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Interstitial brachytherapy in the treatment of advanced and recurrent vulvar cancer

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OBJECTIVE: Our purpose was to evaluate the role of interstitial brachytherapy in vulvar cancer management.

STUDY DESIGN: From 1985-1992 we performed a retrospective study of patients treated at the University of California, Irvine Medical Center, and Long Beach Memorial Medical Center.

RESULTS: Eleven patients received interstitial brachytherapy, with (n = 5) or without (n = 6) external beam radiotherapy, for locally advanced (n = 5) or recurrent (n = 6) vulvar cancer. Local control was achieved in all patients. Ten patients have died of disease at a mean interval of 33 months from the time of treatment, with 9 patients having maintenance of local control at death. One patient is alive without disease after 77 months of follow-up. There were 2 cases of local necrosis (18%) and 1 case of rectovaginal fistula (9%).

CONCLUSION: Local control of advanced vulvar cancer can be achieved with interstitial brachytherapy, with or without external beam radiotherapy. With improved systemic therapy this treatment modality may be used to salvage women with bulky, symptomatic tumors. (Am J Obstet Gynecol 1999;181:91-8.)

Key words: Interstitial brachytherapy, vulvar cancer

With the advancing age of our female population and the attendant large increase in the number of older women, the incidence of vulvar cancer has increased and now accounts for approximately 8% of all gynecologic malignancies.[1] In many series the majority of patients are >70 years old at the time of diagnosis. Up to 50% of patients have advanced disease at presentation, with involvement by direct extension to adjacent structures, including the vagina, urethra, and anus, and by lymphatic embolization to regional groin lymph nodes.[1] Hematogenous dissemination to the liver, lungs, and bones may occur.

Management in cases of locally advanced or recurrent cancer of the vulva has consisted of limited resection, exenterative surgery, primary radiotherapy, or a combination radiotherapeutic and surgical approach. In recent years the use of chemotherapy as a radiosensitizer has also been examined in vulvar cancer treatment programs. Although local control of advanced or recurrent cases of vulvar cancer may be achieved by means of these techniques, with varying degrees of morbidity, often the remission is short-lived. In addition, the survival rate of patients with clinically involved groin nodes is poor, and in patients with pelvic nodal metastases or distant disease, long-term survival is uncommon.

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The clinical problem and review of the literature

In 1956 Brunschwig and Daniel[2] reported a 47% operative mortality rate among 27 patients treated with exenterative surgery for advanced vulvar cancer. With accumulated experience the operative mortality rate has decreased. Indeed, in the early 1970s Boronow[3] calculated a 16% postoperative mortality rate from a review of 227 exenterative procedures for vulvovaginal cancer from the literature; survival at 5 years, however, was only 15%. In 1982, Cavanagh and Shepherd[4] recorded a 47% 5-year survival rate with exenterative surgery but found the high level of morbidity to be unacceptable. The ability of elderly patients (often with debilitating medical illnesses) to tolerate extensive surgery is limited. Additionally, quality-of-life assessments need to be made regarding extirpative procedures, which often necessitate removal of either bladder or rectal viscera, or both. Nevertheless, it is clear that radical surgery offers carefully selected patients the potential for cure.

Earlier in this century primary radiation therapy for vulvar cancer fell into disrepute when Stoeckel[5] and Tod[6] reported 5-year survival rates of only 12% to 25%.

Table I. Medical considerations in this series

Patient No.	*Age (y)*	*Medical history*
1	66	Chronic brain syndrome
2	75	Hypertension
3	69	Hypertension
4	77	Chronic obstructive pulmonary disease
5	59	Congestive heart failure
6	66	Hypertension
7	86	Chronic brain syndrome
8	71	Coronary artery disease
9	58	Hypertension
10	64	Diabetes mellitus, obesity
11	54	Hypertension

In the late 1960s and early 1970s essayists from the Continent suggested that survival in cases of advanced disease may approach 40% at 5 years, with the use of external beam radiation therapy.[7] More contemporary reports have confirmed that with modern radiotherapeutic treatment modalities external beam radiotherapy with or without chemotherapy can be successfully used in the primary management of patients who are not candidates for operation or in an effort to reduce tumor volume and thereby permit less extensive surgery in patients with locally advanced disease.[8-10] However, because the entire vulvar surface and consequently the large number of end arteries receive a full dose of radiation, the vulva is predisposed to the development of vasculitis. This often results in acute moist desquamation and pain, necessitating interruption of therapy.

Treatment of recurrent vulvar cancer presents a greater problem, because the blood supply and lymphatic drainage of the remaining tissue after radical vulvar surgery often are compromised. The anatomy is frequently altered, making surgical and radiotherapeutic approaches more complex and less successful. In addition, patients with recurrent lesions who received external beam radiotherapy as part of primary management often cannot undergo reirradiation because the bladder and rectum have already accumulated a maximal tolerable dose of radiation. Finally, although brachytherapy may permit the application of a radiation boost to the vulva, conventional intracavitary techniques may not be feasible for deeply infiltrating tumors or bulky lesions with complex geometric appearances.

Proposal of an alternative

In an effort to avoid extensive surgery in medically infirm patients and because of the occasional need to reirradiate those with relapse, the radiation oncology department and gynecologic oncology division of Women's Hospital at Long Beach Memorial Medical Center and the University of California, Irvine Medical Center began using interstitial irradiation in the management of locally advanced and recurrent vulvar cancer.

Interstitial brachytherapy permits the precise application of doses of radiation to a particular tumor volume, thus resulting in a homogeneous radiation field with differential sparing of the bladder and rectum. The placement of these radioactive sources by afterloading techniques may result in durable local control, which is superior to that obtained with intracavitary devices or external beam radiation therapy alone. To date, however, there have been no randomized trials to test this hypothesis.

Treatment of locally advanced or recurrent squamous cell carcinomas of the vagina and of the uterine cervix with interstitial brachytherapy has resulted in complete responses, many of which are long-lasting.[11-13] Additionally, in the management of epidermoid anal cancer, the use of interstitial irradiation has resulted in durable local control and survival at 5 years of follow-up.[14] In these clinical scenarios interstitial irradiation has generally been combined with external beam radiotherapy.

The prototype of this series, a 66-year-old white woman in poor health, came to our urgent clinical attention in 1985 with a massive squamous cell carcinoma of the vulva 10 cm in diameter that had spread to involve the rectovaginal septum and the right inguinal lymph nodes. For clearance of the surgical margins, a posterior exenteration and lymphadenectomy would have been necessary. So that extensive surgery could be avoided in this frail patient, she was treated with bilateral inguinal lymphadenectomy, followed by postoperative external beam radiotherapy and interstitial irradiation.

We describe our technique of interstitial brachytherapy in the treatment of vulvar tumors and summarize our experience in treating locally advanced and unresectable recurrent vulvar cancers. Finally, we review algorithms used in the treatment of advanced vulvar cancer at the University of California, Irvine Medical Center and Women's Hospital of Long Beach Memorial Medical Center.

Material and methods

From 1985 to 1992, patients treated at the University of California, Irvine for locally advanced or recurrent vulvar cancer were identified and retrospectively reviewed. All patients were treated with interstitial irradiation. Included in this case series are 2 patients with advanced malignant melanoma of the vulva. Excluded from this series are those patients who received chemotherapy as a radiosensitizer and those patients who had a relapse only at a distant site.

Patient profiles. Eleven patients with locally advanced or recurrent vulvar cancer received interstitial brachytherapy, with or without external irradiation. The median age was 67 years (range, 54-86 years). The medical profiles of these patients are recorded in Table I.

Three groups were treated: group 1, with locally advanced squamous cell carcinoma (n = 4); group 2, with

Table II. Group 1: Primary locally advanced squamous cell carcinoma of vulva

Patient No.	*Age (y)*	*Diagnosis*	*Tumor description**	*Treatment*	*Positive nodes*
1	66	Stage III, grade 2	10 × 7 cm, labia majora, rectovaginal septum; lateralized lesion	Bilateral inguinal lymph node dissection, external beam radiation therapy, iridium 192 interstitial implant	Right inguinal
2	75	Stage III, grade 2	5 × 5.5 cm, labia majora, anal sphincter	Bilateral inguinal lymph node dissection, external beam radiation therapy, iridium 192 interstitial implant	Right inguinal
3	69	Stage IVA, grade 2	5 × 5.5 cm, labia majora, distal urethra, vaginal sidewall, pelvic bone	Bilateral inguinal lymph node dissection, external beam radiation therapy, iridium 192 interstitial implant	Right inguinal
4	77	Stage IVA, grade 2	6 × 7 cm, labia majora, rectovaginal septum	Bilateral inguinal lymph node dissection, external beam radiation therapy, iridium 192 interstitial implant	Bilateral inguinal

*Patients 2, 3, and 4 had central lesions.

Table III. Group 2: Recurrent squamous cell carcinoma of vulva

Patient No.	*Age (y)*	*Positive nodes**	*Tumor description†*	*Treatment‡*
5	59	Right inguinal	5 × 5 cm, perineal relapse, ischiorectal fossa, lung and liver metastases	Iridium 192 interstitial implant
6	66	Right inguinal	9.5 × 6 cm, urethral relapse	Iridium 192 interstitial implant
7	86	Left inguinal	5 × 8 cm, perineal relapse	Iridium 192 interstitial implant
8	71	Right inguinal	6 × 8 cm, urethral relapse	Iridium 192 interstitial implant
9	58	Bilateral inguinal	5 × 6 cm, urethral relapse	Iridium 192 interstitial implant

*Nodal status at time of recurrence.
†These patients had central lesions.
‡These patients underwent radical vulvectomy, bilateral inguinal lymphadenectomy, and external beam radiotherapy as part of primary treatment.

recurrent squamous cell carcinoma (n = 5); and group 3, with malignant melanoma (n = 2).

All 4 patients in group 1 had locally advanced disease at presentation, with clinically involved inguinal lymph nodes. The first patient (the prototype of our series) had a massive lateralized carcinoma involving the rectovaginal septum and clinically involved right inguinal lymph nodes. Surgical resection in this patient would have necessitated removal of part of the rectum. Three patients had central tumors that were considered locally unresectable without sacrifice of either the rectum or the bladder, or both. All 4 patients underwent treatment by bilateral inguinal lymphadenectomy, external beam radiotherapy, and interstitial irradiation. These data are summarized in Table II.

All 5 patients in group 2 had originally been treated by radical vulvectomy, bilateral inguinal lymphadenectomy, and external beam radiotherapy (mean dose, 52 Gy). Each patient subsequently had relapse in the surgical bed with a central lesion. In addition, each of these patients had clinically involved inguinal nodes at the time of recurrence. All 5 patients were treated with interstitial irradiation. These data are summarized in Table III.

The 2 patients in group 3 with malignant melanoma of the vulva were treated as follows. The first patient had a 7 × 7-cm central tumor involving the distal urethra and palpably enlarged inguinal lymph nodes. After a limited surgical excision, the patient received external beam and interstitial irradiation. The second patient originally underwent modified radical vulvectomy, bilateral inguinal and pelvic lymphadenectomy, and external beam radiotherapy. She had a relapse with a lateralized lesion and palpably enlarged inguinal lymph nodes and was treated with interstitial irradiation. Both patients in this group were treated with hyperthermia for 1 hour at 42.2°C in conjunction with interstitial brachytherapy. These data are summarized in Table IV.

Thus a total of 5 patients received interstitial brachytherapy as part of primary therapy of locally advanced disease (4 squamous cell carcinomas, 1 malignant melanoma). Of these 5 patients, 3 had International Federation of Gynecology and Obstetrics (FIGO) stage III tumors and 2 had FIGO stage IVA tumors. Six patients were treated for recurrent disease (5 squamous cell carcinomas, 1 malignant melanoma). Four of these patients originally had FIGO stage III disease, and 2 initially had

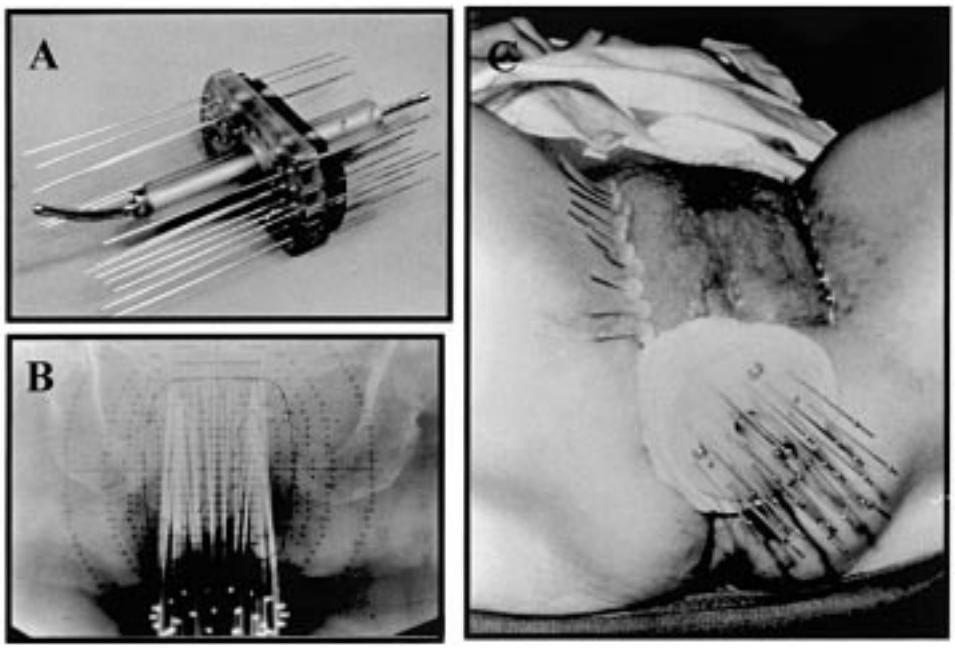


Fig 1. Interstitial implant for locally advanced vulvar cancer. **A,** Interstitial implant created with Syed-Neblett dedicated vulvar plastic template and 17-gauge hollow stainless steel guide needles. **B,** X-ray localization film demonstrating position of guide needles. **C,** Massive tumor involving perianal region and mons pubis with lateral extension. Satisfactory implant technique required both hollow plastic tubes and vulvar template with guide needles.

Table IV. Group 3: Malignant melanoma of vulva

Patient No.	*Age (y)*	*Diagnosis*	*Tumor description*	*Treatment*
10	64	Stage III	7 × 7 cm, labia minora, urethral involvement	Excision, external beam radiation therapy, iridium 192 interstitial implant
11*	54	Stage IVA†	8 × 5 cm, vaginal relapse, lateralized lesion; urethral involvement; lung, liver, bone metastases	Iridium 192 interstitial implant

*Patient 11 underwent modified radical vulvectomy, bilateral inguinal and pelvic lymphadenectomy, and external beam radiotherapy at the time of primary treatment (inguinal nodes positive, bilaterally; pelvic nodes negative, bilaterally).
†Original FIGO stage before recurrence.

FIGO stage IVA disease. The 4 FIGO stage IVA cancers were classified as such because of pelvic bone involvement (n = 2), bilateral inguinal node involvement (n = l), or both (n = l).

All squamous cell carcinomas were moderately differentiated. Tumors 5 to 10 cm in diameter (mean, 7.2 cm) were treated. All patients had clinically involved inguinal lymph nodes at presentation, which were confirmed on pathologic analysis to contain metastatic disease.

Summary of radiotherapy. External beam radiotherapy was administered before interstitial irradiation to the 5 patients who were treated for advanced primary disease. With the use of a linear accelerator, teletherapy was administered via parallel and opposed portals, encompassing the groins and pelvic sidewalls. In general, radiation therapy was given during a 28-day period at a dose of 1.8 Gy/d, 5 days a week.

Interstitial brachytherapy was administered to the 9 patients with central lesions by means of a transperineal Syed-Neblett dedicated vulvar template. The implant was created with multiple 17-gauge stainless steel guide needles, inserted transperineally through the template into the tumor-bearing regions of the vulva (Fig l, *A*). The implants were individualized with respect to the number of guide needles and depth of insertion.

After needle placement, x-ray localization films with inactive dummy sources were obtained (Fig 1, *B*) and isodose curves were generated. The placement of radiopaque contrast material in the rectum and a Foley catheter balloon permitted calculation of the radiation dose that would be received by the rectum and bladder. Radioactive iridium 192 seeds were afterloaded into the guide needles, and the prescription dose of minimum radiation was given to the perimetry of the radiated field. Regions encompassed by the isodose curves received a higher dose of radiation.

Table V. Interstitial brachytherapy: Dosimetry, response, and outcome

Patient No.	*Dose (cGy)*	*Needles*	*Seeds*	*Activity**	*Duration (h)*	*Dose (mCi)*	*Complications*	*Local control*	*Status*	*Survival time (mo)†*
Group 1: Primary locally advanced squamous cell carcinoma										
1	5500	11	89	0.371	92	68.1	None	Achieved	Died of disease	10
2	2360	22	110	0.412	22	93.5	None	Achieved	Died of disease	35
3	2800	32	256	0.281	40	148.4	Necrosis	Achieved	Died of disease	46
4	3000	25	250	0.267	50	137.7	Necrosis	Achieved	Died of disease	23
Group 2: Recurrent squamous cell carcinoma										
5	2500	8	56	0.350	46	40.4	Fistula	Achieved	Died of disease	46
6	3000	17	102	0.305	51	64.2	None	Achieved	Died of disease	42
7	3000	13	78	0.305	50	49.1	None	Achieved	Died of disease	42
8	3000	25	150	0.300	38	92.8	None	Achieved	Died of disease	64
9	3000	17	102	0.300	43	63.1	None	Achieved‡	Died of disease	8
Group 3: Malignant melanoma (interstitial implants with 1 h of 42.2°C hyperthermia)										
10	3500	11	77	0.281	64	44.6	None	Achieved	No evidence of disease	77
11	5400	26	323	0.267	96	177.9	None	Achieved	Died of disease	10

Patients 1, 2, 3, 4, and 10 received external beam radiation therapy as part of the treatment program for advanced disease. Patients 4, 5, 6, 7, 8, 9, and 11 had previously received external beam radiation therapy as part of primary therapy.
*Activity per seed in milligram radium equivalents.
†Survival time calculated from time of diagnosis (patients 1-4, 10) or from time of recurrence (patients 5-9, 11).
‡Local control maintained for 8 months.

Two patients (Nos. 1 and 11) had lateralized lesions at presentation that extended beyond the regions encompassed by the Syed-Neblett dedicated vulvar template. Therefore a satisfactory implant was created for these 2 patients, with the use of both the vulvar template and plastic tubes threaded over guide needles through the lateral regions of the tumor (Fig 1, *C*). After computerized dose distribution plotting and volume analysis, both the plastic tubes and the template needles were afterloaded with the radioisotope iridium 192.

Results

The mean teletherapy dose administered to the 5 patients who were treated for primary disease was 50.4 Gy. Characteristics of the interstitial implants, outcome of treatment, and survival are summarized in Table V. The mean interstitial tumor dose administered with the dedicated vulvar template was 2866 cGy (range, 2360-3500 cGy). The average number of hours that the radioactive sources were in place was 44 hours (range, 22-64 hours). The 2 patients who also received interstitial irradiation by means of both the dedicated vulvar template and the laterally placed plastic tubes received tumor doses of 5400 and 5500 cGy. Radioactive sources with this technique were left in place for >90 hours in each patient. The mean interstitial dose was 79.02 mCi (vulvar template) and 23.0 mCi (plastic tubes). All interstitial implant procedures were well tolerated by the patients. There were no cases of moist desquamation or other acute local toxic effects.

Patients were followed up for a mean of 37 months (range, 8-77 months) from the time of presentation with either locally advanced primary or recurrent disease. There were 2 cases (18%) of local necrosis attributable to radiation therapy, one of which required surgical debridement. One patient (9%) had severe treatment-related morbidity consisting of a rectovaginal fistula.

Local control at the perineum was achieved in all 11 patients. Local control in excess of 2 years (range, 2-6 years) was maintained in 9 patients (82%). In 1 patient treatment failed locally, and a relapse within the radiation field occurred 8 months after treatment with interstitial brachytherapy.

Despite local perineal control, 10 patients (91%) have died of disease at a mean interval of 33 months from the time of treatment (range, 8-64 months). Six of these patients died with widespread metastases, and 4 died of recurrent and progressive disease within the pelvis. One patient remained without evidence of disease at a 77-month follow-up.

Comment

Because cancer of the vulva is a relatively uncommon clinical entity, there are no large series from which to draw definitive conclusions as to what constitutes optimal management for advanced disease. Published works report on experiences in which, for the most part, treatment has been individualized and has resulted in a variety of therapeutic modalities implemented within a given case series. Thus the algorithm for advanced or recurrent vulvar cancer management is devoid of consistency, clarity, and linearity. Although we were not encouraged by the poor survivorship among patients in the current series, it is our opinion that any contribution to an incomplete decision tree may potentially be useful.

In developing a treatment program for patients with locally advanced primary and recurrent vulvar malignancies, the goal of therapy needs to be carefully defined.

Prognosis is poor for patients who have clinically involved groin lymph nodes at presentation. In addition, groin node relapses are usually fatal. In many cases only local control of massive symptomatic vulvar lesions (eg, urethral obstruction, infection, bleeding) may be accomplished. Thus palliation would be the end point and not necessarily a cure. This also holds true for women with bulky vulvar disease with concurrent distant metastases. Interstitial brachytherapy should provide sufficient comfort even when used primarily as palliative therapy because patients can have relief of ulcerative symptoms and tumor drainage; in this series all procedures were well tolerated.

Our data clearly demonstrate that local control of advanced vulvar cancer can be achieved with interstitial brachytherapy. Local control was maintained in 9 patients for >2 years, and these patients ultimately died with disease outside the radiation field. It is difficult to separate the contribution to local control provided by external beam radiotherapy in the 5 patients treated with combined external beam and interstitial irradiation for locally advanced primary disease. However, it is likely that acute local toxic effects may have been unacceptable if only external beam irradiation had been used in the management of these large lesions. Similarly, electron therapy would have resulted in significant local toxic effects because the skin receives a higher dose with this radiation technique, thus preventing the administration of a sufficient tumor dose. Permanent implants represent a form of brachytherapy potentially applicable to the treatment of vulvar lesions but do not allow for control of the radioactive sources or dose distribution, which is important in limiting radiation exposure to the surface. Finally, the complex tumor geometric types that we encountered were considered suitable for a tailored and individualized interstitial brachytherapy approach.

It is of interest that 6 patients with recurrent disease received only interstitial irradiation, and local control in excess of 3½ years was achieved in 4. Especially noteworthy is the fact that, although the 6 recurrences constituted retreatments (external beam radiation therapy had been used in the primary disease setting), only 1 patient had severe treatment-related morbidity.

The use of interstitial irradiation in the management of vulvar cancer is not a new concept. Reporting on 26 patients treated at Catholic University Medical Center in Rome, Carlino et al[15] found interstitial brachytherapy to be an effective complement to surgery. Prempree and Amornmarn[16] published their experience in managing recurrent vulvar cancer with interstitial brachytherapy alone or in combination with external beam radiation therapy. They observed 100% disease-free survival at 5 years in 8 patients with limited recurrences; however, only 4 of 13 patients with extensive recurrences responded to interstitial irradiation. Finally, in a report of 11 patients treated with interstitial brachytherapy for vulvar or distal vaginal malignancy, Hoffman et al[17] recorded disease-free survival ranging from 1 to 4 years for the 5 patients with vulvar cancer. Four of the patients had severe perineal radionecrosis. In contrast to our series, none of the patients included in the Hoffman article had pathologically involved inguinal lymph nodes, and none had FIGO stage IV disease at presentation.

As in cases of locally advanced squamous cell carcinomas of the vulva, there exists no general consensus on therapy for locally advanced malignant melanoma of the vulva. The use of interstitial radiotherapy for these malignancies has not been described previously. Because the only long-term survivor in our series was 1 of 2 patients with advanced malignant melanoma of the vulva, we remain optimistic in treating forthcoming cases in a similar manner.

During the preceding quarter century, 2 therapeutic alternatives to exenterative surgery for locally advanced primary and recurrent carcinoma of the vulva have been introduced. Boronow[3] has spent considerable time examining this clinical problem and, in 1973, proposed a combined surgical and radiotherapeutic approach. At the Mississippi Baptist Medical Center, his treatment program consisted of radical vulvectomy with or without bilateral inguinal lymphadenectomy to treat the external genital phase of the disease, combined with external beam radiotherapy or intracavitary brachytherapy, or both, to treat the internal genital phase, with adequate overlap of the fields to protect the surgical margins. The rationale was that the cancer and its dual regional spread patterns would be treated, while at the same time both the bladder and rectum would be preserved. During the succeeding years, Boronow et al[18, 19] periodically reviewed their results and, at the time of their last published communication, had treated a total of 48 patients, with a projected overall 5-year survival rate of 72% for the study population. Certainly, the low incidence of clinically or pathologically involved inguinal-femoral lymph nodes among their cases contributed substantially to their impressive results.

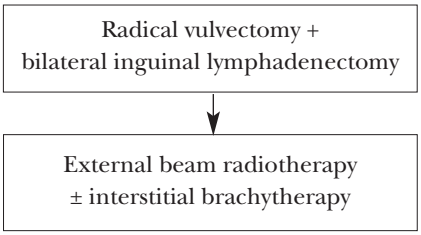
The impact of chemoradiation on vulvar cancer treatment programs has been evaluated in recent years. Both single-institution experiences and preliminary results from the ongoing Gynecologic Oncology Group Protocol 101 cooperative trial have been encouraging.[20-24] External beam therapy with synchronous radiopotentiating chemotherapy (usually 5-fluorouracil) may obviate the need for exenteration or extensive surgery in patients whose medical conditions preclude surgery. Although the responses are usually prompt and dramatic, they are often not sustained. Furthermore, long-term results with chemoradiation have been disappointing, both for local control and for survival, especially in patients with metastases to the inguinal lymph nodes.

At the University of California, Irvine, we constructed 3 treatment algorithms to manage locoregional advanced or recurrent carcinoma of the vulva. Common to each is the use of interstitial brachytherapy to provide a radiation boost to the perineum (if needed) to effect local control. In addition, for elimination of the hazards of operating in a previously irradiated field (eg, fistula formation), surgery after radiotherapy is rarely necessary in any of the algorithms. We are cognizant that large lymph nodes will not be consistently sterilized with external beam radiotherapy.

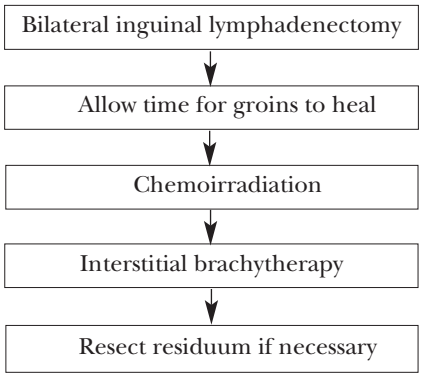
Suspect enlarged but mobile inguinofemoral lymph nodes should be resected (ie, debulked) before radiation therapy because healing of the groin dissection is poor after irradiation (see algorithm 2). Although surgical debulking of fixed or matted inguinofemoral lymph nodes is warranted philosophically, the possibility of femoral vein injury makes this procedure dangerous. Neoadjuvant chemotherapy may increase the subsequent operability of fixed or matted inguinofemoral nodal chains (see algorithm 3). Finally, the use of systemic chemotherapy in algorithms 2 and 3 may (1) serve as a radiosensitizing agent and thereby increase efficacy of radiotherapy, (2) decrease the total cumulative radiation dose and therefore decrease toxic effects of radiation, and (3) possibly palliate or treat distant metastases, if present.

We acknowledge that these algorithms represent a departure from what has been considered "standard" therapy and, like Boronow et al,[18, 19] accept the obligation to review our results periodically in subsequent communications.

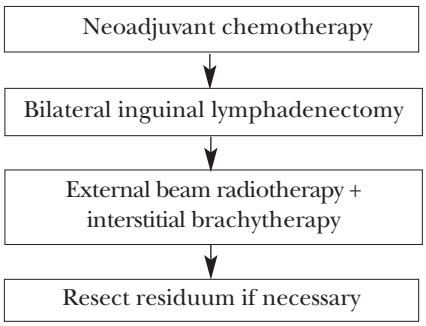
Algorithm 1: Clinically negative inguinofemoral nodal chains with compromised surgical margins. This algorithm is based on the work of Boronow et al[3, 18, 19] with 1 modification: Interstitial irradiation is used in place of intracavitary irradiation to supply a radiation boost to the tumor-bearing region. Radical vulvectomy with bilateral inguinal lymphadenectomy to treat the external genital phase of the disease is followed by radiotherapy tailored to protect the surgical margins and treat the internal genital phase of the disease.



Algorithm 2: Suspect, enlarged, mobile inguinofemoral lymph nodes. Designed around the accumulating experience in the use of radiosensitizing agents in the management of locally advanced vulvar cancer,[20-24] this algorithm consists of bilateral groin node dissection of enlarged, mobile nodes, followed by chemoradiation (eg, cisplatin or 5-fluorouracil and external beam radiotherapy) and an interstitial brachytherapy boost to the vulva.



Algorithm 3: Matted or fixed inguinofemoral lymph nodes. Founded on the experience of Sardi et al[25] in using neoadjuvant chemotherapy (a 21-day regimen consisting of vincristine, bleomycin, and cisplatin) to increase the operability of bulky squamous cell carcinomas of the uterine cervix, this algorithm has been developed for patients with advanced disease and matted or fixed inguinofemoral nodes.



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