Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013; 63(1):11-30.	Review/Other-Tx	N/A	To provide the expected numbers of new cancer cases and deaths in 2013 nationally and by state, as well as an overview of current cancer statistics using data through 2009, including incidence, mortality, and survival rates and trends. The article also estimate the total number of deaths averted as a result of the decline in cancer death rates since the early 1990s, and provide the actual reported numbers of deaths in 2009 by age for the 10 leading causes of death and the 5 leading cancer types.	In 2009, Americans had a 20% lower risk of death from cancer than in 1991, when cancer death rates peaked. Despite this substantial progress, all demographic groups have not benefitted equally, particularly for cancers such as colorectal and breast, for which mortality declines have been attributed to earlier detection and improvements in treatment. Further progress can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those groups in the lowest socioeconomic bracket as well as other disadvantaged populations.	4
2. Creasman WT, Phillips JL, Menck HR. The National Cancer Data Base report on cancer of the vagina. *Cancer.* 1998; 83(5):1033-1040.	Review/Other-Tx	4,885 cases of vaginal cancer	To determine practice patterns in the management of vaginal malignancy.	Between 1985-1994, 4,885 cases of vaginal cancer were submitted to National Cancer Data Base. More than 90% were epithelial neoplasia with approximately 25% of these in situ lesions only. Squamous carcinoma was more common as the age of the patient progressed. Adenocarcinomas represented nearly all the carcinomas in the group of patient's age <20 years and were observed less frequently with advanced age. Relative survival at 5 years was stage-related: stage 0: 96%; stage I: 73%; stage II: 58%; and stages III-IV: 36%. Melanoma had an extremely poor prognosis with a 5-year survival rate of only 14%. A significant number of sarcomas occurred in children for whom chemotherapy played a major role in treatment. Chemotherapy was used less frequently in the older patients. Survival was better in the younger patients (90% vs 30% in the older patients).	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
3. Daling JR, Madeleine MM, Schwartz SM, et al. A population-based study of squamous cell vaginal cancer: HPV and cofactors. *Gynecol Oncol.* 2002; 84(2):263-270.	Observational-Tx	156 women with vaginal cancer and 2,041 control women	To evaluate risk factors for in situ and invasive vaginal cancer and their potential relationship to prior exposure to HPV.	Women with vaginal cancer were more likely to have 5 or more lifetime sexual partners (OR = 3.1, 95% CI, 1.9 to 4.9), to have an early age at first intercourse (<17 years OR = 2.0, 95% CI, 1.2 to 3.5), and to be current smokers at diagnosis (OR = 2.1, 95% CI, 1.4 to 3.1) than control women. Approximately 30% of all cases had been treated for a prior anogenital tumor, most often of the cervix. Prior hysterectomy was a risk factor only among women who had no history of prior anogenital cancer (OR = 3.9, 95% CI, 2.5 to 6.1). Antibodies to HPV16 L1 were strongly related to risk of vaginal cancer (OR = 4.3, 95% CI, 3.0 to 6.2). We detected HPV DNA in tumor blocks from over 80% of the patients with in situ and 60% of the patients with invasive cancers.	2
4. Current FIGO staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia. *Int J Gynaecol Obstet.* 2009; 105(1):3-4.	Review/Other-Tx	N/A	Current International Federation of Gynecology and Obstetrics (FIGO) staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia.	N/A	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Bipat S, Glas AS, van der Velden J, Zwinderman AH, Bossuyt PM, Stoker J. Computed tomography and magnetic resonance imaging in staging of uterine cervical carcinoma: a systematic review. *Gynecol Oncol.* 2003; 91(1):59-66.	Review/Other-Dx	57 articles	To systematically review the available evidence on the diagnostic performance of CT and MRI in staging of cervical carcinoma.	57 articles were included. In 49 articles one imaging modality was evaluated (MRI, 38; CT, 11), and in 8 articles, both. Inclusion criteria were: minimum of 10 patients included, histopathology as reference standard, sufficient data presented to construct 2(x) 2 tables. The exclusion criterion was: data reported elsewhere in more detail. Sensitivity estimates for parametrial invasion were 74% (95% CI, 68%-79%) for MRI and 55% (95% CI, 44%-66%) for CT, and for lymph node involvement, 60% (95% CI, 52%-68%) and 43% (95% CI, 37%-57%), respectively. MRI and CT had comparable specificities for parametrial invasion and lymph node involvement. For bladder invasion and rectum invasion the sensitivities for MRI were respectively 75% (95% CI, 66%-83%) and 71% (95% CI, 53%-83%), higher compared with CT. The specificity in evaluating bladder invasion for MRI was significantly higher compared with CT: 91% (95% CI, 83%-95%) for MRI and 73% (95% CI, 52%-87%) for CT. The specificities for rectum invasion were comparable. Differences in patient sample size, publication year, methodological criteria, and MRI techniques had no effect on the summary estimates.	4
6. Hricak H, Gatsonis C, Chi DS, et al. Role of imaging in pretreatment evaluation of early invasive cervical cancer: results of the intergroup study American College of Radiology Imaging Network 6651-Gynecologic Oncology Group 183. *J Clin Oncol.* 2005; 23(36):9329-9337.	Observational-Dx	208 patients	To compare MRI and CT with each other and to FIGO clinical staging in the pretreatment evaluation of early invasive cervical cancer, using surgicopathologic findings as the reference standard.	Complete data were available for 172 patients; surgicopathologic findings were consistent with FIGO stages IA to IIA in 76% and stage ≥IIB in 21%. For the detection of advanced stage (≥IIB), sensitivity was poor for FIGO clinical staging (29%), CT (42%), and MRI (53%); specificity was 99% for FIGO clinical staging, 82% for CT, and 74% for MRI; and NPV was 84% for FIGO clinical staging, 84% for CT, and 85% for MRI. MRI (AUC, 0.88) was significantly better than CT (AUC, 0.73) for detecting cervical tumors (P=.014). For 85% of patients, FIGO clinical staging forms were submitted after MRI and/or CT was performed.	3

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Taylor MB, Dugar N, Davidson SE, Carrington BM. Magnetic resonance imaging of primary vaginal carcinoma. *Clin Radiol.* 2007; 62(6):549-555.	Review/Other-Dx	25 patients	To describe the MRI features of vaginal carcinoma and to suggest a role for MRI in its management.	The median patient age was 54 years (range 31-86 years). Tumor maximum diameter ranged from 1.6-11.3 cm (mean 3.7 cm). Most tumors were of iso-intense signal to muscle on T1-weighted images and hyper-intense to muscle on T2-weighted images. 88% of patients had tumor extending beyond the vagina and 56% of patients had FIGO stage III or above tumors. 16 patients were treated with RT (2 with chemoradiotherapy), 5 with surgery and 4 with supportive care. 10 patients (40%) died of their disease during the study period. The MRI stage of the tumor correlated with survival.	4
8. Choi HJ, Ju W, Myung SK, Kim Y. Diagnostic performance of computer tomography, magnetic resonance imaging, and positron emission tomography or positron emission tomography/computer tomography for detection of metastatic lymph nodes in patients with cervical cancer: meta-analysis. *Cancer Sci.* 2010; 101(6):1471-1479.	Review/Other-Dx	41 articles	Meta-analysis was performed to compare diagnostic performances of CT, MRI, and PET or PET/CT, for detection of metastatic lymph nodes in patients with cervical cancer.	In a patient-based data analysis, PET or PET/CT showed the highest pooled sensitivity (82%) and specificity (95%), while CT showed 50% and 92%; and MRI, 56% and 91%, respectively. The AUC (0.9641) and Q* (0.9106) of PET or PET/CT were significantly higher than those of MRI (AUC = 0.8270; Q* = 0.7599), both P<0.001. In region- or node-based data analysis, sensitivities of CT (52%) and PET or PET/CT (54%) were higher than that of MRI (38%), P<0.02 and P<0.001, respectively, while specificities of MRI (97%) and PET or PET/CT (97%) were higher than that of CT (92%), both P<0.001. The AUC and Q* showed no significant difference among CT, MRI, and PET or PET/CT.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Loft A, Berthelsen AK, Roed H, et al. The diagnostic value of PET/CT scanning in patients with cervical cancer: a prospective study. *Gynecol Oncol.* 2007; 106(1):29-34.	Observational-Dx	120 patients	To investigate the clinical value of PET/CT as a supplement to FIGO staging in patients with cervical cancer stage ≥1B.	27 patients underwent radical surgery; 4 of these had PET/CT scans revealing pathological foci in the pelvis. Three (11%) were true positive; one was false positive. 22 patients had true negative PET/CT scans concerning pelvic lymph nodes. One patient had a false negative node. For these patients, we found the PPV to be 75%, NPV 96%, sensitivity 75%, specificity 96%. Regarding para-aortal nodal disease in the total population of 119 patients, 15 patients had true positive scans. The number of true negatives was 103, resulting in PPV 94%, NPV 100%, sensitivity 100% and specificity 99%. PET/CT scans showed distant metastases in 19 patients, 10 were true positive and 9 were false positive. The remaining 100 patients were considered true negative for distant metastases and for these patients, we found PPV 63%, NPV 100%, sensitivity 100% and specificity 94%.	3
10. Schwarz JK, Siegel BA, Dehdashti F, Grigsby PW. Association of posttherapy positron emission tomography with tumor response and survival in cervical carcinoma. *JAMA*. 2007;298(19):2289-2295.	Observational-Dx	92 women	To validate the association between the metabolic response on the 3-month post-therapy FDG-PET and long-term survival outcome.	Post-therapy FDG-PET showed a complete metabolic response in 65 patients (70%), a partial metabolic response in 15 (16%), and progressive disease in 12 (13%). Their 3-year PFS rates were 78%, 33%, and 0%, respectively (P<.001). Multivariate analysis demonstrated that the HR for risk of recurrence based on the post-therapy metabolic response showing progressive disease was 32.57 (95% CI, 10.22-103.82). A partial metabolic response had an HR of 6.30 (95% CI, 2.73-14.56). These were more predictive of survival outcome than the pretreatment lymph node status (HR, 3.54; 95% CI, 1.54-8.09).	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Lamoreaux WT, Grigsby PW, Dehdashti F, et al. FDG-PET evaluation of vaginal carcinoma. *Int J Radiat Oncol Biol Phys.* 2005; 62(3):733-737.	Observational-Dx	23 patients	To compare the results of CT and FDG-PET in the detection of the primary tumor and lymph node metastases in carcinoma of the vagina.	Of the 21 patients with an intact primary tumor, CT visualized it in 9 (43%). CT also demonstrated abnormally enlarged groin lymph nodes in 3 patients and both groin and pelvic lymph nodes in 1 patient (4/23, 17%). FDG-PET identified abnormal uptake in all 21 intact primary tumors (100%). Abnormal uptake was found in the groin lymph nodes in 4 patients, pelvic lymph nodes in 2, and both groin and pelvic lymph nodes in 2 patients (8/23, 35%). The 3-year PFS and OS estimate was 73% and 68%, respectively.	3
12. Cutillo G, Cignini P, Pizzi G, et al. Conservative treatment of reproductive and sexual function in young woman with squamous carcinoma of the vagina. *Gynecol Oncol.* 2006; 103(1):234-237.	Review/Other-Tx	4 women	To determine feasibility and the efficacy of conservative surgery of reproductive and sexual function in young women with vaginal carcinoma.	Mean operative time of conservative surgical treatment was 161 min. No intraoperative or postoperative complications were observed. In one patient, definitive pathologic examination revealed microscopic involvement of the paracolpium. Thus, after carrying out laparoscopic ovarian transposition, adjuvant RT, consisting of pulsed-dose rate brachytherapy and external RT was delivered in this woman. After a follow-up time of 51, 45, 21 and 9 months, respectively, all patients are regularly menstruating, sexually active and clinically free of disease.	4
13. Al-Kurdi M, Monaghan JM. Thirty-two years experience in management of primary tumours of the vagina. *Br J Obstet Gynaecol.* 1981; 88(11):1145-1150.	Observational-Tx	99 patients	A retrospective study is presented of patients with a diagnosis of primary tumor of the vagina who were managed at the Gynaecological Oncology Department.	The corrected 5 year survival rates for patients given definitive treatment were: stage I, 71% (10/14), stage II, 29% (10/34), stage III, 25% (2/8), stage IV, 22% (2/9). The overall corrected 5 year survival rate when definitive treatment was given was 37% (24/65).	2
14. Davis KP, Stanhope CR, Garton GR, Atkinson EJ, O'Brien PC. Invasive vaginal carcinoma: analysis of early-stage disease. *Gynecol Oncol.* 1991; 42(2):131-136.	Observational-Tx	89 patients	To review the treatment and outcome of patients with stages I and II vaginal carcinoma treated with surgery, with surgery and radiation, or with radiation alone at the Mayo Clinic between 1960 and 1987.	The median duration of follow-up was 4.4 years. The 5-year survival (Kaplan-Meier method) was 82% for patients with stage I disease and 53% for those with stage II disease (P=0.009). Analysis of survival according to treatment did not show statistically significant differences.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Ball HG, Berman ML. Management of primary vaginal carcinoma. *Gynecol Oncol.* 1982; 14(2):154-163.	Observational-Tx	58 patients	To examine the problems in staging vaginal carcinoma, patterns of persistent and recurrent disease, and complications of surgical therapy.	27 patients were stage I, 18 stage II, 6 stage III, and 5 stage IV. In 2 patients staging information was not available. 30 patients underwent operative therapy including 19 with stage I disease. The adjusted actuarial survival for the entire group was 50% at 5 years and 46% at 10 years. The 5-year survival for stage I treated with operation was 84% and with RT was 55%.	2
16. Otton GR, Nicklin JL, Dickie GJ, et al. Early-stage vaginal carcinoma--an analysis of 70 patients. *Int J Gynecol Cancer.* 2004; 14(2):304-310.	Observational-Tx	70 women	To assess outcomes and define prognostic factors for early-stage vaginal carcinoma.	The 5-year survivals for stages I and II carcinomas were 71% and 48%, respectively ($P<0.05$). 61 patients (87%) had squamous cell carcinomas with a 5-year survival of 68% vs 22% for adenocarcinomas ($P<0.01$). Those women with grade 3 tumors had a 5-year survival of 40% vs 69% for grades 1 and 2 ($P<0.05$). Tumor size and site were not significant prognostic factors. Patients treated by surgery alone or with combined surgery and RT had a significantly improved survival compared to the radiation alone group ($P<0.01$). 85% of recurrences were locoregional. The median time to relapse was 12 months after initiation of therapy.	2
17. Rubin SC, Young J, Mikuta JJ. Squamous carcinoma of the vagina: treatment, complications, and long-term follow-up. *Gynecol Oncol.* 1985; 20(3):346-353.	Observational-Tx	75 cases	To review and present long-term follow-up of cases of primary squamous cell carcinoma of the vagina treated at the University of Pennsylvania.	5-year survival for the entire group was 45%. Patients treated with radical surgery other than exenteration did well, with 7/8 surviving 5 years. Serious treatment complications were mostly related to RT and primarily involved the bowel and bladder. 3 patients died of complications. Recurrence carried a grave prognosis as 30/33 patients with recurrence died of disease. Most recurrences were diagnosed within the first year following treatment. Patients with advanced disease were more likely to have distant recurrences. Although RT is generally the treatment of choice, radical surgery can yield excellent results when used in carefully selected patients.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
18. Stock RG, Chen AS, Seski J. A 30-year experience in the management of primary carcinoma of the vagina: analysis of prognostic factors and treatment modalities. *Gynecol Oncol.* 1995; 56(1):45-52.	Observation-Tx	100 cases	To examine the natural history of primary invasive carcinoma of the vagina, define prognostic factors, compare treatment modalities, and determine optimal treatment strategies.	Treatment with surgery, disease limited to one third of the vaginal canal, and FIGO stage I and II disease are significantly favorable prognostic factors for DFS. Treatment with surgery was superior to RT alone in stage II patients (P=0.00004).	2
19. Tjalma WA, Monaghan JM, de Barros Lopes A, Naik R, Nordin AJ, Weyler JJ. The role of surgery in invasive squamous carcinoma of the vagina. *Gynecol Oncol.* 2001; 81(3):360-365.	Observational-Tx	84 patients	To define the role of surgery in managing patients with a primary squamous vaginal cancer.	The median follow-up was 45 months (range: 0.6-268). The patients were primarily treated by surgery in 67% and by RT alone in 33% of cases. The 5- and 10-year OS was, respectively, 74% and 58%. For stage I the figures were 91% and 70%. These survival rates compared favorably with those of published series of cases managed by RT alone. Univariate analysis showed that age (P=0.004), size (P=0.009), site (P=0.016), lymph node status (P=0.022), FIGO stage (P=0.027), and treatment (P=0.003) were relevant prognostic factors. Multiple regression analysis, however, revealed that only age (P=0.009) and size (P=0.037) were independent prognostic variables.	2
20. Shah CA, Goff BA, Lowe K, Peters WA, 3rd, Li CI. Factors affecting risk of mortality in women with vaginal cancer. *Obstet Gynecol.* 2009; 113(5):1038-1045.	Review/Other-Tx	2,149 women	To estimate the current effect of demographics, pathology, and treatment on mortality among women with vaginal cancer.	The mean age +/- standard deviation at diagnosis was 65.7+/-14.3 years. Approximately 66% of all cases were non-Hispanic whites. Incidence was highest among African-American women (1.24 per 100,000 person-years). The 5-year disease-specific survival was 84% (stage I), 75% (stage II), and 57% (stage III/IV). In a multivariate adjusted model, women with tumors >4 cm and advanced disease had elevated risks of mortality (HRs 1.71 and 4.67, respectively). Compared with women with squamous cell carcinomas, patients with vaginal melanoma had a 1.51-fold (95% CI, 1.07-2.41) increased risk of mortality. Surgery alone as a treatment modality had the lowest risk of mortality. The risk of mortality has decreased over time, as women diagnosed after 2000 had an adjusted 17% decrease in their risk of death compared with women from 1990-1994.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
21. Ling B, Gao Z, Sun M, et al. Laparoscopic radical hysterectomy with vaginectomy and reconstruction of vagina in patients with stage I of primary vaginal carcinoma. *Gynecol Oncol.* 2008; 109(1):92-96.	Review/Other-Tx	4 patients	To retrospectively evaluate the technique, feasibility and oncological safety of laparoscopic radical hysterectomy with vaginectomy and reconstruction of vagina in patients with stage I primary vaginal carcinomas.	The average operative time was 305 min (range 260-350 min). The average estimated blood loss was 325 ml (range 250-400 ml), and the medial number of the lymph nodes removed was 16 (range 13-20). All surgical margins and nodes removed were negative histopathologically. There were no intra-operative and postoperative complications. The mean stay day after surgery was 7 days (range 6-8 days). The mean length of a neo-vagina was 13 cm (range 12-15 cm) and the introitus admitted two fingers in breadth. The mean follow-up was 46 months (range 40-54 months). All patients are clinically free of disease and have satisfactory sexual life. None require dilation of the introitus. During the first 6 months, all the patients had little complaints of excessive leucorrhoea.	4
22. Benedetti Panici P, Bellati F, Plotti F, et al. Neoadjuvant chemotherapy followed by radical surgery in patients affected by vaginal carcinoma. *Gynecol Oncol.* 2008; 111(2):307-311.	Observational-Tx	11 patients	To analyze the feasibility and results obtained by neoadjuvant chemotherapy followed by surgery in patients affected by invasive vaginal cancer with paravaginal tissue involvement not reaching the pelvic side wall.	All patients were subjected to the 3 planned chemotherapy courses. 3 (27%) patients achieved a complete clinical response and 7 (64 %) patients achieved a partial clinical response. All patients were subjected to radical hysterectomy and vaginectomy. At a median follow up of 75 months 2 (18%) patients suffered a disease recurrence and one of these died of disease.	3

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
23. de Crevoisier R, Sanfilippo N, Gerbaulet A, et al. Exclusive radiotherapy for primary squamous cell carcinoma of the vagina. *Radiother Oncol.* 2007; 85(3):362-370.	Observational-Tx	91 patients	To retrospectively analyze results of EBRT with brachytherapy for primary vaginal squamous cell carcinoma.	The 5-year cause specific survival rates were: 83% for stage I, 76% for stage II, 52% for stage III, and 2 of the 4 stage IVa patients died 9 and 36 months after treatment. The 5-year pelvis control rates were: 79% for stage I and II and 62% for stage III. Recurrences as a first event were local only in 68% of cases, nodal only in 10%, metastatic only in 13% and combined in 9%. In multivariate analysis: stage (I and II vs II and IV), response to EBRT (evaluated at brachytherapy), and the number of brachytherapy applications were statistically significant for cause specific survival. Grade 2-3 toxicities were as follows (Franco-Italian Glossary): rectum (n=3), sigmoid colon and small bowel (n=8), bladder (n=5), ureter (n=4) and vagina (n=13). Anterior location of the tumor increased bladder toxicity (P=0.01) and total reference air kerma was higher in patients who experienced grade 2-3 urinary or digestive toxicity (P=0.03).	2
24. Frank SJ, Jhingran A, Levenback C, Eifel PJ. Definitive radiation therapy for squamous cell carcinoma of the vagina. *Int J Radiat Oncol Biol Phys.* 2005; 62(1):138-147.	Observational-Tx	193 patients	To evaluate outcome and describe clinical treatment guidelines for patients with primary squamous cell carcinoma of the vagina treated with definitive RT.	Disease-specific survival and pelvic disease control rates correlated with FIGO stage and tumor size. At 5 years, disease-specific survival rates were 85% for the 50 patients with stage I, 78% for the 97 patients with stage II, and 58% for the 46 patients with stage III-IVA disease (P=0.0013). 5-year disease-specific survival rates were 82% and 60% for patients with tumors ≤4 cm or >4 cm, respectively (P=0.0001). At 5 years, pelvic disease control rates were 86% for stage I, 84% for stage II, and 71% for stage III-IVA (P=0.027). The predominant mode of relapse after definitive RT was local-regional (68% and 83%, respectively, for patients with stages I-II or III-IVA disease). The incidence of major complications was correlated with FIGO stage; at 5 years, the rates of major complications were 4% for stage I, 9% for stage II, and 21% for stage III-IVA (P<0.01).	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
25. Kirkbride P, Fyles A, Rawlings GA, et al. Carcinoma of the vagina--experience at the Princess Margaret Hospital (1974-1989). *Gynecol Oncol.* 1995; 56(3):435-443.	Observational-Tx	153 patients	Charts of patients with vaginal carcinoma or carcinoma in situ seen at Princess Margaret Hospital between 1974 and 1989 were analyzed with respect to treatment modality, radiation dose and technique, complications, and survival.	The overall 5-year actuarial cause-specific survival was 66%. The 5-year cause-specific survivals by stage were stage 0 (C-I-S) 100%, stages I/II 77%, and stages III/IV 56%. Late complications from treatment were infrequent and in only 12 patients were such complications classified as severe. Univariate analysis indicated that size and stage of tumor, histological grade, patient age, and radiation dose >7000 cGy were significant factors in predicting survival, although in a multivariate analysis only size and stage retained significance. 51 patients had a prior gynecological malignancy arising 1-37 years previously, of which 34 had cervical cancers.	3
26. Kucera H, Vavra N. Radiation management of primary carcinoma of the vagina: clinical and histopathological variables associated with survival. *Gynecol Oncol.* 1991; 40(1):12-16.	Observational-Tx	434 patients	To present the influence of clinical and histological prognostic factors on 5-year survival figures of patients treated for invasive primary carcinoma of the vagina between 1952 and 1984.	In stage I, 5-year survival was 76.7%; in stage II, 44.5%; in stage III, 31%; and in stage IV, 18.2%. The overall uncorrected 5-year survival rate was 39.9%. The disease is primarily one of the elderly as 78% were found to be >60 years of age. Younger patients had a 5-year survival of 50%; patients between 61 and 75 years of age, 41.2%; and those 76 years of age or older, 34.3%. Patients with presenting symptoms had a cure rate of 36.9%, whereas 61.1% of asymptomatic cases survived. Best results (60%) were obtained when the lesion was in the upper third of the vagina; only 37% of patients with lesions of the middle third and lower third survived more than 5 years. Well-differentiated tumors were associated with a 5-year survival of 62.5%; and poorly differentiated tumors, with a rate of 34.9%.	3

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
27. Perez CA, Grigsby PW, Garipagaoglu M, Mutch DG, Lockett MA. Factors affecting long-term outcome of irradiation in carcinoma of the vagina. *Int J Radiat Oncol Biol Phys.* 1999; 44(1):37-45.	Observational-Tx	212 patients	To evaluate prognostic and technical factors affecting outcome of patients with primary carcinoma of the vagina treated with definitive RT.	Tumor stage was the most significant prognostic factor; actuarial 10-year DFS was 94% for stage 0 (20 patients), 80% for stage I (59 patients), 55% for stage IIA (63 patients), 35% for stage IIB (34 patients), 38% for stage III (20 patients), and 0% for stage IV (15 patients). All in situ lesions except one were controlled with intracavitary therapy. Of the patients with stage I disease, 86% showed no evidence of vaginal or pelvic recurrence; most of them received interstitial or intracavitary therapy or both, and the addition of EBRT did not significantly increase survival or tumor control. In stage IIA (paravaginal extension) and IIB (parametrial involvement) 66% and 56% of the tumors, respectively, were controlled with a combination of brachytherapy and EBRT; 13/20 (65%) stage III tumors were controlled in the pelvis. Four patients with stage IV disease (27%) had no recurrence in the pelvis. The total incidence of distant metastases was 13% in stage I, 30% in stage IIA, 52% in stage IIB, 50% in stage III, and 47% in stage IV. The dose of irradiation delivered to the primary tumor or the parametrial extension was of relative importance in achieving successful results. In patients with stage I disease, brachytherapy alone achieved the same local tumor control (80%-100%) as in patients receiving external pelvic irradiation (78%-100%) as well. In stage II and III there was a trend toward better tumor control (57%-80%) with combined external irradiation and brachytherapy than with the latter alone (33%-50%) (P=0.42). The incidence of grade 2-3 complications (12%) correlated with the stage of the tumor and type of treatment given.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
28. Pingley S, Shrivastava SK, Sarin R, et al. Primary carcinoma of the vagina: Tata Memorial Hospital experience. *Int J Radiat Oncol Biol Phys*. 2000; 46(1):101-108.	Observational-Tx	75 patients	To analyze the treatment outcome of patients with primary carcinoma of the vagina treated at the Tata Memorial Hospital from January 1984 to December 1993.	DFS for the whole group is 50%, and OS is 60%. Most locoregional recurrences and distant failures are noted in the 2 years following treatment. DFS at 5 years is as follows: stage I (5 patients), stage IIA (37 patients), stage IIB (15 patients), stage III (14 patients), and stage IV (4 patients); are 40%, 55%, 60%, 50%, and 25%, respectively. The DFS for patients with complete response (42 patients) to external radiation at 5 years is 68%, with partial response (25 patients) is 35%, and with poor or no response (6 patients) is 18% (P=0.0000). Authors observed brachytherapy was an important part of the treatment, and patients who received brachytherapy (59 patients), either with a vaginal intracavitary applicator (30 patients) or interstitial implant (29 patients) had a DFS of 53% and 56%, respectively, while 15 patients who received external radiation alone had a DFS of 30%. Patients receiving brachytherapy within 4 weeks of external radiation had a DFS of 60% as compared to 30% when the interval was more than 4 weeks.	2
29. Prempree T, Amornmarn R. Radiation treatment of primary carcinoma of the vagina. Patterns of failures after definitive therapy. *Acta Radiol Oncol.* 1985; 24(1):51-56.	Review/Other	88 patients	To analyze patterns of failures after definitive RT in patients with primary carcinoma of the vagina.	The majority of the local failures in early stages of the disease (I, II and a few III) were due to inadequate treatment either by EBRT or brachytherapy. In some cases the inadequate treatments were unavoidable (previous radiation treatment) and in a few they were due to poor brachytherapy technique.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Tran PT, Su Z, Lee P, et al. Prognostic factors for outcomes and complications for primary squamous cell carcinoma of the vagina treated with radiation. *Gynecol Oncol.* 2007; 105(3):641-649.	Observational-Tx	78 patients	To analyze the results of treatment and identify prognostic factors for primary squamous cell carcinoma of the vagina managed with RT at a single institution.	Kaplan-Meier 5-year pelvic control, distant metastasis free survival and disease specific survival probabilities: stage I, 83%, 100%, and 92%; stage II, 76%, 95%, and 68%; stage III, 62%, 65%, and 44%; and stage IV, 30%, 18%, and 13%. On multivariate analysis: stage; treatment hemoglobin; and prior hysterectomy were prognostic for disease-specific survival (P<0.05). The Kaplan-Meier 5-year grade 3/4 complication free estimate of the cohort was 84%. Grade 3/4 complications: tumor size and tumor dose were independently predictive (P<0.05).	2
31. Urbanski K, Kojs Z, Reinfuss M, Fabisiak W. Primary invasive vaginal carcinoma treated with radiotherapy: analysis of prognostic factors. *Gynecol Oncol.* 1996; 60(1):16-21.	Observational-Tx	125 patients	The authors present their experience with RT of patients with primary invasive vaginal carcinoma and discuss the controversial problem of the factors that significantly affect survival.	5-year NED survival was achieved in 42.4% of patients. In the Cox multivariate analysis three variables were independently related to beneficial survival: grade G1 + G2, stage I + II, and age <60 years. Of 66 patients who died of vaginal cancer, locoregional failure was found in 51 (77.3%), locoregional and distant in 5 (7.6%), and distant only in 10 (15.1%) patients. Late radiation morbidity occurred in 16 (12.8%) patients.	2
32. Mock U, Kucera H, Fellner C, Knocke TH, Potter R. High-dose-rate (HDR) brachytherapy with or without external beam radiotherapy in the treatment of primary vaginal carcinoma: long-term results and side effects. *Int J Radiat Oncol Biol Phys.* 2003; 56(4):950-957.	Observational-Tx	86 patients	To report toxicity, prognostic factors, and outcome of HDR brachytherapy in the primary management of vaginal carcinoma.	5-year OS rates for stages 0-IV diseases were 83%, 41%, 43%, 37%, and 0%, respectively. Corresponding 5-year disease-specific survival rates were 100%, 92%, 57%, 59%, and 0%. Regarding 5-year recurrence-free intervals, values of 100%, 77%, 50%, 23%, and 0% (stages 0-IV) were found, respectively. Tumor stage was the most significant prognostic factor. Chronic side effects G 1-4 were observed in ≤2% (bladder, rectum) and 1%-6% (vagina).	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Leung S, Sexton M. Radical radiation therapy for carcinoma of the vagina--impact of treatment modalities on outcome: Peter MacCallum Cancer Institute experience 1970-1990. *Int J Radiat Oncol Biol Phys*. 1993; 25(3):413-418.	Observational-Tx	103 patients	To determine the outcome of radical RT for carcinoma of the vagina.	Results were analyzed from two eras--before and after 1985--reflecting changes in referral pattern, treatment policy, and outcome. 48 patients were treated before 1985 (stage I, 24; stage II, 6; stage III, 15; stage IV, 3) and 36 patients after 1985 (stage I, 20; stage II, 3; stage III, 6; stage IV, 7). After 1985 more patients were treated with combined beam radiation and brachytherapy (23/36 vs 16/48 prior to 1985). More extensive tumors were systematically implanted (Ir 192). (No implants before 1985; 15 implants and 8 intracavitary applications post 1985). Fewer were treated with EBRT alone after 1985; 11/36 (31%) vs 27/48 (55%) before 1985. A small number (7/84-8%) were treated with brachytherapy alone. Survival results were markedly improved after 1985 (22/36-61% vs 16/48-33%) due partly to the shorter period of follow-up, but due also to marked improvement in local control particularly in early stage disease. (1/23 vs 12/30 recurrences in stage I, II disease). Results indicate optimal results with radical RT occur only with adequate dose delivery best achieved with a judicious combination of EBRT and brachytherapy.	2
34. Nori D, Hilaris BS, Stanimir G, Lewis JL, Jr. Radiation therapy of primary vaginal carcinoma. *Int J Radiat Oncol Biol Phys*. 1983; 9(10):1471-1475.	Observational-Tx	36 patients	To examine RT management of primary carcinoma of the vagina.	14 patients (39%) were stage I; 6 patients (17%) were stage II; 3 patients (8%) were stage III; and 13 patients (36%) were stage IV. 9 patients (25%) were treated with external radiation and interstitial implant; 7 patients (20%) were treated with interstitial implant alone; 9 patients (25%) were treated with external radiation alone and 11 patients (30%) with external radiation and intracavitary radiation. The 5-year NED survival was 71% in stage I, 66% in stage II, 33% in stage III and 0% in stage IV.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Rydzewska L, Tierney J, Vale CL, Symonds PR. Neoadjuvant chemotherapy plus surgery versus surgery for cervical cancer. *Cochrane Database Syst Rev.* 2010; (1):CD007406.	Review/Other-Tx	6 trials (1,072 women)	To assess the role of neoadjuvant chemotherapy in women with early or locally advanced cervical cancer.	Although data on PFS was available for all 6 trials (1,036 women), data on OS, resection rates and pathological response were only available for 5 trials (909 to 938 women) and data on recurrence were only available for 3 trials (604 women). Whilst PFS was significantly improved with neoadjuvant chemotherapy (HR = 0.76, 95% CI = 0.62 to 0.94, P=0.01), no OS benefit was observed (HR = 0.85, 95% CI = 0.67 to 1.07, P=0.17). Furthermore, estimates for both local (OR = 0.76, 95% CI = 0.49 to 1.17, P=0.21) and distant (OR = 0.68, 95% CI = 0.41 to 1.13, P=0.13) recurrence and rates of resection (OR = 1.55, 95% CI = 0.96 to 2.50, P=0.07) only tended to be in favor of neoadjuvant chemotherapy, and heterogeneity was observed. Exploratory analyses of pathological response showed a significant decrease in adverse pathological findings with neoadjuvant chemotherapy (OR = 0.54, 95% CI = 0.39 to 0.73, P<0.0001 for lymph node status; OR = 0.58, 95% CI = 0.41 to 0.82, P=0.002 for parametrial infiltration) which despite a high level of heterogeneity was still significant when the random effects model was used. There was also no difference in the effect of neoadjuvant chemotherapy according to total cisplatin dose, chemotherapy cycle length or by cervical cancer stage.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Zanetta G, Lissoni A, Gabriele A, et al. Intense neoadjuvant chemotherapy with cisplatin and epirubicin for advanced or bulky cervical and vaginal adenocarcinoma. *Gynecol Oncol.* 1997; 64(3):431-435.	Review/Other-Tx	22 patients	The authors report their experience with a neoadjuvant intensive regimen including cisplatin and epirubicin for bulky or locally advanced cervical or vaginal adenocarcinoma.	21 subjects received at least four courses of treatment and were therefore evaluable for response. 4 clinically complete and 10 partial responses, accounting for an objective response rate of 67% were observed. 18 subjects (82%) underwent surgery without serious complications. No histopathologic complete response was observed. The response rate is in the lower range observed with other regimens for squamous cell carcinoma. Although feasible, this regimen implies a significant risk of myelotoxicity. This enhanced toxicity may be justified only if balanced by long-term survival.	4
37. Lanciano R, Calkins A, Bundy BN, et al. Randomized comparison of weekly cisplatin or protracted venous infusion of fluorouracil in combination with pelvic radiation in advanced cervix cancer: a gynecologic oncology group study. *J Clin Oncol.* 2005; 23(33):8289-8295.	Experimental-Tx	316 patients; 159 assigned to arm I and 157 assigned to arm II	To compare the outcome of protracted venous infusion fluorouracil with standard weekly cisplatin and concurrent RT.	The study was closed prematurely when a planned interim futility analysis indicated that protracted venous infusion fluorouracil/RT had a higher treatment failure rate (35% higher) and would, most likely, not result in an improvement in PFS compared with weekly cisplatin/RT. The protracted venous infusion fluorouracil/RT arm continues to show a higher risk of treatment failure (relative risk unadjusted, 1.29) and a higher mortality rate (relative risk unadjusted, 1.37). There was no difference in pelvic treatment failure between regimens, but there was an increase in the failure rate at distant sites in the protracted venous infusion fluorouracil arm.	1

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Morris M, Eifel PJ, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med.* 1999; 340(15):1137-1143.	Experimental-Tx	403 women	To compare the effect of RT to a pelvic and para-aortic field with that of pelvic radiation and concurrent chemotherapy with fluorouracil and cisplatin in women with advanced cervical cancer.	Of the 403 eligible patients, 193 in each group could be evaluated. The median duration of follow-up was 43 months. Estimated cumulative rates of survival at 5 years were 73% among patients treated with RT and chemotherapy and 58% among patients treated with RT alone (P=0.004). Cumulative rates of DFS at 5 years were 67% among patients in the combined-therapy group and 40% among patients in the RT group (P<0.001). The rates of both distant metastases (P<0.001) and locoregional recurrences (P<0.001) were significantly higher among patients treated with RT alone. The seriousness of side effects was similar in the two groups, with a higher rate of reversible hematologic effects in the combined-therapy group.	1
39. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med.* 1999; 340(15):1144-1153.	Experimental-Tx	526 women	To perform a randomized trial of RT in combination with three concurrent chemotherapy regimens — cisplatin alone; cisplatin, fluorouracil, and hydroxyurea; and hydroxyurea alone — in patients with locally advanced cervical cancer.	The median duration of follow-up was 35 months. Both groups that received cisplatin had a higher rate of PFS than the group that received hydroxyurea alone (P<0.001 for both comparisons). The relative risks of progression of disease or death were 0.57 (95% CI, 0.42 to 0.78) in group 1 and 0.55 (95% CI, 0.40 to 0.75) in group 2, as compared with group 3. The OS rate was significantly higher in groups 1 and 2 than in group 3, with relative risks of death of 0.61 (95% CI, 0.44 to 0.85) and 0.58 (95% CI, 0.41 to 0.81), respectively.	1
40. Dalrymple JL, Russell AH, Lee SW, et al. Chemoradiation for primary invasive squamous carcinoma of the vagina. *Int J Gynecol Cancer.* 2004; 14(1):110-117.	Review/Other-Tx	14 patients	To report outcomes for patients with primary, invasive, squamous carcinoma of the vagina treated with chemoradiation.	One patient failed locally at 7 months and died of disease at 11 months. 4 patients died of intercurrent illness (46, 92, 104, 109 months) and 9 are alive and cancer-free 74-168 months after treatment (median 100 months). There were no vesicovaginal or enterovaginal fistulae.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Samant R, Lau B, E C, Le T, Tam T. Primary vaginal cancer treated with concurrent chemoradiation using Cis-platinum. *Int J Radiat Oncol Biol Phys.* 2007; 69(3):746-750.	Observational-Tx	12 patients	To evaluate the feasibility of concurrent weekly Cis-platinum chemoradiation in the curative treatment of primary vaginal cancer.	10 patients (83%) were diagnosed with squamous cell carcinoma and 2 patients (17%) with adenocarcinoma. The distribution according to stage was as follows: 6 (50%) stage II, 4 (33%) stage III, and 2 (17%) stage IVA. All patients received pelvic EBRT concurrently with weekly intravenous Cis-platinum chemotherapy (40 mg/m(2)) followed by brachytherapy. The median dose of EBRT was 4500 cGy given in 25 fractions over 5 weeks. 10 patients received interstitial brachytherapy, and 2 patients received intracavitary brachytherapy, with the median dose being 3000 cGy. The 5-year OS, PFS, and locoregional PFS rates were 66%, 75%, and 92%, respectively. Late toxicity requiring surgery occurred in 2 patients (17%).	3
42. Harris EE, Latifi K, Rusthoven C, Javedan K, Forster K. Assessment of organ motion in postoperative endometrial and cervical cancer patients treated with intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys.* 2011; 81(4):e645-650.	Review/Other-Tx	22 patients	To quantify vaginal wall organ motion during the course of postoperative pelvic irradiation using pelvic IMRT.	The total motion of the fiducials center of mass was a median of 5.8 mm (range, 0.6-20.2 mm), and 95% of all center of mass positions fell within 15.7 mm of their original position. Directional margins of 3.1 mm along the right-left axis, 9.5 mm along the superoinferior axis, and of 12.1 mm along the anteroposterior axis encompassed the vaginal fiducials in 95% of treatments. Mean organ deformation for all patients was 3.9 mm, (range, 0-27.5 mm; standard deviation, 3.1 mm), with significant distortions of greater than 10 mm in 17% of secondary image sets.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Jhingran A, Salehpour M, Sam M, Levy L, Eifel PJ. Vaginal motion and bladder and rectal volumes during pelvic intensity-modulated radiation therapy after hysterectomy. *Int J Radiat Oncol Biol Phys.* 2012; 82(1):256-262.	Review/Other-Tx	24 patients	To evaluate variations in bladder and rectal volume and the position of the vaginal vault during a 5-week course of pelvic IMRT after hysterectomy.	The mean full and empty bladder volumes at simulation were 480 cc (range, 122-1,052) and 155 cc (range, 49-371), respectively. Bladder volumes varied widely during IMRT: the median difference between the maximum and minimum volumes was 247 cc (range, 96-585). Variations in rectal volume during IMRT were less pronounced. For the 16 patients with vaginal fiducial markers in place throughout IMRT, the median maximum movement of the markers during IMRT was 0.59 cm in the right-left direction (range, 0-0.9), 1.46 cm in the anterior-posterior direction (range, 0.8-2.79), and 1.2 cm in the superior-inferior direction (range, 0.6-2.1). Large variations in rectal or bladder volume frequently correlated with significant displacement of the vaginal apex.	4
44. Kucera H, Mock U, Knocke TH, Kucera E, Potter R. Radiotherapy alone for invasive vaginal cancer: outcome with intracavitary high dose rate brachytherapy versus conventional low dose rate brachytherapy. *Acta Obstet Gynecol Scand.* 2001; 80(4):355-360.	Observational-Tx	190 patients	To compare the role of remote afterloaded HDR brachytherapy with traditional low-dose-rate brachytherapy for patients with invasive primary vaginal carcinoma.	No significant differences were found for stages, tumor grade or location between the two groups. Crude 5-year survival for all patients was 41% in the former low-dose-rate brachytherapy group, 81% in stage I and 43% in stage II. Overall actuarial 3-year survival and disease-specific survival rates for all patients in the HDR brachytherapy series were 51% and 66%, respectively. Disease-specific 3-year survival attained 83% in stage I and 66% in stage II. There were no significant differences in local and distant recurrences between the treatment modalities. The comparison of treatments with or without EBRT and of complications showed no significant differences between the HDR brachytherapy and low-dose-rate brachytherapy series.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Perez CA, Korba A, Sharma S. Dosimetric considerations in irradiation of carcinoma of the vagina. *Int J Radiat Oncol Biol Phys.* 1977; 2(7-8):639-649.	Observational-Tx	126 patients	To retrospectively study 114 patients with histologically proven invasive carcinoma of the vagina and 12 patients with carcinoma in situ; in evaluation of the dose of radiation. Special emphasis was given to the primary tumor and to the parametrial tissues and correlated with tumor control and survival.	11/12 patients with carcinoma in situ were controlled with interstitial or intracavitary therapy. 36/37 patients with stage I carcinoma showed no evidence of vaginal or pelvic recurrence. Most of them were treated with interstitial or intracavitary therapy or both and the addition of EBRT did not significantly increase survival or tumor control. In stage IIA (paravaginal extension) 12/17 (70.5%) patients were controlled with a combination of brachytherapy and EBRT whereas only 4/16 (25%) treated without the addition of EBRT exhibited tumor control in the pelvis. 4/10 patients with stage III disease were controlled whereas only one of 11 patients with stage IV had control of the pelvic tumor even with relatively high doses of irradiation.	2
46. Beriwal S, Demanes DJ, Erickson B, et al. American Brachytherapy Society consensus guidelines for interstitial brachytherapy for vaginal cancer. *Brachytherapy.* 2012; 11(1):68-75.	Review/Other-Tx	N/A	To present recommendations for the use of interstitial brachytherapy in patients with vaginal cancer or recurrent endometrial cancer in the vagina.	Patients with bulky disease (approximately >0.5 cm thick) should be considered for treatment with interstitial brachytherapy. The American Brachytherapy Society reports specific recommendations for techniques, target volume definition, and dose-fractionation schemes. 3D treatment planning is recommended with CT scan and/or MRI. The treatment plan should be optimized to conform to the clinical target volume and should reduce the dose to critical organs, including the rectum, bladder, urethra, and sigmoid colon. Suggested doses in combination with EBRT and summated equivalent doses in 2 Gy fractions are tabulated.	4

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Dimopoulos JC, Schmid MP, Fidarova E, Berger D, Kirisits C, Potter R. Treatment of locally advanced vaginal cancer with radiochemotherapy and magnetic resonance image-guided adaptive brachytherapy: dose-volume parameters and first clinical results. *Int J Radiat Oncol Biol Phys*. 2012; 82(5):1880-1888.	Observational-Tx	13 patients	To investigate the clinical feasibility of MR image-guided adaptive brachytherapy for patients with locally advanced vaginal cancer and to report treatment outcomes.	The mean gross tumor volume (+/- 1 standard deviation) at diagnosis was 45.3 (+/-30) cm(3), and the mean gross tumor volume at brachytherapy was 10 (+/-14) cm(3). The mean D90 for the high-risk clinical target volume was 86 (+/-13) Gy. The mean D2cc for bladder, urethra, rectum, and sigmoid colon were 80 (+/-20) Gy, 76 (+/-16) Gy, 70 (+/-9) Gy, and 60 (+/-9) Gy, respectively. After a median follow-up of 43 months (range, 19-87 months), one local recurrence and two distant metastases cases were observed. Actuarial local control and OS rates at 3 years were 92% and 85%. One patient with stage IVA and 1 patient with stage III disease experienced fistulas (one vesicovaginal, one rectovaginal), and 1 patient developed periurethral necrosis.	4
48. Lee WR, Marcus RB, Jr., Sombeck MD, et al. Radiotherapy alone for carcinoma of the vagina: the importance of overall treatment time. *Int J Radiat Oncol Biol Phys*. 1994; 29(5):983-988.	Observational-Tx	65 patients	To review treatment results, complications, and the importance of overall treatment time for carcinoma of the vagina treated with RT alone.	The 5-year cause-specific survival rates were, stage 0 (6 patients), 100%; stage I (17 patients), 94%; stage IIA (6 patients), 80%; stage IIB (10 patients), 39%; stage III (2 patients), 79%; and stage IVA (6 patients), 62%. The pelvic control rates at 5 years were: stage 0, 100%; stage I, 87%; stage IIA, 88%; stage IIB, 68%; stage III, 80%; and stage IVA, 67%. The parameters of stage, patient age, total dose to primary site, and overall treatment time were evaluated in a multivariate analysis. The single most important predictor of pelvic control was overall treatment time. If the entire course of RT (external beam + implant) was completed within 9 weeks (63 days), the pelvic control rate was 97%. The pelvic control rate was only 54% if treatment time extended beyond 9 weeks (P=.0003). The rate of severe complications was 12%, and the incidence increased with increasing total primary dose.	2

Management of Vaginal Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Spanos WJ, Jr., Perez CA, Marcus S, et al. Effect of rest interval on tumor and normal tissue response--a report of phase III study of accelerated split course palliative radiation for advanced pelvic malignancies (RTOG-8502). *Int J Radiat Oncol Biol Phys.* 1993; 25(3):399-403.	Experimental-Tx	136 patients	A report of patients randomized between rest intervals of 2 weeks vs 4 weeks to determine if length of rest would influence tumor response or patient toxicity.	There was a trend toward increased acute toxicity incidence in patients with shorter rest interval (S/68 vs O/68; P=.07). Late toxicity was not significantly different between the two groups. Decreasing the interval between courses did not result in a significant improvement in tumor response (CR+PR = 34% vs 26%, P=NS). More patients in the 2 week groups completed all three courses (72% vs 63%). Patients completing cell three courses had a significantly higher overall response rate than for patients completing less than three courses (42% vs 5%) and higher complete response rate (17% vs 1%). A multivariate analysis indicated performance status as the significant predictor for number of courses completed. For Karnofsky Performance Status ≥80, the survival at 12 months was 40% for the 2 week interval and 25% for the 4 week interval.	1

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

AUC = Area under the receiver operating characteristic curve

CI = Confidence interval

CT = Computed tomography

DFS = Disease-free survival

EBRT = External-beam radiation therapy

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

HDR = High-dose-rate

HPV = Human papilloma virus

HR = Hazard ratio

IMRT = Intensity-modulated radiotherapy

MRI = Magnetic resonance imaging

NPV = Negative predictive value

OR = Odds ratio

OS = Overall survival

PFS = Progression-free survival

PPV = Positive predictive value

RT = Radiation therapy