compared to controls, with the IB device providing superior dose reduction across all DVH parameters.

Clinical Significance of Dosimetric Findings

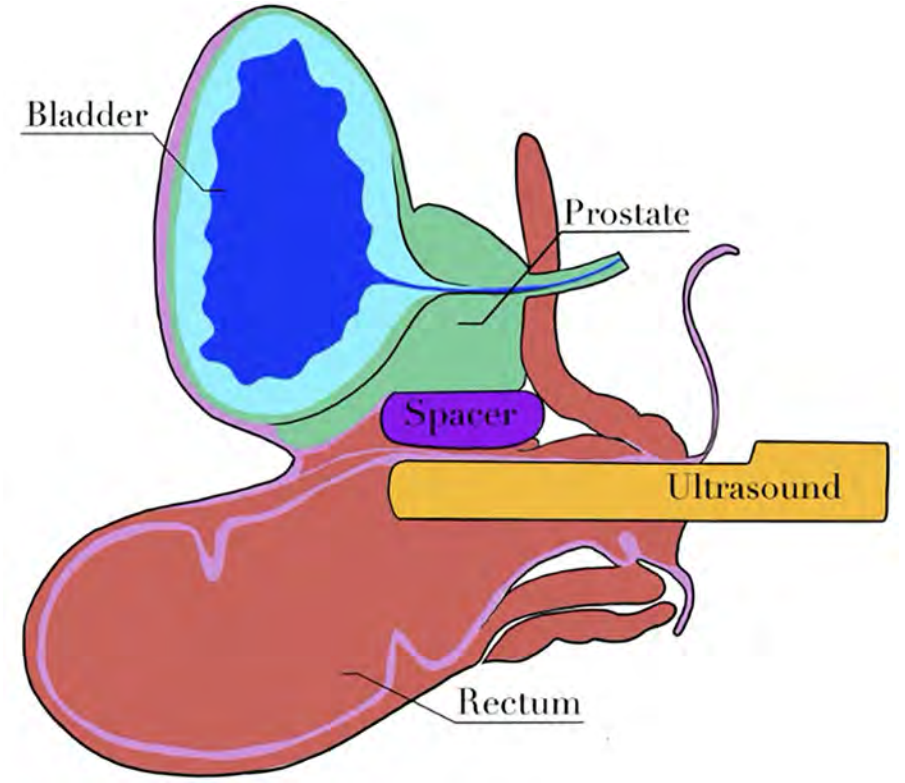
The IB implant achieved substantial dose reductions of 11.5%, 19.7%, and 25% for D0.1cc, D1cc, and D2cc, respectively, compared to controls (all $P < .001$). These reductions translate to mean doses of 71.7 Gy, 65.2 Gy, and 61.2 Gy (EQD2) for the respective parameters. The PEG implant, while also providing statistically significant dose reduction (3%, 7.5%, and 11.9% for D0.1cc, D1cc, and D2cc; all $P < .001$), demonstrated more modest dose-sparing, with mean values of 78.1 Gy, 73.7 Gy, and 69.9 Gy.

Table 3. Clinical Characteristics of Implants

CHARACTERISTIC	IB	PEG
Implant size (cc)	16-20	10-12
Imaging modalities where implant is visible	MRI, CT	MRI, CT when contrast is added

Abbreviations: IB, inflatable balloon; PEG, polyethylene glycol.

Figure 4. Depiction of the implantation of a rectal displacement device (RDD) into the perirectal space. Ultrasound imaging is used during the procedure to guide and validate RDD placement.



Direct comparison between devices revealed the IB implant reduced doses by 8.5%, 12.2%, and 13.2% relative to PEG across all 3 parameters (all $P < .001$).

These findings agree with prior studies showing that both implant technologies significantly reduce radiation dose to the rectum.[9,10] A previous study also agrees that the IB implant is superior to PEG in reducing the rectal dose.[18]

The progressively greater dose-sparing effect observed at larger volumes (D2cc > D1 cc > D.1 cc) for the IB device likely reflects superior spatial symmetry. Well-positioned IB implants typically create 1.7 to 2.0 cm separation between rectum and prostate. Suboptimal PEG symmetry may result in incomplete coverage, where small rectal volumes receive higher doses despite larger volumes benefiting from displacement.

Product Comparison

Beyond these dosimetric distinctions, the 2 devices also differ substantially in their insertion techniques and procedural requirements, see **Table 3**. Insertion procedures of the PEG and IB are relatively quick, typically performed after beacon placement using transrectal ultrasound-guided needle or instrument into the perirectal space. See **Figure 4** for a depiction of the ultrasound-guided implantation procedure. PEG uses hydrodissection followed by a 10 to 12 mL gel injection. IB requires blunt dissection, insertion of the apparatus and balloon, then filled with 16 to 20 mL sterile water. The IB device tip is blunt, requiring more force but is less likely to perforate the rectum.[19] The IB allows opportunities to inflate, deflate, and reposition the balloon, which can improve symmetry. Poor spacer symmetry results in less rectal dose reduction but still offers significant reduction.[20] The separation between the rectum and prostate is typically 1.7 to 2.0 cm with the IB implant. More bleeding usually occurs with IB (typically < 5 mL), but lidocaine administration nearly eliminates pain. The balloon is easily visible on MRI, obviating the need for contrast.

Limitations

The limitations of this study include bias with respect to physician experience; greater experience generally improves outcomes. In this study, both physicians had little experience with IB placements, but PEG data were aggregated from one physician who had performed over 500 placements. Complication rates and symmetry after PEG placement have demonstrated improvement after the first 20 cases.[21] The IB data based on the first 13 cases likely underestimate the technology's potential performance. Another bias relates to prostate volume differences (mean 95 cc in IB group vs 66 cc in others). Randomization would have been ideal, but both devices are rapidly evolving. Beyond PEG and perirectal balloons, hyaluronic acid spacers have demonstrated rectal dose-sparing with supportive prospective evidence. Hyaluronic acid spacers have also demonstrated rectal dose-sparing and are now commercially available.[14] Future comparison studies that include this RDD type are warranted.

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Conclusion

We report the dosimetric analysis of 2 RDDs, a PEG gel implant and an IB implant, for reduction of radiation dose to the rectum during prostate cancer treatment using external beam RT. Both implants are well-tolerated, with a low but possible risk of complications.[14] Both demonstrated statistically significant reduction of received dose to the rectum compared to the absence of implants in control patients. The IB implant demonstrated superior dose reduction to the rectum than the PEG implant. RDDs are a new technology and are under continued development and improvement. Further investigation and comparison of RDDs is warranted as technology improves.

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Unexpected Complete Response to Palliative Radiation Therapy in Non-Small Cell Lung Cancer

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Abstract

Locally advanced non–small cell lung cancer (NSCLC) is generally treated with chemotherapy, long-course radiotherapy, and surgery. The role of palliative radiotherapy is typically reserved for pain management and functional recovery. An elderly patient presented in October 2023 with thoracodorsal pain and functional impairment of the right upper limb. Imaging revealed a bulky mass in the right upper lung lobe with suspected costovertebral infiltration and no distant disease. The multidisciplinary tumor board recommended sequential chemoradiotherapy followed by surgery. Due to worsening pain, radiotherapy (8 Gy × 2 fractions) was administered between the second and third cycles of cisplatin–pemetrexed (with a 25% dose reduction for age) of the four planned cycles.

Restaging demonstrated marked tumor shrinkage. Given persistent arm impairment and favorable tumor response, surgery was prioritized and achieved complete resection. Histopathologic examination unexpectedly revealed a complete pathologic response.

This case suggests that short-course radiotherapy may contribute to tumor downstaging and raises important questions regarding radiosensitivity in NSCLC.

Keywords: lung cancer, palliative radiation therapy, pain management, sequential chemo-radiotherapy, tumor down-sizing, unexpected result, multidisciplinary approach, predictive factors, treatment response, case report

Case Summary

A 75-year-old man, a former heavy smoker, presented in October 2023 with a 3-month history of neuropathic chest pain radiating to the right shoulder, associated with progressive functional impairment and a visual analog scale score of 7 despite treatment with paracetamol and codeine. Contrast-enhanced CT identified a large right upper lobe mass with costovertebral infiltration. Staging with PET and MRI excluded distant metastases, consistent with locally advanced non-small cell lung cancer (NSCLC).

The initial therapeutic plan consisted of neoadjuvant chemo radiation therapy; however, due to worsening pain, palliative radiation therapy (8 Gy × 2 fractions, February 13-16, 2024)

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Informed Consent: Written informed consent was obtained and signed by the patient for publication of this case and associated images.

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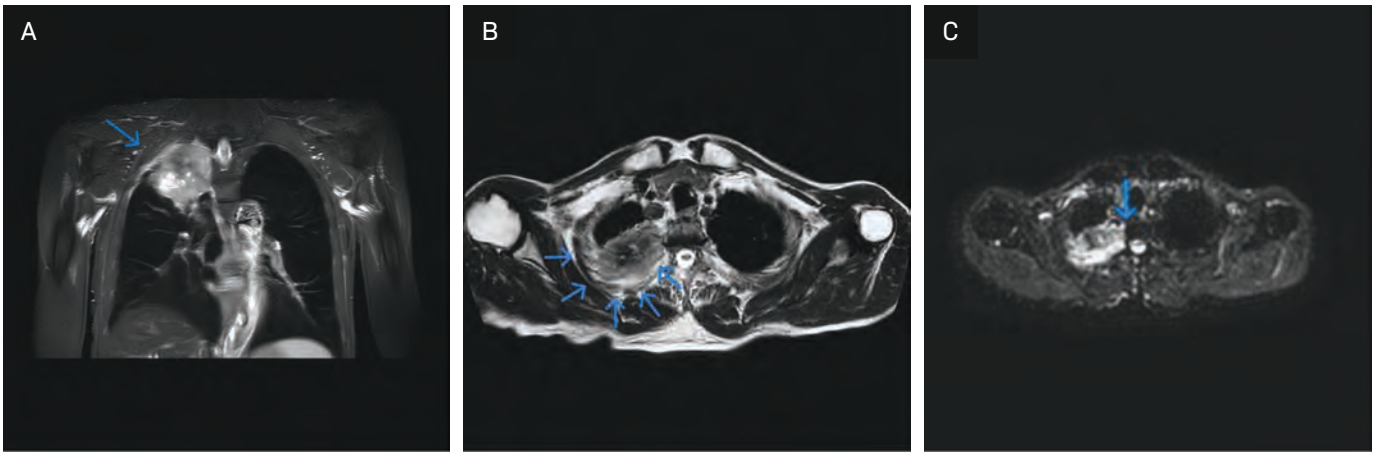
Figure 1. Thoracic MRI demonstrating Pancoast syndrome due to involvement of the right upper lung lobe. Coronal plane (A), axial plane (B), and axial plane showing suspected vertebral infiltration (blue arrow) (C).



was administered between the second and third chemotherapy cycles. At completion of chemotherapy (April 2, 2024), the patient exhibited deterioration in performance status and difficulty maintaining treatment position for definitive radiation therapy, prompting referral for surgical management on April 17, 2024. Histopathologic analysis unexpectedly demonstrated a complete pathologic response with no residual neoplastic tissue, representing an extraordinary response to a purely palliative treatment.

Imaging Findings

The first relevant imaging evaluation was performed in November 2023 because of suspected Pancoast syndrome. MRI (**Figure 1A-C**) revealed a mass measuring 7.2 cm (axial) × 6.8 cm (coronal) × 8.9 cm (sagittal) in the right upper lobe, infiltrating the ipsilateral second through 4th ribs and abutting the second through 4th thoracic vertebrae.

Subsequent whole-body PET (**Figure 2A and B**) demonstrated intense uptake of fluorodeoxyglucose (SUV_max 19.6) corresponding to the known pulmonary mass, measuring 7.8 cm (axial) × 5.0 cm (coronal) × 9.0 cm (sagittal), located in the apical and posterior segments of the right upper lobe. Moderate tracer uptake suggestive of nodal involvement was

Figure 2. PET-CT demonstrating an excavated lesion infiltrating the ribs in the right upper lung lobe. Axial view (A) and sagittal view (B).

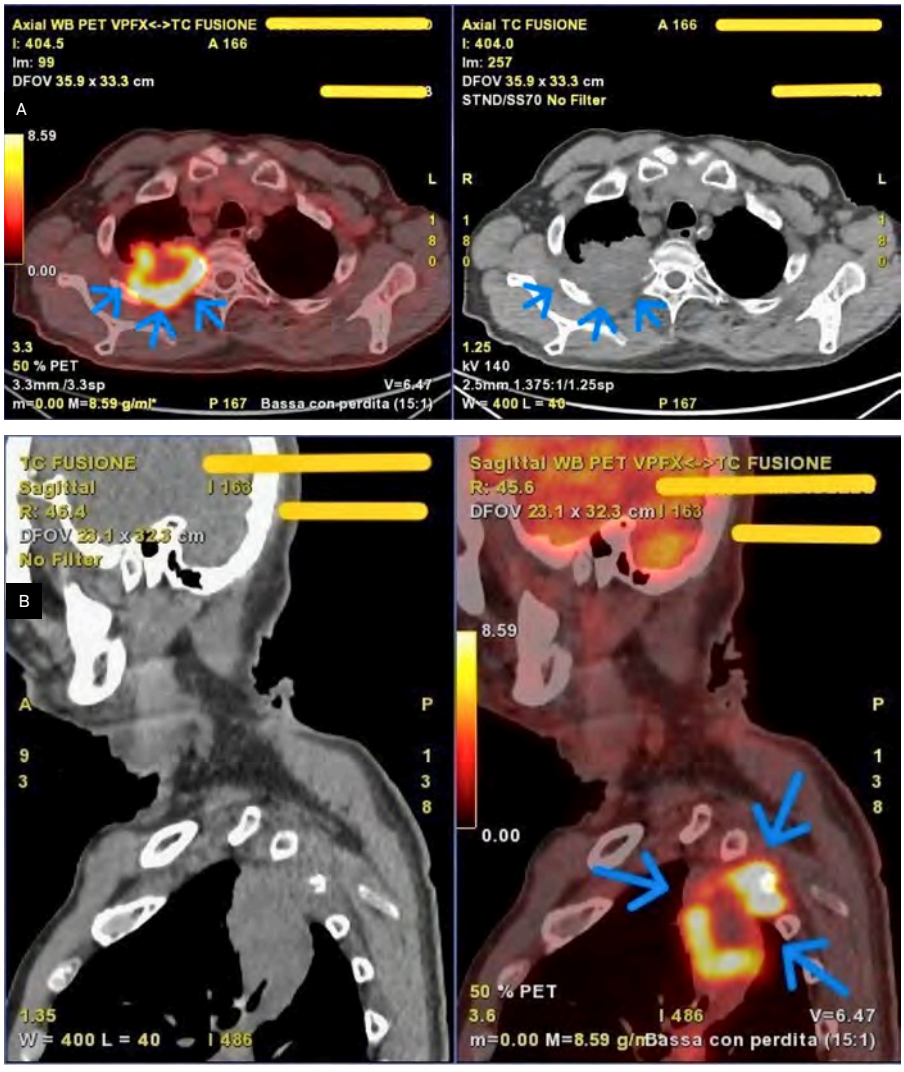


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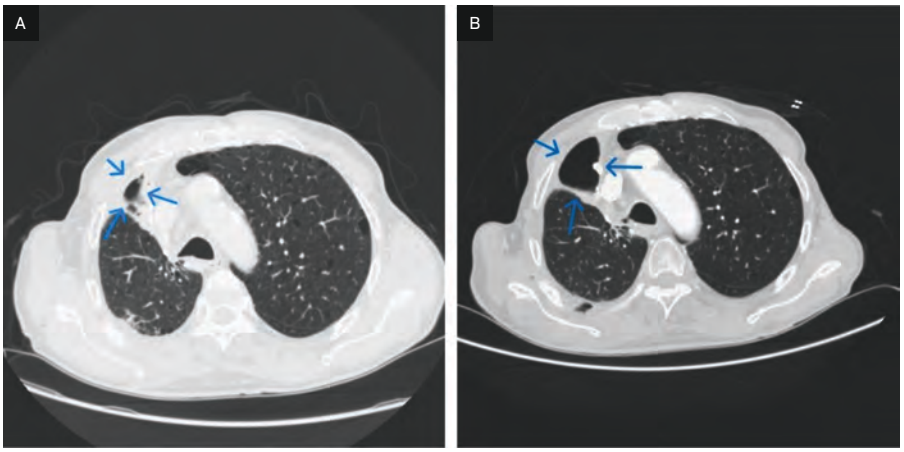
Figure 3. Routine postoperative CT demonstrating right-sided hydropneumothorax. Upper axial plane (blue arrows) (A) and lower axial plane (blue arrows) (B).



observed in the right hilar (SUV_max 3.6) and subcarinal (SUV_max 2.8) regions.

Postoperative thoracic CT (**Figure 3A and B**) revealed a loculated right-sided hydropneumothorax and confirmed the outcomes of right upper lobectomy with resection of the lateral arches of the second and third ribs. A thin residual pleural effusion and minor subpleural consolidation were present. Paraseptal emphysema persisted in the left upper lobe. Enlarged paratracheal mediastinal lymph nodes, measuring up to 2 cm, were subsequently evaluated histologically by endobronchial US-guided biopsy.

Diagnosis

The patient had a history of hypertension treated with ramipril/hydrochlorothiazide and a previous transient ischemic attack managed with daily acetylsalicylic acid. He had a heavy smoking history (> 20 cigarettes per day for 50 years). He was in good general condition (ECOG performance status 1), with mild weight loss and no dyspnea or hemoptysis. Physical examination revealed reduced mobility of the right upper limb and decreased breath sounds in the right upper lung field. Laboratory tests were within normal limits.

Imaging demonstrated a large right upper lobe mass with infiltration of the second through 4th ribs and the second thoracic vertebra, consistent with advanced disease (cT4 cN2 M0, stage IIIB). Differential diagnoses—including primary bone tumors, soft tissue sarcoma, metastatic disease, plasma cell dyscrasia, and infectious etiologies—were excluded through imaging, laboratory evaluation, and clinical assessment. The diagnosis of locally advanced NSCLC without distant metastases was definitively established by US-guided bronchial biopsy.

Discussion

Although Pancoast tumors account for fewer than 5% of all lung cancer cases, the significant morbidity caused by their infiltrative growth at the thoracic outlet, along with ongoing debate regarding optimal treatment strategies in this anatomically complex region, continues to challenge efforts to improve local control and progression-free survival.[1] These tumors originate from the superior pulmonary sulcus and invade the thoracic inlet, including adjacent ribs and vertebrae. The first clinical and radiologic characterization was described by Pancoast in 1932.[2] Approximately 3 decades later, Paulson introduced a combined approach of preoperative radiation therapy followed by posterior surgical resection, reporting encouraging outcomes.[3]

Subsequent therapeutic milestones emerged from pivotal phase II trials in the early 2000s, including SWOG 9416 and JCOG 9806, which demonstrated complete pathologic response rates of 87.3% and 89.4%, respectively, and 5-year overall survival rates of 46% and 61% using combined chemo radiation therapy.[4,5] Technological advancements later enabled dose escalation from the historical 30 to 35 Gy used in earlier protocols to the current standard of 60 Gy, resulting in improved pathologic response and survival outcomes.[6] Radiobiologically, 30 to 35 Gy delivered in 10 fractions corresponds to an EQD2 of 32.5 to 39.4 Gy and a biologically effective dose (BED) of 39 to 47.3 Gy ($\alpha/\beta = 10$), whereas a total dose of 60 Gy corresponds to an EQD2 of 60 Gy and a BED of 72 Gy.

In the scientific literature, neoadjuvant treatment strategies for locally advanced NSCLC include either definitive chemo radiation therapy or a trimodality approach incorporating surgery. The principal randomized studies addressing this question are the Intergroup Trial 0139 and the SAKK 16/00 trial.[7,8] In the SAKK 16/00 study, no survival benefit was demonstrated for the trimodality approach using sequential chemo radiation therapy followed by surgery compared with bimodal treatment consisting of chemotherapy and surgery alone.[8] Across published series, reported rates of complete pathologic response range from 15% to 33%, and rates of nodal downstaging (pN0) range from 25% to 46%.

Other investigations have evaluated dose escalation, altered fractionation schedules, and hyperfractionated regimens, demonstrating higher rates of pathologic complete response. However, to date, no studies have shown that a purely palliative radiation therapy regimen, such as 8 Gy × 2 fractions, can induce a complete pathologic response in non–small cell lung cancer. Therefore, the favorable outcome observed in the present case can only be interpreted

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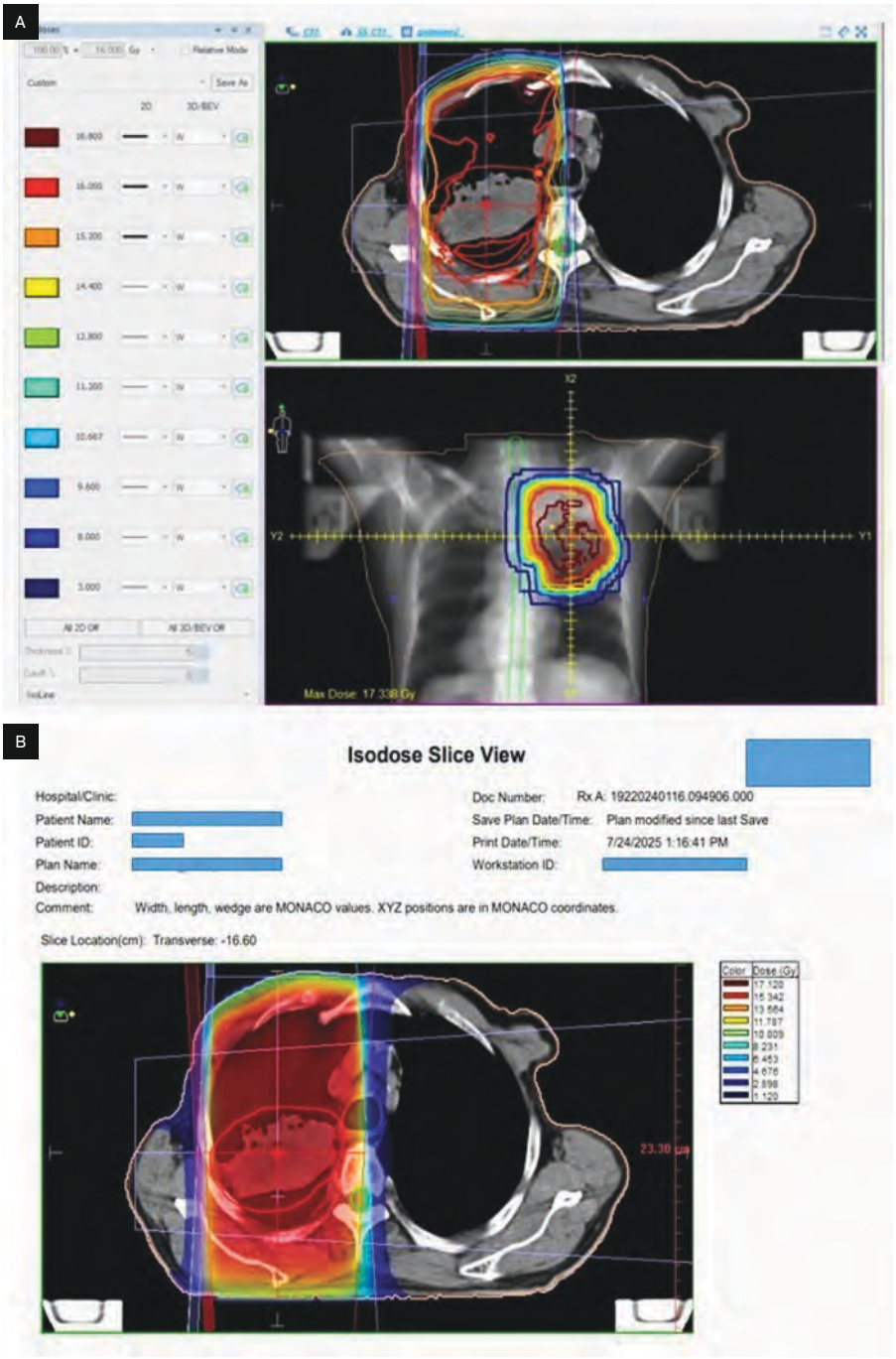
through hypothesized radiobiologic mechanisms.

Large radiation dose fractions are not limited to direct DNA damage, which represents the classical radiobiologic mechanism. At higher dose levels, radiation also affects tumor vasculature by inducing endothelial apoptosis and ischemic injury through vascular collapse. Tumor endothelial cells are particularly sensitive to high single doses, activating ceramide-mediated signaling pathways that result in apoptosis and disruption of the tumor's abnormal vasculature.[9,10] Loss of perfusion amplifies direct tumor cell death. Preclinical models have shown that genetic suppression of endothelial apoptosis confers resistance to high-dose radiation, highlighting the therapeutic relevance of doses ≥8 to 10 Gy per fraction.[9,10]

High-dose hypofractionated radiation therapy has also been shown to induce immunogenic cell death, characterized by the exposure of damage-associated molecular patterns such as calreticulin and CD47 and the release of ATP and HMGB1. These signals activate dendritic cells and promote cytotoxic T-lymphocyte priming against tumor antigens, thereby enhancing systemic antitumor immunity.[11-14] Preclinical studies suggest that multifraction regimens around 8 Gy (eg, 8 Gy × 3 fractions) may be more immunogenic than single ablative doses.[15-18] Although the regimen used in this case consisted of 8 Gy × 2 fractions, it remains within this biologically active window, potentially allowing vascular, immunologic, and cytotoxic effects to converge.

The exceptional response observed in this patient is likely attributable to the combined effects of direct tumor cell killing, vascular normalization, and immune activation, occurring within a narrow therapeutic window and in an anatomic site where even modest tumor regression can result in substantial clinical benefit, including pain relief and functional recovery.

Figure 4. Radiation therapy treatment planning images demonstrating isodose distribution on frontal and axial planes (A) and color wash dose distribution on axial plane (B).



Conclusion

This case represents a remarkable and unexpected complete pathologic response in a patient with superior sulcus NSCLC treated with a short-course palliative radiation therapy regimen of 8 Gy × 2 fractions (**Figure 4**). This outcome challenges conventional dose–response paradigms and suggests that tumor- and host-specific radiosensitivity factors may play a critical role. Further

investigation into ultra-hypofractionated radiation therapy and personalized treatment strategies is warranted.

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Successful Reirradiation of Multiple Recurrent Lymphocytic Hypophysitis: A Case Report

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Abstract

Lymphocytic hypophysitis is a rare autoimmune inflammatory condition of the pituitary gland. For patients with disease refractory to corticosteroids and systemic agents, surgery is often pursued. However, given the anatomy of the suprasellar area, complete resection is difficult, and postoperative recurrence is common. Radiation therapy (RT) represents an alternative to surgery in those not suitable for resection or a means for further treatment in the setting of postsurgical recurrence. Given the rarity of the disease, data on the use of RT and its outcomes are sparse. Even more rare are examples regarding *reirradiation* for this uncommonly encountered condition. To add to the data in this space, we present the case of a patient with multiple recurrent lymphocytic hypophysitis who underwent 2 courses of RT as part of his treatment.

Keywords: Lymphocytic hypophysitis, pituitary dysfunction

Case Summary

The patient originally came to medical attention roughly 6 years prior to his initial course of radiation therapy (RT) after months of progressively worsening headaches. Further workup revealed pan-hypopituitarism and diabetes insipidus. An MRI of the brain demonstrated enlargement, thickening, and enhancement of the pituitary stalk and gland. Systemic staging scans were negative for signs of malignancy. He was started on prednisone (30 mg daily) and azathioprine for presumed neuro-sarcoidosis (azathioprine was eventually stopped after a hospitalization for bacterial meningitis). Ultimately, the decision was made to observe the patient with serial MRI scans while continuing corticosteroids. A few years later, the patient developed bitemporal hemianopsia and associated progression on surveillance imaging. An endoscopic trans-nasal biopsy revealed evidence of chronic inflammation consistent with lymphocytic hypophysitis. He continued steroids, which were eventually tapered to lower doses due to side effects, including steroid-induced diabetes.

Shortly thereafter, he experienced progressive visual changes that correlated with continued inflammatory progression involving the pituitary apparatus and floor of the third ventricle. Progression continued following the start of rituximab. Eventually, he underwent a subtotal resection, resulting in short-term improvement. With continued observation, the patient's imaging remained stable for the next 2 years.

Imaging Findings

After 2 years of stability, imaging revealed further progression with mass-like enhancement involving the suprasellar cistern, optic apparatus, and hypothalamus, associated with worsening vision. The patient's case was discussed at multidisciplinary tumor board with the recommendation for radiation. He then received 24 Gy in 12 fractions with 6 MV photons utilizing 2 non-coplanar VMAT arcs and cone-beam CT for image guidance (**Figure 1**). Areas

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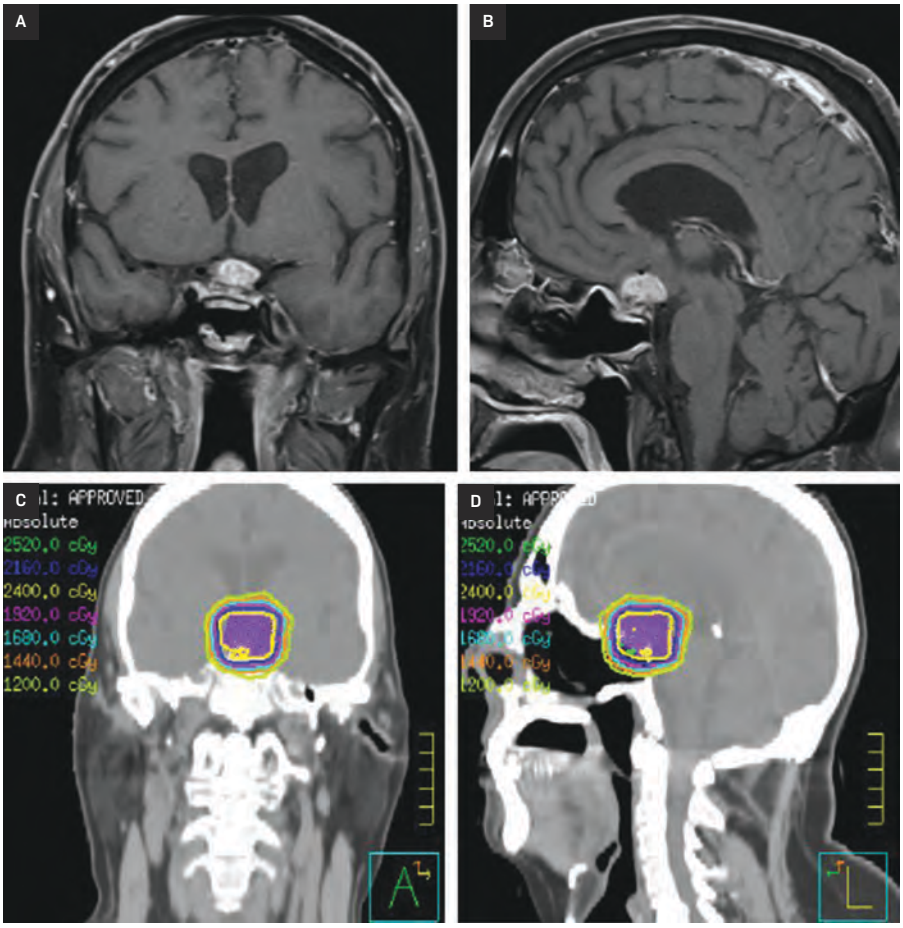
Figure 1. Coronal and sagittal slices of T1-weighted, postcontrast MRI scans of the pituitary gland (A, B). Corresponding radiation therapy (RT) plan for first course of RT, 24 Gy in 12 fractions delivered to the enhancing lesion (C, D).



of progression and enhancement were targeted, including the sella, optic nerves and chiasm, and hypothalamus. He experienced no immediate side effects except for mild fatigue. Within 6 months of his initial course of RT, his vision had improved. At 3 years post RT, he had stable vision with very slight progression on imaging and remained on low-dose steroids. However, by 6 years after RT, the patient's suprasellar lesion had notably enlarged with an increased mass effect on the optic chiasm as well as corresponding declines in his vision (light perception only in the left eye; worsening right-sided peripheral vision).

At this time, after a multidisciplinary discussion, the patient was referred to radiation oncology for consideration of additional RT. Ultimately, he was treated to a dose of 28 Gy in 14 fractions using 6 MV photons with 2 non-coplanar VMAT arcs (**Figure 2**). He again experienced no immediate side effects except for significant fatigue. MRI scans at 3 and 6 months post re-RT demonstrated a decrease in size and enhancement of the suprasellar abnormality with stable vision (**Figure 3**).

Diagnosis

Lymphocytic hypophysitis.

Differential considerations included neuro-sarcoidosis, pituitary adenoma, central nervous system lymphoma, and craniopharyngioma.

Discussion

Lymphocytic hypophysitis is a rare form of pituitary dysfunction, with some estimates placing its annual incidence at 1 in 9 million.[1,2] It is believed to be caused by an autoimmune lymphocytic infiltrate, which leads to destruction of the pituitary gland, often resulting in pan-hypopituitarism.[2] While it most commonly occurs in peripartum women, nonpregnant women and men can also be affected.[2,3] Individuals with this condition often experience intense headaches and visual changes, with a homogeneously enhancing suprasellar mass appreciated on MRI.[3]

First-line treatment typically includes high-dose glucocorticoids and/or other systemic therapies such as rituximab, azathioprine, and mycophenolate.[1-5] Surgery is usually undertaken for those with disease refractory to medical management. RT utilizing either a conventionally fractionated (1.8-2 Gy per treatment, 12-14 treatments) or stereotactic radiosurgery (12-15 Gy per treatment, 1-2 treatments) approach can be used for medically inoperable patients or for individuals with persistent disease after surgery.[3,6-9] Given the rarity of this condition, there is a paucity of data in the literature regarding the use and effectiveness of RT in this setting.[3]

Recently, Khaleghi et al published on their single-center experience of 3 patients treated with RT for lymphocytic hypophysitis.[3] In their systematic review, they were able to identify only 5 other similar cases of lymphocytic hypophysitis treated with radiation. Short-term follow-up limited the analysis of outcomes.

Notably, no patients in the Khaleghi et al series underwent reirradiation with post-RT recurrence.[3] To the best of our knowledge, this report represents the first documented case of reirradiation

Figure 2. Coronal and sagittal slices of T1-weighted, postcontrast MRI scans of the pituitary gland (A, B). Corresponding radiation therapy (RT) plan for the second course of RT, 28 Gy in 14 fractions delivered to the progressively enhancing lesion (C, D).

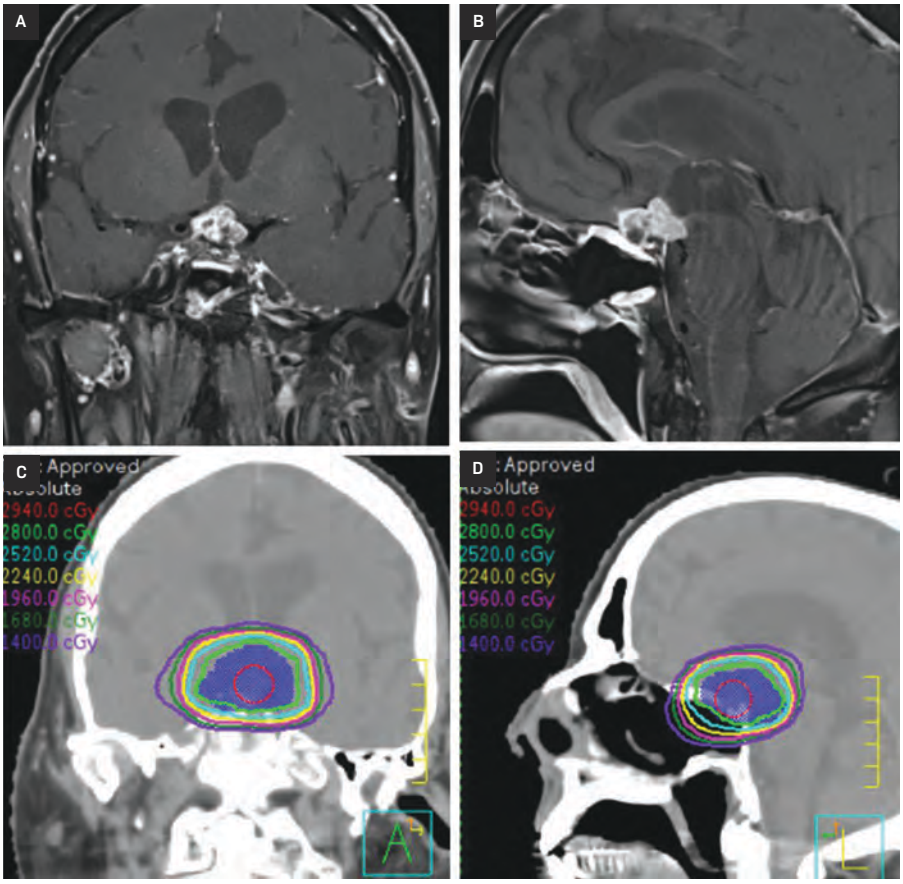
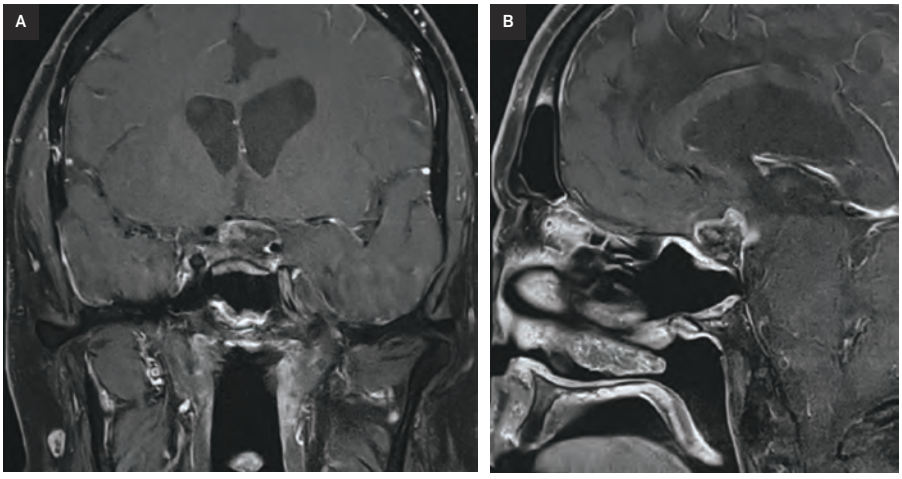


Figure 3. Coronal and sagittal slices of T1-weighted, postcontrast MRI scans of the pituitary gland showing decreased size and enhancement of the suprasellar lesion 6 months post reirradiation (A, B).



for a patient with multiple recurrent lymphocytic hypophysitis. After an initial course of 24 Gy in 12 fractions, our patient was reirradiated 6 years later to a dose of 28 Gy in 14 fractions. There were no significant side effects associated with the first course of RT, and 2 years post-RT there was radiographic regression and visual improvement. Unfortunately, his response was not sustained, and the patient had symptomatic progression despite medical treatment until re-RT, after which his visual changes and headaches stabilized.

Our patient's recurrence is somewhat surprising given the general radiosensitivity of lymphocytic cells. Indeed, for this patient, medical management, surgery, and RT have all been ineffective at producing sustained remission of the infiltrate. With reports in the literature suggesting resolution with medical management and/or RT alone, we wonder whether the underlying biology of this patient's condition is fundamentally different. We have also considered whether stereotactic radiosurgery, and the delivery of ablative doses in just 1 to 2 treatments, would have produced different initial results.[6-9] Despite these considerations, we are encouraged by the patient's initial response to his second course of RT. Our preliminary experience suggests that reirradiation is a safe and effective short-term solution for multiple recurrent lymphocytic hypophysitis. Observation over a more extended period is required to confirm whether these encouraging early results will last over time.

Conclusion

This case report illustrates the short-term feasibility and effectiveness of reirradiation for multiple recurrent lymphocytic hypophysitis. Long-term follow-up is needed to confirm the durability of this approach.

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Procedural Competency in Brachytherapy: Stepping Beyond Case Minimums

Fara Dayani, MD, MAS

Brachytherapy is one of the foundational treatment modalities in radiation oncology. It is an integral component of management across multiple disease sites in the definitive, adjuvant, and recurrent settings. During residency, we gain early and consistent exposure to external beam radiation therapy, developing proficiency in simulation, treatment planning, and patient management.

In contrast, brachytherapy requires a distinct educational approach rooted in technical skill acquisition, real-time procedural decision-making, and the cultivation of procedural competency. Mastery is achieved through a strong cognitive foundation, simulation-based learning, supervised clinical performance, graduated autonomy, and competency-based assessment.

The educational landscape in brachytherapy is heterogeneous,[1-3] with marked variability across training programs driven by differences in patient volume, faculty expertise, institutional practice patterns, and procedural exposure. Current procedural minimums set by the Accreditation Council for Graduate Medical Education (ACGME) represent an important step toward defining baseline expectations for training. These minimums are accompanied by case log forms that deconstruct each procedure into discrete components, spanning from pre-procedure history and physical examination to appropriate post-procedure management.[4]

Notably, the minimum required number of interstitial brachytherapy cases increased from 5 to 7 beginning in the 2023-2024 academic year. However, numerical thresholds may not serve as an adequate measure of technical fluency, procedural competency, or readiness for independent practice.

The variability of resident experience in brachytherapy is reflected in the national trends in brachytherapy procedure volumes. ACGME reports for academic years 2017-2025 demonstrate a national mean of approximately 50 intracavitary brachytherapy cases, with standard deviations ranging from 32 to 45 cases (60%–85% of the national mean), indicating substantial dispersion in case exposure.[5] A similar pattern is observed for interstitial brachytherapy procedures, suggesting markedly different procedural exposure among residents, despite satisfying minimum requirements.[5]

This is further supported by the findings of Basree et al[6] regarding perceived confidence levels of graduating radiation oncology residents from 2020 to 2024 with different treatment techniques. They found that only 25.7% and 22.6% of graduating radiation oncology residents reported comfort in independently performing high-dose

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rate and low-dose rate prostate brachytherapy, respectively, upon completion of residency.

The findings above underscore the importance of incorporating structured, competency-based frameworks into brachytherapy training, in which clearly defined training objectives are mapped to developmental milestones, linked to graduated levels of entrustment, and evaluated using appropriate assessment tools, rather than procedural minimums.

The Joint ABS/GEC-ESTRO Consensus Statement on the objectives of training in brachytherapy for physicians represents a meaningful step in this direction, outlining comprehensive knowledge domains and procedural skills required for safe practice.[7] This approach enables programs to determine whether a resident can perform a procedure safely and effectively.

Competency-based training and assessment does not eliminate the challenges posed by institutional differences in procedural volume and exposure. Therefore, individual training programs must identify and address these gaps. For those in need of additional brachytherapy experience, regional collaborations, external rotations, and initiatives such as the American Brachytherapy Society's "300 in 10" program provide valuable opportunities to supplement training.

As practice patterns continue to evolve, it is essential to ensure equitable access to brachytherapy expertise. This requires standardizing the training curriculum, strengthening procedural competency through meaningful assessment, and creating intentional pathways to further develop and maintain procedural competency.

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