



# The impact of prior external beam radiation therapy on device outcomes following artificial urinary sphincter revision surgery

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**Background:** Previous reports on the effect of radiation therapy on primary artificial urinary sphincter (AUS) device survival have met with conflicting results, and data evaluating this after revision surgery is sparse. Thus, we evaluated AUS device outcomes after revision surgery, and compared them among individuals who did versus did not undergo prior radiation therapy.

**Methods:** A database of patients who underwent AUS revision surgery at our institution was used to perform a retrospective review. Device survival endpoints, including overall survival, infection/erosion, urethral atrophy, and device malfunction were evaluated. Overall device survival (i.e., any repeat surgery) was compared between groups, stratified by external beam radiation status, via Kaplan-Meier method. Proportional hazard regression and competing risk analysis were used to evaluate association between prior radiation therapy and device outcomes.

**Results:** From 1983 to 2016, a total of 527 patients underwent AUS revision surgery. Of these, 173 (33%) patients had undergone prior radiation therapy. Patients with prior radiation therapy were more likely to have diabetes mellitus (22% *vs.* 14%;  $P=0.05$ ), hypertension (71% *vs.* 56%;  $P<0.01$ ), previous vesicourethral anastomotic stenosis (41% *vs.* 19%;  $P<0.0001$ ), as well as prior androgen deprivation therapy (26% *vs.* 6%;  $P<0.0001$ ). Overall, there was not enough evidence to support the existence of a significant difference in device survival among patients with or without a history of radiotherapy, with 1- and 5-year-overall survival of 84% *vs.* 85% and 51% *vs.* 64%, respectively ( $P=0.07$ ). On competing risk analysis, a history of pelvic radiation therapy was not enough evidence to support a significant association with the risk of device infection/erosion, mechanical failure, or urethral atrophy.

**Conclusions:** There was not enough evidence of a difference in the rate of device erosion or infection, cuff atrophy, malfunction, or overall device survival following AUS revision surgery between patients with and without a history of pelvic radiation. These findings may be helpful when counseling patients regarding outcomes after AUS revision.

**Keywords:** Artificial urinary sphincter (AUS); treatment outcome; radiotherapy; urinary incontinence

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## Introduction

Male stress urinary incontinence is most commonly encountered following benign or malignant prostate treatments, and can have a large impact on a patient's quality of life. The artificial urinary sphincter (AUS) is considered the most effective surgery for moderate and severe male stress incontinence (1). Given the mechanical nature of the device, revision surgery is often required over time (2). Prior publications have looked at outcomes of primary AUS implantation after radiation therapy with mixed conclusions (3-7).

Several studies, including a meta-analysis, demonstrate adverse outcomes in patients with prior radiation, specifically a higher rate of device infection and explantation (4-6,8). However, the largest of these studies with a cohort of almost 500 patients did not demonstrate any difference in device outcomes amongst patients undergoing primary AUS placement with a history of radiation therapy (3). Similar findings have been noted in some smaller series as well (9). Differences in the findings between these studies may be secondary to the small sample sizes in many series, how the study cohorts were defined (e.g., timing of radiation therapy), surgical technique, and the length of follow-up available (3,5).

Notably, while these studies evaluate primary placements, there is a paucity of data regarding the impact of radiation therapy on AUS revisions. This is an important consideration as radiation leads to progressive changes in tissues quality over time, thus its impact may be even greater in those undergoing revision (i.e., with more time from radiation treatment). We therefore sought to evaluate outcomes in those patients with a history of prior external beam radiation therapy who underwent AUS revision at our institution.

## Methods

After institutional review board approval was obtained, we performed a retrospective review of post-operative outcomes in male patients that underwent AUS revision between January 1983 and December 2016. Patients were excluded from analysis if they underwent AUS placement for incontinence secondary to neurogenic bladder or pelvic fracture, previously received prostate cryotherapy or brachytherapy, or were under 18 years old.

All implanted devices were the AMS 800TM (Boston Scientific, Marlborough, MA, USA). Our approach to AUS

revision surgery, depending on the underlying cause for revision, has previously been reported (10-12).

Chart review was carried out to identify clinical comorbidities and surgical history of the cohort. History of radiation (defined as external beam radiotherapy) and device outcomes following revision, including urethral erosion/device infection, urethral atrophy, and device malfunction were recorded. Of note, we routinely perform transcorporeal cuff placement for AUS revision procedures. All patients underwent device activation and follow-up at 6 weeks, and subsequent follow-up was performed in clinic on an as needed basis and through mailed questionnaires. Additional follow-up reviewed included written or telephone correspondence.

Patient characteristics were described with descriptive statistics. Continuous variables were summarized with mean and standard deviation (SD); categorical variables are summarized by number count and percentage. The Kaplan-Meier method was used to depict device survival, defined as time from device revision to subsequent revision for any reason or device explantation. In addition, competing risks survival analysis was performed to evaluate factors specifically related to device failure due to malfunction, urethral atrophy, and urethral erosion/infection, respectively. Statistical analysis was performed using SAS.

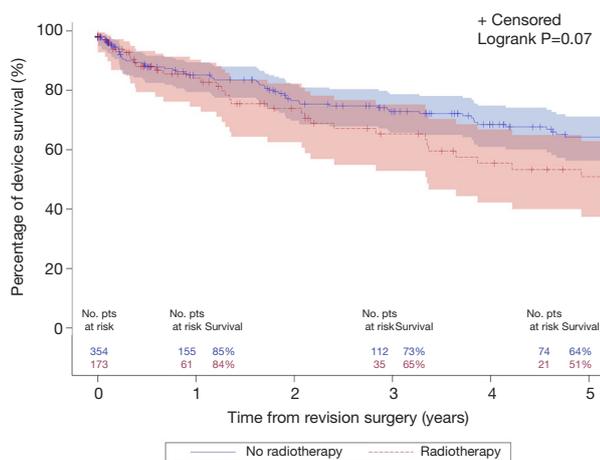
## Results

A total of 527 patients underwent AUS revision surgery at our institution from 1983 to 2016. Of the revision AUS cohort, 173 (33%) had received external beam pelvic radiation therapy prior to their AUS revision surgery. Clinical and demographic features of the cohort, stratified by radiation status, are shown in *Table 1*. Patients with prior radiation therapy were more likely to have a history of diabetes mellitus (22% vs. 14%;  $P=0.05$ ), hypertension (71% vs. 56%;  $P<0.01$ ), vesicourethral anastomotic stenosis (41% vs. 19%;  $P<0.0001$ ), and use of androgen deprivation therapy (26% vs. 6%;  $P<0.0001$ ) compared to those without prior radiation exposure.

The median follow-up for the entire cohort was 2.4 years (IQR, 0.3–7.0 years), during which time 121 patients underwent an additional AUS surgery including 41 explantations for infection/erosion (16 among radiation cohort), 42 revisions for device malfunction (15 among radiation cohort), 28 revisions for urethral atrophy (6 among radiation cohort, and 10 for device failures (tubing kink, etc.) (2 among radiation cohort). Notably, exposure to

**Table 1** Clinical and demographic features of patients undergoing AUS revision surgery, stratified by prior radiation therapy exposure

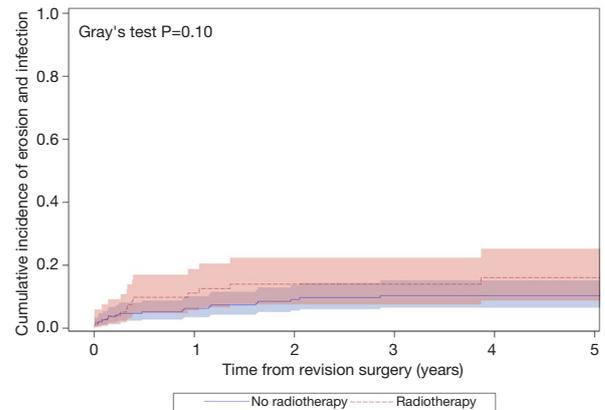
Variable	No radiation therapy, N=354	Radiation therapy, N=173	P value
Mean age at time of revision surgery (SD)	73.5 (8.4)	73.1 (7.7)	0.4
Mean body mass index, kg/m <sup>2</sup> (SD)	28.2 (3.9)	28.9 (4.5)	0.06
Diabetes mellitus (%)	28 (13.5)	29 (21.6)	0.05
Hypertension (%)	115 (55.8)	95 (70.9)	0.005
Coronary artery disease (%)	49 (23.7)	36 (26.9)	0.5
Prior vesicourethral anastomotic stenosis (%)	39 (19.2)	53 (40.5)	<0.0001
Prior androgen deprivation therapy (%)	13 (6.4)	34 (26.4)	<0.0001
Current or prior smoker (%)	106 (52.4)	66 (51.6)	0.9
Prior Radical prostatectomy (%)	298 (84.2)	134 (77.5)	0.06
Prior Benign prostate tissue resection (%)	47 (13.3)	30 (17.3)	0.2



**Figure 1** Overall survival of AUS revisions in patient with prior radiation. AUS, artificial urinary sphincter.

prior radiation therapy was not associated with a significant difference in 5-year overall device survival (51% vs. 64%; P=0.07; *Figure 1*). In addition, there was no significant difference in specific device outcomes, including: infection/erosion (P=0.10; *Figure 2*), malfunction (P=0.18; *Figure 3*), and urethral atrophy (P=0.57; *Figure 4*).

We then assessed the association of radiation therapy on device outcomes, controlling for pertinent patient clinical and demographic factors. Here, radiation therapy exposure was not significantly associated with the risk of adverse overall device survival after revision surgery (*Table 2*). Likewise, radiation therapy was not associated with the risk of subsequent device revision for infection/erosion, or

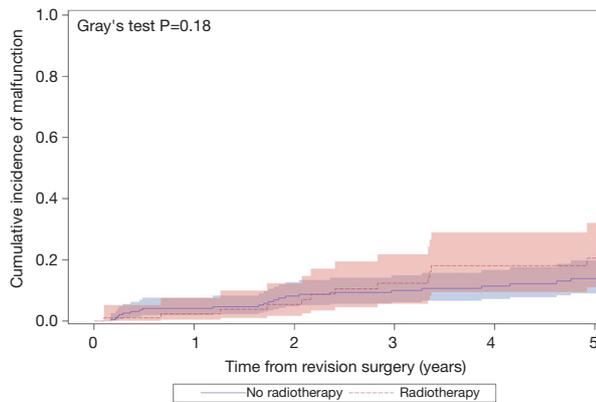


**Figure 2** Cumulative incidence of erosion and infection compared between those with and without radiation exposure.

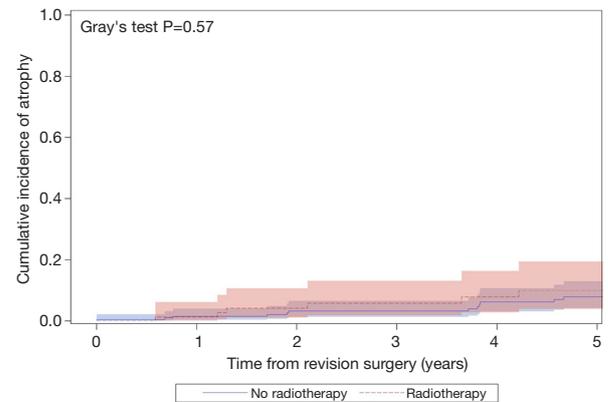
malfunction (*Table 3*). Increased age at time of revision was associated with increased risk of device infection/erosion (HR 1.04; 95% CI, 1.002–1.1; P=0.04) and a decreased risk of malfunction (HR 1.0; 95% CI, 0.9–1.0; P=0.01). Diabetes mellitus was associated with a significantly increased risk of device malfunction (HR 2.4; 95% CI, 1.1–5.4; P=0.03). No variables studied, including radiation therapy, were associated with the risk of revision for urethral atrophy.

**Discussion**

We found here, in a large cohort of AUS revision procedures, that prior external beam radiotherapy was



**Figure 3** Cumulative incidence of malfunction compared between those with and without radiation exposure.



**Figure 4** Cumulative incidence of atrophy compared between those with and without radiation exposure.

**Table 2** Hazard regression analysis of factors associated with overall device survival following AUS revision

Variable	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Radiation	1.4	0.9–2.1	0.08	1.5	0.9–2.4	0.1
Age at revision	1.0	0.9–1.0	0.61	1.0	1.0–1.1	0.2
BMI	1.0	1.0–1.1	0.21	1.0	1.0–1.1	0.3
HTN	1.1	0.7–1.8	0.62	1.0	0.6–1.7	0.9

**Table 3** Competing risk analysis of factors associated with device survival by device outcome

Variable	Infection/erosion			Mechanical failure		
	HR	95% CI	P value	HR	95% CI	P value
Radiation	1.7	0.9–3.2	0.1	1.5	0.7–3.2	0.3
Age at revision	1.04	1.002–1.1	0.04	0.95	0.91–0.98	0.01
Diabetes mellitus				2.4	1.1–5.4	0.03

not associated with an increased risk of adverse overall device survival or the rate of revision for atrophy, erosion/infection, or malfunction. We did find that increased age was associated with higher rates of infection/erosion, and that a history of diabetes mellitus was also associated with higher rates of device malfunction after revision surgery. These are important considerations for those providers counseling patients preoperatively on AUS revision outcomes.

While patients that underwent radiation therapy were more likely to have comorbidities of diabetes mellitus and hypertension, device survival was not significantly

different between the two groups. It is notable that despite no statistically significant difference, about half of the patients in the radiated cohort required subsequent device revision at 5 years (*Figure 1*). Patients in the radiation group were predictably more likely to have a history for vesicourethral anastomotic stenosis and use of androgen deprivation therapy. Likewise, no significant association was identified when controlling for these features. Interestingly, the adverse impact of diabetes mellitus and age on device malfunction and device infection/erosion events are similar to those we identified in a cohort of patients undergoing primary device implantation (13,14). Although unclear

why diabetes mellitus leads to increased rates of device malfunction, increased age may be a surrogate measure for worsening urethral vascularity accounting for a predisposition for device erosion.

Multiple studies have evaluated the impact of prior radiation therapy on primary AUS outcomes, and have met with conflicting results (3-7). This study is unique in its evaluation of a population of patients undergoing revision surgery. This is an important consideration as many men undergoing primary placement will ultimately require revision (2). It is important to understand how this cohort of AUS patients may differ from patients undergoing primary AUS surgery, particularly given a higher rate of device failure in this group (15).

Of note, surgical technique may play a role in the favorable findings described in this study. For instance, we routinely perform transcorporeal cuff placement which may have a protective effect particularly for erosion and atrophy among all revision cases (when periurethral dissection is needed), and particularly among patients with compromised tissue quality (16,17). This surgical approach may be of particular benefit to older patients who were found to be at increased risk of erosion in our cohort, likely due to worsening vascular supply. Of note, erosion/infection was the complication most commonly reported in prior studies where radiation was associated with adverse outcomes (4-6). Further study is needed to delineate the role that operative technique plays in outcomes of AUS revision in patients with prior radiotherapy.

Limitations of our study include the fact that it represents a single tertiary care institution and an high volume AUS practice, which may not be generalizable to all practices. In addition, given the retrospective nature of the study we do not have all pertinent clinical features, such as the time between radiotherapy and AUS surgery, available for evaluation. Testosterone levels were not evaluated in this study and may have influenced these data. Additionally, this study reports the rates of device survival, but this does not account for potential differences in functional outcomes. Finally, it is possible that with additional power or longer follow-up, differences in outcomes may be further elucidated.

## Conclusions

Overall, we found that there is not enough evidence supporting that AUS revision in patients with prior external beam radiotherapy will not have comparable and acceptable

outcomes to those without prior radiation. These findings will assist urologists with clinical decision making and counseling men with a history of radiation therapy who are considering AUS sphincter revision.

## Acknowledgments

None.

## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by Mayo Clinic Institutional Review Board (No. 18-011648) and informed consent was taken from all the patients.

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