VIA MEDICA

CASE REPORT

Oncology in Clinical Practice
2024, Vol. 20, No. 5, 370–379
DOI: 10.5603/ocp.96805

ISSN 2450-1654
eISSN 2450-6478

Rectal ulceration and rectourethral fistula as rare complications of radiotherapy for prostate cancer — a case report and literature review

Krzysztof Kowalik[1,*], Anna Gruszczyńska[2], Katarzyna Hetman[3], Katarzyna Kołaczyk[4], Michał Falco[5], Krystian Kasperowicz[6], Andrzej Modrzejewski[1]

[1]Clinical Department of General Surgery, Pomeranian Medical University, Szczecin, Poland
[2]Department of Forensic Medicine, Pomeranian Medical University, Szczecin, Poland
[3]Department of Clinical Oncology, West Pomeranian Oncology Center, Szczecin, Poland
[4]Department of Imaging Diagnostics and Interventional Radiology, University Clinical Hospital No. 1 of the Pomeranian Medical University, Szczecin, Poland
[5]Clinical Department of Radiotherapy, Pomeranian Medical University, West Pomeranian Oncology Center, Szczecin, Poland
[6]Faculty of Health and Life Sciences, Northumbria University in Newcastle upon Tyne, United Kingdom

Abstract

We present a case of a patient with inoperable prostate cancer [Gleason 10 (5 + 5), cT3b]. The patient was treated with radical radiotherapy because he had numerous internal conditions, and he had been disqualified from radical prostatectomy. The man developed radiation colitis after radiotherapy. This inflammation led to rectal ulceration. Another complication of radical irradiation was a rectourethral fistula. In this case, the reaction occurred within 6 months of the initiation of irradiation, i.e. during the period of early effect, whereas the presentation of the reaction (ulcer, fistula) corresponded to the late effect. This led us to classify the presented case as a consequential late effect. This article presents possible complications and treatment options for prostate radiotherapy. We reviewed the available literature and discussed our patient's case in the context of other authors' experiences.

Keywords: prostate cancer, adenocarcinoma, radiotherapy, complications, rectal ulceration, rectourethral fistula

Introduction

Prostate cancer (PCa) is the second most common malignancy among men [1]. It is initially hormone-sensitive, which is exploited in its treatment through the use of anti-androgenic drugs. Approximately 94% of prostate cancer patients have locally confined, curable disease, with treatment options including active monitoring, surgery, or radiation therapy (RTH) [2]. Radiation therapy is a common approach for the management of locally advanced prostate cancers [3, 4].

*Correspondence: Krzysztof Kowalik, Clinical Department of General Surgery, Pomeranian Medical University, ul. Piotra Skargi 9–11, 70–965 Szczecin, Poland (krzysztof.kowalik.uro@gmail.com)
Received: 2 August 2023; Accepted: 5 December 2023; Early publication: 16 January 2024

Prostate cancer is categorized into risk groups, including low-risk [prostate specific antigen (PSA) concentration < 10 ng/mL, Gleason score < 7, cT1-2a], intermediate-risk (PSA concentration 10–20 ng/mL, or Gleason score = 7, or cT2b), and high-risk (PSA concentration > 20 ng/mL or Gleason score > 7, or cT2c, or any PSA and any Gleason score with cT3-4, or presence of metastasis).

In older patients with multiple coexisting conditions in the high-risk group (cT3/4), radical prostatectomy (RP) is often omitted, and radical radiotherapy or RTH in combination with hormone therapy (HT) is used as the sole treatment option. Hormone therapy is recommended for patients in the intermediate and high-risk groups.

For patients in the intermediate-risk group, a combination of radiotherapy and hormone therapy lasting 4–6 months is recommended. For patients in the high-risk group, combining radiotherapy and hormone therapy for approximately 2–3 years should be considered [5]. RP is reserved only for patients with expected long survival (> 10 years) [2].

The use of HT in PCa inhibits the stimulating effect of male sex hormones on cancer cells [6]. However, monotherapy with HT is not recommended [5]. It is important to note that the response to hormonal treatment is temporary, and disease progression is observed despite maintaining castration levels of testosterone during standard androgen deprivation therapy (when using gonadotropin-releasing hormone agonists or antagonists) [5].

Both, RTH and HT can lead to a range of complications. HT in PCa treatment may increase the risk of myocardial infarction and erectile dysfunction, decrease libido, cause insulin resistance, fatigue, mood changes, and pathological fractures [6]. On the other hand, the most common complications following RTH include injury to the rectal wall and, less frequently, bladder injury. Other relatively rare complications in patients undergoing RTH for PCa include rectal bleeding (4.7% of patients), hematuria (4%), urinary voiding dysfunction (3.5%), and radiation proctitis (1.1%) [7].

Case report

A 75-year-old male patient was diagnosed with prostate cancer [Gleason score 10 (5 + 5)] and was scheduled for radiotherapy with hormone therapy because he was disqualified from radical prostatectomy. PSA level before treatment was 79 200 ng/mL.

Abdominal computed tomography (CT) revealed a prostate gland measuring 44 mm × 37 mm with calcifications. Contrast-enhanced areas were observed in the anterior part of the gland, extending towards the posterior wall of the bladder. Thickening of the bladder wall up to 5 mm was also noted. Additionally, multiple diverticula with a diameter of up to 17 mm were observed in the bladder base. The examined lymph nodes did not show enlargement, and no metastatic lesions were observed on the CT scan. 10 (5 + 5). In accordance with the European Association of Urology (EAU) guidelines, we also performed bone scintigraphy, which did not reveal typical features of metastatic lesions.

After obtaining the results of abdominal CT and bone scintigraphy (no metastases), it was decided not to perform multi-parametric magnetic resonance imaging (mpMRI) (due to low or moderate risk of metastasis).

Pelvic MRI performed before HT helped determine disease stage. In the obtained images, there were tumor foci in both prostate lobes with infiltration of both seminal vesicles and the prostate capsule but no infiltration of adjacent organs.

A chest CT scan revealed a subpleural pulmonary nodule with a diameter of 4.1 mm and right paratracheal lymph nodes measuring up to 9 mm in the short axis. Bone scintigraphy performed two weeks earlier did not show typical signs of metastatic lesions. A prostate biopsy confirmed the presence of adenocarcinoma with a Gleason score 10 (5 + 5).

Based on the tests and disease staging, the patient was classified as cT3b/4NxM0. He was scheduled for radical radiotherapy with HT. Hormone therapy with degarelix was started 3 months before radiotherapy initiation. Radiotherapy planning was based on computed tomography performed in the therapeutic position (2 mm slices were obtained) with an empty rectum and full bladder. The structures were contoured according to the common practice [International Commission on Radiation Units and Measurements (ICRU) protocol] (Fig. 1).

Gross tumor volume (GTV) included the prostate and seminal vesicles (image fusion with MRI was used). Two clinical tumor volume structures (CTV) were created. CTV1 was obtained by 1 cm expansion of GTV with healthy structures, and CTV2 included regional, external, internal, and distal common iliac and presacral lymph nodes. The planning target volume was obtained by expansion of CTV1 by 6 mm (no more than 4 mm into the rectum) and CTV2 by 8 mm. Healthy structures (rectum, bladder, colon, intestine, and femoral bones) were drawn according to the Radiation Therapy Oncology Group (RTOG) atlas recommendations. Rectum was defined as a structure including the anal canal and colon up to the sigmoid, drawing on the external border of the rectal wall. Planning was conducted in the Eclipse planning system (VARIAN Medical Systems®). The dose limits to healthy structures were defined according to the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) data. The plan consisted of two steps. A dose of 45 Gy in 25 fractions was delivered to PTV2 and 54 Gy was delivered to PTV1. A dose of 22 Gy was delivered to PTV1 in the following 10 fractions.

The rectal dose constraints were not fulfilled for volume obtaining less than 70 Gy (V_{70Gy}), V_{65Gy}, V_{60Gy}, and V_{50Gy}. The dose limit for V_{75Gy} was fulfilled (Fig. 2 and 3).

According to the presented data, the risk of grade 3 or higher late rectal toxicity was higher than 10% (Tab. 1).

The irradiation plan was based on volumetric modulation arc therapy, combined with image-guided radiotherapy. The planned dose was delivered using

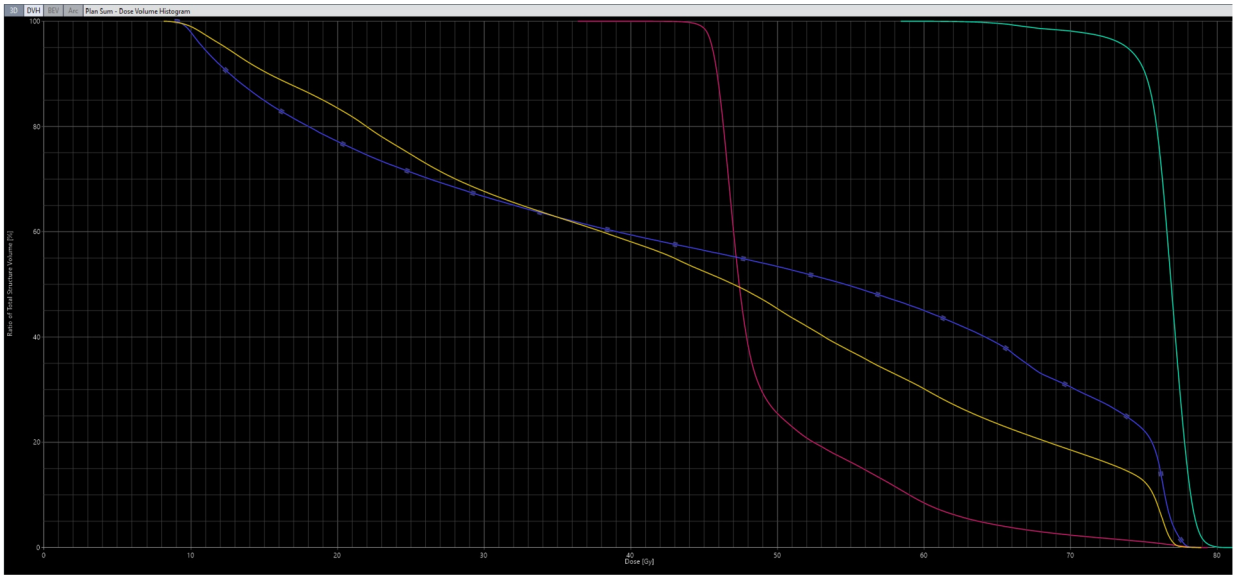

Figure 1. Dose-volume histogram; Green line — PTV2 (Planning Target Volume 2) covering the prostate and seminal vesicles — the prescribed dose 76 Gy; Pink line — PTV1 covering obturator, internal, external, distal common iliac, and presacral lymph nodes — the prescribed dose 45 Gy; Yellow line — bladder; Blue line — rectum

Halcyon linac (VARIAN Medical Systems®). Before every fraction, cone beam computed tomography (CBCT) was performed. Grade 1 early side effects from the rectum and bladder were observed during treatment. The irradiation was finished according to the prepared schedule.

Four months later, the patient presented to the doctor with anal pain. The patient denied rectal bleeding. On rectal examination, a large ulcerated mass causing oncological concern was palpable in the anal canal. A colonoscopy revealed approximately 30 mm of infiltration in the distal part of the rectum, involving half of its circumference. Biopsy samples taken during the examination showed abundant chronic inflammatory infiltration with mononuclear cells, neutrophilia, and congestion. No evidence of tumor growth was observed. A small prostate gland with a volume of 14 mL and loss of layered structure was observed. No significant abnormalities were reported.

Contrast-enhanced MRI of the pelvis showed focal thickening of the posterior rectal wall measuring approximately 30 mm, with the distal end located about 60 mm above the anal sphincter. The loss of layered architecture of the rectum was also described (Fig. 3A, B).

Approximately three months after the initial colonoscopy, a follow-up examination revealed persistent ulceration covered with granulation tissue, involving over half of the circumference of the rectum. The mucosa around the ulceration appeared red and swollen. Angiectasias after radiation therapy were visible in the sigmoid colon.

Due to the persistent rectal ulceration, the patient underwent laparoscopy with conversion to laparotomy using the Hartmann procedure to create a colostomy. A Veress needle was inserted through an incision above the umbilicus, creating a CO_2 pneumoperitoneum. Trocars and a visual access port were inserted into the abdominal cavity. Adhesions encountered during the procedure were released, and infiltration of the rectal wall into the bladder and anterior abdominal wall was observed. Perforation of the intestine was noticed during the release of the rectum, leading to the decision to convert to laparotomy. A midline incision in the lower abdomen was made to expose the peritoneal cavity. Adhesions were released, and the rectum was partially excised, including the segment with the perforation. The intestine was closed with a linear stapler. The resected segment was brought outside the abdominal cavity, and an end colostomy was created. Peritoneal lavage was performed, and a drain was placed in the peritoneal recess. The abdominal cavity was closed.

In the postoperative period (on the second day after surgery), the patient experienced general weakness, increasing dyspnea, elevated inflammatory parameters [C-reactive protein (CRP) — 309 mg/L, white blood cells (WBC) — 15,103/μL, procalcitonin (PCT) — 11.46 ng/mL], and renal insufficiency [estimated glomerular filtration rate (eGFR) 25 mL/min/1.73 m^2, creatinine concentration 226 μmol/L]. The patient's condition was assessed as moderate. Pulmonary embolism was excluded by angiographic CT. *Enterobacter cloacae*, *Pseudomonas aeruginosa*, and *Escherichia coli* were isolated from

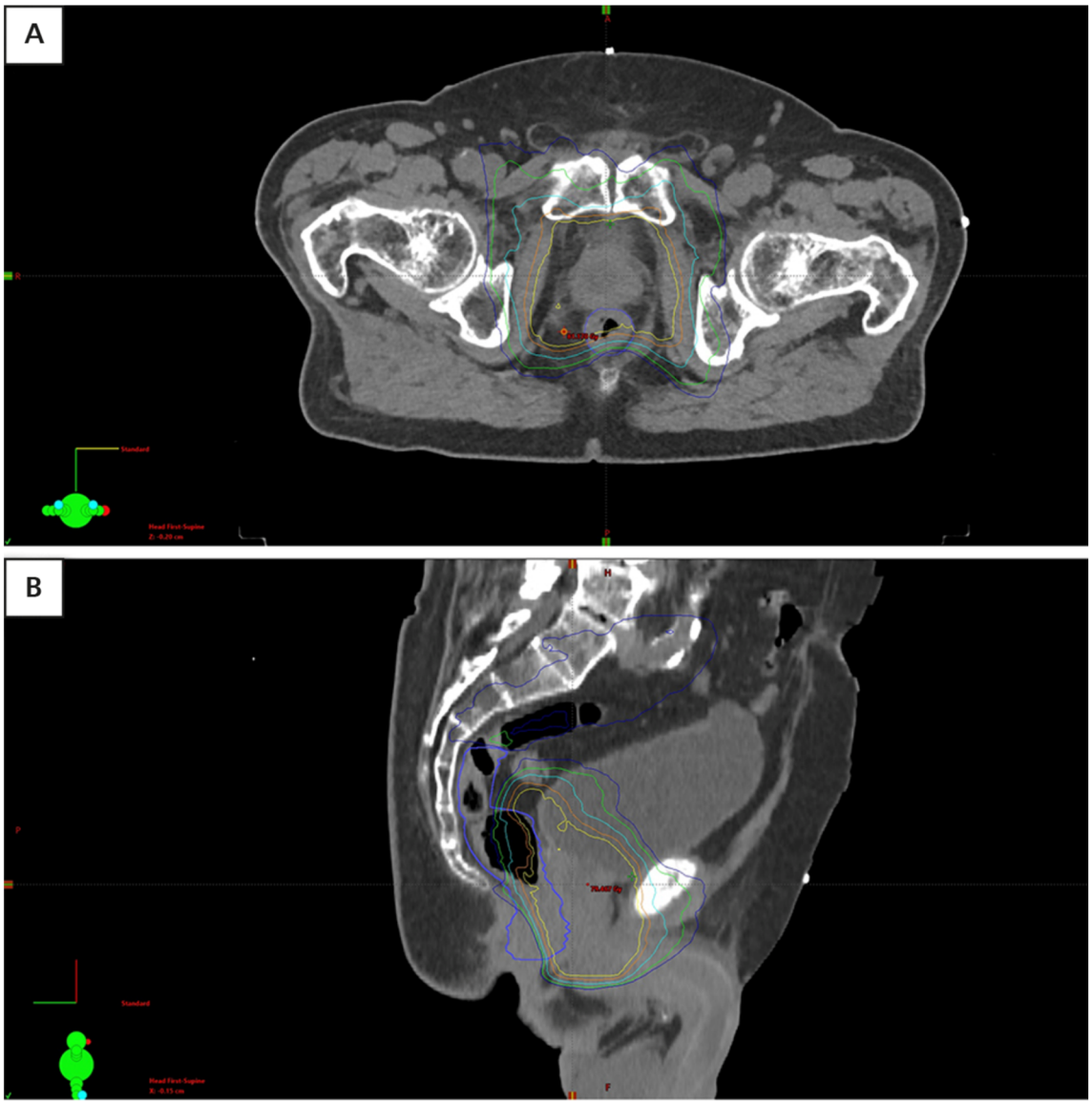

Figure 2. A. Transverse cross-section with maximal dose; **B.** Sagittal cross section; Dark blue — 45 Gy isodose, Green — 50 Gy, Light blue — 60 Gy, Orange — 70 Gy, Yellow — 75 Gy

the wound swab culture, while methicillin-resistant coagulase-negative staphylococci (*Staphylococcus hominis subsp. hominis*) were isolated from the blood culture. Initially, empirical antibiotic therapy was administered due to pneumonia. Targeted antibiotic therapy based on culture results was implemented after obtaining the cultures.

After two weeks from colostomy creation, no pathological changes were observed in the follow-up colonoscopy. After a significant improvement in the patient's general condition, he was discharged from the hospital after 22 days of hospitalization.

Twelve days later, the patient was readmitted to the Surgical Department due to inflammation around the colostomy and stoma dehiscence. Laboratory tests showed an increase in inflammatory parameters (CRP — 207 mg/L). A colonoscopy revealed edematous and congested mucosa just beyond the anal sphincter. The patient was started on parenteral nutrition, and the colostomy was cleansed from devitalized tissues. A decrease in inflammatory parameters was observed during hospitalization. After achieving improvement in the patient's general condition, he was discharged.

One month later, the patient was admitted to the Urology Department due to a suspected rectourethral fistula. Laboratory tests showed elevated inflammatory parameters (WBC — 16.70 × 10^3/μL, CRP — 114 mg/L) and normocytic anemia (HGB — 8.2 g/dL, RBC — 2.96 × 10^6/μL, HCT — 26.2%, MCV — 88.5 fL). The total PSA level was within the normal range, measuring less than 0.01 ng/mL.

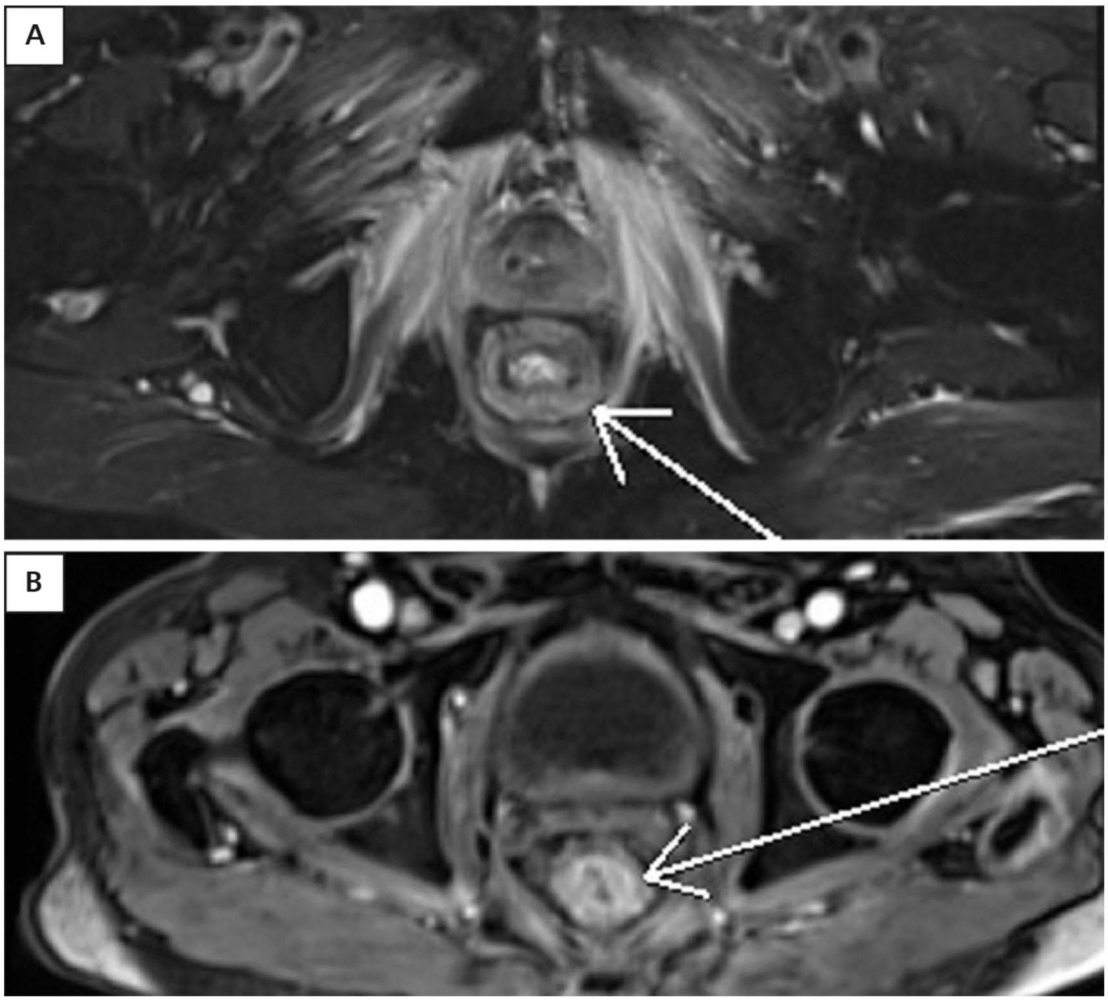

Figure 3. Transverse T2-weighted fat-suppressed image (**A**) shows the increased signal intensity within the muscles of the pelvic floor representing typical features of edema after radiation therapy. Note rectal wall thickening with submucosal high signal intensity (arrow) also consistent with edema. The presence of submucosal edema and intense postgadolinium enhancement (arrow) depicted in T1-weighted fat-saturated image (**B**) is consistent with inflammation

Table 1. Rectal dose limits, planned dose to the rectum, and late rectal toxicity according to the Quantec data

	Planned dose	**Dose limit**	**Late Rectal toxicity rate**	
			≥ 2	**≥ 3**
V75[1]	13% (9 cm^3)	< 15%	< 15%	< 10%
V70[2]	26% (17 cm^3)	< 20%	< 15%	< 10%
V65[3]	37% (25 cm^3)	< 25%	< 15%	< 10%
V60[4]	44%	< 35%	< 15%	< 10%
V50[5]	52%	< 50%	< 15%	< 10%

[1]volume below 75 Gy; [2]volume below 70 Gy; [3]volume below 65 Gy; [4]volume below 60 Gy; [5]volume below 50 Gy

The patient underwent an endoscopic procedure of the urethra and bladder to evaluate them. A fistula in the prostatic part of the urethra was visualized. The fistula was also visible on previously performed MRI (Fig. 4). No suspicious bladder masses were found. A Foley catheter was inserted into the urethra, and the balloon was palpable on rectal examination. An attempt was made to reinsert the Foley catheter into the urethra, and it was left in place until the fistula healed. The patient was discharged in good general condition. The rectourethral fistula was confirmed to be healed after over a month.

Discussion

Late adverse effects occur after 6 months following radiotherapy completion. In some cases, they can manifest after many years because they affect tissues with low proliferative potential, which can undergo fibrosis and necrosis as a result of exposure to ionizing radiation. Late complications are caused by damage to the cells that build up the tissue in question, small blood and lymph vessels, and by direct damage to the parenchyma. The extent of the lesions is determined by the dose of ionizing radiation and the volume of the irradiated area, among other factors [8].

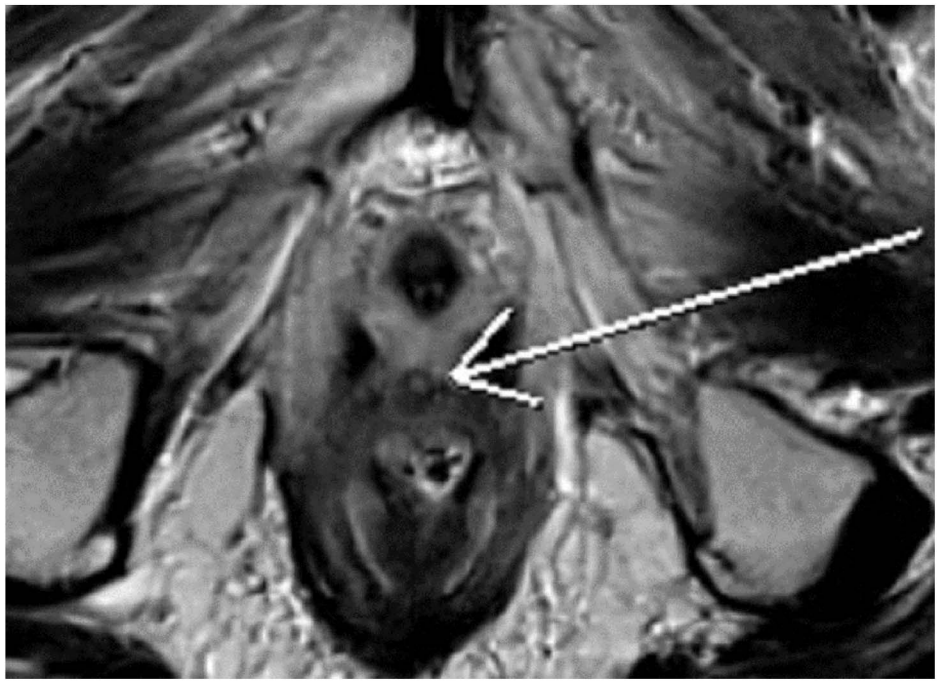

Figure 4. Transverse T2-weighted image shows the sinus tract of the rectourethral fistula (arrow) located within the rectal wall in the 12 o'clock position

To assess the severity of radiation reactions, various five-grade scales are used, such as the World Health Organization (WHO), Radiation Therapy and Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer (EORTC), and Common Terminology Criteria Adverse Events (CTCAE). Gastrointestinal disorders presented in the CTCAE scale include anal inflammation, anal fissure, rectal fistula, rectal bleeding, and rectal mucosal inflammation (presence of ulcers or inflammatory processes in the rectum). Grade I rectal mucosal inflammation is characterized by asymptomatic or mild symptoms, and intervention is not recommended at this stage. Grade II involves more severe symptoms, requiring medical intervention and limiting the patient's ability to perform daily activities. Grade III exhibits severe symptoms that significantly restrict independent functioning. Grade IV involves life-threatening complications, necessitating urgent surgical intervention. Grade V rectal mucosal inflammation leads to the patient's death. Rectal fistula refers to the presence of abnormal connections between the rectum and another organ or anatomical site.

In the case of rectal fistula, it can be observed that Grade I is asymptomatic, Grade II presents symptoms, but surgical intervention is not necessary. Grade III requires surgery, and Grade IV has a life-threatening risk, necessitating urgent surgical intervention. Grade V results in the death of the patient [9].

Late complications are rarely reversible. Changes such as necrosis of the irradiated area, persistent diarrhea and constipation, and intestinal obstruction are challenging to treat. Chronic complications of radiotherapy include the development of fistulas, such as tracheoesophageal, rectovesical (in men), and rectovaginal (in women). Not all complications occur with the same frequency. Fistula formation is among the rare side effects [10].

Based on a 2012 study, which involved a review of patient records from the years 1999–2009 at the Cleveland Clinic, long-term (ten-year) toxicity of three treatment methods was assessed [7]. The gastrointestinal (GI) and genitourinary (GU) toxicity profiles were compared among three groups of patients treated with intensity-modulated radiotherapy (IMRT), brachytherapy, or radical prostatectomy. The IMRT group received a five-field IMRT plan to a total dose of 70 Gy in 28 daily fractions of 2.5 Gy. Patients who were not eligible for IMRT were treated with a radiotherapy plan to a total dose of 78 Gy in 39 daily fractions of 2.0 Gy. For low-risk patients, the treatment target was the prostate gland, while for high-risk patients, it included the prostate and seminal vesicles. Dose constraints applied to the bladder did not exceed 30% to receive more than 55 Gy (with a maximum dose of 74 Gy) and to the rectum did not exceed 30% to receive more than 50 Gy (with a maximum level of 74 Gy). Low rates of late GI and GU toxicity were reported for all three treatment methods. Late GU toxicity was highest for patients undergoing radiotherapy, with a rate of 10.5%. GI toxicity was also highest in the case of radiotherapy (RTH), with

a rate of 11.2% after ten years. Among RTH complications requiring intervention, rectal bleeding (4.7%) and radiation proctitis (2.3%) were identified. Most adverse effects resolved during follow-up or after intervention.

The ProtecT study showed that patients treated with external beam radiotherapy (EBRT), such as intensity-modulated radiotherapy (IMRT)/volumetric modulated arc therapy (VMAT) + image-guided radiotherapy (IGRT), plus six months of androgen deprivation therapy (ADT) reported adverse effects in the form of persistent diarrhea, fecal urgency, urinary incontinence, and rectal bleeding. On the other hand, patients treated with IMRT had fewer adverse effects [6]. After RTH, 5% of men experienced bloody stools. The study indicated a high incidence of rectal bleeding in men after radiotherapy and a gradual increase in this symptom in actively monitored patients [11, 12].

Studies have shown that the onset of symptoms related to late complications occurs after 2 years following treatment completion. Risk factors for the development of radiation reactions include older age, larger rectal volume, prior abdominal surgeries, use of androgen deprivation therapy (ADT) along with RTH, and concomitant conditions such as diabetes, hemorrhoids, and inflammatory bowel disease. It has also been demonstrated that the occurrence of early complications within the rectum predisposes the development of late adverse effects in the same location [13]. A study by Kuban et al. [14] demonstrated that GI complications were more frequent in patients (28%) receiving a higher radiation dose (78 Gy) compared to patients (15%) treated with three-dimensional conformal radiotherapy (3DCRT) at a dose of 70 Gy. The frequency of complications could be reduced by decreasing the radiation dose to the rectum [14].

Peeters et al. [15] compared the impact of a dose of 68 Gy and 78 Gy on the occurrence of early and late complications. They found that a higher dose was associated with an increased frequency of rectal bleeding.

Matzinger et al. [16] conducted a study comparing the frequency of adverse events in patients after receiving doses of 70 Gy, 74 Gy, or 78 Gy of 3DCRT or IMRT [16]. It was found that occurrence of complications depends on the type of radiotherapy used, as IMRT is associated with less radiation to the rectum than 3DCRT. Results from Zelefsky et al. [17] showed that patients treated with IMRT doses up to 81 Gy experienced the following complications: rectal bleeding (in 1.6% of patients) and Grade 3 rectal toxicity (according to the National Cancer Institute Common Toxicity Criteria) (in 0.1% of cases).

Studies by Meerleer et al. [18] indicated that IMRT with a dose of up to 75 Gy causes late Grade 3 GI toxicity in 2.9% of patients and Grade 2 GI toxicity in 13.2% of patients. Grade 3 GU toxicity occurred in 2.9% of patients, and Grade 2 GU toxicity occurred in 30.8% [17]. Another study reported that 9% of patients, one year after the completion of EBRT or brachytherapy, reported adverse events in the rectal region, such as urgency, urinary incontinence, and pain. A study by Budäus et al. [13] indicated that the negative impact of radiation therapy on the urinary system stopped after 12 months of treatment. It was shown that patients who experienced acute adverse events are at higher risk of developing late complications [13].

In 2018, early and late complications were compared in prostate cancer patients treated with proton beam therapy (PBT) or IMRT. Among the observed GI complications were diarrhea, fecal incontinence, rectal bleeding, and proctitis. GI adverse events were less frequent than GU events. The most common GI adverse event was proctitis, occurring in 37.9% of patients treated with IMRT and 48.3% of patients treated with PBT. Late complications were rare in both the IMRT and PBT groups, with rates of 36.4% and 22.7%, respectively. The most frequently described adverse event was Grade 1 proctitis, occurring in 22.7% of patients treated with IMRT and 4.5% of patients treated with PBT, followed by Grade 1 rectal bleeding (13.6% in IMRT and 4.5% in PBT) [19].

Chronic radiation proctitis occurs in approximately 5% of patients within five years after treatment. Symptoms are most common within two years after prostate cancer radiotherapy [20]. There are several methods for treating chronic proctitis, including argon plasma coagulation during colonoscopy or flexible sigmoidoscopy [21].

Urinary and gastrointestinal fistulas are rare complications after radiotherapy. Approximately 60% of rectourethral fistulas, as in the described case, are iatrogenic, caused by treatments such as radiotherapy or prostatectomy [22]. There are limited data on the occurrence of fistulas after radiotherapy, which may be due to insufficient reporting or the classification of these issues as adverse GU or GI events.

According to a 2023 study, patients treated with radiotherapy have a low short-term risk of developing fistulas [23]. A meta-analysis of six cohort studies involving patients who underwent pelvic radiotherapy was conducted. The overall frequency of fistulas in these studies was 0.2% with a 95% confidence interval (CI) of 0.1–0.4, an I2 value of 0%, and a p value below 0.608. The study did not demonstrate a significant increase in the risk of fistulas in patients who underwent repeat radiotherapy (0.3%; 95% CI 0.1–0.4; p = 0.762) or in those treated with a combination of chemotherapy and radiotherapy (0.4%; 95% CI –0.3 to –1.2; p = 0.664) compared to patients who received only the initial course of radiotherapy. The authors stress the importance of detailed reporting of such

complications, as this will help to better understand the problem and determine the extent of this adverse event.

In 2012, a case was reported of a patient with recurrent prostate cancer who developed a rectourethral fistula after high-intensity focused ultrasound (HIFU) treatment. The patient had previously undergone radical prostatectomy and EBRT for pT3N0Mx, Gleason 8 prostate cancer. Due to the small size of the fistula, it was decided to manage it conservatively by placing a Foley catheter permanently. The patient also received antibiotics (metronidazole 500 mg and ceftriaxone 1 g for 10 days, followed by ciprofloxacin 500 mg twice daily for a month). Monthly retrograde urethrograms were performed on an outpatient basis. At the 60-day follow-up after catheter placement, no fistula was observed. The Foley catheter was removed, and after 15 days, a repeat retrograde urethrogram confirmed the absence of the fistula [23]. Despite low efficacy of conservative treatment for rectourethral fistulas described in the literature, the patient's fistula healed without surgical intervention [24, 25]. A similar outcome was observed in our case. In our patient, a Foley catheter was also placed, and the fistula healed on the catheter without surgical treatment.

A study by Ahmed et al. [26] evaluated whether the development of rectourethral fistulas is caused by HIFU or is a consequence of previous radiotherapy. It was found that fistulas occurred in 6.5% of patients who underwent prior radiotherapy followed by HIFU, while no fistulas were observed in patients treated with HIFU alone [26].

Some of the mentioned radiation complications require surgical treatment and reconstructive procedures. Complications such as infections, bleeding from the genitourinary or gastrointestinal system, and urinary tract obstruction require hospitalization [27]. The presence of a urinary fistula necessitates measures to facilitate urine drainage. The presence of a fistula increases the risk of other complications and delays the patient's recovery [28, 29]. A rectourethral fistula can cause fecal passage through the urethra, leading to urinary tract infection and subsequent sepsis. The presence of such complications requires urgent surgical treatment to close the fistula and create separate channels for stool and urine [24].

In 2017, a study described six patients who developed rectourethral fistulas for various reasons. The initial treatment involved creating a suprapubic cystostomy and colostomy. After three months, the urethral defect was closed with a graft from the buccal mucosa, and the fistula was closed and sutured to the surrounding perianal tissues using a gracilis muscle flap between the urethra and rectum. No recurrence of the fistula was observed during follow-up [22].

Improvements in the radiotherapy planning and delivery process, such as dose modulation that increases dose conformity, help limit the extent of tissue exposed to radiation [13]. To reduce the radiation dose to the rectum, a biodegradable spacer pad can be used. It increases the distance between the prostate and the rectum. The spacer pad can be made of a liquid gel (hydrogel) or a balloon. A meta-analysis demonstrated that using a spacer pad resulted in 5–8% of rectal tissues receiving a lower radiation dose [30].

Proper patient preparation also prevents late complications. Radiation therapy for prostate cancer patients is performed when patients have a full bladder. Adequate filling of the bladder moves the small bowel out of the irradiated area, thus reducing the radiation dose the bowel will receive [31]. Before starting radiation therapy, the patient should have an empty rectum. If it is filled with gases or fecal masses, the prostate may be displaced, resulting in greater irradiation of the healthy area and increased side effects [32].

Image guidance such as CBCT and MR-Linacs also play an important role.

Image-guided radiotherapy most often uses CT scans, which can be kilovoltage (kV) static images or CBCT. They are used for initial treatment planning. CBCT produces good-quality images that allow evaluation of lesions such as bladder filling and rectal dilatation. However, the technique does not allow intrafraction monitoring [33].

Daily MR-Linacs enables assessing interfractional motion. By adjusting radiotherapy treatment for dynamic motion and filling of the rectum and bladder, radiation reactions can be significantly reduced. It also allows visualization of internal organs more accurately than CT and better protection of the organs at risk (OARs). MR-Linacs can also be performed during radiation therapy, improving the accuracy of the irradiation [34]. Preliminary data from a prospective study [35] evaluating MR-Linacs and describing GI side effects show that the rate of early second-degree complications was 5%, and third-degree reactions did not occur.

The presented case concerns a patient with locally advanced prostate cancer. Therefore, the patient belonged to a high-risk group for progression. The presence of infiltration of the seminal vesicles contributed to the need to deliver a high dose on a large area of tissues located anteriorly and close to the rectum. The institutional protocol provides for irradiation of pelvic lymph nodes in a group of patients with high-risk prostate cancer. In retrospect, it seems that it was justified to consider either refraining from irradiating the lymph nodes or reducing the area of irradiation of the surrounding tissues, especially near the rectum.

Another method is megavoltage (MV) X-ray imaging using implanted fiducial markers (FM). This technique is inexpensive and easy to use [36]. It involves implanting three radiation-impermeable markers on

the periphery of the prostate gland. Most commonly, two FMs are located at the posterior base of the prostate and one marker is placed at the apex. The displacement of the markers is about 1–2.8 mm [37].

Electromagnetic transponders, which are implanted in a similar manner to fiducial markers, enable initial treatment planning and real-time evaluation of the intrafraction motion [38]. The Calypso® 4D Localization System™ allows markers to be localized 10 times per second. This reduces treatment margins, thereby reducing the incidence of side effects. Not all patients can benefit from this treatment technique, as there are specific and limited eligibility criteria [39].

Transabdominal ultrasound-based localization systems allow positioning, imaging, and shift correction in a short period of time. They are inexpensive and fast but are highly dependent on the person performing the ultrasound, which can be associated with low accuracy [40, 41].

Based on the presented case, we think it is necessary to strive to limit the deposition of high and medium doses of irradiation in the rectum. In our case, the reaction occurred within 6 months of the initiation of irradiation, i.e. during the period of early effects. The presentation of the reaction (ulcer, fistula) corresponded to a late effect. This led us to classify the presented case as a consequential late effect. The risk of such a reaction does not have to depend only on the parameters of the treatment plan although the irradiation plan used may have influenced its occurrence.

Conclusions

1. After prostate cancer radiotherapy, a rectourethral fistula and rectal ulceration are rare complications.
2. Rectal ulceration resulting from radiotherapy can mimic a rectal tumor.
3. Rectal ulceration at the site of colostomy closure and prior pelvic radiotherapy can contribute to the formation of an iatrogenic rectourethral fistula.

Article Information and Declarations

Ethics statement

Verbal informed consent was obtained from the patients fortheir anonymized information to be published in this article.

Author contributions

K.K., A.G., M.F.: prepared the first draft of the manuscript, manuscript revision and literature review; K.H., A.M.: final preparation of the manuscript and substantive supervision; K. Kołaczyk: development of images from diagnostic imaging; K. Kasperowicz: translation of the article and linguistic revision.

Funding

The paper did not require any financial investment.

Acknowledgements

None.

Conflict of interest

Authors declare no conflict of interest.

Supplementary material

None.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68(6): 394–424; erratum in: CA Cancer J Clin. 2020;70(4):313, doi: 10.3322/caac.21492, indexed in Pubmed: 30207593.
2. Guidelines NCCN for Treatment Prostate Cancer Version 4.2023. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.
3. Cooperberg MR, Broering JM, Carroll PR. Time trends and local variation in primary treatment of localized prostate cancer. J Clin Oncol. 2010; 28(7): 1117–1123, doi: 10.1200/JCO.2009.26.0133, indexed in Pubmed: 20124165.
4. Kramer KM, Bennett CL, Pickard AS, et al. Patient preferences in prostate cancer: a clinician's guide to understanding health utilities. Clin Prostate Cancer. 2005; 4(1): 15–23, doi: 10.3816/cgc.2005.n.007, indexed in Pubmed: 15992457.
5. https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2023_2023-03-27-131655_pdvy.pdf.
6. Pawłowska E, Jassem J. Review of Polish and international guidelines on hormonal therapy in localized prostate cancer. Nowotwory. Journal of Oncology. 2017; 66(5): 403–407, doi: 10.5603/njo.2016.0071.
7. Hunter GK, Reddy CA, Klein EA, et al. Long-term (10-year) gastrointestinal and genitourinary toxicity after treatment with external beam radiotherapy, radical prostatectomy, or brachytherapy for prostate cancer. Prostate Cancer. 2012; 2012: 853487, doi: 10.1155/2012/853487, indexed in Pubmed: 22577562.
8. Rucińska M, Powikłania radioterapii. Onkol Dypl. 2023; 20(2). https://podyplomie.pl/onkologia/38796,powiklania-radioterapii.
9. Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0 Published: November 27, 2017 U.S. Department of Health and Human Services.
10. Kim Y, Roscoe JA, Morrow GR. The effects of information and negative affect on severity of side effects from radiation therapy for prostate cancer. Support Care Cancer. 2002; 10(5): 416–421, doi: 10.1007/s00520-002-0359-y, indexed in Pubmed: 12136225.
11. Hamdy F, Donovan J, Lane J, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med. 2016; 375(15): 1415–1424, doi: 10.1056/nejmoa1606220, indexed in Pubmed: 27626136.
12. Donovan J, Hamdy F, Lane J, et al. Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. N Engl J Med. 2016; 375(15): 1425–1437, doi: 10.1056/nejmoa1606221, indexed in Pubmed: 27626365.
13. Budäus L, Bolla M, Bossi A, et al. Functional outcomes and complications following radiation therapy for prostate cancer: a critical analysis of the literature. Eur Urol. 2012; 61(1): 112–127, doi: 10.1016/j.eururo.2011.09.027, indexed in Pubmed: 22001105.
14. Kuban D, Tucker S, Dong L, et al. Long-Term Results of the M. D. Anderson Randomized Dose-Escalation Trial for Prostate Cancer. Int J Radiat Oncol Biol Phys. 2008; 70(1): 67–74, doi: 10.1016/j.ijrobp.2007.06.054, indexed in Pubmed: 17765406.
15. Peeters STH, Heemsbergen WD, van Putten WLJ, et al. Acute and late complications after radiotherapy for prostate cancer: results of a multicenter randomized trial comparing 68 Gy to

78 Gy. Int J Radiat Oncol Biol Phys. 2005; 61(4): 1019–1034, doi: 10.1016/j.ijrobp.2004.07.715, indexed in Pubmed: 15752881.
16. Matzinger O, Duclos F, van den Bergh A, et al. EORTC Radiation Oncology Group. Acute toxicity of curative radiotherapy for intermediate- and high-risk localised prostate cancer in the EORTC trial 22991. Eur J Cancer. 2009; 45(16): 2825–2834, doi: 10.1016/j.ejca.2009.07.009, indexed in Pubmed: 19682889.
17. Zelefsky MJ, Deasy JO. Improved long-term outcomes with IMRT: is it better technology or better physics? Int J Radiat Oncol Biol Phys. 2013; 87(5): 867–868, doi: 10.1016/j.ijrobp.2013.09.004, indexed in Pubmed: 24267964.
18. Meerleer GDe, Fonteyne V, Meersschout S, et al. Salvage intensity-modulated radiotherapy for rising PSA after radical prostatectomy. Radiother and Oncol. 2008; 89(2): 205–213, doi: 10.1016/j.radonc.2008.07.027, indexed in Pubmed: 18771809.
19. Dutz A, Agolli L, Baumann M, et al. Early and late side effects, dosimetric parameters and quality of life after proton beam therapy and IMRT for prostate cancer: a matched-pair analysis. Acta Oncol. 2019; 58(6): 916–925, doi: 10.1080/0284186X.2019.1581373, indexed in Pubmed: 30882264.
20. Matta R, Chapple CR, Fisch M, et al. Pelvic Complications After Prostate Cancer Radiation Therapy and Their Management: An International Collaborative Narrative Review. Eur Urol. 2019; 75(3): 464–476, doi: 10.1016/j.eururo.2018.12.003, indexed in Pubmed: 30573316.
21. Weiner J, Schwartz D, Martinez M, et al. Long-term results on the efficacy of argon plasma coagulation for patients with chronic radiation proctitis after conventionally fractionated, dose-escalated radiation therapy for prostate cancer. Pract Radiat Oncol. 2017; 7(1): e35–e42, doi: 10.1016/j.prro.2016.07.009, indexed in Pubmed: 27663931.
22. Prabha V, Kadeli V. Repair of recto-urethral fistula with urethral augmentation by buccal mucosal graft and gracilis muscle flap interposition - our experience. Cent European J Urol. 2018; 71(1): 121–128, doi: 10.5173/ceju.2018.1353, indexed in Pubmed: 29732218.
23. Sadighian M, Hakam N, Amend G, et al. Radiation-induced Fistulas in Patients With Prior Pelvic Radiotherapy for Prostate Cancer: A Systematic Review and Meta-analysis. Urology. 2023; 176: 121–126, doi: 10.1016/j.urology.2023.03.015, indexed in Pubmed: 36963666.
24. Topazio L, Perugia C, Finazzi-Agro E. Conservative treatment of a recto-urethral fistula due to salvage HIFU for local recurrence of prostate cancer, 5 years after radical prostatectomy and external beam radiotherapy. BMJ Case Rep. 2012; 2012, doi: 10.1136/bcr.03.2012.6115, indexed in Pubmed: 23144340.
25. Thompson IM, Marx AC. Conservative therapy of rectourethral fistula: five-year follow-up. Urology. 1990; 35(6): 533–536, doi: 10.1016/0090-4295(90)80111-y, indexed in Pubmed: 2353382.
26. Ahmed HU, Ishaq A, Zacharakis E, et al. Rectal fistulae after salvage high-intensity focused ultrasound for recurrent prostate cancer after combined brachytherapy and external beam radiotherapy. BJU Int. 2009; 103(3): 321–323, doi: 10.1111/j.1464-410X.2008.08026.x, indexed in Pubmed: 19021611.
27. Wallis CJD, Mahar A, Cheung P, et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. Lancet Oncol. 2014; 15(2): 223–231, doi: 10.1016/S1470-2045(13)70606-5, indexed in Pubmed: 24440474.
28. Mundy AR, Andrich DE. Posterior urethral complications of the treatment of prostate cancer. BJU Int. 2012; 110(3): 304–325, doi: 10.1111/j.1464-410X.2011.10864.x, indexed in Pubmed: 22340079.
29. Bassett MR, Santiago-Lastra Y, Stoffel JT, et al. Neurogenic Bladder Research Group, Trauma and Urologic Reconstructive Network of Surgeons. Urinary Diversion for Severe Urinary Adverse Events of Prostate Radiation: Results from a Multi-Institutional Study. J Urol. 2017; 197(3 Pt 1): 744–750, doi: 10.1016/j.juro.2016.10.091, indexed in Pubmed: 27810450.
30. Miller LE, Efstathiou JA, Bhattacharyya SK, et al. Association of the Placement of a Perirectal Hydrogel Spacer With the Clinical Outcomes of Men Receiving Radiotherapy for Prostate Cancer: A Systematic Review and Meta-analysis. JAMA Netw Open. 2020; 3(6): e208221, doi: 10.1001/jamanetworkopen.2020.8221, indexed in Pubmed: 32585020.
31. Nasser NJ, Fenig E, Klein J, et al. Maintaining consistent bladder filling during external beam radiotherapy for prostate cancer. Tech Innov Patient Support Radiat Oncol. 2021; 17: 1–4, doi: 10.1016/j.tipsro.2021.01.002, indexed in Pubmed: 33553698.
32. Rowe LS, Mandia JJ, Salerno KE, et al. Bowel and Bladder Reproducibility in Image Guided Radiation Therapy for Prostate Cancer: Results of a Patterns of Practice Survey. Adv Radiat Oncol. 2022; 7(5): 100902, doi: 10.1016/j.adro.2022.100902, indexed in Pubmed: 35847548.
33. Stenmark MH, Hamstra DA. Image-Guided Strategies for Prostate Cancer. In: Thomas CHR. ed. Radiation Medicine Rounds Prostate Cancer. Demos Medical Publishing 2011: 113–130.
34. Randall JW, Rammohan N, Das IJ, et al. Towards Accurate and Precise Image-Guided Radiotherapy: Clinical Applications of the MR-Linac. J Clin Med. 2022; 11(14), doi: 10.3390/jcm11144044, indexed in Pubmed: 35887808.
35. Bruynzeel AME, Tetar SU, Oei SS, et al. A Prospective Single-Arm Phase 2 Study of Stereotactic Magnetic Resonance Guided Adaptive Radiation Therapy for Prostate Cancer: Early Toxicity Results. Int J Radiat Oncol Biol Phys. 2019; 105(5): 1086–1094, doi: 10.1016/j.ijrobp.2019.08.007, indexed in Pubmed: 31419510.
36. Kudchadker RJ, Lee AK, Yu ZH, et al. Effectiveness of using fewer implanted fiducial markers for prostate target alignment. Int J Radiat Oncol Biol Phys. 2009; 74(4): 1283–1289, doi: 10.1016/j.ijrobp.2009.02.033, indexed in Pubmed: 19427750.
37. Kupelian PA, Willoughby TR, Meeks SL, et al. Intraprostatic fiducials for localization of the prostate gland: monitoring intermarker distances during radiation therapy to test for marker stability. Int J Radiat Oncol Biol Phys. 2005; 62(5): 1291–1296, doi: 10.1016/j.ijrobp.2005.01.005, indexed in Pubmed: 16029784.
38. Willoughby TR, Kupelian PA, Pouliot J, et al. Target localization and real-time tracking using the Calypso 4D localization system in patients with localized prostate cancer. Int J Radiat Oncol Biol Phys. 2006; 65(2): 528–534, doi: 10.1016/j.ijrobp.2006.01.050, indexed in Pubmed: 16690435.
39. Litzenberg DW, Balter JM, Hadley SW, et al. Prostate intrafraction translation margins for real-time monitoring and correction strategies. Prostate Cancer. 2012; 2012: 130579, doi: 10.1155/2012/130579, indexed in Pubmed: 22111005.
40. McNair HA, Mangar SA, Coffey J, et al. A comparison of CT- and ultrasound-based imaging to localize the prostate for external beam radiotherapy. Int J Radiat Oncol Biol Phys. 2006; 65(3): 678–687, doi: 10.1016/j.ijrobp.2006.01.022, indexed in Pubmed: 16751060.
41. Scarbrough TJ, Golden NM, Ting JY, et al. Comparison of ultrasound and implanted seed marker prostate localization methods: Implications for image-guided radiotherapy. Int J Radiat Oncol Biol Phys. 2006; 65(2): 378–387, doi: 10.1016/j.ijrobp.2006.01.008, indexed in Pubmed: 16563658.