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FIRST RUSSIAN EXPERIENCE OF THE STEREOTACTIC RADIOTHERAPY ON THE PROSTATE BED

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Purpose. Assess the safety of postoperative radiation therapy on the area of the prostate bed (PB) using extreme dose hypofractionation (5 fractions of 6.6–7 Gr). **Materials and methods.** from April 2019 to March 2020 at the National Medical Center of Oncology named after N.N. Petrov of the Ministry of Health of the Russian Federation in the first 15 patients of the prostate cancer carried out stereotactic radiation therapy (SRT) on the PB. Depending on the clinical situation, adjuvant and salvage SRT were distinguished. Linear electron accelerators with 6 MeV energy are used for treatment. Three factional regimes were evaluated: 5 factions of 6.6 Gr, 5 factions of 6.8 Gr and 5 factions of 7 Gr. The clinical target volume is defined by RTOG (2010). **Results.** The median of follow-up was 7.6 (1.3-11.6) months. Of the 15 patients, adjuvant SRT performed three observed, and the remaining 12 patients – salvage SRT (4 – early, 8 – delayed). Acute radiation toxicity was estimated in 12 patients. Early impairment from the lower urinary tract 1 degree was observed in 8 (66.7%) 12 of them. Toxicity of 2 or more degree in the early period was not observed. Clinical signs of early 1st degree toxicity from the rectum were found in five (41.7%) of the bowel of the 12 observed. One patient (8.3%) there was a mixture of blood in the feces, which required a medical correction, which was considered as toxicity of the 2nd degree. **Conclusions.** Postoperative SRT of the PB region is a promising modern method of radiation treatment of patients with prostate cancer. The presented methods of adjuvant and salvage SRT are feasible in clinical practice and are characterized by an acceptable level of early radiation toxicity.

Keywords: radical prostatectomy; biochemical progression; local relapse; adjuvant; salvage; stereotactic radiation therapy.

ПЕРВЫЙ ОТЕЧЕСТВЕННЫЙ ОПЫТ СТЕРЕОТАКСИЧЕСКОЙ ЛУЧЕВОЙ ТЕРАПИИ НА ОБЛАСТЬ ЛОЖА УДАЛЕННОЙ ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

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Цель. Оценка безопасности послеоперационной лучевой терапии на область ложа удаленной предстательной железы (ЛУПЖ) с использованием режимов экстремального гипофракционирования дозы (5 фракций по 6,6–7 Гр). **Материалы и методы.** С апреля 2019 г. по март 2020 г. в ФГБУ «НМИЦ онкологии им. Н.Н. Петрова» Минздрава России 15 больным раком предстательной железы проведена стереотаксическая лучевая терапия (СТЛТ) на область ЛУПЖ. В зависимости от клинической ситуации различали адъювантную и спасительную СТЛТ. Для лечения использовали линейные ускорители электронов с энергией тормозного излучения 6 МэВ. Оценивались три режима фракционирования: 5 фракций по 6,6 Гр, 5 фракций по 6,8 Гр и 5 фракций по 7 Гр. В качестве клинического объема облучения определено ЛУПЖ с границами оконтуривания по RTOG (2010).

Результаты. Медиана наблюдения за пациентами составила 7,6 [2,2; 9,9] (1,3–11,6) месяцев. Из 15 больных адъювантная СТЛТ выполнена трем наблюдаемым, а оставшимся 12 пациентам — спасительная СТЛТ (4 — ранняя, 8 — отсроченная). Показатели ранней лучевой токсичности оценены у 12 пациентов. Ранние нарушения со стороны нижних мочевыводящих путей 1-й степени отмечены у 8 (66,7 %) из 12 человек. Токсичность 2-й и более степеней в раннем периоде не наблюдалась. Клинические признаки ранней токсичности 1-й степени со стороны прямой кишки выявлены у пяти (41,7 %) из 12 наблюдаемых. У одного пациента (8,3 %) отмечена примесь крови в кале, потребовавшая проведения медикаментозной коррекции, что расценивалось как токсичность 2-й степени. **Выводы.** Послеоперационная СТЛТ области ЛУПЖ — перспективный современный метод лучевого лечения больных раком предстательной железы. Представленные методики адъювантной и спасительной СТЛТ осуществимы в клинической практике и характеризуются приемлемым уровнем ранней лучевой токсичности.

Ключевые слова: радикальная простатэктомия; биохимический рецидив; местный рецидив; адъювантная; спасительная; стереотаксическая лучевая терапия.

INTRODUCTION

Radical prostatectomy is one of the most common methods of treatment of prostate cancer (PC) in patients of various risk groups. The operation has undergone significant changes over the last 20 years. Retropubic and perineal radical prostatectomy with open approach now more and more replacing by laparoscopic (endoscopic) surgery, which is increasingly being conducted with a robot-assisted version [1]. The technical advantages of robotic surgery are reduction of intra-and postoperative complications, however it did not significantly affect the oncological effectiveness of treatment [2]. Unfortunately, the frequency of recurrent PC following does not actually differ by surgery approach. Depending on the stage of the disease, the frequency of recurrence are in the range of 30%–50% over 10 years of follow-up [3, 4]. The main cause of local postoperative progression is the abandonment of a positive surgical margin [5–7]. Despite the overall positive dynamics of reducing the frequency of positive surgical margins, the detection of tumor cells in the resection margins after a radical prostatectomy remains the most common characteristic of pathomorphological conclusion among all prostate cancers, especially in locally advanced forms of the disease [8].

Adjuvant or life-saving radiotherapy for patients with PC with a high risk of a relapse after radical prostatectomy is a generally recognized approach [9–11]. The standard mode of fractionation for both primary radical and postoperative remote radiotherapy is to sum up a single boost dose (SBD) of 1.8–2 Gy. The accumulated experience shows that in order to achieve local control of PC, escalation of the total boost dose (TBD) to more than 70 Gy is necessary [12]. Under the standard fractionation mode, this requires at least 35 irradiation sessions. In recent years, a sufficient number of moderate hypofractionation modes (SBD2.5–4.0 Gy) have been introduced into a clinical practice that reduce the duration of treatment [13]. Thus, the possibility of using an extreme hypofractionation or stereotactic radiation therapy (SRT) seems justified and promising. An SBD of more than 4.1 Gy per bed area of the removed prostate (BRP), with an even more limited number of fractions (usually 5–7), has demonstrated excellent results in the treatment of primary patients [14].

The aim of the study was to evaluate the safety of a postoperative radiation therapy on the area of the BRP using extreme hypofractionation modes of the dose (five fractions of 6.6–7 Gy).

MATERIALS AND METHODS

From April 2019 to April 2020 there were 15 patients with PC, who underwent postoperative SRT in an extreme hypofractionation mode at the Petrov National Research Center of Oncology of the Ministry of Health of the Russian Federation. The study included patients with verified PC who had undergone a radical prostatectomy.

Depending on the clinical situation, adjuvant and life-saving SRT were distinguished. As part of the last variant of a radiation treatment, early and delayed SRT were released.

The indication for adjuvant SRT was the presence of one or more adverse risk factors for relapse according to the pathomorphological study of the operating material: extracapsular invasion (rt3a) and/or a clinically significant positive surgical margin, or tumor invasion of the seminal vesicles (rt3b). The clinical significance of a positive surgical margin was determined based on several positions: by length (more than 3 mm [5–7]); by reason of abandonment (extraprostatic-associated with rt3a); and by number-multiple, regardless of the extent of the tumor in the margin of resection of individual localities.

Life-saving SRT was made for patients at various times of occurrence of a biochemical (clinical local) relapse. Early life-saving SRT was given at a prostate specific antigen (PSA) level up to 0.5 ng/mL. Delayed life-saving SRT was given at a PSA level equal to or greater than 0.5 ng/mL.

The following criteria were taken into account when choosing the amount of exposure limited to the area of the BRP:

- absence of data about regional lymph glands based on the results of the pathomorphological examination of the operating material (rn0) or radiation examination after a radical prostatectomy in case of a suspected relapse [positron emission tomography combined with a computed tomography (PET/CT) with ^{68}Ga-PSMA or ^{11}C-choline, magnetic resonance imaging (MRI), or CT] (adjuvant and life-saving SRT);
- lack of data on the presence of distant metastases (adjuvant and life-saving SRT);
- no PSA persistence (adjuvant SRT);
- International Society of Urological Pathology (ISUP) group 1–3 (life-saving SRT);
- the time of the beginning of a biochemical relapse is more than 18 months (life-saving SRT); and
- PSA doubling time is more than 12 months (life-saving SRT).

Biochemical relapse as an indication for radiation treatment was determined in accordance with generally accepted criteria: a consecutive twofold increase in the level of total PSA at a value of more than 0.2 ng/mL [10]. Patients with signs of biochemical progression were stratified into low- and high-risk groups [15].

Local relapse after a radical prostatectomy was considered to be a sign of isolated progression of PC in the BRP area (prostate ± seminal vesicles) against the background of PSA growth that met the criteria for the relapse. PET/CT with ^{68}Ga-PSMA or ^{11}C-choline was used as the main method for diagnosing local relapses. If PET/CT was not possible, contrast MRI was used. Histological verification of a local relapse was not performed due to the high frequency of false negative results of biopsy of the BRP area [16].

Contraindications to a radiation treatment included the following conditions:

- stricture of vesicourethral anastomosis (presence of clinically significant infravesical obstruction);
- previously performed radiation treatment on the pelvic area;
- acute infectious disease; and
- chronic inflammatory diseases of the rectum.

Before treatment we evaluated the quality of urination (International Prostate Symptom System index, Quality of Life (QoL) [(WHO, 1993), and urination diary], the maximum rate of urination according to uroflowmetry data, and the volume of residual urine.

An important condition for the formulation of indications for any variant of a postoperative radiotherapy is the need to exclude the stricture of vesicourethral anastomosis. The frequency of this varies, according to the literature, and ranges from 1.6% to 29.9% [17]. With short periods of formation of vesicourethral anastomosis stricture (the stage of a compensation and subcompensation), uroflowmetry may be uninformative. In case of inconclusive results during the urodynamic study, we recommend performing urethrocystoscopy and ascending urethrography.

In the case of adjuvant SRT, the timing of its implementation after radical prostatectomy ranged from 2 to 6 months. (average, 4 months). The start time of a radiation treatment was determined individually, taking into account the following factors: restoration of urine retention, and postoperative features (complications, failure of the anastomosis, duration of standing urethral catheter, presence of lymphocytes, and fistulas in the pararectal tissue). The beginning of life-saving SRT was due to the registration of a biochemical relapse. Due to insignificant follow-up periods, the effectiveness of the tested SRT protocols (biochemical progression) was not evaluated.

The safety of the studied SRT modes was assessed by the frequency and severity of radiation reactions and complications. The analysis of a radiation toxicity was made in accordance with the generally accepted RTOG/EORTC criteria, also taking into account the terminology recommendations of CTCAE v. 5.0 [18]. We released early (within the first three months after the end of a radiation treatment) radiation-related toxicity in the urinary tract (RRTUT) and the lower gastrointestinal tract (rectum) (RPTLGT), as well as a late (nine months after the end of a radiation treatment) complications of an online radiation therapy from the urinary tract and rectum.

The SRT method of the BRP area. In order to increase the accuracy of radiation energy delivery to tissues, X-ray contrast markers similar to the primary SRT of PC were used. For this purpose, a day before pre-radiation topometric preparation under the control of a transrectal ultrasound by perineal access, two markers were installed: anteriorly (10 mm), and at the level of vesicourethral anastomosis, retreating to the right and left of the median line by 5 mm (Fig. 1, *c*).

An additional third place mark could be set in the subtrigonal zone along the median line. In the presence of radiopaque foreign bodies (staples and clips) in the area of the BRP, the use of markers seems impractical (Fig. 1, *d*).

Preparing the lower urinary tract without catheterization involved urination 1.5 h before the irradiation session. After urination, the patient was not recommended to drink liquid, to allow for comfortable filling of the bladder (approximately150 ± 10 mL). Bladder catheterization was made before topometry and each SRT session. A two-way Foley CH 14–16 catheter was installed, and a 10 mL balloon was installed. Both insufficient and excessive injection of fluid into the catheter balloon can contribute to deforming the contours of the neck of the bladder. The bladder cavity was filled with 150 mL of 0.9% NaCl solution, after which a moderate traction was made behind the catheter pavilion, and a plastic clip was applied to it in the area of the external opening of the urethra.

The topometric study included an MRI and CT scan in the position of the therapeutic placement with the patient immobilized on the treatment table according to the standard SRT method. In addition to the images obtained during topometry, PET/CT se-

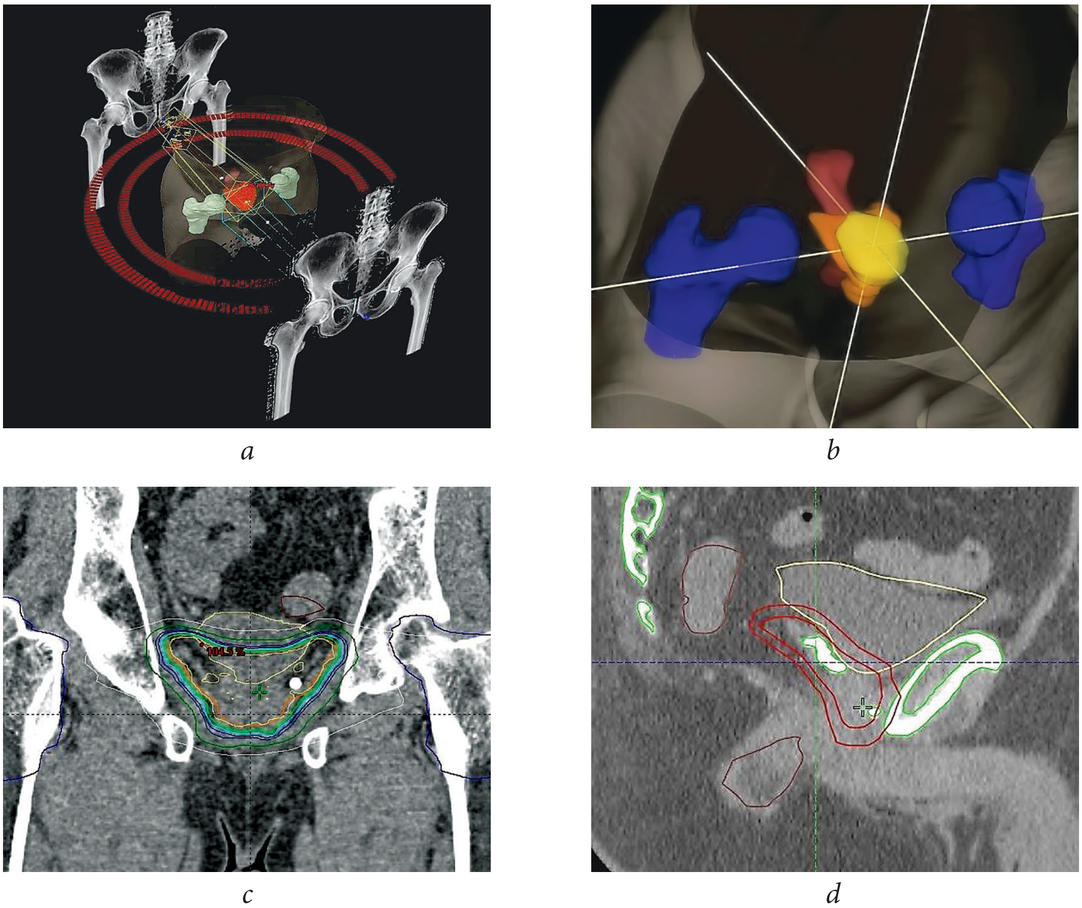

Fig. 1. Dosimetric support of the stereotactic radiotherapy on the prostate bed: *a* – example of a 3D model of a treatment plan using two dynamic arches (RapidArc); *b* – 3D model of irradiated prostate bed (orange) and organs at risk: bladder (yellow), rectum (dark red), femur heads (blue); *c* – an example of isodose distribution (coronal scan), to the left of the vesico-urethral anastomosis is visible X-ray contrast gold seed; *d* – clinical and planned target volumes (sagittal scan), x-rays of contrast staples used as landmarks are visible in the area of the prostate bed

Рис. 1. Дозиметрическое обеспечение СТЛТ области ЛУПЖ: *a* — пример 3D-модели плана лечения с использованием двух динамических арок с модуляцией интенсивности (RapidArc); *b* — 3D-модель облучаемого ЛУПЖ (оранжевый цвет) и критических органов: мочевого пузыря (желтый), прямой кишки (темно-красный), головок бедренных костей (синий); *c* — пример изодозного распределения (корональный скан), слева от везикоуретрального анастомоза видна рентгеноконтрастная метка; *d* — клинический и планируемый объемы облучения (сагиттальный скан), в области ложа семенных пузырьков видны рентгеноконтрастные скобы, используемые в качестве ориентиров quences were used (for C-SRT). After performing the procedure of combining the MRI, CT, and PET/CT images imported into the planning system Calipso V. 4.0 (Varian), the target (BRP) and surrounding normal tissues were contoured in accordance with the recommendations of RTOG (2010) [19] (Table 1).

The following organs were identified as critical: the rectum, bladder, and femoral heads. Since the frequency of erectile dysfunction of postoperative patients is close to 90%, the circumference of the penis bulb was not made.

To translate the doses given to patients with SRT into equivalent doses (equieffective dose – EQD_2), which are supplied during an online radiotherapy in the standard fractionation mode (TYPE2 Gy), we used the concept of converting each mode to an equivalent mode of 2 Gy per fraction, which gives the same biological effect (Table 2).

Radiation treatment was given in the form of five daily (with the exception of weekends) irradiation sessions using linear electron accelerators NovalisTx, Clinac or Truebeam (Varian) with an energy of 6 MeV inhibitory photon irradiation, allowing the dose to be applied using RapidArc technology (Fig. 1, *a*).

RESULTS

Clinical characteristics of patients. The median monitoring time for patients was 7.6 [2.2; 9.9] (1.3–11.6) months. The average patient age was 66.5 ± 6.3 (58–81) years, and the average body mass index was27.1 [23.5; 306] (21.5–326) points.

Retropubic radical prostatectomy was performed for three patients. Laparoscopic prostatectomy was performed for 10 patients, and a robotic procedure was performed for two patients. The median duration of SRT for the BRP area after a previous surgery was 32 [11; 56] (4.0–78.0) months. Out of 15 patients, adjuvant SRT was performed on three observed patients, and the remaining 12 patients received life-saving SRT (four early, eight delayed). All patients receiving life-saving SRT belonged to a low-risk group for a biochemical relapse.

The median PSA at the start of adjuvant and a life-saving SRT was 0.55 [0.25; 1.35] (0.06–3.0) ng/mL. PSA persistence was recorded for two patients of the group receiving life-saving SRT after a radical prostatectomy.

The distribution of patients depending on the pathologic stage and degree of tumor differentiation (ISUP, 2014) is as follows: pT2, eight patients (53.3%); pT3A, three patients (20%); and pT3b,

Table 1 / Таблица 1

Prostate bed contouring during post-prostatectomy radiotherapy

Оконтуривание ложа предстательной железы во время лучевой терапии после простэктомии

Borders of a contouring	Level of a contouring	
	below the upper edge of the pubic symphysis	above the upper edge of the pubic symphysis
Front boundary	Posterior surface of the pubic symphysis	Posterior 1–2 cm of the bladder wall
Back boundary	Anterior wall of the rectum	Mesorectal fascia
Lower boundary	8–12 mm below vesicourethral anastomosis	Ending level of *d. deferens* or 3–4 cm above the level of the symphysis
Lateral boundary	Muscles: *m. levator ani*, *m. obturator internus*	Visceral fascia (*fascia sacrorectogeni-topubic*)

Table 2 / Таблица 2

The values of the total and equivalent doses administered during the investigated fractionation modes

Значения суммарных и эквивалентных доз, подводимых при исследуемых режимах фракционирования

Adjuvant SRT	Life-saving SRT	
	biochemical relapse	local relapse
5 fractions of 6.6 Gy (SBD 33 Gy)	5 fractions of 6.8 Gy (SBD 34 Gy)	5 fractions of 7 Gy (SBD 35 Gy)
EQD_2 76,4 Gy	EQD_2 80,6 Gy	EQD_2 85,0 Gy

Note. SRT – stereotactic radiation therapy.

four patients (26.7%); and group I, three patients (20%); group II, six patients (40%); and group III, six patients (40%), accordingly. Perineural and lymphovascular invasion were observed in seven (46.7%) and two (13.3%) cases, accordingly. In most cases, the tumor was represented by acinar adenocarcinoma: 11 (73.3%) patients. Three (20%) patients showed small acinar, and one (6.7%) showed the foam cell variant of PC. The tumor in the resection margin was recorded for six (40%) patients, of which five people had an extended character of extension. Due to leaving a positive surgical margin, patients were grouped as follows: four were extraprostatic and two were intraprostatic. For two (13.3%) patients, seminal vesicles remained in the area of the BRP.

Local relapse was diagnosed for eight (66.7%) of 12 patients. Among these, two patients in other institutions underwent histological verification of suspicious changes. Ten of the 15 patients (66.7%) underwent PET/CT with ^{68}Ga-PSMA. The zone of vesicourethral anastomosis was the location of relapse for six patients, and the area of the bed of seminal vesicles (subtrigonal zone) was the location for two patients. The average volume of the recurrent nodule was 1.79 (0.85–3.5) cm^3.

Persistent postoperative urinary incontinence at the beginning of radiation treatment was observed for four (26.7%) of 15 patients. Initially, no patient was diagnosed with a pathology from the rectum. Erectile function sufficient for sexual activity was absent for all patients.

At the beginning of radiation treatment, six (40%) of 15 patients were undergoing a hormone deprivation therapy. Given the presumably local nature of the progression of PC, it was not recommended to continue deprivation therapy after SRT.

Early radiation toxicity. In accordance with the follow-up period, it was possible to assess the indicators of early urinary and early rectal radiation toxicity (RRTUT and RPTLGT) for 12 patients.

Early disorders of the lower urinary tract were represented by changes that can be attributed to changes of the 1st degree, which do not require any correction. Clinically, they were characterized as increased urination (more than double compared to the baseline level), as well as episodes of insignificant volume loss of urine due to *de novo* urgency. In total, grade 1 RRTUT was observed foreight (66.7%) out of 12 people. Disbalance of the 2nd or more degree in the early period were not recorded.

Disbalance of a rectal function after the studied SRT regimens in most cases were represented by complaints characteristic of grade 1RRTUT: an increase in the frequency of urges to defecate, which does not require medical correction, or pain in the rectum, which does not require the appointment of analgesics. Similar changes were detected for five (41.7%) of 12 patients. One (8.3%) patient had an admixture of blood in the feces (grade 2 RPTLGT), which required medical correction.

DISCUSSION

Postoperative radiation therapy is an essential component of the treatment of patients with PC. Radiation exposure may be justified by the need to a supplement surgical intervention in the framework of the so-called multimodal approach (adjuvant radiation therapy), as well as considered as a forced measure in the event of a relapse of the disease (lifesaving radiation therapy). Radiobiological studies, as well as accumulated clinical experience, have led to the widespread use of various variants of a moderate hypofractionation of the dose (SBD2.5–4.0 Gy) in recent years [10, 11]. However, the total duration of treatment, even with hypofractive radiation (19–25 fractions), is 30–45 days. Extreme hypofractionation or SRT of PC involves summing up TBD through a limited (usually five fractions) number of irradiation sessions. Thus, together with pre-radiation preparation, the duration of a treatment is only 9–10 days, which makes it possible to reduce the patient's hospital stay by at least three times.

One of the most difficult issues of radiation treatment of patients with PC after a radical prostatectomy is the choice of an adequate amount of radiation. In certain clinical situations (damage of regional lymph nodes or suspicion of it), locoregional exposure is necessary, implying irradiation of the regional lymph flow pathways (TBD44–50 Gy) with an additional dose load on the BRP area to TBD above 70 Gy (according to the European Association of Urologists (EAU) 2019 clinical recommendations, a minimum of 66 Gy) [10]. This approach makes it possible to increase the control over the disease, but it is characterized by more expressed radiation toxicity [20].

Irradiation of the BRP area is the second standard option for a postoperative radiation treatment of PC. A clinically significant positive surgical margin, rT3a/b, or histologically or radiologically verified local relapse, provided that there is no data on the spread of the process beyond the area of the BRP, provide a reason to reduce the amount of radiation to the borders of the anastomosis zone and removed seminal vesicles. Cases of isolated biochemical relapse present known difficulties in determining the volume of an online radiotherapy. In our opinion, to optimize a postoperative radiation therapy for isolated biochemical relapse, it is advisable to use the algorithm for distributing patients with a biochemical relapse into risk groups, proposed and then tested by specialists of the EAU (EAU risk groups) in 2018 [15, 21]. The main predictors were the sum of Gleason scores, the time of the beginning of biochemical relapse, and the time of PSA doubling, which demonstrated the most significant link with overall, cancer-specific and metastasis-free survival. Nowadays, this approach is recommended for the selection as a therapeutic tactic of an active treatment or observation [10]. Attributing the patient to a group of a low-risk biochemical relapse probably gives reason to limit the BRP making a life-saving online radiotherapy.

Special attention must be for abiochemical phenomenon as the persistence of PSA after a radical prostatectomy. It determines the always “saving” nature of an radiotherapy. PSA levels that reach a minimum level of 0.1 ng/mL or higher after a radical prostatectomy are associated with a high probability of further disease progression, even if the removed regional lymph nodes are intact [22]. Since PSA persistence is one of the most unfavorable scenarios of patients requiring fairly aggressive, and often combined treatment [23], isolated lupus irradiation of BRP is justified only if the pathomorphological conclusion of the removed prostate allows explaining the relatively high postoperative level of the marker (extended positive surgical margin, presence of residual prostate tissue). In our study, there were two cases of PSA persistence that were combined with a clinically significant positive surgical margin, which gave grounds to limit the BRP making a life-saving SRT.

The practical implementation of SRT in the area of a probable or diagnosed local relapse after a radical prostatectomy is possible in two ways. In the first case, the viewable nodule is irradiated, and in the second case, the entire BRP is irradiated with standard boundaries according to RTOG (2010). The second variant seems to us more appropriate. Thus, determining the boundaries of a macroscopic relapse is not possible in the case of adjuvant SRT, except in rare cases when visible prostate tissue (apex, seminal vesicles) is left during the operation. For the same reason, this option is rarely implemented in isolated biochemical relapse. The main method for diagnosing local relapse is PET/CT with ^{68}Ga-PSMA, in which, regardless of the PSA level, the average detectability of local progression is approximately 35% [24], and with PSA values below 1 ng/mL, the sensitivity of the technique is 50% [25]. At the same time, it is proven that the earliest possible conduct of a life-saving online radiation therapy (PSA threshold value less than 0.5 ng/mL) it has a significant impact on the prognosis of the disease [26].

The first to report their experience with SRT for patients with a local relapse after a radical prostatectomy were B. Detti et al [27]. A study published in 2016 reported the results of life-saving SRT performed using CyberKnife linear electron accelerators for 16 patients with a median monitoring of 10 months. The researchers evaluated the safety of two fractionation modes: five fractions of 6 Gy to SBD30 Gy (a history of a radical prostatectomy and an online radiotherapy to the pelvic area) and five fractions of 7 Gy (only radical prostatectomy). The visible nodule in the area of the BRP was considered the clinical target radiation volume. The observed patients did not have any cases of an expressed radiation toxicity of the 3rd degree in the lower urinary tract or rectum.

The second approach, i.e., irradiation of the entire BRP according to RTOG (2010), was presented by L.K. Ballas et al [28]. They presented comparative results of radiation toxicity indicators in three modes of an extreme hypofractionation: 15 fractions of 3.6 Gy, 10 fractions of 4.7 Gy, and five fractions of 7.1 Gy. The minimum monitoring period was 6 months (median, 14.1 months). The study included 24 patients who had SRT given as both adjuvant and life-saving procedures. No cases of grade 3 radiation toxicity in the lower urinary tract and rectum were observed during the monitoring period.

In early 2020, the results of the first randomized phase I study were presented by S. Sampath et al [29]. The aim of the study was to assess the toxicity of three modes of dose escalation to the BRP area in the form of three modes ofa dose fractionation: SBD35, 40, and 45 Gy, summed up as five daily fractions in a group of 26 patients. The clinical target radiation volume included the entire area of the BRP. The energy was delivered using the TrueBeam STX linear electron accelerator in the form of two coplanar arches (RapidArc). The median follow-up was 60 months for 35 Gy, 48 months for 40 Gy, and 33 months for 45 Gy. The link between the value of SBD and the severity of radiation complications was insignificant. Late toxicity ≤2nd and ≥3rd degree in the rectum was 11% and 0%, accordingly, and in the urinary tract, 38% and 15%, accordingly. The authors concluded that escalating the dose to 45 Gy does not significantly increase the severity of radiation complications, has similar levels of late toxicity of the 3rd degree, and does not provide a higher level of biochemical control compared to SBD in 40 Gy.

The greatest experience of life-saving SRT is described in the work of G. Francolini et al [30], who analyzed the results of a treatment of 90 patients in three radiotherapy centers in Italy [30]. Radiation therapy was given in five fractions with SBD of 30–40 Gy. Most often, 35 Gy was added in five fractions (77.8%). In all cases, a macroscopic/radiographic nodule in the area of the BRP was irradiated. We used linear electron accelerators CyberKnife or VeroR. The median monitoring was 21.2 (2–64) months. Concomitant hormone deprivation therapy was given to 17 (19%) patients. A complete biochemical response, defined as a decrease in PSA of less than 0.2 ng/mL (nadir), was achieved for 39 (43.3%) of 90 patients. Biochemical relapse was defined as BHR1 (PSA increase >10% from the pre-STLT level) and BHR2 (PSA increase above 0.2 ng/mL for patients with PSA nadir <0.2 ng/mL or two consecutive PSA increases >25% relative to nadir for patients with PSA nadir <0.2 ng/mL). Twenty-five (27.8%) patients showed signs of a biochemical progression with a median absence of BHR1 equal to 36.4 months. For 32 (35.5%) patients, the disease progression was recorded in accordance with the BHR2 criteria and the median of the absence time of 24.3 months. The analysis of cases of relapses showed that local relapse was noted in two cases. In 11 cases, there were distant metastases present, and for 12 patients at the time of examination, it was not possible to determine the cause of PSA growth. During the entire observation period, no cases of a radiation toxicity of the 3rd or higher degree were recorded.

Analysis of the literature published to date allows us to conclude that there is increasing interest in studying the possibility of applying postoperative SRT to patients with PC to the area of the BRP, which can be implemented in two different ways. This study presents the results of the first domestic experience of using SRT for patients after a radical prostatectomy to affect the area of the BRP. Primary approbation of various methods of a radiation treatment was made. The choice of modes of a dose fractionation (tab. 2) is associated with the long-term results of the most studied and a widespread mode of fractionation of primary SRT of PC – 37.25 Gy for five fractions [14]. A shortmonitoring period of our patients does not allow us to draw conclusions about the effectiveness of these fractionation modes to achieve a local control over the tumor process. However, the comparability of the amount of energy supplied by us with the primary SRT allows us to assume a high efficiency of treatment with obviously smaller local volumes of tumor masses in the area of the BRP. The preliminary data obtained indicate that the proposed treatment schemes are well-tolerated. Low toxicity and short treatment times will probably make this method of treatment more attractive for a number of patients in adjuvant conditions, when it is difficult to make a decision about the need for a long-term additional radiation.

CONCLUSION

The obtained preliminary data allow us to conclude that postoperative SRT of the BRP area is a promising modern method of a radiation treatment of patients with PC. The presented methods of an adjuvant and life-saving SRT are easily implemented in a clinical practice and are characterized by an acceptable level of an early radiation toxicity.

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