Radical Extirpation With Intraoperative Radiotherapy for Locally Recurrent Gynecologic Cancer: An Institutional Review

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Abstract

Objective: To report survival outcomes in patients with locally recurrent gynecologic cancers managed with curative-intent radical extirpation, perioperative external beam radiotherapy, and intraoperative radiotherapy (IORT).

Patients and Methods: We conducted a retrospective cohort analysis of 44 patients with locally recurrent gynecologic cancer treated at a single tertiary-care center (Mayo Clinic in Arizona) over a 15-year period (January 1, 2004, to July 31, 2019). This cohort included patients with uterine (n = 21, 47.7%), ovarian (n = 3, 6.8%), cervical (n = 11, 25.0%), vaginal (n = 2, 4.5%), vulvar (n = 1, 2.3%), and unknown primary (n = 6, 13.6%) cancer. Curative-intent radical extirpation included pelvic exenteration (n = 13, 29.5%), laterally extended endopelvic resection (n = 22, 50.0%), excision of para-aortic lymph node metastasis (n = 8, 18.2%), and radical vaginectomy (n = 1, 2.3%). Of the 44 patients in our cohort, 37 (84.1%) received IORT and 7 (15.9%) had intended to receive IORT but did not receive it.

Results: The median follow-up for the 44 patients was 12 months (range, 1 to 161 months). For patients who received IORT, the median progression-free survival (PFS) and overall survival (OS) were 13 and 21 months, respectively, and the 3-year cumulative incidence of central, locoregional, and distant recurrence was 27.0% (10 of 37), 40.5% (15 of 37), and 37.8% (14 of 37), respectively. Surgical margins were classified as negative (28 of 44, 63.6%), microscopic (11 of 44, 25.0%), or macroscopic (5 of 44, 11.4%). Negative, microscopic, and macroscopic surgical margins resulted in 3-year PFS of 51.8%, 20.5%, and 0%, respectively (P = .01) and 3-year OS of 62.9%, 20.0%, and 0%, respectively (P = .035). Progression-free survival (P = .69) and OS (P = .88) were not different between patients with negative surgical margins who received (n = 21) and did not receive (n = 7) IORT. Ten of 37 patients (27.0%) had development of grade 3 or higher toxicities, with 1 death due to sepsis.

Conclusion: Complete tumor resection at the time of curative-intent radical extirpation achieved higher rates of PFS and OS regardless of IORT administration.
challenging with a high risk for toxicity.\textsuperscript{10-12} Intraoperative radiotherapy (IORT) is a modality that allows for additional radiation to be delivered safely, primarily by physically displacing normal tissues such as bladder and bowel away from radiation exposure.\textsuperscript{1} The literature suggests that use of IORT for recurrent gynecologic malignancies may improve local control and long-term overall survival (OS).\textsuperscript{10,13-15} In this study, we describe our experience with IORT at the time of extirpative surgical treatment in patients with locally recurrent gynecologic malignancies.

PATIENTS AND METHODS
The Mayo Clinic Institutional Review Board approved this retrospective medical record review (IRB #18-009261). The medical records of 44 patients treated at Mayo Clinic in Arizona from January 1, 2004, to July 31, 2019, were reviewed. All patients with locally recurrent gynecologic cancer underwent radical extirpation with intention for IORT. Radical extirpative procedures included pelvic exenteration, laterally extended endopelvic resection, excision of para-aortic lymph node metastases, and radical vaginectomy. Candidates for IORT were medically fit patients with locally recurrent gynecologic cancer not amenable to surgical resection alone and without evidence of distant metastasis.\textsuperscript{1}

Pretreatment evaluation included a complete history and physical examination, routine laboratory studies, and imaging to assess the extent of local disease and to rule out distant metastasis (computed tomography, magnetic resonance imaging, and positron emission tomography at the discretion of the treating physician). A multidisciplinary tumor board of physicians from gynecologic oncology, medical oncology, radiation oncology, and surgical pathology determined appropriate treatment plans. If a patient had a history of radiation therapy, outside records were reviewed to determine if additional preoperative irradiation was feasible. Radiation dose was based on the time interval from prior radiation therapy, the prior radiation therapy dose, and the location of the radiation therapy field. Systemic chemotherapy was added as indicated based on tumor histology and characteristics.

Surgical resection was performed, and the abdomen was fully explored to ensure that there was no evidence of other sites of metastases. Surgical specimens were oriented and sent for frozen section to confirm margin status. Surgical margins were classified as negative, microscopic, or macroscopic residual tumor. Exenteration and the ability to achieve complete tumor resection were not prerequisites for administration of IORT. The final decision to administer IORT was made intraoperatively by both the gynecologic oncologist and the radiation oncologist. Intraoperative radiotherapy techniques used at Mayo Clinic have been described previously.\textsuperscript{16} A dedicated linear accelerator (Mebetron, IntraOp Medical, Inc) was used in specialized operating suites for delivery of IORT. Intraoperative radiotherapy was prescribed at appropriate doses (range, 10 to 18 Gy) to the 90\% isodose level and took into account the amount of residual tumor and its proximity to critical structures. The size of the IORT applicator encompassed the tumor bed plus a 2- to 3-cm margin. The thickness of the tumor bed was estimated by direct measurement or by preoperative imaging. The appropriate energy (range, 6 to 15 MeV) of IORT was selected to ensure adequate dose coverage to the full thickness of the tumor bed.

Progression-free survival (PFS) was defined as the time from radical surgical treatment to disease recurrence or progression. Overall survival was defined as the time from radical surgical treatment to death from all causes. After surgical treatment, surveillance was scheduled in 3-month intervals for the first 2 years and then in 6-month intervals until 5 years after treatment. Disease progression was determined using physical examination findings and/or imaging ordered at the discretion of the treating physician. Disease recurrence was classified as central, locoregional, or distant relapse. Central recurrence was defined as disease appearing within the IORT field. Locoregional recurrence was defined as disease within the IORT field in addition to local lymph nodes. Distant recurrence was defined as disease outside the pelvis. Patients who were alive and disease-free at last follow-up were treated as censored observations. Toxicity was scored using the National Cancer Institute’s Common Terminology
Criteria for Adverse Events (formerly, Common Toxicity Criteria).

The Mann-Whitney U test was used to analyze continuous variables as appropriate. Frequency distributions were compared using the χ² test and Fisher exact test for categorical variables. Progression-free survival and OS were estimated using the Kaplan-Meier method and log-rank test. Progression-free survival and OS were compared between patients who received and did not receive IORT. Univariate analysis was performed to assess the clinical and pathologic risk factors for survival including residual tumor, tumor pathology, site of recurrence, tumor size, history of external beam radiotherapy (EBRT) at initial diagnosis, perioperative EBRT at recurrence, and IORT. Risk factors with statistical significance were selected for further analysis with the multivariate Cox proportional hazards regression model. In all cases, P<.05 was considered statistically significant. SPSS Statistics for Windows, version 23.0 (IBM Corp) and Prism 6.0c (GraphPad Software) statistical software were used for statistical analyses.

RESULTS

Of the 44 patients with recurrent disease who underwent radical surgical treatment with intention for IORT, 37 (84.1%) received IORT and 7 (15.9%) ultimately did not receive IORT due to complete tumor resection. The median time from initial diagnosis to first recurrence or disease progression was 36 months (range, 3 to 360). Patients were divided to 2 groups according to the time of initial treatment to recurrence: 12 or more months vs less than 12 months. There were no survival differences in PFS (hazard ratio, 1.236; 95% CI, 0.4845 to 3.155; P=.66) and OS (hazard ratio, 1.188; 95% CI, 0.4611 to 3.060; P=.73) after IORT.

The 37 patients who underwent extirpation with IORT were diagnosed as having the following cancers: uterine, 20 (54.1%); ovarian, 2 (5.4%); cervical, 8 (21.6%); vaginal, 2 (5.4%); vulvar, 1 (2.7%); and unknown primary, 4 (10.8%). Tumor characteristics including histologic subtypes are listed in Table 1, with endometrioid endometrial adenocarcinoma being most common (n=11, 29.7%). The median age of this cohort was 62 years (range, 29 to 89 years). Sites of recurrence (Table 2) occurred centrally (n=5, 13.5%), at the pelvic sidewall (n=16, 43.2%), lymph nodes (n=8, 21.6%), or multiple sites (n=8, 21.6%). The median tumor size was 5 cm (range, 1 to 12 cm).

Treatments received at initial diagnosis and at recurrence are listed in Table 2. At recurrence, 35 patients (94.6%) received preoperative radiation therapy prior to planned extirpation, with a median dose of 45 Gy (range, 19.8 to 57 Gy); 23 patients (62.2%) received both EBRT at the time of initial diagnosis and radiation therapy prior to extirpation, receiving a median cumulative dose of 95.4 Gy (range, 75.2 to 110 Gy); and 10

| TABLE 1. Tumor Characteristics Stratified by Histology in the IORT Cohort |
|---------------------------------------------------------------|
| Cancer type          | No. (%) of patients (N=37) |
|--------------------|-----------------------------|
| **Uterine**         |                             |
| Endometrioid        | 11 (29.7)                   |
| UPSC                | 2 (5.4)                     |
| Leiomysarcoma       | 3 (8.1)                     |
| Clear cell adenocarcinoma | 1 (2.7)            |
| ESS                 | 2 (5.4)                     |
| Mullerian sarcoma   | 1 (2.7)                     |
| **Ovarian**         |                             |
| Serous adenocarcinoma | 1 (2.7)                   |
| Undifferentiated adenocarcinoma | 1 (2.7)        |
| **Cervical**        |                             |
| Squamous            | 7 (18.9)                    |
| Adenocarcinoma      | 1 (2.7)                     |
| **Vaginal**         |                             |
| Squamous            | 1 (2.7)                     |
| Adenocarcinoma      | 1 (2.7)                     |
| **Vulvar**          |                             |
| Squamous            | 1 (2.7)                     |
| **PUO**             |                             |
| Squamous            | 1 (2.7)                     |
| Adenocarcinoma      | 1 (2.7)                     |
| Mullerian           | 1 (2.7)                     |
| adenocarcinoma      | 1 (2.7)                     |
| Spindle cell        | 1 (2.7)                     |

ESS, endometrial stromal sarcoma; IORT, intraoperative radiotherapy; PUO, pelvic of unknown origin; UPSC, uterine papillary serous carcinoma.)
patients received chemotherapy (27.0%) prior to surgery.

Ten patients (27.0%) underwent pelvic exenteration, 18 (48.6%) had laterally extended endopelvic resection, 8 (21.6%) underwent excision of para-aortic lymph node metastasis, and 1 (2.7%) had radical vaginectomy. Thirty-five of the cases (94.6%) were performed via laparotomy (1 conversion from laparoscopy to laparotomy) and 2 as minimally invasive with robotic assistance.

Two patients underwent en bloc vessel resection as a result of tumor attachment or invasion.

Tumor specimens were submitted to surgical pathology for frozen section to confirm margin status. Twenty-one patients (56.8%) had negative surgical margins, with 4 of whom (10.8%) having no viable tumor. Eleven patients (29.7%) had microscopic and 5 (13.5%) had macroscopic margin involvement. Thirty-three patients (89.2%) had a single IORT field while 4 (10.8%) had multiple IORT fields, with a median dose of 12.5 Gy (range, 10 to 18 Gy) and median energy of 9 MeV (range, 6 to 15 MeV).

At the end of this study period, median follow-up was 12 months (range, 1 to 161 months). Fourteen patients (37.8%) experienced complete remission without relapse, and 1 patient is alive with subsequent disease recurrence. Twenty-two patients (59.5%) died, all due to disease progression except for 1 patient who died of perioperative complications. There were 10 central recurrences (27.0%), 15 locoregional recurrences (40.5%), and 14 distant recurrences (37.8%) after IORT.

There were 16 occurrences of toxicity or complications in 10 patients (27.0%). The 16 occurrences included 2 gastrointestinal fistulas, 5 pelvic abscesses, 2 pulmonary embolisms, 2 perioperative hemorrhages, 1 gastrointestinal obstruction, 1 peripheral neuropathy, 1 ureteral stenosis, and 2 other events. The 2 other events were upper extremity compartment syndrome and postoperative atrial fibrillation in one patient each. There was one grade 5 complication with patient death 4 days postoperatively due to gastrointestinal anastomotic leak leading to septic shock.

The overall median PFS of 13 months (3-year PFS, 33.5%) and median OS of 21 months (3-year OS, 38.3%) are depicted in the Figure using Kaplan-Meier survival curves. On univariate analysis, 3-year PFS for patients with negative, microscopic, and macroscopic margins was 51.8%, 20.5%, and 0%, respectively ($P=0.006$), and 3-year OS was 62.9%, 20.0%, and 0%, respectively ($P=0.035$). Patients with small tumors were more likely to have complete surgical resection, with a median tumor diameter of 4.4 cm in patients.
with negative surgical margins compared with 6.5 cm in patients with microscopic or macroscopic residual tumor ($P = .037$). Perioperative EBRT ($P = .20$), dose of EBRT ($P = .78$), administration of concurrent chemoradiotherapy or chemotherapy alone ($P = .54$), site of recurrence ($P = .83$), and administration of IORT ($P = .53$) were not associated with achievement of complete surgical resection.

**Extirpation Without IORT**

In the group that did not receive IORT, 1 patient had uterine cancer, 1 had ovarian cancer, 3 had cervical cancer, and 2 had unknown primary cancers (Table 3). Of the 7 patients, 3 underwent pelvic exenteration and 4 underwent laterally extended endopelvic resection. All patients had negative margins at intraoperative pathologic assessment. One patient underwent en bloc vessel resection with subsequent vessel replacement graft. Three patients experienced major perioperative complications related to abscess formation.

There were 4 (57.1%) recurrences after extirpative surgical treatment, which were all distant recurrences. Three patients (42.9%) achieved complete remission with 46 to 56 months of PFS at the end of the study period (Figure).

**IORT vs No IORT**

In patients who had complete tumor resection, there was no difference in PFS ($P = .69$) and OS ($P = .88$) between those who received IORT and those who did not. Additionally, in this same group of patients with complete tumor resection, there was no difference in locoregional control ($P = .29$) or distant control ($P = .21$) between those who received IORT and those who did not.

**DISCUSSION**

In this study, we reviewed outcomes of patients with locally recurrent gynecologic malignancies who received extirpative surgical treatment with or without IORT. Patients who underwent extirpative operations with complete tumor resection had improved PFS and OS compared with patients who had suboptimal resection regardless of IORT administration.

The primary goal of curative-intent extirpative operations should be complete tumor resection. The role of IORT at the time of radical surgical treatment in patients with locally recurrent gynecologic malignancies is promising, but data are limited to only small retrospective studies.10,13,17 The most encouraging results are seen in cases with no or microscopic residual tumor after debulking procedures, suggesting variable but improved disease control and survival with use of IORT.10,13,17 In a retrospective analysis of 39 patients with locally recurrent gynecologic cancer, microscopic or macroscopic residual tumor after radical surgical treatment with IORT produced central and locoregional control rates of 81% and 67.4%, respectively.10 The cohort had a 5-year PFS and OS of 55% and 50%, respectively.10 In another study of 86 patients with locally recurrent cervical cancer treated with radical surgical treatment and IORT, negative, microscopic, and macroscopic resection margins produced significant differences in distant control (61%, 45%, and 25%, respectively) and PFS (45%, 27%, and 14%, respectively).15 Most recently, a

| Variable                  | No. (%) of patients (N=7) |
|---------------------------|---------------------------|
| **Tumor type**            |                           |
| Cervical                  | 3 (42.9)                  |
| Ovarian                   | 1 (14.3)                  |
| Uterine                   | 1 (14.3)                  |
| PUO                       | 2 (28.6)                  |
| **Type of surgery**       |                           |
| LEER                      | 4 (57.1)                  |
| PE                        | 3 (42.9)                  |
| **Residual tumor**        |                           |
| Negative                  | 7 (100.0)                 |
| Microscopic               | 0 (0.0)                   |
| Macroscopic               | 0 (0.0)                   |
| **Site of recurrence**    |                           |
| Central                   | 0 (0.0)                   |
| Locoregional              | 0 (0.0)                   |
| Distant                   | 4 (57.1)                  |

IORT, intraoperative radiotherapy; LEER, laterally extended endopelvic resection; PE, pelvic exenteration; PUO (pelvic of unknown origin).

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**TABLE 3. Treatments and Disease Status at Recurrence in the Cohort.**
retrospective study of 32 patients who received radical surgical treatment with IORT, 5-year PFS was 40.9% in patients with microscopic residual tumor in contrast to 9.1% with macroscopic residual tumor, and 5-year OS was 77.3% for microscopic and 54.5% for macroscopic residual tumor.3

Prognosis for patients with locally recurrent or persistent gynecologic malignancies is poor overall, and often central recurrence is the primary site.3 In patients with distant metastasis, survival rates are dismal.2,4 The literature supports central and locoregional control to decrease risk of distant metastasis.2 In concordance with prior retrospective studies, our results suggest that complete tumor resection is imperative for central control, PFS, and OS. In patients who received IORT, sites of recurrence were more likely to be locoregional (n=13, 40.5%) or distant (n=14, 37.8%). Central recurrence was more common in patients with microscopic (n=4,
40.0%) and macroscopic (n=4, 40.0%) resid-
ual tumor. In the cohort that received IORT, 
there was improved 3-year PFS with negative 
surgical margins, in contrast to microscopic 
or macroscopic, of 51.8%, 20.5%, and 0.0%, 
respectively (P=0.06) and 3-year OS of 
62.9%, 20.0%, and 0.0%, respectively 
(P=0.035). In patients who did not receive 
IORT, sites of recurrence were all distant 
(n=4, 100.0%). Our study also found that 
small tumors were more likely to have com-
plete tumor resection (P=0.037), with a median 
tumor diameter of 4.4 cm. These data suggest 
that patients who would have the most sur-
vival benefit from curative-intent extirpati-
ve operations are those with small tumors 
amenable to complete resection.

Additionally, our results suggest that IORT 
may improve disease control and survival out-
comes if optimal surgical resection is achieved 
and multimodality treatment comprising peri-
operative EBRT and IORT is employed. Our re-
sults are in agreement with another 
retrospective study by Calvo et al indicating 
benefit of EBRT integrated with radical surgical 
treatment and IORT in cases of locally recurrent 
gynecologic malignancies. The administration 
of EBRT preoperatively or postoperatively 
should be considered because the addition of 
EBRT delivers a higher cumulative radiation 
dose than IORT alone. At our institution, we 
administer EBRT preoperatively because it opti-
mizes delivery of radiation therapy without delay in the event of postoperative complica-
tions. However, our study did not find that 
preoperative EBRT led to complete tumor 
resection (P=0.20) and that only tumor size 
was related to complete resection (P=0.037). 
Further study is needed to determine if preop-
erative EBRT aids in tumor volume reduction.

Intraoperative radiotherapy is beneficial 
for its ability to deliver high-dose radiation 
therapy to the site of recurrence, decreasing 
risk of radiation to surrounding critical struc-
tures. These cases are not without their com-
plications, however, and it is challenging to 
distinguish if complications are related to radia-
tion therapy or to radical surgical treatment. 
In our study, multimodality treatment with 
perioperative EBRT, optimal surgical resec-
tion, and IORT had acceptable toxicity, 
congruent with toxicity rates presented in 
the literature. Grade 3 or higher toxicities 
developed in 10 patients (27.0%), and 1 pa-
tient died 4 days postoperatively due to gastro-
intestinal anastomotic leak resulting in septic 
shock. The 5-year PFS for locally recurrent gy-
ecologic cancer without treatment is 10%. It 
is important to counsel patients on the natural 
history of the disease and its poor survival out-
comes without treatment. The discussion on 
curative-intent radical surgical treatment with 
both EBRT and IORT should include lack of 
prospective data on associated toxicities and 
the limited retrospective data on survival out-
comes.

One of the strengths of this study was the 
radiicality of the operations performed, almost 
half (48.6%) being laterally extended endopel-
vic resection procedures. Three patients un-
derwent en bloc vessel resection as a result of 
tumor attachment or invasion (2 patients 
who received IORT and 1 who did not). All 
3 patients had complete remission at the end 
of this study period, suggesting that radicality 
may be warranted if long-term survival in pa-
tients with locally recurrent or persistent gynec-
ologic malignancies can be achieved.

One of the limitations of this study was its 
retrospective nature. This study also included 
a small sample size from a single institution, 
and statistical significance may have been dif-
cult to achieve. Our cohort included a hetero-
geneous sample pathology, and thus the 
results may not be generalizable. Administra-
tion of IORT was an intraoperative decision 
based on surgical resection margins, risk of re-
sidual tumor, and potential for local recur-
rence. The case may be that there were no 
 survival differences between those who 
received and did not receive IORT because of 
inherent selection bias to not administer 
IORT in cases of complete tumor resection, 
cancers with low risk for local recurrence, 
and patients with favorable long-term prog-
nosis. Long-term prospective data are needed 
to determine the survival benefit of IORT in 
patients with suboptimal resection.

CONCLUSION

While the role of IORT in the treatment of 
 recurrent or persistent disease remains 
controversial, our study documents the importance 
of complete tumor resection at the time of 
extirpative surgical treatment in optimizing 
survival benefit. It may behoove physicians

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to select appropriate candidates with the highest probability of complete tumor resection and ability to tolerate radical surgical treatment with high-dose radiation therapy to minimize the chance for cure and minimize overall patient morbidity.

Abbreviations and Acronyms: EBRT, external beam radiotherapy; IORT, intraoperative radiotherapy; OS, overall survival; PFS, progression-free survival

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REFERENCES
1. Backes FJ, Martin DD. Intraoperative radiation therapy (IORT) for gynecologic malignancies. Gynecol Oncol. 2015;138(2):449-456.
2. Tran PT, Su Z, Hara W, Husain A, Teng N, Kapp DS. Long-term survivors using intraoperative radiotherapy for recurrent gynecologic malignancies. Int J Radiat Oncol Biol Phys. 2007;69(2):504-511.
3. Foley OW, Rauh-Hain JA, Clark RM, et al. Intraoperative radiation therapy in the management of gynecologic malignancies. Am J Clin Oncol. 2016;39(4):329-334.
4. Calvo FA, Sole CV, Lozano MA, et al. Intraoperative electron beam radiotherapy and extended surgical resection for gynecological pelvic recurrent malignancies with and without external beam radiation therapy: long-term outcomes. Gynecol Oncol. 2013;130(3):537-544.
5. Haddock MG, Petersen IA, Webb MJ, Wilson TO, Podratz KC, Gunderson LL. IORT for locally advanced gynecological malignancies. Front Radiat Ther Oncol. 1997;31:256-259.
6. Höckel M. Long-term experience with (laterally) extended endopelvic resection (LEER) in relapsed pelvic malignancies. Gynecol Oncol. 2015;137(3):435.
7. Com BV, Lanciano RM, D’Agostino R, et al. The relationship of local and distant failure from endometrial cancer: defining a clinical paradigm. Gynecol Oncol. 1997;66(3):411-416.
8. Fagundes H, Perez CA, Grigsby PW, Lockett MA. Distant metastases after irradiation alone in carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys. 1992;24(2):197-204.
9. Kapp KS, Stuecklschweiger GF, Kapp DS, et al. Prognostic factors in patients with carcinoma of the uterine cervix treated with external beam irradiation and IR-192 high-dose-rate brachytherapy. Int J Radiat Oncol Biol Phys. 1998;42(3):531-540.
10. Garton GR, Gunderson LL, Webb MJ, Wilson TO, Cha SS, Podratz KC. Intraoperative radiation therapy in gynecologic cancer: update of the experience at a single institution. Int J Radiat Oncol Biol Phys. 1997;37(4):839-843.
11. Backes FJ, Billingsley CC, Martin DD, et al. Does intra-operative radiation at the time of pelvic exenteration improve survival for patients with recurrent, previously irradiated cervical, vaginal, or vulvar cancer? Gynecol Oncol. 2014;135(1):95-99.
12. del Carmen MG, McIntyre JF, Goodman A. The role of intraoperative radiation therapy (IORT) in the treatment of locally advanced gynecologic malignancies. Oncologist. 2000;5(1):18-25.
13. del Carmen MG, Eiserer B, Willet CG, Fuller AF. Intraoperative radiation therapy in the management of gynecologic and genitourinary malignancies. Surg Oncol Clin N Am. 2003;12(4):1031-1042.
14. Dowdy SC, Mariani A, Cliby WA, et al. Radical pelvic resection and intraoperative radiation therapy for recurrent endometrial cancer: techniques and analysis of outcomes. Gynecol Oncol. 2006;101(2):280-286.
15. Barney BM, Petersen IA, Dowdy SC, Bakkum-Gamez JN, Klein KA, Haddock MG. Intraoperative electron beam radiotherapy (IORT) in the management of locally advanced or recurrent cervical cancer. Radiat Oncol. 2013;8:80.
16. Gunderson LL, Nelson H, Martenson JA, et al. Intraoperative electron and external beam irradiation with or without 5-fluorouracil and maximum surgical resection for previously unirradiated, locally recurrent colorectal cancer. Dis Colon Rectum. 1996;39(12):1379-1395.
17. Garton GR, Gunderson LL, Webb MJ, et al. Intraoperative radiation therapy in gynecologic cancer; the Mayo Clinic experience. Gynecol Oncol. 1993;48(3):328-332.