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MRI Findings of Radiation-Induced Changes in the Urethra and Periurethral Tissues after Treatment for Prostate Cancer

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Abstract

Purpose—To assess radiotherapy (RT)-induced changes in the urethra and periurethral tissues after treatment for prostate cancer (PCa).

Methods and Materials—This retrospective study included 108 men (median age, 65y; range, 43–87y) who received external-beam radiotherapy (EBRT) and/or brachytherapy for PCa and underwent endorectal-coil MRI of the prostate within 180 days before RT and a median of 20 months (range, 2–63 months) after RT. On all MRIs, two readers independently measured the urethral length (UL) and graded the margin definition (MD) of the urethral wall and the signal intensities (SIs) of the urethral wall and pelvic muscles on 4-point scales.

Results—The mean urethral length decreased significantly from pre- to post-RT MRI (from 15.2 to 12.6 mm and from 14.4 to 12.9 mm for readers 1 and 2, respectively; both p-values < 0.0001). Brachytherapy resulted in greater urethral shortening than EBRT. After RT, SI in the urethral wall increased in 57% (62/108) and 35% (38/108) of patients (reader 1 and reader 2, respectively). The frequency and magnitude of SI increase in pelvic muscles depended on muscle location. In the obturator internus muscle, SI increased more often after EBRT than after brachytherapy, while in the periurethral levator ani muscle SI increased more often after brachytherapy than after EBRT.

Conclusion—After RT for PCa, MRI shows urethral shortening and increased SI of the urethral wall and pelvic muscles in substantial percentages of patients.

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Keywords

MRI; radiation therapy; prostate cancer; urethra

Introduction

Radiation therapy (RT) is the primary treatment approach for about 25% of patients with prostate cancer (PCa) in the United States ¹. Despite high rates of cancer control and excellent overall survival ²⁻⁵, prostate cancer can recur in approximately 30% to 40% of the patients initially treated with RT ^{6, 7}. Several salvage treatment options are available to patients with confirmed local recurrence, including further radiation, salvage radical prostatectomy and focal therapies such as cryotherapy and high-intensity focused ultrasound (HIFU). Complication rates of all these treatment modalities are generally higher when they are performed to treat recurrence as opposed to primary PCa. The higher complication rates are generally attributed to “post-treatment changes” in the irradiated tissue, mainly related to fibrosis with loss of anatomical tissue planes. The different techniques used for delivering RT, including external beam radiotherapy (EBRT) and brachytherapy, can be expected to lead to different patterns of post-treatment changes in the pelvis, and the quantification of these changes could potentially be useful for assessing the appropriateness of salvage treatment options.

Although magnetic resonance imaging (MRI) has a well-known role in depicting post-RT changes in prostatic tissue ⁸⁻¹⁰, little has been published on the use of MRI to assess post-RT changes of the urethra and periprostatic and periurethral tissues ^{11, 12}. The few existing reports are relatively old and unlikely to reflect recent advances in RT technology such as three-dimensional conformal RT or intensity-modulated RT and image-guided brachytherapy techniques. However, as it is well established that the urethral length (UL) correlates with the time to continence after surgery in patients with non-irradiated prostates ¹³⁻¹⁷, documentation of the effects of radiation on the urethral and periurethral tissues may prove to be clinically relevant.

The purpose of our study is to descriptively assess RT-induced changes in the urethra and periurethral tissues on endorectal MRI in patients who were treated for PCa and to evaluate differences in RT-induced tissue changes between patients who underwent EBRT, brachytherapy and combined EBRT and brachytherapy.

Methods and Materials

This retrospective study complied with the Health Insurance Portability and Accountability Act and was approved by our Institutional Review Board. A waiver of informed consent was issued.

Patients

A search of our electronic hospital information system was performed to identify patients who met the following inclusion criteria: 1) pre- and post-RT MRI of the prostate between January 2006 and March 2012, 2) pre-RT MRI performed less than 180 days before start of

RT. Of 127 patients who met those criteria, 11 patients were excluded because the MRI examination was performed without an endorectal coil, 5 patients were excluded because of insufficient signal in the periurethral area due to coil positioning, 2 patients were excluded due to the presence of a Foley catheter during MRI and 1 patient was excluded because of severe image artifacts. The final eligible study population consisted of 108 men (median age at time of pre-RT MRI, 64 years; range, 43–87 years). Forty-five patients underwent EBRT (median dose, 86.4Gy), 29 underwent brachytherapy (median dose, 144Gy,) and the remaining 34 patients underwent a combination of brachytherapy (median prescription dose for iodine-125, 110Gy; for palladium-103, 100Gy and for Iridium-192, 21Gy) and EBRT (median dose, 50.4Gy). The radiation techniques used have been described before^{18–20}. Pre-treatment MRI was performed 180 days or less before initiating RT (median time 66 days; range 4–175 days). Median time between the end of RT and post-treatment MRI was 20 months (range 2–63 months). Prostate volume was recorded from pre- and post-RT radiology reports. Thirty-one patients received androgen deprivation therapy (ADT) before starting RT and 22 patients received ADT before post-treatment MRI. Patient characteristics are summarized in Table 1.

Imaging

MR imaging studies were performed on 1.5-Tesla (T) (n=94) or 3-T units (n=14) (GE Medical Systems, Milwaukee, WI). A body coil was used for excitation; a pelvic phased-array coil with 4 channels (GE Medical Systems, Milwaukee, WI) was used in combination with an endorectal coil (Medrad, Warrendale, PA, USA) for signal reception. Typical acquisition parameters for the axial T1-weighted images were: repetition time (TR)/echo time (TE), 500–950ms/8–11 ms at 1.5T and 633–767 ms/7.3–9.8 ms at 3T; slice thickness, 5 mm; intersection gap, 0–1 mm; FOV, 24–36 cm; matrix, 256 × 128 – 320 × 224. Axial, coronal and sagittal T2-weighted fast spin-echo images were acquired. Typical acquisition parameters were: TR/TE, 3000–6617 ms/101–122 ms at 1.5T and 3650–4474 ms/116–122 ms at 3T; slice thickness, 3–4 mm; intersection gap, 0 mm; FOV, 14–16 cm; matrix, 256 × 192 – 512 × 256. Images were routinely post-processed to compensate for the reception profile of the endorectal coil.

Image Analysis

Two body imaging research fellows performing dedicated research in genitourinary imaging with 1 and 2 years of experience in interpreting prostate MR images, respectively and who were blinded to laboratory and biopsy results independently analyzed the MRI data. Images from pre- and post-RT MRI for each patient were presented to the readers in random order. The length of the membranous urethra (UL) was measured on coronal T2-weighted images (Figure 1). The membranous urethra was measured from the prostatic apex to the level of the urethra at the penile bulb. The transverse and sagittal T2-weighted images were used for cross referencing as necessary. Signal intensity (SI) of the urethral wall as compared to skeletal muscle was classified on T2-weighted images on a 4-point scale (1, hypointense; 2, isointense; 3, hyperintense; 4, very hyperintense) (Figure 1). The same scale was used to grade the SI of the levator ani (LA) muscle on two different levels (periurethral and periprostatic), the internal obturator muscles, and the muscles of the genitourinary diaphragm including the ischiocavernosus and transversus perinei muscles (Figure 2). The

margin definition of the urethral wall was graded on the following previously reported 4-point scale: 1, well defined; 2, 1/3 of the circumference ill-defined; 3, 2/3 ill-defined; 4, 3/3 ill defined¹⁵ (Figure 3).

Statistical Analysis

Interreader agreement for continuous variables was assessed using the intraclass correlation coefficient (ICC), while the Cohen's Kappa (κ) coefficient with quadratic weights was used for categorical variables. Both, the ICC and kappa-values were interpreted as follows: 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement²¹.

Descriptive statistics including the mean, median, range and standard deviation (SD) were calculated for UL. Comparisons between radiation treatment groups for descriptive statistics were made using the Kruskal Wallis Test. With respect to measurements on MRI, the paired Student's T-test was used for continuous variables and the Stuart Maxwell Test^{22, 23} for ordinal variables to assess the difference between pre-radiation and post-radiation MRI parameters for each reader. Additionally, to evaluate significant differences between patients who underwent EBRT, those who underwent brachytherapy and those who underwent both treatments, ANOVA was used for continuous variables and the Kruskal Wallis Test for ordinal variables. Post-hoc analyses were conducted using Tukey's HSD. Spearman's rho was used to assess correlations between measurements on MRI and time from end of RT to imaging.

All statistical analyses were performed with SAS 9.2 (SAS Institute Inc., Cary, NC, USA) and Stata 11 (StataCorp, College Station, TX, USA). Results with p-values < 0.05 were considered statistically significant.

Results

Of the 108 patients in the study, 45 (42%) underwent EBRT, while 29 (27%) underwent brachytherapy. The remaining 34/108 patients (31%) had both, EBRT and brachytherapy.

Interreader agreement

Interreader agreement for measurement of the UL was excellent on both pre- and post-RT MRI, with intraclass correlation coefficients of 0.89 (95% CI: 0.85–0.92) and 0.90 (95% CI: 0.86–0.93), respectively. On pre- and post-RT MRI interreader agreement was fair for margin definition (with kappa values of 0.39 and 0.39, respectively), and fair to moderate for grading of the signal intensity of the urethral wall (with kappa values of 0.34 and 0.43, respectively). In the grading of the signal intensity of all muscles analyzed, interreader agreement ranged from slight to substantial, with kappa values ranging from 0.13 to 0.79.

Urethral Length

Both readers' measurements indicated a significant reduction of the UL from pre- to post-RT MRI (Figure 1); the mean ULs measured by readers 1 and 2 were 15.2 ± 4.0 mm and 14.6 ± 4.00 mm, respectively, on pre-RT MRI and 12.6 ± 3.6 mm and 12.9 ± 3.5 mm,

respectively, on post-RT MRI ($p < 0.0001$ for both readers). The decrease in UL did not differ significantly between patients who received ADT between pre- and post-RT MRI and those who did not have any ADT ($p = 0.832$ for reader 1 and $p = 0.871$ for reader 2). The decrease in UL showed a weak to moderate correlation ($\rho = 0.39$ and $\rho = 0.40$ for readers 1 and 2, respectively) with the timing of post-RT MRI.

Analysis by Treatment Subgroup—Mean decreases in urethral length from pre- to post-RT MRI in patients undergoing EBRT, brachytherapy and concurrent EBRT and brachytherapy were 1.41 mm, 3.01 mm, and 3.84 mm, respectively, for reader 1 and 0.80 mm, 1.44 mm, and 2.39 mm, respectively, for reader 2. The decreases were significant for both readers in all subgroups except the EBRT subgroup, where the difference was only significant for reader 1 (p values for the mean UL decreases in the EBRT, brachytherapy, and concurrent EBRT and brachytherapy subgroups were 0.003, < 0.0001 , and < 0.0001 , respectively, for reader 1 and 0.11, 0.01, and 0.0001, respectively, for reader 2).

Margin Definition of the Urethra and Signal Intensity of the Urethral Wall and Pelvic Muscles

Margin definition decreased from pre-RT to post-RT MRI in 91/108 patients (84%) for reader 1 and in 69/108 patients (64%) for reader 2 (Figure 3).

In 2/108 patients (2%) reader 1 rated the margin as more clearly defined on post-RT MRI than on pre-RT MRI. For reader 2, this was the case in 10/108 patients (9%). Margin definition was unchanged between pre- and post-RT MRI in 15/108 patients (14%) for reader 1 and 29/108 patients (27%) for reader 2. The decrease in margin definition showed only weak correlation ($\rho = 0.27$ and $\rho = 0.17$ for readers 1 and 2, respectively) with the timing of post-RT MRI.

The SI in the urethral wall increased after RT in 62/108 patients (57%) for reader 1 and 38/108 patients (35%) for reader 2. The SI in the urethral wall was lower after RT in 4/108 patients (4%) for reader 1 and 12/108 patients (11%) for reader 2; it stayed the same in 42/108 patients (39%) for reader 1 and 58/108 patients (54%) for reader 2 (Table 2). The distribution of SI changes found after RT in the pelvic muscles is summarized in Table 2. There was no correlation between the magnitude of change in the SI of the urethral wall ($\rho = 0.10$ and $\rho = -0.03$ for readers 1 and 2, respectively) and the timing of post-RT MRI.

Analysis by Treatment Subgroup—Readers 1 and 2 found decreased definition of the urethral wall in 37/45 (82%) and 28/45 (62%) patients who underwent EBRT, 25/29 (86%) and 20/29 (69%) patients who underwent brachytherapy and 29/34 (85%) and 21/34 (62%) patients who underwent EBRT and brachytherapy, respectively. The magnitude of change in margin definition did not differ significantly between treatment groups ($p = 0.10$ for reader 1 and $p = 0.50$ for reader 2).

Table 3 shows the percentages of patients with post-RT SI changes in the urethral wall and pelvic muscles, subdivided by type of radiotherapy administered. The magnitude of change in the SI of the urethral wall from pre- to post-RT MRI did not differ significantly between the treatment groups ($p = 0.12$ for reader 1 and $p = 0.42$ for reader 2).

The magnitude of SI change in the obturator internus muscle from pre- to post-RT MRI differed significantly between two or more of the three treatment groups ($p<0.0001$, reader 1 and $p=0.04$, reader 2); post-hoc analyses showed that for both readers, the difference was significant between patients who underwent EBRT and those who underwent brachytherapy ($p<0.05$). Likewise, the magnitude of SI increase change in the periurethral portion of the levator ani muscle differed significantly between at least two of the treatment groups ($p=0.03$, reader 1 and $p=0.02$, reader 2) (Figure 2); post-hoc analyses showed that for both readers, the difference was significant between patients who underwent EBRT and those who underwent a combination of EBRT and brachytherapy ($p<0.05$). For the remaining muscles analyzed, SI changes did not differ significantly between patients in any of the three treatment groups. For both readers, the SI of the obturator internus muscle increased substantially more often after EBRT than after brachytherapy while, conversely, the SI of the periurethral portion of the levator ani muscle increased more often after brachytherapy than after EBRT (Table 3).

Discussion

To our knowledge, this is the first study in patients with prostate cancer that describes changes in the MRI features of the urethra and periurethral tissues after RT and also distinguishes between the changes induced by different types of RT (EBRT, brachytherapy, and combined EBRT and brachytherapy). We found that after RT, MRI showed urethral shortening that was significant in all treatment groups for reader 1 and in the brachytherapy and combined EBRT and brachytherapy groups for reader 2. The definition of the urethral wall declined in most patients, regardless of the type of RT delivered. Furthermore, the signal intensity of the urethral wall and pelvic muscles increased in substantial percentages of patients, with these percentages varying markedly in certain muscles depending on the type of radiation administered.

According to the findings of both readers, the shortening of the urethra after RT – documented here for the first time -- was greater in patients who had brachytherapy or combined therapy than in patients who had only EBRT. In patients who have undergone radical prostatectomy for primary PCa, shorter urethral length on pretreatment MRI has been associated with longer time to continence after surgery^{13, 15–17}. It remains to be determined whether post-RT shortening of the urethra could be related to the higher incidence of postoperative incontinence observed in patients who undergo salvage prostatectomy.

Further research is needed to determine the nature and clinical significance of the tissue changes that result in increased SI and reduced margin definition of the urethral wall after RT. Of note, in every pelvic muscle we assessed, both readers detected SI increases in a minimum of 26% of patients, regardless of which type of radiation treatment was administered. Sugimura et al.¹² described an increase in SI in the obturator internus muscle after pelvic radiation; however, only 2 of the 51 patients in their study had radiation to the prostate, while the others underwent RT because of gynecologic neoplasms or malignancies of the gastrointestinal tract. In our study, increased SI of the obturator internus muscle was found in 60–80% of patients undergoing EBRT but only 31–45% of patients undergoing brachytherapy, suggesting that this muscle falls within the radiation field more frequently

during EBRT. Conversely, we found that the periurethral part of the levator ani muscle showed an increase in SI in 79–91% of patients who underwent brachytherapy or combined therapy but only 56%–75% of patients who had EBRT. This difference may be related to the fact that, in order to decrease the dose to the urethra and cover the apex of the prostate well, it is sometimes necessary to place brachytherapy seeds more peripherally.

Our study was limited in that it was a retrospective analysis of patients presenting over more than 6 years. While changes in MRI parameters during this period were minimal, they may have affected quantitative analysis. Furthermore, we assessed a heterogeneous patient cohort with different types and dosages of applied RT. Also, due to range of 2–63 months between RT and post-RT MRI, there may have been an influence on tissue findings caused by the time course after RT rather than the RT itself. However, Spearman analyses did not evidence strong correlation between imaging findings and timing of post-RT MRI. Finally, because few patients in our study underwent salvage prostatectomy, we were not able to correlate MRI features with histopathologic findings. However, our results provide an important foundation for further research. Ideally, further studies should focus on correlating MRI findings with toxicity. Potentially, quantitative measurements from imaging could be correlated with surgeons' intraoperative assessments of surgical difficulty during salvage RP, as well as clinical outcomes of salvage RP or RT such as complications, time to continence, and/or quality-of-life scores²⁴. If significant correlations are identified, awareness of RT-induced tissue changes on MRI may prove useful for selecting and planning salvage treatment for patients with recurrent PCa.

In summary, we found urethral shortening, decreased urethral margin definition, and increased SI of the urethral wall and pelvic muscles in patients who underwent RT of the prostate. Additionally we demonstrated differences in urethral shortening and SI changes in the pelvic muscles depending on the type of RT applied. These findings may have implications on the treatment planning regarding salvage therapy in patients with biochemical recurrence after RT. Potentially, awareness of RT-induced tissue changes on MRI may prove useful for selecting and planning salvage treatment for patients with recurrent PCa.

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Figure 1.

Coronal T2-weighted images from a 68-year old patient who underwent EBRT (8640 cGy) for prostate cancer. Measurements taken by readers 1 and 2 indicated that the urethral length measured from prostatic apex to penile bulb (red lines) decreased by 7 mm and 8 mm, respectively, between pre-RT MRI (A) and post-RT MRI (B). Axial T2-weighted images pre-RT (C) and post-RT (D) of a 54-year old man who underwent brachytherapy (144Gy) demonstrates an increase in SI of the urethral wall from “isointense” (C) to “hyperintense” (D).

Figure 2.

Left-hand column: T2-weighted images from a 70-year-old patient who underwent EBRT (8640 cGy). The images demonstrate an increase in SI between pre- and post-RT MRI in the obturator internus muscle (arrowheads). Right-hand column: T2-weighted images from a 59-year old patient who underwent brachytherapy (144 Gy) for prostate cancer. The images demonstrate an increase of SI (asterisks) between pre- and post-RT MRI in the periurethral part of the levator ani muscle (LA periurethral).

Figure 3. Axial and coronal T2-weighted images from a 73-year old patient who underwent brachytherapy (144 Gy) for prostate cancer. The urethral wall is sharply demarcated on pre-RT MRI (arrowheads). On post-RT MRI, the margin of the urethral wall (arrowheads) is less sharply demarcated.

Table 1

Patient demographics

Age at post-RT MRI (years); median (range)	66.9 (45.2–91.1)	71.8 (51.9–91.1)	64.7 (50.2–81.6)	64.9 (45.2–79.3)	0.002
PSA at time of diagnosis [ng/mL]; median (range)	6.4 (1.3–391.0)	9.6 (1.8–284.0)	5.7 (1.8–11.7)	5.3 (1.3–391.0)	<0.0001
Time between pre-RT MRI and start of radiotherapy (months); median (range)	2.2 (0.1–5.8)	2.7 (0.4–5.8)	1.4 (0.1–5.7)	2.1 (0.2–4.6)	0.0066
Time between end of radiotherapy and post-RT MRI (months); median (range)	19.9 (2.0–62.2)	24.1 (2.0–61.8)	18.4 (6.5–38.9)	19.2 (4.3–62.2)	0.5275
ADT between pre- and post-RT MRI; n (%)	22 (21)	16 (15)	1 (1)	5 (5)	0.0024

Note: RT = radiation treatment; EBRT = external beam radiation therapy; Brachy = brachytherapy

Table 2

Changes in the signal intensity of the urethral wall and the pelvic muscles in all patients

	Reader 1			Reader 2		
	Increasing S.I.	No change in S.I.	Decreasing S.I.	Increasing S.I.	No change in S.I.	Decreasing S.I.
Urethral wall	62/108 (57%)	42/108 (39%)	4/108 (4%)	38/108 (35%)	58/108 (54%)	12/108 (11%)
Periurethral levator ani muscle^{††}	88/107 (82%)	18/107 (17%)	1/107 (1%)	76/108 (70%)	31/108 (29%)	1/108 (1%)
Periprostatic levator ani muscle	104/108 (96%)	4/108 (4%)	0/108 (0%)	96/107 (90%)	10/107 (9%)	1/107 (1%)
Internal obturator muscle	79/108 (73%)	28/108 (26%)	1/108 (1%)	54/108 (50%)	52/108 (48%)	2/108 (2%)
Transversus perinei muscle^{††}	52/105 (50%)	53/105 (50%)	0/105 (0%)	40/100 (40%)	49/100 (49%)	11/100 (11%)
Ischio-cavernosus muscle^{††}	37/104 (36%)	65/104 (62%)	2/104 (2%)	27/103 (26%)	66/103 (64%)	10/103 (10%)

^{††} Some cases could not be assessed, as the field of view did not include the relevant structure or the quality of the image of the relevant structure was deemed insufficient by the reader.

Table 3

Changes in the signal intensity of the urethral wall and the muscles of the genitourinary diaphragm subdivided by type of radiotherapy

Signal intensity changes during radiotherapy									
Reader 1	EBRT			Brachytherapy			EBRT+Brachy		
	Increasing S.I.	No change in S.I.	Decreasing S.I.	Increasing S.I.	No change in S.I.	Decreasing S.I.	Increasing S.I.	No change in S.I.	Decreasing S.I.
Urethral wall	23/45 (51%)	18/45 (40%)	4/45 (9%)	16/29 (55%)	13/29 (45%)	0/29 (0%)	23/34 (68%)	11/34 (32%)	0/34 (0%)
Periurethral levator ani muscle [†]	33/44 (75%)	10/44 (23%)	1/44 (2%)	24/29 (83%)	5/29 (17%)	0/29 (0%)	31/34 (91%)	3/34 (9%)	0/34 (0%)
Periprostatic levator ani muscle	42/45 (93%)	3/45 (7%)	0/45 (0%)	29/29 (100%)	0/29 (0%)	0/29 (0%)	33/34 (97%)	1/34 (3%)	0/34 (0%)
Internal obturator muscle	36/45 (80%)	9/45 (20%)	0/45 (0%)	13/29 (45%)	15/29 (52%)	1/29 (3%)	30/34 (88%)	4/34 (12%)	0/34 (0%)
Transversus perinei muscle [†]	19/44 (43%)	25/44 (57%)	0/44 (0%)	16/28 (57%)	12/28 (43%)	0/28 (0%)	17/33 (52%)	16/33 (48%)	0/33 (0%)
Ischio-cavernosus muscle [†]	14/43 (33%)	28/43 (65%)	1/43 (2%)	9/28 (32%)	19/28 (68%)	0/28 (0%)	14/33 (42%)	18/33 (55%)	1/33 (3%)
Reader 2	EBRT			Brachytherapy			EBRT+Brachy		
	Increasing S.I.	No change in S.I.	Decreasing S.I.	Increasing S.I.	No change in S.I.	Decreasing S.I.	Increasing S.I.	No change in S.I.	Decreasing S.I.
Urethral wall	14/45 (31%)	24/45 (53%)	7/45 (16%)	11/29 (38%)	14/29 (48%)	4/29 (14%)	13/34 (38%)	20/34 (59%)	1/34 (3%)
Periurethral levator ani muscle [†]	25/45 (56%)	20/45 (44%)	0/45 (0%)	24/29 (83%)	5/29 (17%)	0/29 (0%)	27/34 (79%)	6/34 (18%)	1/34 (3%)
Periprostatic levator ani muscle	39/45 (87%)	5/45 (11%)	1/45 (2%)	27/29 (93%)	2/29 (7%)	0/29 (0%)	30/33 (91%)	3/33 (9%)	0/33 (0%)
Internal obturator muscle	27/45 (60%)	17/45 (38%)	1/45 (2%)	9/29 (31%)	19/29 (66%)	1/29 (3%)	18/34 (53%)	16/34 (47%)	0/34 (0%)
Transversus perinei muscle [†]	14/41 (34%)	20/41 (49%)	7/41 (17%)	9/27 (33%)	15/27 (56%)	3/27 (11%)	17/32 (53%)	14/32 (44%)	1/32 (3%)
Ischio-cavernosus muscle [†]	11/42 (26%)	26/42 (62%)	5/42 (12%)	6/28 (21%)	19/28 (68%)	3/28 (11%)	10/33 (30%)	21/33 (64%)	2/33 (6%)

[‡] Some cases could not be assessed, as the field of view did not include the relevant structure or the quality of the image of the relevant structure was deemed insufficient by the reader.