The Role of Radiation in Urological Malignancies

2

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Introduction

Urologic malignancies represent a diverse group of neoplastic processes that include primary prostate, kidney and bladder cancers, which represent some of the most common cancers encountered in the United States of America (USA); seminomatous testicular germ cell tumors (GCT), which are less common tumors principally of younger men as well as primary ureter; and urethral and penile cancers, which are only rarely encountered in clinical practice. Collectively in 2014, more than 385,000 people in the USA are expected to be diagnosed with a urologic malignancy, accounting for an estimated 60,500 deaths [1]. Radiation therapy (RT) plays an important role in the definitive treatment of all of the aforementioned urologic cancers with the exception of kidney and ureter malignancies, where RT is primarily indicated for palliation of advanced or metastatic disease. Within urologic subsites, where RT is utilized with curative intent, there is considerable heterogeneity of RT type, technique, and use of concurrent systemic agents. Within subsites where surgery is utilized upfront, RT also plays an important role in an adjuvant or salvage capacity.

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Prostate Cancer

In 2014, an estimated 233,000 new cases of prostate cancer are expected in the USA, reconfirming prostate cancer's status as the most common genitourinary (GU) malignancy among US males [1]. Along with radical prostatectomy (RP) and active surveillance (AS), RT continues to be a mainstay of treatment in select patients.

Definitive RT for prostate cancer can be administered in the form of external beam RT (EBRT), interstitial brachytherapy (IB), or a combination of the two treatment modalities. In clinical practice, patients with prostate cancer are routinely classified as having low-, intermediate-, or high-risk disease based on their pretreatment prostate-specific antigen (PSA) level, clinical tumor stage, and biopsy specimen Gleason Grade [2]. Within this framework, definitive EBRT may be appropriate therapy for select patients in any of the three categories, while IB is typically appropriate as monotherapy for patients with low-risk disease or as a boost following EBRT for patients with intermediate-risk disease.

The choice of RT modality, the anatomic target, radiation dose, fractionation, and potential use of concurrent hormonal therapy are also based on a patient's risk factors, medical comorbidities, life expectancy and the potential impact of the proposed intervention on quality of life

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[3]. In addition, emerging evidence suggests that treatment choice and survival may also be influenced by demographic and socioeconomic factors outside of traditional, patient, tumor, and treatment characteristics [4].

The anatomic target for definitive EBRT is the intact prostate with inclusion of the seminal vesicles and/or pelvic lymph nodes based on the extent of disease and tumor characteristics. Additional margins are added to the target volume to account for microscopic tumor extension and daily setup uncertainty. Pelvic RT targeting the regional lymphatics has been employed in the past for patients felt to be at high risk for lymphatic spread of disease, though to date has provided no clear benefit in either control or survival based on level one data [5, 6].

Trends in the treatment of early-stage prostate cancer between 1973 and 2004 show relatively stable use of RT as first-line therapy for patients under 65. However, a steady increase in the use of RT for patients aged 65 and over has been identified [7]. Although AS has been increasingly gaining acceptance in the management of elderly patients, men aged 70 and over with favorable-risk prostate cancer continue to receive EBRT over 50% of the time [8].

With regards to optimal EBRT dose, several important prospective randomized control trials (RCTs) have shown that patients undergoing definitive EBRT derive a local control and survival benefit from escalation of dose to the prostate and seminal vesicles [5, 9–12]. As a result of increased dose to adjacent pelvic organs, patients in the dose-escalated arms on these trials were observed to have significantly increased toxicity including rates of late grade 2 or higher gastrointestinal (GI) toxicities ranging from 17.5 to 33% at between 5 and 10 years of follow-up [5, 9–12].

Advances in technology and evolution of treatment technique from traditional 2-dimensional to present day utilization of intensity modulated RT (IMRT) have enabled dose-escalation without commensurate increases in acute and late toxicity. Retrospective analyses have shown that patients treated to the intact prostate with IMRT have a statistically significant reduction in GI toxicities compared to patients treated to similar doses with 3-dimensional chemoradiation therapy (3D-CRT). Zelefsky et al. published the results of 1571 patients treated for intact prostate cancers with either 3D-CRT or IMRT at Memorial Sloan Cancer Center to doses ranging from 66 to 81 Gy. The use of IMRT was shown to significantly reduce the risk of GI toxicities compared to 3D-CRT (13% vs 5%, $p<0.001$) [13]. Likewise, subset analysis of the Dutch dose-escalation study of 68 Gy vs 78 Gy for intact prostate cancers demonstrated that the use of IMRT over 3D-CRT resulted in significant reductions in acute grade 2 or higher GI toxicity (20% vs 61%, $p=0.001$) [14]. Given improvement in the treatment toxicity profile, IMRT has increasingly been used in place of 3D conformal techniques. As demonstrated in a recent Surveillance, Epidemiology, and End Results (SEER) data analysis, use of IMRT increased from 0.15% in 2000 to 95.9% in 2008 [15]. Along with IMRT, daily imaging, real-time prostate tracking and methods to reduce rectal motion are now widely employed to safely deliver increased dose to the prostate while minimizing dose to normal structures of the pelvis and account for both inter-fractional and intra-fractional motion. Use of these techniques has enabled some groups to dose-escalate beyond 80 Gy with limited toxicity [16].

Prostate cancer cells are unique among human malignancies in that they have an alpha-to-beta ratio that is estimated to be lower than that of adjacent normal tissues [17]. Hypofractionated intensity modulated RT (HIMRT) to the prostate may hypothetically exploit this radiobiologic principle to provide increased tumor control without increasing overall toxicity. HIMRT also reduces overall treatment time and therefore expense, an important consideration given that dose-escalated conventional IMRT (CIMRT) with daily radiation fractions of 1.8–2 Gy can take up to 9 weeks to complete at considerable cost to the patient and health care system. A prospective trial from Fox Chase Cancer Center randomized patients with low-, intermediate- and high-risk prostate cancers to receive either CIMRT with 76 Gy in 2 Gy fractions vs HIMRT with 70.2 Gy in 2.7 Gy fractions. This study did not find any significant difference between treatment arms in

terms of 5-year biochemical and/or clinical failure rates (21.4% vs 23.3%, CIMRT vs HIMRT, $p = 0.745$). In addition, there was no difference in late toxicities and HIMRT treatment could be completed in 2.5 fewer weeks than CIMRT [18]. Additional multicenter prospective studies will be required to confirm the safety and efficacy of HIMRT for the treatment of intact prostate cancers.

Owing to the distinct dosimetric advantages of proton beam RT (PBRT) over conventional photon-based EBRT, including minimal entrance dose and no exit dose, proton beam therapy has become an increasingly attractive modality for treatment of intact prostate cancers. Presently, proton therapy for intact prostate cancer can be delivered in a highly conformal manner using two opposed lateral fields that reduce dose to the bladder and rectum as compared to CIMRT. To date, no prospective randomized study has been performed to directly compare outcome measures between PBRT and CIMRT. However, retrospective data have suggested that despite improved dosimetry, there may be little clinical advantage for PBRT over CIMRT but considerable extra expense. A retrospective comparison of Medicare beneficiaries treated for prostate cancer between 2008 and 2009 identified 27,647 men treated with PBRT and 27,094 patients treated with IMRT. The findings demonstrated that patients receiving PBRT were younger, healthier, and from more affluent areas than those patients receiving CIMRT and at 12 months posttreatment there was no difference in GI or GU toxicity between the two patient groups. Median Medicare reimbursement was US$32,428 for PBRT and US$18,575 for CIMRT [19]. Interestingly, in a SEER data analysis of patients treated for prostate cancer between 2002 and 2007, propensity score-match analyses between 684 men treated with PBRT and 6666 men treated using IMRT showed that IMRT patients actually had a lower risk of GI morbidity than those receiving PBRT [15].

Prostate IB conceptually represents an "inside-out" method of RT in which high doses of radiation are delivered to the target volume that rapidly fall off thereby limiting dose to adjacent organs at risk. Low-dose rate (LDR) IB may be performed via permanent implantation of LDR isotopes such as Palladium-103 or Iodine-125 and local control rates achieved with LDR IB in men with clinically localized, low-risk prostate cancer are comparable with those achieved with RP [20, 21]. Alternatively, high-dose rate (HDR) IB may be performed via temporary implantation of catheters in the prostate through which HDR isotopes are inserted and then removed after a prescribed duration of time. Despite its value as monotherapy for low-risk prostate cancer, SEER analysis shows that between 2004 and 2009 monotherapy IB use decreased from 30.4 to 25.6%, a finding the authors attribute to the rise in popularity of EBRT techniques including IMRT and PBRT, which are reimbursed at higher rates than IB. For patients with intermediate-risk prostate cancer, EBRT may be combined with an LDR or HDR IB boost. With respect to combined therapy utilization, SEER analysis shows a less drastic decline in utilization from 13.8% in 2004 to 12.3% in 2009 [22].

In addition to playing an integral role in the definitive treatment of intact prostate cancer, EBRT has also been employed postoperatively as either adjuvant therapy for patients with high-risk pathologic or surgical features or as salvage therapy for patients with a biochemical failure based on PSA or in those found to have a clinical local recurrence. In the setting of adjuvant or salvage treatment, the RT treatment target is the surgical resection bed with consideration for treatment of the pelvic lymph nodes and therapy is delivered with EBRT alone without any role for IB. Three large RCTs demonstrated that patients with at least one of the following: extra-capsular extension, positive surgical margins, or seminal vesicle involvement after RP derive a biochemical failure free survival benefit from adjuvant RT to the surgical prostate bed [23–25]. Two of the trials included patient subgroups with detectable PSA levels post-RP that received salvage RT. In these studies, salvage RT significantly reduced metastatic recurrence rates [24] and biochemical failure [23] among patients with detectable PSA post-RP, respectively.

Prior to the publication of these key postoperative RT RCTs, only 18.2% of patients received

adjuvant RT after RP with high-risk features [26]. Based on these trials, several clinical guidelines have been presented and updated to reflect these findings. As part of their published clinical guidelines, the American Society for Radiation Oncology (ASTRO) and the American Urologic Association (AUA) now jointly recommend adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy and salvage RT to patients with PSA or local recurrence after RP [27]. However, it appears as though biases may still influence practice patterns regarding adjuvant and salvage RT. A national web-based survey of post-RP RT beliefs was mailed to 926 radiation oncologists and 591 urologists showed that 68 % of respondents recommended adjuvant RT based on adverse pathologic features. However urologists were much less likely to recommend adjuvant RT than radiation oncologists (78 % vs 44 %, Radiation Oncologists vs Urologists, $p < 0.001$). Likewise, PSA thresholds for recommending salvage RT were significantly higher among Urologist responders than responding Radiation Oncologists [28].

The past two decades have witnessed an incredible evolution in RT for prostate cancer that has resulted in impressive gains in biochemical control and reduction in toxicity. The improvement in the therapeutic ratio has resulted largely from technological advances that have enabled dose-escalation with sparing of adjacent normal tissues. Additional gains may come from further refinement of image-guidance techniques and organ-motion compensation that enable reduction in the size of target margin expansions. In addition, novel treatment modalities and techniques that utilize hypofractionation to exploit the unique radiobiology of prostate cancers may also prove to further increase local tumor control without adding toxicity. Given the anticipated changes in health care economics and the massive expense of modern prostate cancer treatments, new treatment strategies will need to be rigorously tested and evaluated through multi–institutional trials to prove their safety, efficacy, and superiority to current standards of care.

Bladder Cancer

Bladder cancer is the second most common GU malignancy in the USA, with 74,690 total new cases expected in 2014 [1]. The large majority of patients with new bladder cancers present with superficial tumors that are commonly managed with local therapies, with radiation playing only a limited role in select patients. However, patients found to have muscle-invasive bladder cancers have significantly worse survival and require more aggressive management. RT is presently an integral component of trimodal bladder preservation therapy, which has emerged as an important alternative to radical surgery in this patient population.

Historically, the treatment options for muscle-invasive bladder cancer without distant disease included partial or radical cystectomy (RC), RT to the pelvis alone in those patients deemed to be poor surgical candidates or some combination of surgery and either preoperative or postoperative radiation. Despite similar disease-free survival (DFS) outcomes in nonrandomized studies, RC and pelvic lymphadenectomy has generally been favored over radical radiation for medically operable patients [29]. While considerable advances in surgical technique have occurred in recent decades, a reduction in quality of life remains an unavoidable consequence of urinary diversion following RC.

In light of the morbidity of RC and historical 5-year survival of only 40–60 % an international effort attempted to refine bladder preservation therapy via the addition of concurrent radiosensitizing chemotherapy [30, 31]. This work culminated in the current approach to bladder preservation consisting of maximal transurethral resection of bladder tumor (TURBT) followed by concurrent induction CRT. Patients achieving complete response on cystoscopy proceed to consolidation CRT therapy and close follow-up, while those without complete response were recommended to undergo RC. Prospective analyses of this technique have demonstrated overall survival (OS) rates of 50–60 % with 75 % bladder preservation [32].

Despite results demonstrating nearly equivalent survival when compared to historical trials and greater preservation of bladder and urinary function, strongly held views regarding treatment efficacy may be limiting widespread adoption of bladder-preservation therapy. A retrospective SEER analysis of patterns of care for nearly 27,000 patients with muscle-invasive bladder cancers treated between 1988 and 2006 found that 87% of patients received definitive surgery alone or with adjuvant RT. Importantly, the SEER database did not include details regarding chemotherapy use but 10.9% of patients received EBRT up-front with or without surgery and ostensibly many of the patients in this group would have received chemotherapy concurrent with their EBRT. Medical operability was also not available from the data but the patients who received EBRT up-front were more likely to be older, female, and have squamous cell carcinomas or poorly differentiated tumor. Interestingly, the year of diagnosis was not an independent variable for predicting the use of bladder preservation, suggesting that even as prospective data emerged suggesting a benefit to concurrent CRT there was little change in the firmly entrenched beliefs of the superiority of RC [33].

To date, no direct comparison of modern, CRT-based bladder preservation therapy and RC has been successfully conducted for muscle-invasive disease. A study designed by the Medical Research Council in the United Kingdom attempting to compare these two treatment modalities in a prospective manner closed after accruing only 45 patients in 30 months. Given potential biases in the USA regarding CRT for bladder cancer, it is likely a similar RCT here would meet the same fate. Despite this, ongoing research is refining and expanding the role of RT in bladder cancers in other ways. The Radiation Therapy Oncology Group (RTOG) is presently conducting a legacy phase II study investigating whether bladder preservation with definitive CRT is appropriate for patients who have undergone maximal TURBT revealing grade 2–3, stage T1 bladder cancers for whom RC is being considered. For patients who are older or medically inoperable there may also be an emerging role for bladder-sparing hypofractionated IMRT with concurrent chemotherapy. A preliminary study from Canada of 24 patients treated in this manner to a dose of 50 Gy in 2.5 Gy fractions with concurrent gemcitabine or cisplatin revealed a complete response rate of 83% with acceptable toxicity rates [34].

Seminomatous Testicular Cancer

Testicular cancers are the most commonly diagnosed malignancy of men between the ages of 20 and 45 with an estimated 8820 new cases expected in 2014 [1]. Cancers of the testis can be broadly subdivided into pure seminomatous germ-cell tumors (SGCT) and nonseminomatous germ-cell tumors (NSGCT). RT plays an important role in the treatment of testicular SGCT but does not typically have a role in the treatment of nonseminomatous testicular cancers where chemotherapy is presently the foundation of therapy.

Testicular SGCT are remarkably sensitive to both chemotherapy and radiation with high salvage rates following relapse. As such, following transinguinal orchiectomy patients with stage I disease may be candidates for adjuvant EBRT, chemotherapy, or surveillance.

In general, there has been a trend over the last decade to omit or limit adjuvant RT for early-stage testicular seminoma. SEER data from 1999 indicated that during the late 1990s 84% of patients with localized testicular SGCT received RT after orchiectomy [35]. However, this routine practice was called into question after data emerged indicating a 2.6-fold increase in the long-term development of secondary non-germ cell malignancy after subdiaphragmatic RT for long-term survivors of testicular seminoma [36]. In light of the increased risk of secondary malignancy, high rates of salvage after recurrence and emerging data on observation, the National Comprehensive Cancer Network (NCCN) guidelines were changed in 2009 to reflect a preference for observation. Follow-up analysis of SEER data demonstrated that the same year adjuvant RT use fell to 37.7% [37]. Even with these recommendations, select patients with stage I disease remain

candidates for adjuvant RT, including those with findings of a primary tumors >4 cm, rete testis involvement or for those patients at high risk for noncompliance with the recommended stringent follow-up measures required during observation.

The utilization of radiation, including targets and doses, has been influenced by several key randomized trials. The MRC-UK TE 10 study randomized early stage patients receiving adjuvant EBRT to treatment of the para-aortic (PA) nodal chain and ipsilateral iliac lymph nodes vs PA nodal chain alone. The trial found equivalent 5-year survival in each group [38]. Thus, for stage I patients without other risk factors or nodal disease, radiation is typically delivered to the PA nodal chain alone, omitting the pelvic nodes, with classic field borders extending from T10–11 down through L5–S1, and laterally 2 cm beyond the vertebral bodies with an additional 1 cm border on left renal hilum and sacroiliac joint if the primary tumor was left-sided. In an effort to determine the appropriate dose, MRC-UK TE 18 randomized patients with stage I disease treated to the above field to either 20 Gy in 2 Gy fractions vs 30 Gy in 2 Gy fractions and found no difference in 5-year relapse rates. Based on this, the current recommended doses are for 20–25 Gy in 1.25–1.5 Gy fractions [39].

For stage I patients, there are several treatment options including observation, radiation and chemotherapy. However, patients with stage IIA–IIB seminoma have a higher likelihood of pelvic nodal failure and so radiation remains the standard of care. Radiation fields typically utilize an extended "dog-leg" field to treat both the PA nodal chain and at-risk ipsilateral iliac lymph node regions. The field borders for patients with IIA–IIB disease, as employed in MRC-UK TE 10, include a superior edge of T10–T11, inferior border at mid-obturator foramen, ipsilateral border from renal hilum down to L5–S1 interspace then diagonally in parallel with the ipsilateral border then vertically downwards to mid-obturator level (Fig. 2.1). As in stage I patients, the "dog-leg" field used in IIA–IIB disease is treated to 25 Gy in 1.25 Gy fractions with consideration for an additional boost to involved lymph nodes (Fig. 2.2). In spite of the benefits of radiation in stage IIA–IIB, patients with stage IIC and higher seminoma commonly receive adjuvant chemotherapy first as opposed to RT due to a higher concern for distant over local failure.

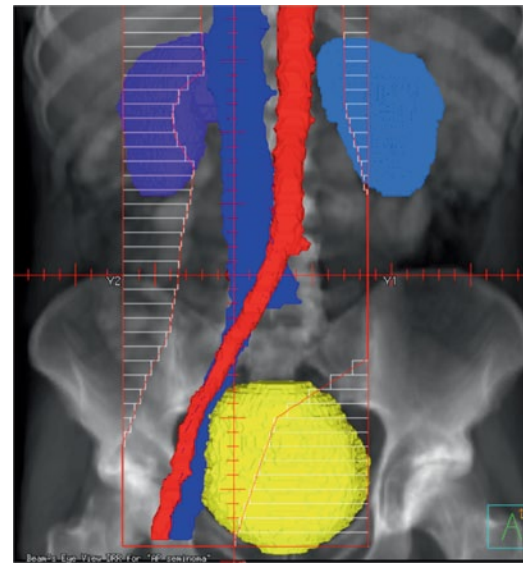

Fig. 2.1 RT fields for a stage I seminoma

Urethral Cancer

Primary urethral cancers are extremely rare malignancies. SEER analysis from 1973 to 2002 identified an annual age-adjusted incidence rate of 4.3 per million US men and 1.5 per million US women [40]. A multimodal approach to treatment is commonly employed with a goal of organ preservation whenever possible; however, given the relative rarity of the disease and historical lack of treatment uniformity, the role of RT is not well described through randomized clinic trials.

RT has historically played a limited role in the treatment of male urethral cancers. Rabbani et al. identified 2065 men from the SEER database from 1988 to 2006 with primary urethral cancer. Of these patients, 78% had urothelial carcinoma histology, 67% presented with less than or equal to T1 disease and 61% of patients were managed with simple surgical excision alone. Only 10% of patients received radical resection and RT was utilized to only 10% of

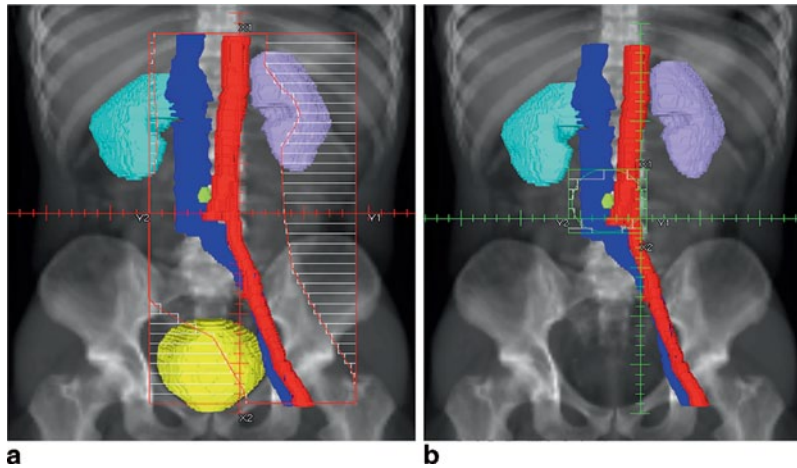

Fig. 2.2 **a** Initial RT fields for a stage IIA seminoma. Enlarged PA node in *yellow-green*. **b** Boost field for stage IIA seminoma

patients as well. The SEER database did not distinguish between proximal vs distal tumors and so it is unclear how tumor site may have influenced treatment choice [41]. Outcomes regarding male urethral cancers treated with radiation are limited. In one of the larger retrospective series on the topic, Dalbagni et al., retrospectively reviewed 46 men with primary urethral carcinoma treated at Memorial Sloan Kettering Cancer Center (MSKCC) between 1958 and 1996. Forty patients received surgery alone and 6 received RT followed by salvage surgery. In this study, none of the RT patients responded to RT though the authors posit that this was due in large part to selection bias and higher T stage among RT patients [42]. Radical CRT for more advanced male urethral carcinoma has showed promise in at least one small, single-institution analysis. Eighteen men in this study with T2–4, N0–2 disease were treated on a protocol of 45–55 Gy, to a field encompassing the inguinal, external iliac lymph nodes and genitalia from the perineum to the upper sacrum using AP/PA technique with a boost of 12–15 Gy to the primary lesion. Radiation was given concurrently with mitomycin and 5-fluorouracil (5-FU). Results demonstrated that 83 % of patients had a complete response to treatment with 5-year overall and disease-specific outcomes of 60 and 83 %, respectively. Three of the nonresponders and four of the complete responders who recurred required salvage surgeries [43].

Radiation has a more established role in the treatment of female urethral cancers though outcomes remain poor irrespective of the choice of treatment modality. Several long-term retrospective series have analyzed the role of RT in female urethral cancers. Grigsby et al. published the results of 44 patients with urethral carcinoma, of whom 12 received RT with surgery (either pre- or postoperatively, dose range: 30–73.68 Gy, median 50.4 Gy) and 25 received EBRT and brachytherapy (EBRT doses 12–70 Gy, median 42.72 Gy; brachy doses 15–145 Gy, median 80 Gy). EBRT fields included bilateral groins in all women. The 5-year OS rate was 42 % and the 5-year cause-specific survival was 40 % with the aggressive treatment regimens resulting in high complication rates [44]. Similarly, Garden et al. reviewed the outcomes of 97 women treated for primary urethral carcinoma at MD Anderson Cancer Center. Of those, 86 received radiation after excision or biopsy, including 35 treated with combined EBRT and IB (EBRT doses 20–70 Gy, median 46 Gy, Brachy doses 20–70 Gy, median 30 Gy), 21 treated with EBRT only (40–71 Gy, median 61 Gy), and 30 with IB only (45–75 Gy, median 60 Gy). There was significant heterogeneity among treatment techniques and fields employed. The overall

actuarial 5-, 10-, and 15-year survival rates for all 97 patients were 41, 31, and 22%, respectively, and the type of treatment did not predict outcome [45]. Princess Margaret Hospital published results of 34 women with urethral carcinomas treated with radiation that was directed to the primary lesion in 15 patients vs the primary tumor and regional lymph nodes in 19 patients. Of these patients, 20 received combined EBRT and brachytherapy. The median dose to the primary tumor, accounting for the contributions of both EBRT and brachytherapy doses for all 34 patients, was 57 Gy (range 30–83 Gy). The 7-year actuarial overall and cause-specific survivals were 41 and 45%, respectively, and brachytherapy reduced the risk of local recurrence by a factor of 4.2 [46].

Penile Cancer

Penile cancer is a rare GU malignancy in the USA with estimated 1600 new cases in 2014, accounting for less than 1% of male malignancies [1]. Although uncommon in Europe and the USA, it represents a more significant cause of male cancer in the Indian subcontinent, Africa, and Latin America. The conventional treatment for early stage penile squamous cell carcinoma has been total or partial penectomy, which results in rates of local control in excess of 90% [47]. In recent years, however, there has been a trend towards organ-sparing treatments including definitive EBRT and/or brachytherapy as a means to limit functional and psychosexual morbidity associated with penectomy. In the USA, however, use of RT for treatment of penile cancers remains limited. A recent SEER database analysis of 2427 men with penile cancer treated between 1988 and 2006 demonstrated 90.0% received surgery alone, 2.2% received EBRT alone, and 7.4% received EBRT after surgery. One subject received brachytherapy alone and eight subjects received brachytherapy after surgery either with or without EBRT. Patients who received EBRT alone or in conjunction with surgery were more likely to have advanced T and N stages. The study authors posit that underutilization of RT for penile cancer is a function of referral bias, with patients presenting first to a dermatologist or urologist being offered specialty-specific therapy instead of referral to a radiation oncologist [47].

Despite the lack of widespread utilization, retrospective data have shown promising results for definitive RT for penile cancers. Ozsahin et al. published the results of a multicenter retrospective review of 60 patients with penile carcinoma. In total, 27 patients underwent surgery with or without adjuvant radiation vs 29 who underwent definitive EBRT alone. After biopsy, four patients refused RT. Of the patients receiving definitive EBRT, local control was obtained in 39% and four patients who recurred underwent salvage surgery resulting in a penis preservation rate of 52%. The 5-year and 10-year probability of surviving with an intact penis was 43% and 26%, respectively, and there was no significant survival difference between the patients treated with definitive RT and primary surgery (56% vs 53%; $p = 0.16$) [48]. A review of 67 men with T1–T3 penile cancers treated at two Canadian centers with penile-conserving primary brachytherapy revealed 10-year actuarial OS and cause-specific survival rates of 59% and 83.6%, respectively. Salvage penectomy was required for eight local failures and two cases of necrosis, for an actuarial penile preservation rate at 5 years of 88% and 10 years of 67% [49].

Although the role of adjuvant RT for penile cancer is not well defined in the literature, it appears to be most important in patients with positive pelvic lymph nodes. Franks et al. retrospectively analyzed the results of 23 men with pathologic N1–N3 penile cancer treated with adjuvant RT after local surgery and unilateral or bilateral groin dissection. The RT dose was 45 Gy in 20 fractions to the pelvis and bilateral groins delivered AP/PA. A 12-Gy boost in five fractions could be given if indicated. 3-year OS and locoregional relapse-free survival was 66% and 56%, respectively [50].

Summary

RT has a well-established and continually evolving role in the treatment of many of the most common and some of the rarest GU malignancies in the USA. Outcomes in many of these disease sites have sufficiently improved such that patients will live long enough to manifest not only the acute but also late-effects of treatment. There is an important duty on the part of all medical practitioners involved in the care of patients with GU malignancies to learn to appropriately prevent, diagnose and manage these treatment-related toxicities.

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