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CRITICAL REVIEW

Gender-Affirming Surgery and Cancer: Considerations for Radiation Oncologists for Pelvic Radiation in Transfeminine Patients

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Abstract: Access to gender-affirming surgery is increasing for many transgender and nonbinary people in the United States, and radiation oncologists must be equipped to care for patients who have undergone such surgery in the region of their planned radiation treatment field. There are no guidelines for radiation treatment planning after gender-affirming surgery, and most oncologists do not receive training in the unique needs of transgender people with cancer. We review common gender-affirming genitopelvic surgeries for transfeminine people, including vaginoplasty, labiaplasty, and orchiectomy, and summarize the existing literature on the treatment of cancers of the neovagina, anus, rectum, prostate, and bladder in these patients. We also describe our systematic treatment approach and rationale for pelvic radiation treatment planning.

Introduction

Over 1.6 million people in the United States identify as transgender or nonbinary, meaning that they have a gender identity that does not correspond to their sex assigned at birth.[1] Although not all transgender or nonbinary people are interested in or undergo gender-affirming hormone therapy or surgery, the number of gender-affirming surgeries performed in the United States is increasing, from 2700 in 2015 to 16,400 in 2020.[2,3] Common sites of surgery include the head and neck (eg, facial feminization surgery, tracheal shaving), chest (eg, breast augmentation, chest masculinization), and pelvis (eg, vaginoplasty, labiaplasty, phalloplasty). Among transgender women, 12% report having had vaginoplasty or labiaplasty, and another 54% report having an interest in these procedures.[4] As gender-affirming surgeries become more widely available, radiation oncologists will be more likely to encounter transgender patients who have had or plan to have gender-affirming surgery. This may be particularly relevant for genitopelvic surgeries

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in transfeminine patients due to the proximity of surgically reconstructed tissues, including the neovagina, to radiation fields for pelvic cancers or metastases within the pelvis and cancers directly involving reconstructed tissues.

Most oncologists do not feel that they have adequate knowledge of the unique needs of transgender people with cancer,[5,6] and, to our knowledge, there are no guidelines for pelvic radiation treatment after gender-affirming surgery. We present a review of the existing literature and offer a systematic approach to pelvic radiation treatment in transgender women and transfeminine people, including those who have undergone gender-affirming surgery and those considering it.

We conducted a literature search using PubMed for studies reporting on the incidence of pelvic cancers (including cancers of the neovagina, anus, rectum, prostate, and bladder and pelvic metastatic disease) in the transgender population and studies on the treatment of pelvic cancers in transfeminine people. We also reviewed the reference list of each included study to identify additional relevant studies. Radiation treatment plans for patients with neovaginal, anal, and rectal cancers are provided as illustrative examples.

Given the limited existing level of evidence, consisting of case reports and expert opinion, we sought to develop recommendations by extrapolation from published data, where available, and by consensus agreement among our expert panel. The initial group comprised physicians treating cases at our institutions; additional institutional experts were included based on their disease site specialty. Further solicitation was obtained from national providers with clinical experience in treating transgender patients to supplement beyond a single institutional experience. The final panel included clinicians from 4 institutions, including radiation oncologists specializing in gynecologic, genitourinary, and gastrointestinal cancers and a urologic surgeon specializing in vaginoplasty.

Gender-affirming genitopelvic surgery for transfeminine people

Gender-affirming surgeries are complex individualized procedures based on a patient's transition goals, anatomy, and surgeon experience and expertise. This section is intended to provide an overview of the most common feminizing gender-affirming surgeries and details that may be relevant to radiation planning. Importantly, when treating a patient, we recommend reviewing operative notes in detail and, if possible, discussing with the patient's gender-affirming surgeon and reviewing their pelvic and genital anatomy with a radiologist.

Vaginoplasty

Vaginoplasty is the creation of a neovagina and vulva from tissue, most commonly originating from the penis and scrotum. This is often, but not always, combined with penectomy and orchiectomy. The most common surgical approach is penile inversion vaginoplasty, through which the neovaginal canal is created from a penile skin flap that is inverted into a space developed between the prostate and rectum (Fig. 1).[7,8] Other techniques include peritoneal vaginoplasty, where scrotal and penile skin is supplemented with peritoneal flaps to form the neovaginal apex.[9] Enteric vaginoplasty is rarely performed, often using the rectosigmoid colon or ileum to line the neovaginal canal.[10]

The following factors should be considered when planning for pelvic radiation after vaginoplasty. The source of neovaginal tissue must be determined and can include penile skin flap, scrotal and perineal skin graft or flap, extragenital full-thickness skin graft, pedicled ileal or rectosigmoid flap, and peritoneal flaps.[9,11,12] The neovaginal space is created with the same approach used in perineal

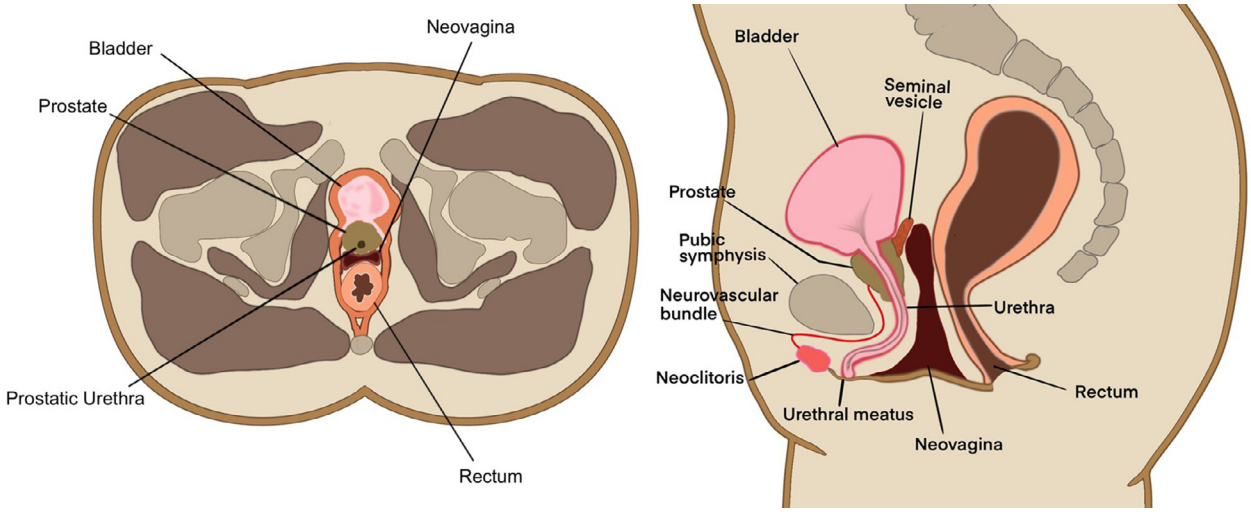

Fig. 1. Genitopelvic anatomy after gender-affirming vaginoplasty. The neovagina is positioned between the prostate and rectum. The neoclitoris and associated neurovascular bundle is inferior to the pubic symphysis, and the urethral meatus is inferior to the neoclitoris. Illustration created by Lisa Fountain.

prostatectomy by blunt dissection between the ventral rectal fascia (posterior Denonvillier's fascia) and the prostate up to the peritoneal reflection.[11] The neoclitoris is constructed from the glans penis and positioned at the base of the corpora, located inferior to the pubic symphysis, with the adductor longus tendon used in some cases as a landmark.[11] The dorsal neurovascular bundle, composed of the dorsal penile nerve and vessels, is folded and positioned superior to the neoclitoris. Urethral reconstruction is performed similarly to perineal urethrostomy, and the meatus may be positioned at two-thirds the distance from the introitus to the neoclitoris, directly below the urinary sphincter.[7,11]

Vulvoplasty/labiaplasty/minimal-depth vaginoplasty

Vulvoplasty, labiaplasty, and minimal-depth vaginoplasty are procedures that often include the removal of the penis and testicles, formation of a neoclitoris, a shortened urethra, inner and outer labia, and a neovaginal introitus without the creation of a neovaginal canal. Vulvoplasty as a standalone procedure is less common than vulvoplasty combined with vaginoplasty, with those undergoing standalone vulvoplasty representing about 9% of patients in 1 cohort.[13] Reasons for choosing minimal-depth vaginoplasty over full-depth vaginoplasty include not being interested in receptive vaginal intercourse, not needing vaginal dilators, and reduced risk of complications. Medical or surgical contraindications to full-depth vaginoplasty include prior rectal surgery or pelvic radiation.[13,14]

Orchiectomy

Gender-affirming orchiectomy may be performed as a component of vaginoplasty or vulvoplasty or may be performed on its own. Gender-affirming orchiectomy is generally performed as a simple orchiectomy through a midline scrotal incision with the removal of the spermatic cords.[15] The scrotal skin, fat, and fascia are usually preserved for potential use in future surgeries. Reasons for undergoing orchiectomy alone can include removing endogenous testosterone production as an alternative to antiandrogen therapy, offering a less complex option for gender-affirming genital surgery, and increased accessibility to patients outside of specialized gender surgery centers.[15]

Pelvic cancers in transfeminine people

Neovaginal and neovulvar cancer

Cancer of the neovagina is rare, with 5 prior case reports involving transfeminine patients and rare cases in patients assigned female at birth with congenital vaginal agenesis.[16-21] Of these 5 case reports, 2 patients presented with localized disease and were planned for treatment with surgery followed by adjuvant chemoradiation. The first patient underwent total resection of the neovagina,[21] followed by chemotherapy and radiation. The second patient was found to have dense adhesions, the attempted resection was aborted, and the patient was then treated with 45 Gy external beam radiation to the pelvis followed by high-dose-rate brachytherapy 6 Gy × 3 fractions.[19] The third patient presented with locally advanced disease with rectovaginal fistula and underwent diverting colostomy followed by palliative carboplatin and fluorouracil.[20] The fourth and fifth patients presented with metastatic disease, for which one patient was treated with cisplatin and radiation to the primary tumor, pelvis, and bone metastases,[18] whereas the other was treated with palliative radiation alone.[17] Two of these patients died within 6 months of diagnosis, 1 died 2 years after diagnosis, and 2 remained alive without evidence of disease at 2 years. Notably, the patient treated with definitive radiation developed significant vaginal stenosis.[19]

We recommend treating localized or locally advanced neovaginal squamous cell carcinoma using similar principles to vaginal cancer, incorporating paradigms from the tissue of origin and with some notable exceptions. Primary vaginal cancers are more often treated with definitive chemoradiation due to the difficulty of resecting tumors close to other pelvic organs; radiation for primary vaginal cancer generally involves a combination of external beam radiation and brachytherapy (intracavitary or interstitial).[22] For neovaginal cancers, the use of brachytherapy may be technically challenging as the neovagina has less redundant tissue and may not be feasible in patients with pre-existing vaginal stenosis. Additionally, as the tissue of origin of neovaginal cancers is an epithelialized surface and not mucosal tissue, there may be a considerable risk of necrosis of the neovagina with brachytherapy due to the generally larger fraction sizes and more heterogeneous dose distribution. Lastly, patients are at high risk of developing vaginal stenosis at baseline after vaginoplasty, and the risk increases with radiation. (Please see the *Patient counseling and radiation treatment planning recommendations* section regarding vaginal dilator counseling and use.) As such, definitive chemoradiation with an external beam boost may be preferable to a brachytherapy boost for locally advanced cancer of the neovagina. This contrasts with the standard treatment recommendations for vaginal cancer of the native vagina.[23]

For treatment planning, we fuse diagnostic magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET CT) images for delineation of the primary tumor (Fig. 2). Regarding nodal coverage, we consider including inguinal as well as external and internal iliac nodal regions for cancers of the neovagina when an external genital flap is used. We recommend treating 1 nodal echelon above the most superiorly involved node for patients with macroscopic pelvic nodal involvement.[24] We recommend treating the elective nodal volumes to a dose of 45 Gy and boosting the gross primary tumor to 70 Gy. Radiographically positive nodes should be treated to a dose

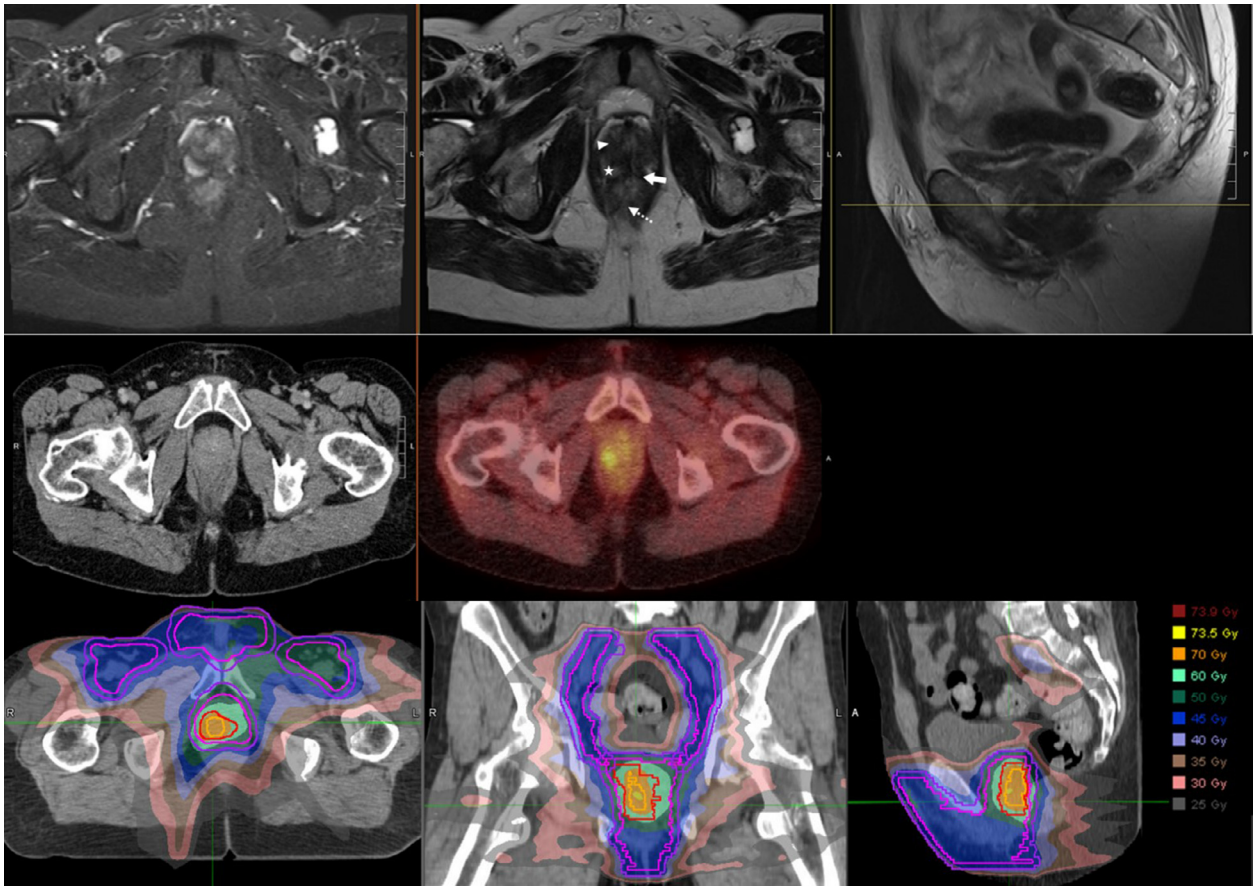

Fig. 2. Diagnostic imaging and graphical treatment plan for a patient with localized squamous cell carcinoma of the proximal neovagina treated with definitive chemoradiation with cisplatin. To account for disruption of the neovaginal and vulvar lymphatics by prior surgery, elective nodal coverage included the bilateral inguinal nodes as first echelon and internal and external iliac nodes as second echelon. The vulva, neovagina, and nodal planning target volume (PTV) was treated with 45 Gy in 1.8 Gy per fraction (fx); the neovaginal gross tumor volume (GTV) was treated during the initial course to 50 Gy in 2 Gy per fx; and the GTV was also boosted sequentially to a total dose of 70 Gy in 2 Gy per fx. This patient remains alive at 18 months posttreatment without evidence of recurrence. Top: Short tau inversion recovery (STIR) and T2 weighted MRI of a 2-cm neovaginal apex mass at diagnosis (arrowhead: prostate; solid arrow: neovagina; dashed arrow: rectum; asterisk: tumor). Middle: Fluorodeoxyglucose positron emission tomography/computed tomography (PET CT) images at diagnosis. Bottom: Representative images from radiation treatment plan with contours and isodose lines shown. Orange = GTV 70 Gy, red = GTV 50 Gy, magenta = CTV 45 Gy, purple = PTV 45 Gy. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of at least 60 Gy. Weekly cisplatin should be given concurrently to act as a radiosensitizer.[25] For tumors arising from penile or scrotal skin flaps, the anticipated first echelon nodal basin is the inguinofemoral nodes.[26,27] For vulvar cancers extending to the neovaginal canal, the inguinofemoral, obturator, internal iliac, and external iliac nodal regions should be included; additionally, the mesorectal and presacral nodes should be included for involvement of the posterior neovaginal wall and rectovaginal septum.[24] For patients with rectosigmoid flaps forming the neovaginal apex, the superior extent of the mesorectal and presacral nodal volume should be at the rectosigmoid junction or at least 2 cm proximal to the superior extent of macroscopic disease, whichever is more proximal.[28] Prescription doses should be comparable to those used to treat cisgender women with vaginal and unresected vulvar cancer. When target volumes include tissues reconstructed from rectosigmoid or small bowel flaps, doses should be constrained to bowel tolerances to avoid bowel tissue toxicity, though this must be balanced with the need to use doses required to eradicate gross disease. Intensity modulated radiation therapy (IMRT) should be used for external beam radiation therapy.

For patients with peritoneal flaps forming the neovaginal apex, there are limited data on the lymphatic drainage of the pelvic peritoneum. An animal study has shown primary peritoneal drainage to celiac, superior mesenteric, and periportal nodes.[29] Although this evidence is not sufficient to inform elective nodal coverage, we would be concerned about early intraperitoneal dissemination of disease involving the neovaginal apex if formed from a peritoneal flap.

Furthermore, although consideration may be given to treat a whole abdominal field when the entire peritoneal cavity is at risk, this is not recommended due to increased toxicity.

When treating cancer of the neovulva, extrapolation from the treatment of vulvar cancer per National Comprehensive Cancer Network guidelines may be applied, as this tissue of origin is similar to epithelialized vulvar tissue.[24] Treatment paradigms for resectable vulvar cancers involve radical resection and nodal evaluation, potentially followed by adjuvant radiation or chemoradiation, depending on risk factors.[23] In the setting of cancer of the neovulva, the native lymphatics have been disrupted by gender-affirming surgery, rendering sentinel lymph node assessment inaccurate; hence, inguinofemoral lymph node dissection may yield a more accurate assessment of lymph node status. Unresectable vulvar cancers can be treated with neoadjuvant or, more commonly, definitive chemoradiation. IMRT is recommended to reduce the dose to uninvolved organs at risk.[30]

Anal cancer

Limited data suggest that rates of anal cancer may be higher in transgender populations. In a National Cancer Database study, a greater proportion of anal cancers occurred in transgender individuals compared with cisgender individuals.[31] A study of the New York State Cancer Registry reported a proportional incidence ratio of 29.7 for anal cancer in transgender versus cisgender individuals,[32] which may be related to increased rates of anal human papillomavirus infection and other risk factors in transgender women.[33,34] We have not identified any radiation treatment recommendations for anal cancer in transgender patients. Rague et al. reported on a transgender woman undergoing vaginoplasty and received a diagnosis intraoperatively of anal cancer upon discovering a mass on a digital rectal exam.[35] Frozen section of the mass showed squamous cell carcinoma, and the operation was converted to a vulvoplasty without creating a neovaginal canal to avoid a lengthy recovery before beginning chemoradiation for her anal cancer.

In the treatment of anal cancer, IMRT has been shown to reduce hematologic, gastrointestinal, and dermatologic toxicity.[36] In Radiation Therapy Oncology Group (RTOG) 0529, among 42 female patients, grade 1 vaginal stenosis was reported in 1 patient (2%), and grade 2 vaginal stenosis was reported in 5 patients (12%).[37] Placement of a vaginal dilator during radiation treatment has been shown to reduce the mean vaginal dose in cisgender women undergoing radiation for anal cancer,[38] and limiting the mean vaginal dose to <43 Gy has been associated with reduced severity of vaginal stenosis.[39] As grafts or flaps used to line the neovagina have increased susceptibility to vaginal stenosis, placement of a vaginal dilator or cylinder during treatment may reduce the dose to the anterior neovaginal wall, recognizing, however, that this may not be tolerable for many patients. An alternative is to simulate the patient with and without the dilator in place so that treatment can continue if the dilator becomes intolerable. (Please see the *Patient counseling and radiation treatment planning recommendations* section regarding vaginal dilator counseling and use.)

Elective nodal coverage for anal cancers should routinely include the inguinal and external iliac regions and the mesorectal, presacral, and internal iliac nodes.[28] In treating anal cancer after vaginoplasty, these nodal regions remain at risk, as well as any additional nodal regions identified based on the tissue of origin if the neovagina is at risk, as described previously (Fig. 3). If the neovagina is not at risk, then an early, open discussion should be had with the patient on the significant risk of vaginal stenosis and efforts that can be made to maintain patency during and after treatment.

Rectal cancer

Rectal cancer rates do not appear to differ significantly between transgender and cisgender populations.[31] We are unaware of any previously published reports or recommendations for treating transfeminine people with rectal cancer.

Expected toxicities of radiation treatment for transfeminine patients with rectal cancer will vary based on tumor location. The RTOG 0822 trial evaluated the use of IMRT in chemoradiation for locally advanced rectal cancer. The protocol specified a clinical target volume (CTV) expansion of 1.5 cm radial and 2.5 cm craniocaudal of the rectal gross tumor volume (GTV) and a 0.5 cm planning target volume (PTV) expansion.[40] For upper and midrectal tumors treated with these expansions, it may be possible to spare the majority of the neovagina and the vulva without compromising target coverage (Fig. 4). Although IMRT has not been shown to reduce gastrointestinal toxicity in rectal cancer, RTOG 0822 reported grade 1 vaginal stenosis in 2 of 30 female patients (7%) and grade 2 stenosis in 1 patient (3%). Reducing vaginal dose with IMRT may be particularly beneficial after vaginoplasty as neovaginal tissue is predisposed to vaginal stenosis. For lower rectal cancers, as with anal cancers, placement of a vaginal dilator may decrease the anterior vaginal dose. (Please see the *Patient counseling and radiation treatment planning recommendations* section regarding vaginal dilator counseling and use.)

For rectal cancers, the superior extent of the mesorectal and presacral nodal volume should be at the rectosigmoid junction or at least 2 cm proximal to the superior extent of macroscopic disease, whichever is more proximal.[28] Standard dosing for treatment of rectal cancer is recommended with consideration to minimize dose to the nearby neovagina and vulva.

Prostate cancer

The risk of prostate cancer in transfeminine people on androgen suppression therapy or those who have undergone orchiectomy is low, estimated at 0.04% and increasing to 0.13% for those who began hormone therapy after age 40.[41]

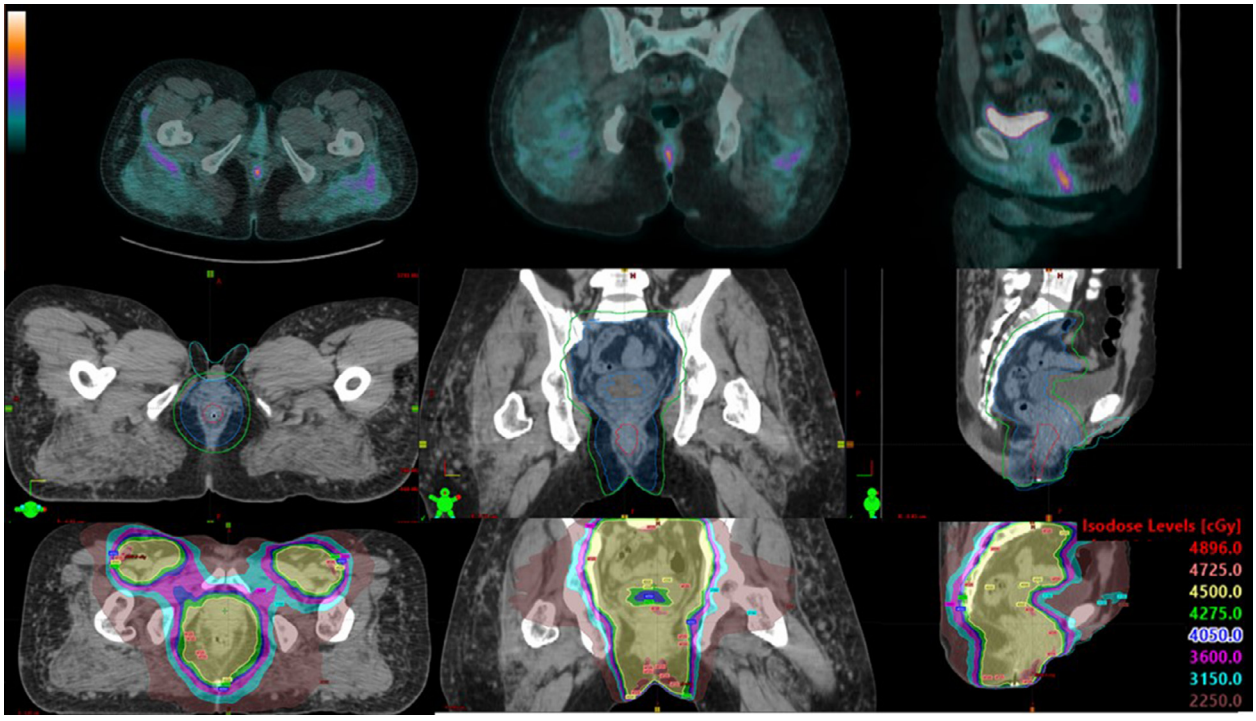

Fig. 3. Diagnostic imaging and graphical treatment plan for a patient with prior vaginoplasty and a cT1N0 anal squamous cell carcinoma treated with definitive chemoradiation. The primary tumor and inguinal, external iliac, internal iliac, presacral, and perirectal nodes were treated to 45 Gy with IMRT. Dose constraints used on the external genitalia were V35 < 50% (actual, 14.1%), V40 < 35% (7.9%), and V50 < 5% (0.0%). Vaginal sparing was not feasible because the neovagina was within the treatment volume, and vaginal dilator placement was not tolerable due to pain. This patient remains alive at 5 years after completing treatment without evidence of disease but with significant vaginal narrowing. Top: Fluorodeoxyglucose positron emission tomography/computed tomography (PET CT) at diagnosis of anal tumor. Middle: Radiation simulation computed tomography (CT) with contours. Red = gross tumor volume (GTV), dark blue = clinical target volume (CTV), green = planning target volume (PTV) 45 Gy, light blue = external genitalia. Bottom: Representative images from radiation treatment plan with isodose lines shown. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

However, the overall risk of death from prostate cancer is increased in transfeminine people (hazard ratio, 1.9), which may be due to more aggressive disease in people on feminizing hormone therapy.[31] Meanwhile, prostate cancer risk in transgender individuals without hormonal therapy is estimated to be comparable to cisgender men. More than 10 cases of prostate cancer in transfeminine patients have been reported in the literature.[42,43]

In formulating treatment recommendations, it is important to consider that prostate cancer that develops in people on feminizing hormone therapy is likely castration-resistant. Thus, patients may be less likely to benefit from androgen deprivation therapy.[43] Additionally, if the prostate size is decreased due to hormone therapy (median of 14 cc in 1 study of transgender women on estrogen therapy),[44] brachytherapy may not be feasible. Patients who have undergone vaginoplasty are at increased risk of rectovaginal or urethrovesico-neovaginal fistula formation with radical prostatectomy and vaginal stenosis after radiation.[45] Studies comparing similar biologically effective doses of conventionally fractionated versus moderately hypofractionated prostate radiation have shown similar rates of late grade 2+ gastrointestinal (GI) and genitourinary (GU) toxicity or reduced GI toxicity with hypofractionation.[46-48] However, these data may not be applicable to the risk of fistula formation for patients undergoing prostate radiation after vaginoplasty.

Due to the close proximity of the neovagina to the prostate and seminal vesicles, there may be an increased risk of neovaginal necrosis within the high-dose region. If the neovaginal apex is formed from bowel, this area should be separately contoured and constrained within bowel tolerances. If adhering to neovaginal dose constraints would compromise target coverage and clinical outcomes, the risks and benefits of target coverage versus protection of neovaginal tissue should be discussed with the patient and their multidisciplinary care team, including their gender-affirming surgeon. Daily image guidance should be used to allow adequate target coverage with the smallest possible margins. Considering these factors, conventional or moderately hypofractionated radiation may be preferable to SBRT or brachytherapy after vaginoplasty, but further studies are necessary. Rectal spacers have been shown to reduce GI toxicity in cisgender

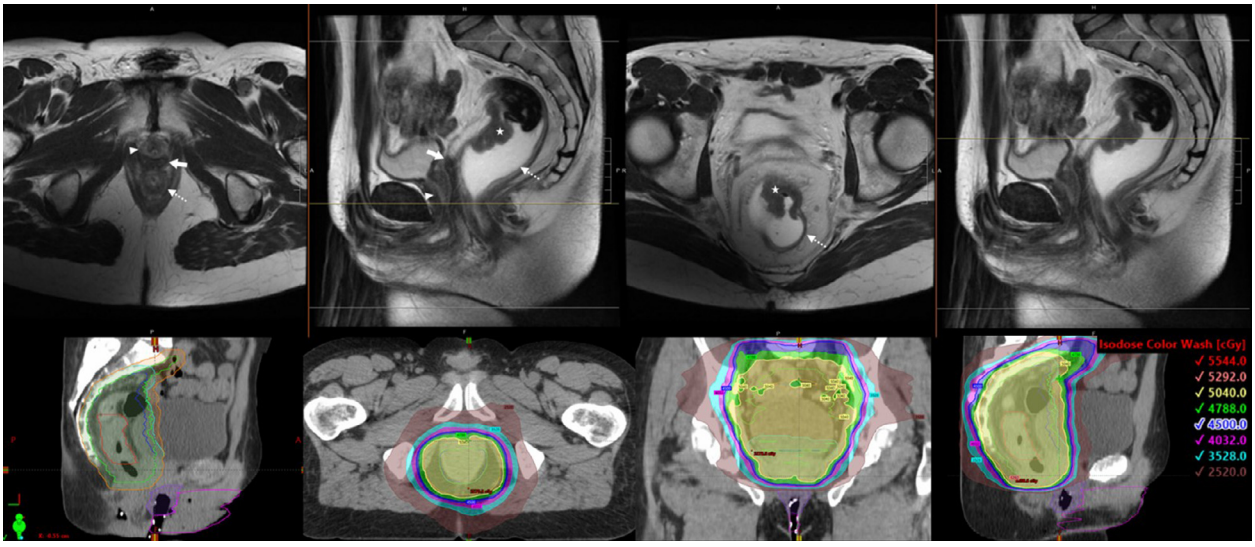

Fig. 4. Diagnostic imaging and graphical treatment plan for a patient with prior vaginoplasty and a cT3N1 rectal adenocarcinoma treated with chemoradiation, low anterior resection and transanal mesorectal excision, and adjuvant chemotherapy. The patient was treated with IMRT to 45 Gy to the pelvis with a 5.4 Gy cone down boost. The inferior aspect of the gross tumor volume (GTV) was approximately 5 cm from the anal verge, and the clinical target volume (CTV) was expanded 2 cm inferiorly with a 7 mm planning target volume (PTV) expansion, resulting in only the neovaginal apex being adjacent to the full dose region. Dose to genitalia was minimized (external genitalia mean <30 Gy, actual 3.2 Gy, neovagina mean <35 Gy, actual 11.8 Gy). She continued estrogen therapy, and at 44 months after completing radiation, this patient is alive without evidence of disease. She uses a vaginal dilator weekly, and her neovaginal depth decreased from 14 to 12.7 cm, but dilator diameter/size has not changed. Top: T2 weighted MRI at diagnosis of rectal tumor located at 7 to 12 cm from the anal verge (arrowhead: prostate; solid arrow: neovagina; dashed arrow: rectum; asterisk: tumor). Bottom left: Sagittal image of radiation simulation computed tomography (CT) with contours. Red = GTV, dark blue = CTV 50.4 Gy, light blue = PTV 50.4 Gy, green = CTV 45 Gy, orange = PTV 45 Gy, purple = neovagina, pink = genitalia. Bottom right: Representative images from radiation treatment plan with isodose lines shown. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

men undergoing prostate radiation;[49,50] however, patients with prior anorectal surgery or urogenital abnormalities have been excluded. In the case of prior vaginoplasty, rectal spacer placement between the prostate and anterior neovaginal wall is likely impractical due to fibrosis caused by the creation of the neovaginal canal; however, such investigations have not been performed to our knowledge.

For patients considering gender-affirming surgery after prostate cancer treatment, the risk of rectal injury or fistula with vaginoplasty is significantly increased after radical prostatectomy or radiation due to scarring in the rectoprostatic space where the neovagina would be constructed.[11,45] Vaginoplasty after radical prostatectomy would increase the risk of urinary incontinence and be more difficult to manage, as artificial sphincter placement is not an option after removing the corpus spongiosum.[45] Conversely, prostate surgery or radiation are not contraindications to vulvoplasty or gender-affirming orchiectomy.

Additionally, monitoring for prostate cancer recurrence after radical prostatectomy or radiation has not been studied in transgender patients. The reliability of prostate-specific antigen (PSA) monitoring for recurrence in patients who develop prostate cancer in a low androgen state due to gender-affirming hormone therapy or orchiectomy has not been established. Elevated PSA at diagnosis has been reported for transgender patients on hormone therapy,[42] suggesting that PSA surveillance may benefit such patients. Magnetic resonance imaging to identify local recurrence may also be challenging to interpret after vaginoplasty, particularly if baseline imaging is unavailable.

Bladder cancer

Bladder cancer rates are known to differ based on biologic sex, with lower incidence in cisgender females than cisgender males.[51] Although the main known risk factor for bladder cancer is tobacco smoking, sex-based differences persist when controlling for smoking status.[52] There are limited data to suggest that estrogen may inhibit bladder carcinogenesis and androgen-androgen receptor signaling may be involved in experimental models of bladder carcinogenesis.[53]

In a National Cancer Database study, rates of bladder cancer for transgender populations appear to lie between the rates for cisgender females and cisgender males; however, there may be an increased risk of death from bladder cancer in transgender people (hazard ratio, 2.9).[31] We are

not aware of published case reports of bladder cancer in transgender patients. Further studies are necessary to understand the role of sex hormones in bladder cancer and the management of bladder cancer in transgender patients. Due to the lack of existing published cases of bladder cancer in transgender patients, recommendations are limited. At a minimum, care must be taken to reduce the dose to uninvolved sexual organs while maintaining the dosing and elective nodal coverage required to treat bladder cancer effectively.

Pelvic metastatic disease

Patients may also present with pelvic metastases in proximity to surgically reconstructed tissues. We have not identified any case reports on managing pelvic metastasis in transgender patients. When treating metastatic disease for symptom management, it is appropriate to adhere to general principles of palliative radiation, including the use of hypofractionated regimens and simple patient setup and treatment planning.[54] When treating pelvic metastatic disease to definitive doses, considerations are similar to those for primary pelvic cancers, including obtaining MRI and PET CT imaging, when possible, to identify tumor and normal structures, determining the tissue of origin and dose tolerance of surgically reconstructed tissues, and using techniques such as vaginal dilator placement, IMRT, and image guidance to reduce dose to normal tissue.

Patient counseling and radiation treatment planning recommendations

We offer the following recommendations when considering pelvic radiation in transfeminine patients (Table 1). First, when a patient is referred for consultation to a cancer center with specialized gynecologic, gastrointestinal, and genitourinary services, the multidisciplinary oncology team should discuss which service is best suited to treat the patient. Considerations include physician expertise with the patient's primary tumor type and pelvic anatomy, team experience with techniques such as vaginal dilator placement, when relevant, and patient comfort with the assigned service (eg, a transgender woman may feel uncomfortable having a team that specializes in treating "Men's cancers"). Moreover, care teams for all disease site services should receive training to provide inclusive care for transgender patients. The patient's history of gender-affirming surgery and any future goals should be reviewed during consultation and treatment consent discussions. Patients considering future surgery should be made aware that they will likely be unable to undergo full-depth vaginoplasty after pelvic radiation due to scar tissue formation and high risk of rectovaginal or urethro-vesico-vaginal fistula; meanwhile, orchiectomy and vulvoplasty may still be possible. For patients with a neovagina, consent discussions should include the risk of vaginal stenosis, increased complication risk or inability to undergo future surgical revisions, and the likely need for ongoing vaginal dilator use. Patients should be asked about any reproductive

Table 1 Summary of recommendations for a systematic approach to patient care, counseling, and radiation treatment planning

Category	Recommendations
Consultation	• Determine the appropriate multidisciplinary team/disease center best suited to meet the patient's needs • Review patient's history of gender-affirming surgery • Discuss any future goals for gender-affirming therapy • Discuss reproductive goals, if any, and refer to respective reproductive team(s)
Radiation consent discussions	• Risk of vaginal stenosis • Need for ongoing vaginal dilator use • Increased risk of complications with future genitopelvic surgeries • Potential contraindication to some surgeries (ie, full-depth vaginoplasty)
Patient counseling	• Offer counseling about sexual health effects of pelvic radiation • Ask if patients have preferred terminology for describing their genitopelvic anatomy • Ask which forms of sexual function, if any, are important to your patient including penile erectile function, ejaculatory function, neoclitoral sensation, neovaginal intercourse sensation, and anal intercourse sensation • Discuss anticipated toxicities, as relevant to your patient, including erectile dysfunction, ejaculatory dysfunction, diminished penile, neoclitoral, or prostatic sensation, vaginal stenosis, and anorectal ulceration or stenosis • Discuss risk/benefits of initiation or continuation of feminizing hormones
Radiation treatment planning	• Fuse pelvic MRI and PET CT images to simulation CT to define tumor and genital anatomy • Minimize radiation dose to surgically reconstructed tissues, when possible, through placement of vaginal dilator during simulation and treatment, contouring and dose constraints for genital tissues, and IMRT planning
Multidisciplinary care	• Engage with patient's transgender health team including medical specialists, surgeons, behavioral health providers, and support groups

goals and, if relevant, be referred to appropriate reproductive teams.

Patients should also be offered counseling about the sexual health effects of pelvic radiation. We approach these conversations with the knowledge that patients who experience gender incongruence or dysphoria[55] may have preferences about the language used to describe gendered body parts. For discussions regarding sexual function, and in other discussions around genitopelvic anatomy, it is best to ask if there are terms that patients would like for their medical team to use in describing their genitopelvic anatomy. Clinicians should ask patients which forms of sexual function, if any, are important to them, including penile erectile function, ejaculatory function, neoclitoral sensation, neovaginal intercourse sensation, and receptive anal intercourse sensation. This information should be used to provide relevant counseling about the expected effects of cancer treatments, potentially including erectile dysfunction, ejaculatory dysfunction, climacturia, anodyspareunia, vaginal stenosis, as well as diminished penile, neoclitoral, or prostatic sensation.

Before radiation planning, we recommend thoroughly reviewing prior genitopelvic gender-affirming surgery notes and available imaging with the patient's gender-affirming surgeon and a radiologist. An MRI pelvis with vaginal contrast or vaginal marker can be helpful to better define anatomy post vaginoplasty. PET CT can also be useful for cancers of the neovagina to identify primary and regional disease. When feasible, placement of a vaginal dilator during radiation treatments may be beneficial to reduce the dose to the anterior vaginal wall in patients treated for rectal or anal cancer.[38] Importantly, it is critical to reinforce with patients the importance of regular dilator use during and after radiation. Early intervention with pelvic floor physical therapy may be beneficial if dilator use is challenging. Patients may also benefit from regular follow-up visits with a sexual health provider knowledgeable in postradiation sequelae.

With respect to radiation treatment planning, the fusion of pelvic MRI and PET CT with the simulation CT is useful to better delineate the neovagina and other genital structures. Given that the blood supply to surgically reconstructed genital tissues is likely less robust than natal tissues, an attempt to minimize radiation dose to these structures should be made with the goal of reducing the risk of late toxicities. Currently, there are no established guidelines on dose constraints for reconstructed genital/pelvic tissues; thus, one must generally extrapolate from available normal tissue contouring resources and attempt to minimize dose to the neovagina and external genitalia, when achievable, without compromising target coverage. Such resources include the RTOG/NRG pelvic normal tissue contouring guidelines, which recommend contouring the penile bulb as an organ at risk but do not include any female genitopelvic organs;[56] anal cancer contouring guidelines, which recommend contouring and limiting dose to the external genitalia;[57,58] and bulboclitoris contouring recommendations that have been developed for sparing the bulboclitoris in anal cancer radiation.[59]

Finally, engaging the patient's gender-affirming health care team from initial diagnosis through treatment and survivorship is critical. This may include surgeons, medical specialists trained in transgender health, behavioral health care providers, and support groups. Engaging in a multidisciplinary discussion of the risks and benefits is important for patients who have been on or are interested in feminizing hormone therapy. Although both malignancy and exogenous estrogen increase the risk of thromboembolism, this must be weighed against the substantial benefits of hormone therapy on mental health and quality of life.[60] Through a thoughtful approach, transfeminine people receiving pelvic radiation can receive inclusive and intelligent care that will allow for appropriate treatment of their cancer while maintaining their other gender-affirming care needs and, importantly, respecting the patient's identity and dignity.

In light of the limited available data on radiation treatment for transgender people with cancer, future research should prioritize multi-institutional experiences with radiation treatment in patients who have undergone gender-affirming surgery, as well as the inclusion of transgender people in clinical trials. This will require a thoughtful design of trial inclusion and exclusion criteria (eg, inclusion criteria that specify "men with prostate cancer" would exclude transgender women). Radiation treatment recommendations are also needed for transmasculine people who have undergone gender-affirming genitopelvic surgeries. We suggest that the American Society for Radiation Oncology (ASTRO) Health Equity Diversity and Inclusion Council consider forming a working group or task force to promote the inclusion of transgender people in radiation oncology research and build a formal process for developing and refining treatment guidelines as more data become available.

Conclusion

Transfeminine people with cancer who have undergone or are planning to undergo gender-affirming genitopelvic surgeries have unique treatment needs and considerations. Radiation oncologists should be aware of common gender-affirming genitopelvic surgeries. They should be able to take a comprehensive history, understand their patient's gender affirmation goals, and use this information to inform the overall treatment plan. Patients should be counseled about anticipated radiation risks to surgically reconstructed tissues and any implications for future gender-affirming care. When possible, a systematic approach to radiation planning should include a thorough review of prior operative notes, diagnostic imaging, patient history, and patient anatomy with the patient's gender-affirming surgeon and a radiologist. Surgically reconstructed tissues, such as the neovagina and neoclitoris, should be contoured, and efforts should be made to limit radiation dose to these structures when uninvolved. Patients may benefit from involvement of their

gender-affirming health care team throughout their cancer treatment and survivorship.

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