

Evaluation and treatment of female stress urinary incontinence after pelvic radiotherapy

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Introduction: Pelvic radiotherapy is associated with both acute and chronic voiding dysfunction. A review of the success and complications of surgical treatments for female stress urinary incontinence after pelvic radiotherapy has not been summarized in the published literature.

Methods: A systematic review of female stress urinary incontinence after pelvic radiotherapy was conducted using MeSH terminology (1988-2018).

Results: There is limited published literature on the treatment of stress urinary incontinence in women following pelvic radiotherapy. Long term indwelling urethral catheter should be avoided in all women given the risk of iatrogenic hypospadias. Surgical treatments can be classified into those for the intact versus failed outlet. Urethral bulking injections have been studied in a prospective fashion specifically in women with stress urinary incontinence after radiotherapy and although not randomized, have the highest level of evidence. Patients should be screened for a history of prior radiotherapy before considering sling placement. Artificial urinary sphincter is associated with a high rate of erosion after prior radiotherapy. The role of Burch colposuspension in patients with prior radiotherapy is poorly defined. Urinary diversion should be considered for patients with a devastated outlet.

Conclusions: Since the long-term effects of radiotherapy on lower urinary tract voiding function are typically irreversible and progressive, further research is needed to mitigate the adverse effects of irradiation and identify more durable treatment options for women with radiation induced bladder dysfunction and stress urinary incontinence.

KEYWORDS

female, radiotherapy, treatment, urinary incontinence

1 | INTRODUCTION

1.1 | Genitourinary morbidity following radiotherapy

According to recent statistics published by the American Cancer Society; urologic, gynecologic, and colorectal

malignancy arising from the pelvis accounted for up to one-third of all new cancer diagnoses in the United States.¹ The National Cancer Institute reports that approximately half of all cancer patients in the United States will receive radiation therapy.² Genitourinary radiotoxicity in the acute phase includes urinary urgency, frequency, nocturia, dysuria,

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bladder spasm, urothelial ulceration, and hemorrhage with an incidence of 20-80%. Following an asymptomatic latent period, epithelial atrophy, reduction in capacity, loss of compliance, and bladder necrosis manifests as a result of progressive vascular damage, obliterative arteritis, ischemia, and fibrosis.³

The Radiation Therapy Oncology Group (RTOG) has clearly defined genitourinary adverse events (Table 1).⁴ Morbidity following radiotherapy can be divided into acute genitourinary toxicity, occurring within 90 days of radiation, and late/chronic effects. Given the close proximity of the cervix and vaginal cuff to the bladder, grade 1 and 2 urinary adverse events are present in up to 45% of patients at 5-years and major complications related to grade 3 adverse events noted in 14% of patients at 20-years (Table 1).⁵⁻⁷

Despite a considerable disease burden, only a handful of investigators have sought to characterize the urodynamic changes which occur following radiotherapy for the treatment of female pelvic malignancy.⁸⁻¹⁰ In the most recent of these investigations, Katepratoom found that radiation typically resulted in storage dysfunction when compared to radical hysterectomy alone.¹⁰ In this study of 35 radiated bladders evaluated with urodynamics, radiation was associated with lower maximum cystometric capacity, poor bladder compliance, increased sensation, increased detrusor overactivity,

and similar proportion of patients with urodynamic stress incontinence. Consistent with the paucity of data on radiation induced urodynamic dysfunction in women, is need for a systematic review on the evaluation and treatment of female stress urinary incontinence after pelvic radiotherapy.

The American Urologic Association (AUA), Society of Urodynamics Female pelvic medicine & Urogenital reconstruction (SUFU), International Continence Society (ICS), and European Association of Urology (EAU) have published guidelines regarding the management of female urinary incontinence and the performance of urodynamics.¹¹⁻¹⁴ A systematic review of published literature in the PubMed database from 1988 to 2018 on female stress urinary incontinence after pelvic radiotherapy was conducted using MeSH terminology (Figure 1) and guidelines established by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).¹⁵

2 | EVALUATION

2.1 | Lower urinary tract symptoms and pathophysiology

Lower urinary tract complaints in women with radiation induced urinary incontinence can include both voiding and

TABLE 1 RTOG radiation morbidity scoring criteria (acute vs late/chronic)

Grade	Genitourinary toxicity	%
Acute (<90 days)		
0	No change	
1	Frequency of urination or nocturia twice pretreatment habit; dysuria, urgency not requiring medication	20-80%
2	Frequency of urination or nocturia that is less frequent than every hour; dysuria, urgency, bladder spasm requiring local anesthetic (eg, Pyridium)	28-45%
3	Frequency with urgency and nocturia hourly or more frequently; dysuria, pelvis pain or bladder spasm requiring regular, frequent narcotic; gross hematuria with/without clot passage	
4	Hematuria requiring transfusion; acute bladder obstruction not secondary to clot passage, ulceration, or necrosis	
Late/chronic		
0	None	
1	Slight epithelial atrophy; minor telangiectasia (microscopic hematuria)	Minor 45% (5 years)
2	Moderate frequency; generalized telangiectasia; intermittent macroscopic hematuria	
3	Severe frequency and dysuria; severe telangiectasia (often with petechiae); frequent hematuria; reduction in bladder capacity (<150 cc)	Major 7.7% (3 years) 9.3% (5 years) 11.1% (10 years) 13% (15 years) 14.4% (20 years)
4	Necrosis/contracted bladder (capacity <100 cc); severe hemorrhagic cystitis	

RTOG, Radiation Therapy Oncology Group.

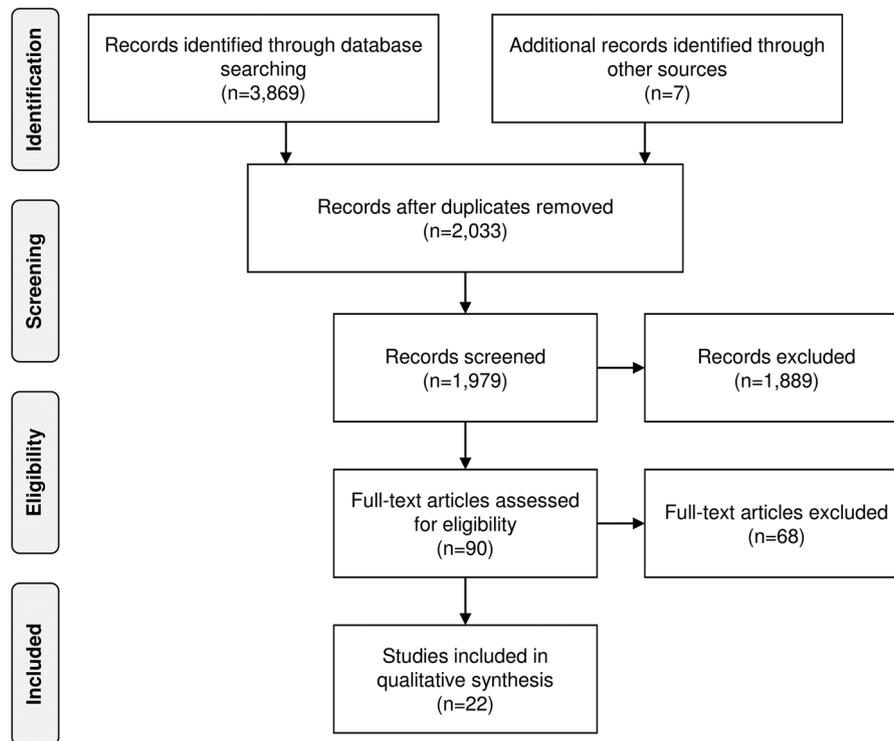


FIGURE 1 PRISMA 2009 Flow Diagram¹⁵ as a result of search strategy using MeSH terms (alphabetical order): cholinergic antagonists, cystitis, electromagnetic radiation, female, neck, phenazopyridine, radiation, radiotherapy, therapeutics, urethra, urinary bladder, urinary diversion, urinary incontinence, women

storage symptoms as defined by ICS standardized terminology.¹⁶ The mechanistic failure to empty urine can result from dysfunction of the bladder, dysfunction of the outlet, or a combination of both a weak bladder and obstruction of the outlet.¹⁷ The underlying pathophysiology of acute urinary symptoms following pelvic radiotherapy are typically subsequent to a leaky urothelium, with detrusor overactivity manifest as urinary frequency, nocturia, urgency, dysuria, and incontinence. Involuntary leakage of urine should be characterized as either stress (effort, exertion, sneezing, or cough), urgency (accompanied/preceded by urge), or mixed incontinence (combination of stress and urgency).¹⁶

2.2 | Principles of evaluation

Since a majority of radiated patient's will report storage symptoms, the AUA/SUFU guidelines¹⁸ form a nice framework for the assessment of overactive bladder and urinary incontinence following pelvic radiation. The minimum evaluation should include a careful history, physical exam, and urinalysis.¹⁸ History related to the pelvic cancer should be elucidated, including dose, timing, and route of irradiation; concomitant pelvic surgery; and expected survival. Review of systems should assess for the presence of recurrent urinary tract infections, hematuria from radiation cystitis, bowel symptoms from radiation proctitis, and

fecaluria concerning for fistula. Past medical history should ascertain medical co-morbid conditions. Past surgical history should assess prior mesh for prolapse or incontinence. At the clinician's discretion, additional tests may include cystoscopy, renal bladder ultrasound, and free uroflowmetry with post-void residual if concern for incomplete bladder emptying.¹⁸ Intake-voiding diary can be used to assess maximum capacity, urinary frequency, diurnal variations in functional capacity (nocturnal vs daytime), timing of incontinence, and correlation with fluid intake. Urodynamics may be obtained in the complicated patient when *invasive, potentially morbid or irreversible treatments are considered*.¹¹

3 | CONSERVATIVE MANAGEMENT

3.1 | Observation during early phase after radiotherapy

During the treatment of gynecologic cancer, radiotherapy templates are created by the radiation oncologist to minimize bladder irradiation. Typically the bladder neck and urethra receive the highest genitourinary radiation dose during cervical cancer treatment. During the acute phase, histology of the bladder demonstrates reversible inflammation characterized by loss of the glycosaminoglycan layer, sloughing of urothelial cells, loss of uroplakin, edema, blood vessel

dilation, leaky urothelium, and epithelial hyperplasia.¹⁹ Since most acute symptoms are self limiting during the first 90 days following radiotherapy, they are typically managed by the radiation oncologist or the patient's primary care provider.²⁰

3.2 | Pharmacologic treatment during the acute phase

Standard treatments for the exacerbation of acute symptoms include phenazopyridine, anticholinergics, and hydration.²⁰ Phenazopyridine is commonly prescribed for its known local analgesic effect on the lower urinary tract when it is excreted into the urine. Despite widespread acceptance of this medication for the symptomatic treatment of bacterial cystitis and anecdotal use in radiation cystitis patients, there has been no published clinical investigational trial on the use of phenazopyridine for the treatment of radiation induced bladder dysfunction.

Anticholinergics are commonly prescribed by the radiation oncologist during the acute phase of radiotherapy for exacerbation of urinary frequency, urgency, and urgency incontinence.²⁰ Two recent clinical trials were identified on the use of anticholinergics for radiation induced bladder dysfunction (Table 2).^{21,22} In a single arm observational study of 249 women treated with solifenacin 5 mg daily for post-irradiation bladder dysfunction, at a mean 38 month interval following radiotherapy, Jaszczynski et al²² found a significant improvement in cystometric capacity, number of micturitions per day, nocturia, urgency episodes, and urinary incontinence. In a subsequent publication by Yan et al,²¹ trospium 20 mg twice daily resulted in significant improvement in IPSS and quality of life, when added to tamsulosin therapy for lower urinary tract symptoms after prostate brachytherapy. This study did not enroll women, and no additional prospective published trials were identified for the use of anticholinergics for radiation induced symptoms in women.

3.3 | Non-surgical stress urinary incontinence treatment

When considering etiologies of stress incontinence, intrinsic sphincter deficiency may exist in isolation, or include a component of stress provoked detrusor overactivity. Common non-surgical treatment options include incontinence liners/pads, pelvic floor muscle exercises, and anti-incontinence pessaries.^{14,23,24} The clinical data regarding success specific to radiation induced bladder dysfunction for each of these is limited (Table 2).

Changes in pelvic floor function after radiotherapy were recently summarized in a review by Bernard in 2016, which included 13 studies, 692 participants, of which 160 were women.²³ Specific detrimental structural changes include poor pelvic floor musculature contractile response (level 1B

evidence), at a mean 78 weeks following radiotherapy. In a cross sectional study of 11 women with urinary incontinence, a mean 3.1 years after hysterectomy with radiotherapy, incontinence severity was found to correlate with rate of pelvic floor force development, number of contractions and endurance. When compared to 18 controls with hysterectomy alone, women with prior radiotherapy demonstrated decreased maximum pelvic floor contractile force, rate of force generation, and number of contractions.²⁴

4 | SURGICAL MANAGEMENT

The late/chronic phase of radiation cystitis occurs years to decades later, and on histology demonstrates chronic inflammatory fibrosis. Typical findings include increased collagen deposition, fibroblast infiltration, atrophy of smooth muscle, edema, obliterative endarteritis, and hemorrhage.¹⁹ Since radiation induced bladder dysfunction typically presents years to decades following irradiation, the optimal timing of surgical interventions for radiation induced outlet dysfunction has not been exhaustively studied in a randomized controlled trial fashion. Success and complications of the available literature on surgical treatments for female stress urinary incontinence with an intact non-devastated outlet after pelvic radiotherapy are summarized (Table 3).

4.1 | Urethral bulking agents

Urethral bulking agents were the subject of a recent Cochrane review by Kirchin et al.²⁵ For many of the trials evaluating bulking injection, patients were excluded if they had a history of prior radiotherapy.²⁶ Out of all the surgical treatments for stress incontinence (Table 3), only bulking agents have been studied in a prospective fashion, and specifically enrolled women with a history of prior radiotherapy.^{27,28} In the most recent publication by Krhut et al, 24 women with a history of pelvic radiotherapy and severe stress urinary incontinence were enrolled in a multi-center study of Bulkamid® (polyacrylamide hydrogel), and complete continence was achieved in 25% of women after radiation, compared to 36% of non-irradiated women. In an earlier study by Plotti of 24 women with de-novo stress incontinence after radical hysterectomy treated with Macroplastique® (polydimethylsiloxane), 10 out of 24 patients (42%) reported cure of incontinence after urethral bulking.²⁷ This study enrolled five women with prior radiotherapy, and no intraoperative or postoperative complications were noted at 12 months after injection. These two reports of urethral bulking agents were the only published in the literature which prospectively enrolled women with a history of prior radiotherapy. Complications specific to radiotherapy were reported by Castillo-Vico et al,²⁹ and include the presence of a

TABLE 2 Non-surgical irradiation bladder treatment/assessment

Author	Cohort (n)	Follow-up	Objective findings	Subjective findings	Notes
Anticholinergic treatment					
Jaszczynski (2016)	n = 300 (n = 249 women); Single arm observational study solifenacin 5 mg daily for post-irradiation bladder	6 months	Improvement in cystometric capacity ^a , volume at first desire ^a , and Pdet@capacity ^a	Improvement in # micturitions/day ^a , nocturia ^a , urgent episodes ^a , and incontinence ^a	38 month (mean) interval between RT and treatment. Solifenacin well tolerated
Yan (2017)	n = 60 vs 64; RCT PrCA s/p brachytherapy, tamsulosin 20 mg BID + tamsulosin vs tamsulosin alone	6 months	No difference in Qmax and PVR from baseline	Improvement in IPSS ^a and QoL ^a in tamsulosin group. No difference in voiding score.	No women
Pelvic floor musculature					
Bernard (2016)	n = 692 (13 studies) Systematic review of effect of RT on pelvic floor muscle function (n = 160 women)	N/A	RT affects structure of PFM (level 2B), no change in anal sphincter thickness (level 2B)	RT worsens PFM contractile response (level 1B)	78 weeks (mean) interval between RT and PFM assessment
Bernard (2017)	n = 11; Descriptive cross sectional study of women with UI after Hx and RT (vs 18 women with Hx without UI)	N/A	PFM maximum force, rate of force development, and # of contractions reduced in RT group	UI severity correlates with rate of force development, # of contractions, endurance, age, and vaginal length	3.1 years (mean) interval between RT and PFM assessment

Hx, hysterectomy; IPSS, International Prostate Symptom Score; N/A, not applicable; NR, not reported; OAB, overactive bladder; Pdet, detrusor pressure; PFM, pelvic floor muscle; PrCA, prostate cancer; PVR, post void residual; Qmax, maximum flow rate; QoL, quality of life; RCT, randomized controlled trial; RT, radiotherapy.

Most recent literature reported since 2010 (where available). Reference list: Jaszczynski et al,²² Yan et al,²¹ Bernard et al,²³ Bernard et al.²⁴

^aSignificant improvement.

periurethral granuloma 4 months after dextranomer/hyaluronic acid copolymer injection. There were no additional publications identified for the other urethral bulking agents (collagen, calcium hydroxylapatite, ethylene vinyl alcohol, and carbon spheres) in irradiated women.²⁵

4.2 | Midurethral sling (synthetic and biologic)

Similar to bulking agents,²⁵ patients with a history of pelvic irradiation have been specifically excluded from many of the clinical trials (OPUS,³⁰ VALUE,³¹ SISTER³²) assessing anti-incontinence procedures.³³ Therefore few studies report outcomes in women with a history of radiotherapy who subsequently underwent sling placement (Table 3). The largest was published by Chuang and Kuo,³⁴ in 16 women with prior radiotherapy and radical hysterectomy, followed for a minimum of 3 months. At a mean 5.9 year interval between radiotherapy and surgical intervention, a 100% (n = 2) rate of recurrent stress incontinence was noted at 6 months postoperatively. Similarly, in a prospective observational study of 120 women treated with tension-free vaginal tape (TVT) sling by Al-Singary, there were two women enrolled with prior radiotherapy. At a 26 month mean follow-up, 72% of women were dry on cough test, and there

were no erosions, however, 100% (n = 2) of the irradiated women reported subjective sling failure. Likewise, in a series of 75 women treated with TVT, including two with radiotherapy, Kinn reported an overall 80% cure rate at a 2 year minimum follow-up, however, noted a 50% rate of erosion in women previously treated with radiation. Additional results of the available published literature on sling complications after prior radiotherapy are summarized (Table 3). Based on these limited published data, there appears to be a strong association between subjective sling failure and rates of erosion after prior radiotherapy.

4.3 | Autologous fascia pubovaginal sling

There was limited published literature identified for autologous fascia and biologic slings following radiotherapy. O'Reilly published a series of 121 women with fascia lata sling and stress urinary incontinence, and included one woman with prior radiotherapy. In their results only eight women had recurrent stress incontinence at a mean 6.5 month follow-up. However, following radiotherapy, there was a 100% (n = 1) rate of incontinence noted at 12 months. In this patient, a 10 cmH₂O leak point pressure was noted preoperatively, which was only increased to 21 cmH₂O after sling.

TABLE 3 Intact outlet—Surgical treatments for female stress incontinence after pelvic radiotherapy

Author	Cohort (n)	Follow-up	Objective findings	Subjective findings	Notes
Urethral bulking agents					
Castillo-Vico (2007)	n = 1 prior RT; Case report, periurethral granuloma after Dx/HA injection	4 months	NR	Incontinence cured at the 1-month follow-up	18 year interval between RT and injection
Plotti (2009)	n = 24 (n = 5 prior RT); Single arm prospective observational study of Macroplastique in women with de-novo SUI after radical Hx	12 months (minimum)	Frequency of incontinence on the 3-day voiding diary reduced (14.5 ± 5.8 vs 4.3 ± 7.9 episodes per 3 days, P < 0.05)	Overall success rate was 84% (10 patients cured and 10 improved)	No intraoperative or postoperative early complications were found. Preoperative urethral hyper-mobility noted in the 4 patients who were not success
Krhot (2016)	n = 46 (n = 24 prior RT); Multi-center single arm prospective observational study of Bulkamid in women with severe SUI (with vs without prior RT)	12.4 months (mean)	No clinically significant between group changes in urodynamic parameters after Bulkamid (VV, Qmax, PVR, Cap, MUCP)	Complete continence in 25% of patients after RT (vs 36.4% without RT). Improved urine leakage ^a , ICIQ-UI ^b and PPBC ^b both groups	Mean 93 month (range 16-384) interval between RT and injection
Midurethral sling (synthetic)					
Kinn (2001)	n = 75 (n = 2 prior RT); Case series of TVT in women with SUI	2 years (minimum)	NR	80% cured, 9% improved, 11% failure	Two women had vaginal erosion, and 1 had prior RT. 50% of RT patients had erosion
Al-Singary (2005)	n = 120 (n = 2 prior RT); Single arm prospective observational study of TVT for urodynamic SUI or MUI	26 months (mean); 6-42 months (range)	72% dry on cough test	18% (n = 16) subjective patient reported failures (leakage >1x/day and/or persistent urgency/frequency syndrome)	87 of 120 patients completed study. No erosions. Of the 16 TVT failures, two had prior RT. 100% of RT patients were subjective failure
Jankiewicz (2005)	n = 1 prior RT; Case report, Tyco IVS retropubic sling after cervical cancer RT	4 months	Negative cough test	Full control over micturition and significant improvement in QoL	10 year interval between RT and TOT
Chuang (2009)	n = 49 (n = 16 prior RT); Case series of urologic complications after radical Hx (n = 7 treated with sling)	3 months (minimum)	NR	Seven patients (n = 2 prior RT) treated with pubovaginal sling for ISD (6 of 7 continent for >3 months; 4 of 7 recurrent mild SUI at >6 months)	5.9 ± 4.5 year interval between RT and surgical intervention. 100% of RT sling patients (n = 2) had recurrent mild SUI at >6 months
Hazewinkel (2009)	n = 2 (n = 1 prior RT); Case series TVT-Secur after radical Hx	6 months	NR	SUI no longer present 6 weeks after surgery in RT patient	5 year interval between RT and TVT-Secur. Erosion × 2 in RT patient (6 and 10 weeks after surgery)

(Continues)

TABLE 3 (Continued)

Author	Cohort (n)	Follow-up	Objective findings	Subjective findings	Notes
Midurethral sling (biologic)					
O'Reilly (2002)	n = 121 (n = 1 prior RT); Case series cadaveric fascia lata sling in women with SUI	6.5 months (mean); 4-13 months (range)	RT LPP 10 cmH ₂ O preoperative and 21 cmH ₂ O postoperative	8 of 121 women had recurrent SUI	100% of RT patients (n = 1) had recurrent SUI at 12 months
Lowman (2007)	n = 1; Case report, TVT with porcine interposition graft after vulvar cancer RT	3 months	Positive cough stress test at 3 months	80% subjective improvement in symptoms, occasional SUI	19 year interval between RT and surgical intervention
Artificial urinary sphincter					
Mundy (1989)	n = 30 (n = 9 prior RT); Case series total urethral substitution (n = 4 treated with AUS)	NR	50% sphincter weakness incontinence with AUS	2 of 4 patients (colonic substitution and AUS) failed and required diversion "not satisfactory"	All post-RT had hysterectomy. Interval between RT and surgery NR.
Duncan (1992)	n = 29 (n = 7 prior RT); Case series AUS in women	NR	NR	4 of 12 patients had "satisfactory result" (n = 7 prior RT)	8 of 12 patients cuff erosion (n = 7 prior RT).
Vayleux (2011)	n = 215 (n = 9 prior RT); Case series AUS in women	6 years (mean)	Overall 73.5% continent (0-1 pad per day). Failure (Incontinence) after AUS in 23.7%	Overall 79% satisfied	Pelvic radiotherapy (Continence failure OR 4.37, CI 1.02-18.5). Erosion in three of nine RT patients

AUS, artificial urinary sphincter; Cap, capacity; CI, confidence interval; Dx/HA, dextranomer/hyaluronic acid copolymer; Hx, hysterectomy; ICIQ-UI, International Consultation on Incontinence Questionnaire—short form; IVS, intravaginal slingsplasty; LPP, leak point pressure; MUCP, maximum urethral closure pressure; MUI, mixed urinary incontinence; NR, not reported; OR, odds ratio; PPBC, Patient Perception of Bladder Condition questionnaire; PVR, post void residual; Qmax, maximum flow rate; RT, radiotherapy; SUI, stress urinary incontinence; TVT, tension-free vaginal tape; VV, voided volume. Literature reported since 1989 (where available). Reference list: Castillo-Vico et al,²⁹ Plotti et al,²⁷ Krhut et al,²⁸ Kinn,⁴⁵ Al-Singary et al,⁴⁶ Jankiewicz et al,⁴⁷ Chuang and Kuo,³⁴ Hazewinkel et al,⁴⁸ O'Reilly and Govier,⁴⁹ Lowman et al,⁵⁰ Mundy,³⁸ Duncan et al,³⁶ Vayleux et al.³⁵

^aSignificant improvement.

4.4 | Burch colposuspension

There were no published outcomes specific to radiotherapy identified for women treated with Burch colposuspension. Radiotherapy was cited as a specific exclusion criteria, for instance in the 2011 Cochrane review³³ of the Stress Incontinence Surgical Treatment Efficacy Trial (SISTER) which randomized 655 women to Burch colposuspension or fascia sling.³² Since there is a lower implant burden with Burch colposuspension when compared to synthetic sling, rates of erosion would be expected to be lower for Burch than sling. However, given the magnitude of adverse changes in bladder physiology after radiotherapy, and a mere 49% stress incontinence success rate published in the SISTER trial of non-radiated women, the postulated efficacy of Burch would be expected to be even lower in irradiated women. Given the paucity of published literature on Burch after radiotherapy, the utility of this treatment is poorly defined.

4.5 | Artificial urinary sphincter

In women with stress urinary incontinence and prior radiotherapy, the published literature on the artificial urinary sphincter is limited. In a case series by Vayleux of 215 women treated with artificial urinary sphincter, there were nine women previously treated with radiotherapy, which on multivariate analysis was significantly associated with continence failure (OR 4.37, CI 1.02-18.5).³⁵ Additionally, a 33% sphincter erosion rate ($n = 3$) was noted at a mean follow-up of 6 years. Prior to this, the only other study of artificial urinary sphincter identified by search criteria which included outcomes in women after radiotherapy, was published by Duncan.³⁶ In this case series of 29 women treated with artificial sphincter, 8 out of 12 patients had cuff erosion which necessitated explant, including 7 of whom previously received radiation. Given the high rate of sphincter failure, the authors advocate screening out women with a history of radiotherapy.

4.6 | Spiral sling and urethral reconstruction

The completely circumferential spiral urethral sling has been well described by several authors as a treatment option for the devastated bladder outlet with recurrent stress urinary incontinence.³⁷ There were no studies identified which specifically reported outcomes in women with prior radiotherapy who underwent spiral sling. For the woman with a devastated outlet, in whom the outlet is to be reconstructed, Mundy described a 30 patient case series of several approaches for urethral substitution in women, including four with prior radiotherapy treated with colonic substitution and artificial urinary sphincter.³⁸ In those treated with colonic substitution and artificial sphincter, 50% of the patients failed and required urinary diversion. The authors

advise that a pedicle labial skin tube neo-urethroplasty should be considered for patients with prior radiotherapy.

4.7 | Urinary diversion

For the failed bladder outlet with devastated urethral sphincter and/or bladder neck, and a continence mechanism which cannot be salvaged, diversion is a standard of care treatment option. Long term indwelling urethral catheter should be avoided in women given the high likelihood of iatrogenic hypospadias. Suprapubic cystostomy catheter urinary diversion without an outlet procedure is an option in select patients with devastated outlet and some degree of sphincter and/or bladder neck continence. An outlet enhancing procedure with one of the surgical treatments traditionally used for the intact outlet (Table 3), may be required in addition to a suprapubic catheter if there is some degree of surgically salvageable outlet function. Alternatively, bladder neck closure may be considered, with the understanding that poor wound healing after radiation places the patient at elevated risk of failure.³⁹

Published outcomes for urinary diversion in women after pelvic radiotherapy are summarized (Table 4). Excluding fistula from our search strategy, there were no published series identified specifically for the indication of urinary incontinence after radiotherapy. The time interval between radiotherapy and urinary diversion is typically on the order of years to decades.⁴⁰⁻⁴³ Options for diversion after radiotherapy include either a continent reservoir or an incontinent ileal conduit with or without vesicovaginostomy. In a series by Banerji of 28 women undergoing ileal conduit at a mean 9.8 years after cervical cancer radiotherapy, 18 women underwent concomitant vesicovaginostomy using a resectoscope and Collin's knife to allow vaginal secretions to drain and prevent pyocystitis.⁴⁰ Ideally the bowel segment selected for the pouch should be outside of the radiotherapy field to improve tissue healing, reduce fibrosis, and improve continence. In a series by Stolzenburg of 24 patients undergoing Colon Mainz pouch III, the authors report a mean pouch capacity of 294 mL at a mean follow-up of 35 months, and 20 patients were noted to be fully continent.⁴⁴ In the 18 patients who were previously radiated, pouch capacity was noted to be adequate at 308 mL, which the authors attribute to the location of the ascending and transverse colon used for the pouch, located outside of the previously radiated field. In a similar series by Wilkin et al,⁴¹ 26 women underwent Indiana pouch at time of exenteration for recurrent gynecologic cancer, with 12 having had prior radiotherapy. In this series, 3 out of 12 patients had pouch incontinence from the efferent limb. For the patient with a devastated outlet and end stage bladder, diversion remains a standard of care treatment option, as long as the quality of life benefits⁴⁰ are carefully weighed against a reported 65-83% postoperative complication rate.^{41,43}

TABLE 4 Failed outlet—Urinary diversion outcomes in women after pelvic radiotherapy

Author	Cohort (n)	Follow-up	Objective findings	Subjective findings	Notes
Urinary diversion					
Blaivas (2005)	n = 76 (n = 3 prior RT); Case series augmentation enterocystoplasty or diversion (n = 58 women)	8.9 years (mean)	NR	2 of 3 (66%) of RT patients cured or improved	18-20 year interval between RT and surgery (n = 2 women)
Wilkin (2005)	n = 26 (n = 12 prior RT); Case series Indiana pouch at time of exenteration for recurrent gynecologic cancer	12 months (minimum); 48.5 months (mean, prior RT group)	3 of 12 patients pouch incontinence efferent limb	83% of RT patients had one or more complications	32 month (mean) interval between RT and surgery
Stolzenburg (2007)	n = 24 (n = 18 prior RT); Case series colon Mainz pouch III (n = 19 women)	35 months (mean)	Mean pouch capacity 294 mL (308 mL after prior RT)	20 of 24 patients fully continent	Interval between RT and surgery NR
Al Hussein Al Awamlh (2015)	n = 29; Case series cystectomy and diversion after pelvic RT (n = 5 women)	37.3 months (median)	NR	65.5% 30-day postoperative complications	87 month (median) interval between RT and first symptoms
Banerji (2015)	n = 28; Case series ileal conduit after cervical cancer RT (n = 18 vesico-vaginostomy)	13.2 months (mean)	NR	Global Impression of Change Scale 5.2/7 (vs 3/7 w/o conduit, P = 0.06)	9.8 year (mean) interval between RT and cystitis

NR, not reported; RT, radiotherapy.

Literature reported since 2005 (where available). Reference list: Blaivas et al,⁴² Wilkin et al,⁴¹ Stolzenburg et al,⁴⁴ Al Hussein Al Awamlh et al,⁴³ Banerji et al.⁴⁰

5 | CONCLUSIONS

Pelvic radiotherapy is associated with both acute and chronic voiding dysfunction. There is limited published literature on the treatment of stress urinary incontinence in women following pelvic radiotherapy. Long term indwelling urethral catheter should be avoided in all women given the risk of iatrogenic hypospadias. Surgical treatments can be classified into those for the intact versus failed outlet. Urethral bulking injections have been studied in a prospective fashion specifically in women with stress urinary incontinence after radiotherapy and although not randomized, have the highest level of evidence. Patients should be screened for a history of prior radiotherapy before considering sling placement. Artificial urinary sphincter is associated with a high rate of erosion after prior radiotherapy. The role of Burch colposuspension in patients with prior radiotherapy is poorly defined. Urinary diversion should be considered for patients with a devastated outlet.

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CONFLICTS OF INTEREST

The author declares that they have no conflicts of interest in relation to the content of the manuscript.

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REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin.* 2015;65:5–29.
2. Radiation Therapy for Cancer. National Cancer Institute. <http://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/radiation-fact-sheet>. Accessed December 29, 2015.

3. Stewart FA. Mechanism of bladder damage and repair after treatment with radiation and cytostatic drugs. *Br J Cancer Suppl.* 1986;7:280–291.
4. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). *Int J Radiat Oncol Biol Phys.* 1995;31:1341–1346.
5. McIntyre JF, Eifel PJ, Levenback C, Oswald MJ. Ureteral stricture as a late complication of radiotherapy for stage IB carcinoma of the uterine cervix. *Cancer.* 1995;75:836–843.
6. Takeshi K, Katsuyuki K, Yoshiaki T, et al. Definitive radiotherapy combined with high-dose-rate brachytherapy for Stage III carcinoma of the uterine cervix: retrospective analysis of prognostic factors concerning patient characteristics and treatment parameters. *Int J Radiat Oncol Biol Phys.* 1998;41:319–327.
7. Eifel PJ, Levenback C, Wharton JT, Oswald MJ. Time course and incidence of late complications in patients treated with radiation therapy for FIGO stage IB carcinoma of the uterine cervix. *Int J Radiat Oncol Biol Phys.* 1995;32:1289–1300.
8. Lajer H, Thranov IR, Bagi P, Aage Engelholm S. Evaluation of urologic morbidity after radiotherapy for cervical carcinoma by urodynamic examinations and patient voiding schemes: a prospective study. *Int J Radiat Oncol Biol Phys.* 2002;54:1362–1368.
9. Lin HH, Sheu BC, Lo MC, Huang SC. Abnormal urodynamic findings after radical hysterectomy or pelvic irradiation for cervical cancer. *Int J Gynaecol Obstet.* 1998;63:169–174.
10. Katepratoom C, Manchana T, Amornwichee N. Lower urinary tract dysfunction and quality of life in cervical cancer survivors after concurrent chemoradiation versus radical hysterectomy. *Int Urogynecol J.* 2014;25:91–96.
11. Winters JC, Dmochowski RR, Goldman HB, et al. Urodynamic studies in adults: AUA/SUFU guideline. *J Urol.* 2012;188:2464–2472.
12. Gammie A, Clarkson B, Constantinou C, et al. International Continence Society guidelines on urodynamic equipment performance. *Neurourol Urodyn.* 2014;33:370–379.
13. Lucas MG, Bosch RJJ, Burkhard FC, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *Eur Urol.* 2012;62:1130–1142.
14. Kobashi KC, Albo ME, Dmochowski RR, et al. Surgical treatment of female stress urinary incontinence: AUA/SUFU guideline. *J Urol.* 2017;198:875–883.
15. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.
16. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn.* 2002;21:167–178.
17. Wein AJ. Classification of neurogenic voiding dysfunction. *J Urol.* 1981;125:605–609.
18. Gormley EA, Lightner DJ, Faraday M, Vasavada SP. American Urological Association, Society of Urodynamics, Female Pelvic Medicine. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol.* 2015;193:1572–1580.
19. Zwaans BMM, Chancellor MB, Lamb LE. Modeling and treatment of radiation cystitis. *Urology.* 2016;88:14–21.
20. Berkey FJ. Managing the adverse effects of radiation therapy. *Am Fam Phys.* 2010;82:381–388, 394.
21. Yan M, Xue P, Wang K, Gao G, Zhang W, Sun F. Does combination therapy with tamsulosin and tropsium chloride improve lower urinary tract symptoms after SEEDS brachytherapy for prostate cancer compared with tamsulosin alone?: A prospective, randomized, controlled trial. *Strahlenther Onkol.* 2017;193:714–721.
22. Jaszczyński J, Kojs Z, Stelmach A, et al. Post-irradiation bladder syndrome after radiotherapy of malignant neoplasm of small pelvis organs: an observational, non-interventional clinical study assessing VESicare®/solifenacin treatment results. *Med Sci Monit.* 2016;22:2691–2698.
23. Bernard S, Ouellet M-P, Moffet H, Roy J-S, Dumoulin C. Effects of radiation therapy on the structure and function of the pelvic floor muscles of patients with cancer in the pelvic area: a systematic review. *J Cancer Surviv.* 2016;10:351–362.
24. Bernard S, Moffet H, Plante M, Ouellet M-P, Leblond J, Dumoulin C. Pelvic-floor properties in women reporting urinary incontinence after surgery and radiotherapy for endometrial cancer. *Phys Ther.* 2017;97:438–448.
25. Kirchin V, Page T, Keegan PE, et al. Urethral injection therapy for urinary incontinence in women. *Cochrane Database Syst Rev.* 2017;7:CD003881.
26. Schulz JA, Nager CW, Stanton SL, Baessler K. Bulking agents for stress urinary incontinence: short-term results and complications in a randomized comparison of periurethral and transurethral injections. *Int Urogynecol J Pelvic Floor Dysfunct.* 2004;15:261–265.
27. Plotti F, Zullo MA, Sansone M, et al. Post radical hysterectomy urinary incontinence: a prospective study of transurethral bulking agents injection. *Gynecol Oncol.* 2009;112:90–94.
28. Krhut J, Martan A, Jurakova M, Nemeč D, Masata J, Zvara P. Treatment of stress urinary incontinence using polyacrylamide hydrogel in women after radiotherapy: 1-year follow-up. *Int Urogynecol J.* 2016;27:301–305.
29. Castillo-Vico M-T, Checa-Vizcaíno MA, Payà-Panadés A, Rueda-García C, Carreras-Collado R. Periurethral granuloma following injection with dextranomer/hyaluronic acid copolymer for stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct.* 2007;18:95–97.
30. Wei JT, Nygaard I, Richter HE, et al. A midurethral sling to reduce incontinence after vaginal prolapse repair. *N Engl J Med.* 2012;366:2358–2367.
31. Nager CW, Brubaker L, Litman HJ, et al. A randomized trial of urodynamic testing before stress-incontinence surgery. *N Engl J Med.* 2012;366:1987–1997.
32. Albo ME, Richter HE, Brubaker L, et al. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. *N Engl J Med.* 2007;356:2143–2155.
33. Rehman H, Bezerra CC, Bruschini H, Cody JD. Traditional suburethral sling operations for urinary incontinence in women. *Cochrane Database Syst Rev.* 2011;Art. No. CD001754. <https://doi.org/10.1002/14651858.CD001754.pub3>.
34. Chuang F-C, Kuo H-C. Management of lower urinary tract dysfunction after radical hysterectomy with or without radiotherapy for uterine cervical cancer. *J Formos Med Assoc.* 2009;108:–626.
35. Vayleux B, Rigaud J, Luyckx F, et al. Female urinary incontinence and artificial urinary sphincter: study of efficacy and risk factors for failure and complications. *Eur Urol.* 2011;59:1048–1053.
36. Duncan HJ, Nurse DE, Mundy AR. Role of the artificial urinary sphincter in the treatment of stress incontinence in women. *Br J Urol.* 1992;69:141–143.

37. Rodriguez AR, Hakky T, Hoffman M, Ordorica R, Lockhart J. Salvage spiral sling techniques: alternatives to manage disabling recurrent urinary incontinence in females. *J Urol*. 2010;184:2429–2433.
38. Mundy AR. Urethral substitution in women. *Br J Urol*. 1989;63:80–83.
39. Willis H, Safiano NA, Lloyd LK. Comparison of transvaginal and retropubic bladder neck closure with suprapubic catheter in women. *J Urol*. 2015;193:196–202.
40. Banerji JS, Devasia A, Kekre NS, Chacko N. Early urinary diversion with ileal conduit and vesicovaginostomy in the treatment of radiation cystitis due to carcinoma cervix: a study from a tertiary care hospital in South India. *ANZ J Surg*. 2015;85:770–773.
41. Wilkin M, Horwitz G, Seetharam A, et al. Long-term complications associated with the Indiana pouch urinary diversion in patients with recurrent gynecologic cancers after high-dose radiation. *Urol Oncol*. 2005;23:12–15.
42. Blaivas JG, Weiss JP, Desai P, Flisser AJ, Stember DS, Stahl PJ. Long-term followup of augmentation enterocystoplasty and continent diversion in patients with benign disease. *J Urol*. 2005;173:1631–1634.
43. Al Hussein Al Awamlh B, Lee DJ, Nguyen DP, Green DA, Shariat SF, Scherr DS. Assessment of the quality-of-life and functional outcomes in patients undergoing cystectomy and urinary diversion for the management of radiation-induced refractory benign disease. *Urology*. 2015;85:394–400.
44. Stolzenburg J-U, Schwalenberg T, Liatsikos EN, et al. Colon pouch (Mainz III) for continent urinary diversion. *BJU Int*. 2007;99:1473–1477.
45. Kinn AC. Tension-free vaginal tape evaluated using patient self-reports and urodynamic testing—a two-year follow-up. *Scand J Urol Nephrol*. 2001;35:484–490.
46. Al-Singary W, Arya M, Patel HRH. Tension-free vaginal tape: avoiding failure. *Int J Clin Pract*. 2005;59:522–525.
47. Jankiewicz K, Markwitz E, Adamiak A, Skorupski P, Rechberger T. Delayed positioning of multifilament tape (IVS transobturator tape) in treatment of stress urinary incontinence caused by the radiotherapy. *Ginekol Pol*. 2005;76:819–823.
48. Hazewinkel MH, Schilthuis MS, Roovers J-P. Stress urinary incontinence in patients treated for cervical cancer: is TVT-Secur a valuable treatment option? *Int Urogynecol J Pelvic Floor Dysfunct*. 2009;20:357–359.
49. O'Reilly KJ, Govier FE. Intermediate term failure of pubovaginal slings using cadaveric fascia lata: a case series. *J Urol*. 2002;167:1356–1358.
50. Lowman J, Moore RD, Miklos JR. Tension-free vaginal tape sling with a porcine interposition graft in an irradiated patient with a past history of a urethrovaginal fistula and urethral mesh erosion: a case report. *J Reprod Med*. 2007;52:560–562.

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