

Vulvar Cancer Guidelines

References



Abang Mohammed, D. K., R. Uberoi, et al. 2000. "Inguinal node status by ultrasound in vulva cancer." *Gynecol Oncol* **77**: 93 -96.

OBJECTIVE: The objective of this study was to determine the value of ultrasound in preoperative assessment of groin node status in vulva cancer. **MATERIALS AND METHODS:** Women with clinically uninvolved groins who were undergoing groin node dissection for vulva cancer in our department over an 18-month period were recruited into the study. A preoperative scan of each groin to be dissected was performed to identify any suspicious lymph nodes containing metastases. Suspicious nodes were defined by two sonographic criteria: short axis diameter >8 mm and a long axis/short axis ratio $L/S \leq 2$. Each suspicious node was sampled by ultrasound -guided fine-needle aspiration FNA. **RESULTS:** Twenty women, with an average age of 70 years, consented to the study. Seventeen had bilateral groin node dissection and three had unilateral groin node dissection. Sixteen of the seventeen dissected groins contained metastases. Short axis had a better overall accuracy 89% but failed to detect a singular micrometastasis. The L/S ratio identified all positive groins but had a high false-positive rate 62% and an overall accuracy of 67%. The combination of both criteria did not improve the overall accuracy when compared with the individual criterion. FNA was not diagnostic in three, representative in two, and falsely negative in one. **CONCLUSION:** Although L/S ratio has a lower overall accuracy, it correctly identified all groins with metastases. This has a great impact on treatment and prognosis. Its high false-positive rate may be improved by more diagnostic FNA. These sonographic criteria show good potential for segregating those with groin metastases requiring surgical treatment from those with uninvolved nodes. This experience has to be expanded to prove its clinical effectiveness.

Abbas, S. and M. Seitz 2011. "Systematic review and meta -analysis of the used surgical techniques to reduce leg lymphedema following radical inguinal nodes dissection." *Surg Oncol* **20**: 88 -96.

BACKGROUND: Inguinal nodes dissection is associated with high rates of morbidity, lymphedema in particular is a chronic disabling condition which is a common complication following this operation. Prevention or minimization of this condition is an important aim when considering this procedure. Many technical modifications are suggested for this purpose. This systematic review aims at assessing the efficacy of the available strategies to reduce the risk and severity of leg lymphedema. **METHODS:** For this review, MEDLINE and EMBASE were searched to identify studies that reported surgical strategies designed to reduce complications of groin dissection and in particular leg lymphedema. Studies that reported outcome of long saphenous vein sparing, fascia preserving dissection, microvascular surgery, sartorius transposition and omental pedicle flap were located. Data were collected using predefined inclusion and exclusion criteria. A combined odds ratio was calculated combining studies suitable for meta-analysis using the random effect model. **RESULTS:** The search result defined few studies that reported results of saphenous vein sparing technique; some of those studies were found suitable for meta-analysis based on the Newcastle-Ottawa scale for non-randomized studies. The meta-analysis showed significant reduction of lymphedema odds ratio 0.24, 95% CI 0.11 - 0.53 and other complications of inguinal node dissection. There were no randomized studies to address this problem; there are also isolated studies that reported benefits of other techniques but none of them was suitable for meta-analysis. **CONCLUSION:** Meta-analysis of the reported studies on sparing the long saphenous vein in inguinal nodes dissection suggests a reduced rate of lymphedema and other postoperative complications. Other methods that may be beneficial are fascia preserving dissection, pedicled omental flap and microsurgery; however sartorius transposition has not been shown to reduce the rate of complications. Randomized controlled trials are needed to prove the benefits of various technical modifications.

Achimas-Cadariu, P., P. Harter, et al. 2009. "Assessment of the sentinel lymph node in patients with invasive squamous carcinoma of the vulva." *Acta Obstet Gynecol Scand* **88**: 1209 -1214.

OBJECTIVE: This study aims to evaluate the feasibility and diagnostic validity of the sentinel lymph node technique in detecting inguinal lymph node metastases in patients with invasive squamous cancer

of the vulva. DESIGN: Retrospective analysis of the in-house tumor registry. SETTING: Dr. Horst Schmidt Klinik, a tertiary gynecologic oncology unit in Wiesbaden, Germany, June 2000-May 2008. POPULATION: All consecutive operated patients with primary envisaged diagnosis were included. METHODS: The sentinel node identification technique was performed and patients were informed accordingly. Patients who consented and were found eligible underwent preoperative lymphoscintigraphy on the day before surgery. MAIN OUTCOME MEASURES: Sentinel node detection in specimen from sentinel lymph node biopsy and from full lymphadenectomy LNE; sentinel lymph node biopsy as a sole surgical groin procedure in patients with histological negative sentinel node; benefit with respect to side effects for sentinel lymph node biopsy compared to full LNE; complication rates; and recurrences of vulvar cancer. RESULTS: In all, 46 of 59 patients with vulvar malignancy underwent inguinofemoral LNE, sentinel lymph node biopsy SLB of the groin followed by LNE, or SLB alone. Most patients had been diagnosed in the early stages of the disease. Since no false positive or false negative results were recorded, the sensitivity, specificity, positive predictive value and negative predictive value of the sentinel lymph node were 100%. However, in 6%, a sentinel lymph node could not be detected intraoperatively indicating a feasibility of 94%. CONCLUSION: The implementation of sentinel lymph node technique for groin staging in squamous cell vulvar cancer seems to provide a feasible and safe technique in tertiary gynecologic oncology.

AHS 2013. "Squamous Cell Carcinoma of the Vulva." <http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-gyne006-vulva.pdf>.

Akl, A., M. Akl, et al. 2000. "Preliminary results of chemoradiation as a primary treatment for vulvar carcinoma." *Int J Radiat Oncol Biol Phys* **482**: 415 -420.

PURPOSE: To assess the role of chemoradiation as a primary treatment for vulvar carcinoma. METHODS AND MATERIALS: Between December 1989 and August 1997, there were 14 patients with the diagnosis of squamous cell carcinoma of the vulva. Two patients were excluded from this study because of advanced stage at presentation. Key information about the remaining 12 patients was extracted from their charts. All patients had biopsy prior to treatment, and were treated with chemoradiation. Radiation was administered to the vulva only. Surgical biopsies from the vulva and inguinal nodal dissection were done 4-6 weeks after radiation treatment. All patients were followed for evaluation of response and clinical detection of recurrence. The period of follow-up ranged from 8 to 125 months. Mean follow-up period was 41 months. RESULTS: All 12 patients showed complete response to the treatment. Only 1 patient 8.3% developed local recurrence at 3 months posttreatment. Another patient 8.3% developed nodal recurrence at 30 months posttreatment. Both patients were salvaged by surgical treatment and remained disease free. The actuarial 5-year disease-free survival was 43%. The actuarial 3-year disease-free survival was 84%. The majority of patients developed mild-to-moderate complications due to chemoradiation. These were well tolerated and responded to medical treatment. None of the patients developed late complications to chemoradiation treatment. CONCLUSIONS: Chemoradiation is an effective primary treatment for vulvar carcinoma as shown by these successfully managed cases.

Akrivos, N., A. Rodolakis, et al. 2011. "Sentinel node in vulvar cancer. To use or not to use technetium?" *Int J Gynecol Cancer* **21**Suppl 3: S905.

Akrivos, N., A. Rodolakis, et al. 2011. "Detection and credibility of sentinel node in vulvar cancer: a single institutional study and short review of literature." *Arch Gynecol Obstet* **2846**: 1551 -1556.

PURPOSE: To evaluate the detectability and credibility of sentinel lymph node (SLN) in vulvar cancer. METHODS: With Tc99m-nanocolloid and methylene blue, we identified SLNs in 34 patients. In 27 cases both tracers were used, while in 7 only blue dye was used. Completion lymphadenectomy was performed in all patients. SLNs and non-SLNs were sent separately for pathologic evaluation. RESULTS: At least one SLN was identified in all patients. Detection rate per groin was not significantly higher in the combined versus blue dye only technique 42/50 vs. 10/14, $p = 0.43$. 99m -Tc

was not superior to blue dye in detecting SLN 42/50 vs. 50/64, $p = 0.65$. Midline location of the tumor did not seem to negatively affect the procedure. Four false negatives were observed in three patients with tumors >4 cm. Negative predictive value of SLN was 100% for grade I tumors ≤ 4 cm in patients ≤ 71 years. **CONCLUSION:** Tc-99m does not seem to be superior to methylene blue in the detection of SLN in vulvar cancer. Patients of younger age with small, well-differentiated tumors appear to be the most suitable candidates for lymphatic mapping.

Andrews, S. J., B. T. Williams, et al. 1994. "Therapeutic implications of lymph nodal spread in lateral T1 and T2 squamous cell carcinoma of the vulva." *Gynecol Oncol* **55**: 41-46.

From 1963 to 1993, 157 patients with primary squamous cell carcinoma of the vulva were treated by radical surgery at the University of Kentucky Medical Center. There were 84 unilateral lesions confined to the labium majus or labium minus. Thirty-seven patients had T1 lesions, median diameter 1.5 cm range 0.5-2.0 cm, and 47 patients had T2 lesions, median diameter 3.4 cm range 2.2-9.0 cm. Radical vulvectomy with bilateral inguinal lymphadenectomy was performed in 56 patients and radical hemivulvectomy with selective inguinal lymphadenectomy in 28 patients. An average of 8 nodes was removed with superficial inguinal lymphadenectomy and 13 nodes with superficial and deep inguinal lymphadenectomy. Deep inguinal lymph node metastases occurred only in patients with positive superficial inguinal lymph nodes. There were no contralateral inguinal lymph node metastases in any lateral T1 or T2 lesion. Following surgery, patients were followed 1-15 years mean 5.0 years and none have been lost to follow-up. Nine patients developed ipsilateral recurrences, but no contralateral recurrences were noted. Seven of these patients developed local recurrences to the ipsilateral vulvar skin and were cured by reexcision. Two patients 2.4%, both of whom had positive ipsilateral superficial and deep inguinal lymph node metastases at the time of initial surgery, developed distant metastases and died of disease 10 and 11 months after treatment. These data suggest that deep inguinal lymph nodal metastases occurred only in patients with superficial inguinal node involvement. Contralateral inguinal lymph nodal metastases are extremely rare in lateral T1 and T2 vulvar squamous cell carcinomas. Radical hemivulvectomy is as effective as radical vulvectomy in the treatment of lateral T1 and T2 vulvar squamous cell cancers.

Ansink, A. C., D. M. Sie-Go, et al. 1999. "Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multicenter study." *Cancer* **86**: 652-656.

BACKGROUND: The aim of this multicenter study was to investigate the feasibility and negative predictive value of sentinel lymph node detection with blue dye in vulvar carcinoma patients. **METHODS:** In patients with squamous cell carcinoma of the vulva without suspicious groin lymph nodes, patent blue V was injected intradermally shortly before surgery. Routine groin lymph node dissection and radical vulvectomy were performed. During the surgery, blue lymph vessels and lymph nodes were identified, and the blue lymph nodes were sent separately for histologic examination. The negative predictive value of the blue lymph nodes for the absence of metastases was assessed by histologic examination of the groin lymph node specimens. **RESULTS:** Fifty-one patients in whom 93 groin lymph node dissections were performed were entered. One or more blue lymph nodes were detected in only 52 groins 56%. Nine 17% of these were tumor positive, and 6 blue lymph nodes were the only tumor positive lymph nodes in the specimen in which they were found. There were two false-negative blue lymph nodes. The negative predictive value was 0.953. **CONCLUSIONS:** It was shown in this multicenter study that sentinel lymph node detection in vulvar carcinoma patients with blue dye only is not feasible because its negative predictive value is too low. Further studies involving the use of a combination of radioactive labeled technetium and blue dye are warranted.

Aragona, A. M., N. Cuneo, et al. 2012. "Tailoring the treatment of locally advanced squamous cell carcinoma of the vulva: neoadjuvant chemotherapy followed by radical surgery: results from a multicenter study." *Int J Gynecol Cancer* **22**: 1258-1263.

OBJECTIVE: To determine the feasibility of performing neoadjuvant chemotherapy (NCH) followed by radical surgery in patients with locally advanced squamous cell carcinoma of the vulva. **METHODS:** Prospective and multicenter trial. Thirty-five patients with a diagnosis of previously untreated locally advanced squamous cell carcinoma of the vulva were given 4 schemes of cisplatin-based NCH and 1 NCH regimen with single bleomycin. Then, they underwent radical surgery of the vulva if clinical response was 50% or more. Age, NCH schemes used, toxicity, response to treatment, type of radical surgery performed, and clinical outcome were evaluated. **RESULTS:** Thirty-three patients completed the proposed schemes, and 30 were assessed for radical surgery. Finally, 27 patients underwent radical surgery: radical vulvectomy or radical local excision plus bilateral inguinofemoral lymphadenectomy. In 2 cases of persistent rectal involvement, posterior pelvic exenteration was performed. Moreover, 24 of 27 patients remain with no evidence of disease to date. Toxicity was acceptable. Median age was 62 years, range, 54 -72 years. Median follow-up was 49 months, range, 4 -155 months. **CONCLUSIONS:** The use of NCH in selected groups may increase surgical feasibility in initially inoperable patients, thus favoring organ preservation and less extensive resections. Adverse reactions were acceptable, and vulvoperineal deleterious effects that may occur after radiotherapy were consequently avoided.

Atamdede, F. and D. Hoogerland 1989. "Regional lymph node recurrence following local excision for microinvasive vulvar carcinoma." *Gynecol Oncol* **34**: 125 -128.

A case of microinvasive squamous cell carcinoma of the vulva is reported in which regional lymph node recurrence was noted after excisional therapy. Review of the initial pathology revealed only 0.72 mm of invasion. The results of a literature survey regarding microinvasive vulvar carcinoma are discussed.

Bafna, U. D., U. M. Devi, et al. 2004. "Carcinoma of the vulva: a retrospective review of 37 cases at a regional cancer centre in South India." *J Obstet Gynaecol* **24**: 403 -407.

A retrospective review of 37 cases of carcinoma of the vulva presenting between 1996 and 2000 has been carried out. Thirty-three cases were managed with curative intent and four cases with advanced loco-regional disease were managed with palliative intent. The surgical treatment consisted of wide excision in one case, radical vulvectomy (RV) in six cases, radical vulvectomy and bilateral groin node dissection (RV+BGND) in 25 cases and radical vulvectomy and unilateral groin node dissection in one case. Nine of these 33 women also received adjuvant chemotherapy preoperatively in the hope of achieving better tumour-free surgical margins. Eight cases had a partial response and one case achieved complete response; the surgical margins were free in all these patients. One case received neoadjuvant radiotherapy to the vulva and pelvis followed by RV+BGND, which revealed no residual tumour. Overall, 26/33 cases had groin/inguinal node dissection and 23 (88.4%) of them had groin wound dehiscence. Thirteen of these 26 patients (50%) had inguinal node metastases: Stage III, four patients; Stage IV, nine patients. All the patients with negative nodes were free of disease while three of four patients with Stage III and two of nine patients with Stage IV with nodal metastases remained free of disease. The only patient with Stage III disease plus inguinal node metastases who recurred had multiple positive nodes with extracapsular spread. It appears that although bilateral involvement of the inguinal lymph nodes carries a worse prognosis, unilateral involvement with or without vaginal involvement carries an excellent prognosis provided multiple nodes are not involved. The role of neoadjuvant chemotherapy as compared to neoadjuvant radiotherapy, in locally advanced tumours, needs to be explored further.

Balat, O., C. Edwards, et al. 2000. "Complications following combined surgery: radical vulvectomy versus wide local excision and radiotherapy for the treatment of carcinoma of the vulva: report of 73 patients." *Eur J Gynaecol Oncol* **21**: 501 -503.

Cancer of the vulva is uncommon, accounting for only 5% of all gynecologic malignancies, and usually occurs in women over 60 years of age. The historic treatment of choice for invasive squamous cell carcinoma of the vulva is radical vulvectomy with bilateral inguinal lymphadenectomy, which has

produced excellent long-term survival. We retrospectively analyzed the complications of wide local excision plus postoperative radiotherapy compared with those of radical vulvectomy and bilateral lymphadenectomy plus pre-or postoperative radiotherapy in 73 patients with vulvar cancer. There were no significant differences among these treatments in terms of primary tumor control, 5-year disease-free survival, and overall survival. Based on these results, the best treatment alternative for advanced vulvar cancer is wide local excision plus radiotherapy, as this method retains the high survival of traditional therapy but has less morbidity.

Balat, O., C. L. Edwards, et al. 2000. "The long term results of radiotherapy with or without surgery in management of advanced vulvar cancer: report of 76 patients." *Eur J Gynaecol Oncol* **214**: 426 -429.

BACKGROUND: The combination of conservative surgery plus radiotherapy for vulvar cancer has been well established as a therapeutic alternative to extensive radical surgery. This study was undertaken to evaluate the long-term results of radiotherapy with or without surgery in the management of advanced vulvar cancer. **PATIENTS AND METHODS:** The cases of 76 patients who had advanced carcinoma of the vulva treated with different modalities at the University of Texas M.D. Anderson Cancer Center were retrospectively reviewed. Three patients had unstaged disease as a result of previous surgery, 19 had stage II, 40 had stage III, and 14 had stage IV disease. Follow-up ranged from 4 to 17 years median, 11 years. **RESULTS:** Five -year disease-free survivals were 75, 67, 68 and 52% for treatment groups I, II, III, and IV, respectively. Disease was controlled locally in 83, 80, 73 and 56% of patients in groups I through IV, respectively; the overall rate of local control was 79%. There was no significant difference in primary tumor control, 5-year disease-free survival, or overall survival among the different treatment groups $p=0.1300$. However, these rates did differ significantly $p<0.006$ based on FIGO stage of disease. **CONCLUSION:** In this report, the cure of vulvar cancers with radiotherapy alone 5 -year disease-free survival 52% and local control 56%, the radiotherapeutic salvage of patients with surgical failure and/or large tumors, the improved survival with low morbidity by pre- and postoperative radiotherapy were provocative observations suggesting the value of this therapy for advanced vulvar cancer.

Basta, A., K. Pitynski, et al. 2005. "Sentinel node in gynaecological oncology." *Rep Prac Oncol Radiother* **10**: 91-94.

Bell, J. G., J. S. Lea, et al. 2000. "Complete groin lymphadenectomy with preservation of the fascia lata in the treatment of vulvar carcinoma." *Gynecol Oncol* **772**: 314 -318.

OBJECTIVE: The goal of this study was to assess the local groin recurrence of vulvar carcinoma in patients treated by complete groin node dissection with preservation of the fascia lata GNDPFL. **METHODS:** This study is a retrospective chart review of 60 patients with Stage I-IV vulvar carcinoma who underwent radical vulvectomy and GNDPFL between 1990 and 1998. All superficial inguinal nodes and the deep femoral nodes on the anterior and medial surfaces of the femoral vein within the fossa ovalis were removed en bloc while sparing the fascia lata and the cribriform fascia over the femoral artery. **RESULTS:** Of the 60 study patients, 14 patients had Stage I disease, 20 Stage II, 21 Stage III, and 5 Stage IV. The mean number of nodes removed was 10 per groin. Thirty-nine patients had benign nodes on groin dissection. None of these 39 patients developed cancer recurrence in the dissected groins. Twenty-one of the sixty study patients 34% had malignant nodes on groin dissection. Of these 21 patients, 2 experienced cancer recurrence in the groins. Our study describes a groin recurrence rate of 7.6% in patients with fewer than three malignant unilateral groin nodes. Postoperatively, 13% of patients developed lymphedema and 15% formed lymphoceles. **CONCLUSIONS:** The zero groin recurrence rate in patients with negative nodes and the low rate of recurrence in patients with positive nodes indicate that groin lymphadenectomy with preservation of fascia lata is complete, therapeutic, and comparable to radical techniques of lymphadenectomy involving skeletonization of femoral vessels, resection of fascia lata, and muscle transposition.

Bellati, F., R. Angioli, et al. 2005. "Single agent cisplatin chemotherapy in surgically resected vulvar cancer patients with multiple inguinal lymph node metastases." *Gynecol Oncol* **96**: 227 -231.

OBJECTIVE: The aim of this study was to evaluate acute and long-term morbidity, recurrence rate, and overall survival in patients with multiple groin lymph node metastases treated with postoperative chemotherapy. **METHODS:** Patients affected by FIGO stages III, IVA, and IVB pelvic lymph nodes only submitted to surgery were then treated with four cycles of cisplatin 100 mg/m² given 21 days apart. Toxicity, overall, and disease-free survival were evaluated. **RESULTS:** Fourteen patients were evaluated. Median patients age was 58 range 48 -82. Median performance status was 0 -2. All patients completed the treatment. No treatment-related deaths occurred. Only two patients suffered from grade 4 neutropenia during chemotherapy. Three patients suffered from long-term severe lymphedema. Four patients suffered a disease recurrence. Three of these patients were subjected to surgery with no severe postoperative complications. Two of the latter patients are still alive. At a median follow-up of 57.5 months range 23 -79 months actuarial 3 -year overall survival and progression-free survival are 86% and 71%, respectively. **CONCLUSIONS:** In patients affected by vulvar cancer with multiple lymph node metastases, radical surgery followed by chemotherapy is a feasible strategy, with an acceptable short- and long-term complication rate. Results in terms of overall survival and disease-free survival are promising. Furthermore, due to absence of local long-term tissue toxicity, this strategy allows physicians to surgically treat regional lymph node recurrence safely.

Benedetti-Panici, P., S. Greggi, et al. 1993. "Cisplatin P, bleomycin B, and methotrexate M preoperative chemotherapy in locally advanced vulvar carcinoma." *Gynecol Oncol* **50**: 49 -53.

Based on the encouraging results of neoadjuvant chemotherapy NACT and radical surgery RS observed in locally advanced cervical cancer, 21 patients with advanced squamous cell carcinoma of the vulva FIGO stages, IVa, 21; TNM stages, T2N2M0, 6, T3N2M0, 11, T4N2M0, 4 were submitted to two to three cycles of cisplatin P, 100 mg/m², Day 1, bleomycin B, 15 mg, Days 1, 8, and methotrexate M, 300 mg/m² + cfr, Day 8 NACT followed by RS in operable patients. Two patients 10% had a partial response in the primary tumor T and 14 67% CR+PR in the inguinal nodes N). The operability rate following NACT was 90% pathological downstaging rate, 33% but surgery was really radical in 79% of cases. Pathological N response was significantly related to the pathological T downstaging, and a persistently high N positivity rate was detected inguinal, 81%; pelvic, 47%. NACT+RS had an acceptable morbidity but the therapeutic results were less encouraging than expected with a 3-year survival of 24% and stage, pathological T downstaging, and N status all significantly affected survival. Sixty-eight percent of the operated patients recurred 3-17 months from the end of treatment and 50% of them had a distant relapse. PBM NACT did not seem to add any substantial benefit to the surgery alone in this subset of patients with extremely advanced disease. Studies on a chemoradiotherapeutic approach are currently in progress in order to confirm the promising preliminary results.

Berek, J. S., J. M. Heaps, et al. 1991. "Concurrent cisplatin and 5 -fluorouracil chemotherapy and radiation therapy for advanced-stage squamous carcinoma of the vulva." *Gynecol Oncol* **42**: 197 -201.

A phase II trial of concurrent cisplatin and 5-fluorouracil (5-FU) chemotherapy and radiation therapy CT + RT was conducted for the primary treatment of 12 patients with retrospective surgical FIGO stages III-IV squamous carcinoma of the vulva. Eight patients were stage III and four were stage IV. Chemotherapy was used as a radiation sensitizer and it was administered in two 5-day cycles 28 days apart. Cisplatin, 50 mg/m²/day iv on Days 1 and 2 or 100 mg/m² on Day 1 or 2, plus continuous-infusion 5-FU, 1000 mg/m²/day for 4-5 days commencing on Days 1 and 28 of external-beam radiation therapy, are given. The pelvic radiation to a dose of 4400-5400 cGy is administered AP and PA to treat the primary tumor, the groin nodes, and the iliac vessels to the level below the common iliac nodes. Complete tumor responses were seen in 8 of 12 67% patients. Responses were observed in 6 of 8 75% stage III patients and 2 of 4 50% stage IV patients. Partial response were observed in 3 patients, and 1 patient had persistent disease. At the completion of concurrent chemoradiation therapy, radical

vulvectomy or excision was used in 3 patients and posterior exenteration in 1. With a median follow-up of 37 months range, 7 -60 months, 10 patients are alive and free of disease, and 2 patients died at 12 and 15 months. There were no treatment-related deaths and no grade 4 toxicity. The morbidity included moist desquamation of the vulva in all patients, with grade 2 toxicity in 10 and grade 3 in 2. One patient had a deep venous thrombosis that responded to anticoagulation therapy. These data support the use of concurrent cisplatin and 5-FU chemotherapy and radiation therapy as an alternative to primary radical surgery to treat advanced-stage squamous carcinoma of the vulva.

Beriwal, S., D. E. Heron, et al. 2006. "Intensity -modulated radiotherapy for the treatment of vulvar carcinoma: a comparative dosimetric study with early clinical outcome." *Int J Radiat Oncol Biol Phys* **64**: 1395 -1400.

OBJECTIVES: To assess early clinical outcome of intensity-modulated radiation therapy IMRT in the treatment of vulvar cancer and compare dosimetric parameters with 3D conformal radiotherapy 3D CRT. **METHODS:** Fifteen patients with vulvar cancer were treated with IMRT. Seven patients were treated with preoperative chemoradiation, and 8 patients were treated with adjuvant postoperative radiation therapy. Median dose was 46 Gy in the preoperative and 50.4 Gy in the postoperative group. **RESULTS:** The mean volume of small bowel, rectum, and bladder that received doses in excess of 30 Gy with IMRT was reduced when compared with 3D CRT. Treatment was well tolerated, and only 1 patient had acute Grade 3 small-bowel toxicity. Median follow-up was 12 months. In the preoperative group, 5 patients 71% had clinical complete response and 3 patients 42.8% had pathologic complete response. In the adjuvant group, 2 patients had recurrences in the treatment field. No patients had late Grade 3 toxicity. The 2-year actuarial disease-specific survival was 100%. **CONCLUSIONS:** Intensity-modulated RT appears to offer advantages over 3D CRT treatment of vulvar cancer by elimination of dose modulation across overlapping regions and reduction of unnecessary dose to the bladder, rectum, and small bowel. Early results with a small number of patients show promising results, with a low incidence of severe toxicity.

Beriwal, S., G. Shukla, et al. 2013. "Preoperative intensity modulated radiation therapy and chemotherapy for locally advanced vulvar carcinoma: analysis of pattern of relapse." *Int J Radiat Oncol Biol Phys* **85**: 1269 -1274.

PURPOSE: To examine clinical outcomes and relapse patterns in locally advanced vulvar carcinoma treated using preoperative chemotherapy and intensity modulated radiation therapy IMRT. **METHODS AND MATERIALS:** Forty-two patients with stage I-IVA stage I, n=3; stage II, n=13; stage III, n=23; stage IVA, n=3 vulvar cancer were treated with chemotherapy and IMRT via a modified Gynecological Oncology Group schema using 5-fluorouracil and cisplatin with twice-daily IMRT during the first and last weeks of treatment or weekly cisplatin with daily radiation therapy. Median dose of radiation was 46.4 Gy. **RESULTS:** Thirty-three patients 78.6% had surgery for resection of vulva; 13 of these patients also had inguinal lymph node dissection. Complete pathologic response was seen in 48.5% n=16 of these patients. Of these, 15 had no recurrence at a median time of 26.5 months. Of the 17 patients with partial pathological response, 8 47.1% developed recurrence in the vulvar surgical site within a median of 8 range, 5 -34 months. No patient had grade ≥ 3 chronic gastrointestinal/genitourinary toxicity. Of those having surgery, 8 24.2% developed wound infections requiring debridement. **CONCLUSIONS:** Preoperative chemotherapy/IMRT was well tolerated, with good pathologic response and clinical outcome. The most common pattern of recurrence was local in patients with partial response, and strategies to increase pathologic response rate with increasing dose or adding different chemotherapy need to be explored to help further improve outcomes.

Berman, M. L., J. T. Soper, et al. 1989. "Conservative surgical management of superficially invasive stage I vulvar carcinoma." *Gynecol Oncol* **35**: 352 -357.

Fifty patients with stage I squamous cell carcinoma of the vulva were treated by means of wide local excision and either unilateral or bilateral superficial inguinal lymphadenectomy. Depth of invasion per se was not an exclusionary criterion; however, 36 of 37 patients for whom depth of invasion could be

assessed had tumors invasive to a maximum depth of 5 mm. Factors investigated included recurrences and survival in addition to the early and delayed morbidity associated with this operative approach. Recurrent intraepithelial or minimally invasive cancer was documented in six patients, five of whom were treated successfully by a subsequent wide local excision following initial surgery. Only one patient died of recurrent carcinoma 16 months following surgery. The morbidity with this operation was appreciably less than that generally reported with more extensive operations commonly employed in the management of vulvar cancer and is recommended for management of patients with early invasive disease.

Beugeling, M., P. C. Ewing-Graham, et al. 2014. "Pathology slide review in vulvar cancer does not change patient management." *ISRN Surg* **2014**: 385386.

Hypothesis. Pathology slide review in vulvar cancer is only necessary in a restricted number of cases. **Methods.** A retrospective chart review of all cases of vulvar cancer treated in a tertiary centre between January 1, 2000, and April 1, 2006. Histopathology reports from the referring and tertiary centre were compared. **Results.** 121 pathology reports from 112 patients were reviewed. Of the original reports, 56% were deemed adequate, commenting on tumor type and depth of infiltration; of the reviews, 83% were adequate. **Conclusion.** There were no discrepancies that influenced patient management. We suggest that vulvar cancer biopsies need to be reviewed only when the tumor is less than 10 mm in linear extension, when the infiltration is 1 mm or less, when there is no residual tumor on inspection, and in any nonsquamous cancer.

Bipat, S., G. A. Fransen, et al. 2006. "Is there a role for magnetic resonance imaging in the evaluation of inguinal lymph node metastases in patients with vulva carcinoma?" *Gynecol Oncol* **103**: 1001 -1006.

OBJECTIVE: To study the accuracy of magnetic resonance imaging MRI in lymph node detection in patients with vulva carcinoma. **METHODS:** Sixty patients with diagnosed vulva carcinoma underwent MRI examination for preoperative evaluation of lymph nodes. MRI images were read independently and retrospectively by two radiologists, both unaware of physical examination and surgery findings. The following characteristics of each lymph node with a short-axis diameter of ≥ 8 mm were recorded: size axial, sagittal and coronal; aspect homogeneous, with fatty center or partial fat; margin smooth, lobulated/speculated or indistinct; shape: round, ovoid or elongated. Based on these characteristics, each lymph node was classified as malignant or benign and subsequently each groin was classified as malignant or benign. Histopathology obtained at sentinel node procedure or by inguinofemoral lymphadenectomy was used as reference standard. Per groin sensitivity, specificity, positive and negative predictive values were calculated. Kappa statistics on per groin basis were calculated to express interobserver agreement. **RESULTS:** One hundred nineteen groins were examined either by sentinel node procedure or surgery, of which 23 groins were malignant. Sensitivity, specificity, positive and negative predictive values were 52%, 85%, 46% and 87% for observer 1 and 52% 89%, 52% and 89% for observer 2. The interobserver agreement was 104/119 kappa 0.62, representing good agreement. **CONCLUSION:** At this stage there is no role for standard MRI in evaluating lymph node involvement in patients with vulva carcinoma.

Boran, N., F. Kayikcioglu, et al. 2003. "Sentinel lymph node procedure in early vulvar cancer." *Gynecol Oncol* **90**: 492 -493.

Boronow, R. C., B. T. Hickman, et al. 1987. "Combined therapy as an alternative to exenteration for locally advanced vulvovaginal cancer. II. Results, complications, and dosimetric and surgical considerations." *Am J Clin Oncol* **10**: 171 -181.

We have introduced a therapeutic alternative to exenteration for locally advanced vulvovaginal cancer using surgery for the vulvar external genital phase of this disease presentation, combined with radiotherapy for the internal genital phase with adequate overlap of fields to protect surgical margins. The rationale is that this approach treats the cancer and its dual regional spread patterns, while at the

same time preserving the bladder and/or rectum, and should be associated with less morbidity and mortality than exenterative surgery. This report updates our experience with a total of 48 treated cases 37 primary cases and 11 cases of recurrent disease. Of the 37 primary cases, 20 were FIGO stage III, 4 were FIGO stage IV, and 3 other cases represented "field" cancers involving vulva and/or cervix and/or vagina. Utilizing a Life Table analysis, the 5-year survival for the primary cases was 75.6%. Published FIGO survival for stage III is 32% and for stage IV 10.5%. Life Table analysis projects a 62.6% survival for recurrent cases and an overall 72% 5-year survival for all 48 cases treated. With 48 patients treated, 48 bladders and 48 rectums were at risk for surgical removal had exenteration been employed. One patient had a total pelvic exenteration for local failure, and one had a posterior exenteration for local failure. One bladder and one rectum were lost to permanent diversion because of radiation injury. Thus, 5 of these major viscera were lost of the 96 total, and 91 94.8% were retained. Radiation therapy and surgical details have been reviewed relevant to local control and local failure and complications. The continuing evolution of treatment modifications of all modalities will be discussed. The apparent advantages of this combined therapeutic approach over exenterative surgery include high probability of bladder and/or rectal preservation, low primary mortality, low treatment morbidity, and very good results in cancer control.

Bowles, J., K. Y. Terada, et al. 1999. "Preoperative lymphoscintigraphy in the evaluation of squamous cell cancer of the vulva." *Clin Nucl Med* **244**: 235 -238.

PURPOSE: A pilot study was undertaken to determine the lymphatic drainage of vulvar cancer using cutaneous lymphoscintigraphy. **METHODS:** Six patients with biopsy-proved T1 squamous cell cancer of the vulva were studied using 0.4 to 0.6 mCi Tc-99m HSA. Planar imaging was performed after patients received intradermal injections of Tc-99m HSA in a total volume of 0.4 ml at four sites around the vulvar lesion. **RESULTS:** Tumor locations included two midline lesions and three anterior third lesions. One tumor was located in the midthird of the labia majora. There was no clinically suspicious inguinal adenopathy in any patient. Based on classic anatomic descriptions of cutaneous lymphatic drainage, all but one patient would have been predicted to have drainage to both inguinal nodal basins. Cutaneous lymphoscintigraphy was successful in all six patients. Unilateral drainage was shown in five of six patients. Only one patient had bilateral inguinal drainage, and her tumor was located in the left anterior third of the labia minora. **CONCLUSIONS:** Cutaneous lymphoscintigraphy with Tc-99m HSA is easily performed and may be potentially useful in defining lymphatic basins at risk in squamous cell cancer of the vulva.

Brammen, L., A. Staudenherz, et al. 2014. "Sentinel lymph node detection in vulvar cancer patients: a 20 years analysis." *Hell J Nucl Med* **173**: 184 -189.

Our study aimed to analyze postoperative treatment-related morbidity after sentinel lymph node biopsy (SLNB) compared to systematic inguino-femoral lymph node dissection (ILND) and the recurrence rate in patients with vulvar cancer. This single center study included 128 patients diagnosed with vulvar cancer that underwent ILND or SLNB between January 1991 - January 2011 with intraoperative SLN detection and removal. Treatment-related morbidity, as well as recurrence rate of SLNB patients were evaluated. Preoperative sentinel node scintigraphy was successful in 82/89 92% of the patients. A hundred and seventy six nodes were visualized and all positive SLN were detected within 60min. Patients who were treated with ILND underwent a longer operation $P<0.001$, required longer inguinal drainage $P<0.001$, and had a lengthier postoperative hospital stay $P=0.006$. The presence of lymph cysts $P=0.02$, 95% CI 3.4 1 -1-10.6 was significantly higher in ILND patients. No groin recurrence was appreciated in SLNB patients. In conclusion, patients who underwent SLNB were at a lower risk of postoperative morbidity. No groin recurrences were observed in patients who received SLNB.

Brunner, A. H., S. Polterauer, et al. 2008. "The accuracy of intraoperative frozen section of the inguinal sentinel lymph node in vulvar cancer." *Anticancer Res* **286B**: 4091 -4094.

BACKGROUND: Limited data are available for the accuracy of intraoperative frozen section analysis of inguinal sentinel lymph node in patients with vulvar cancer. **PATIENTS AND METHODS:** Forty-four patients with vulvar cancer treated with separate incisions for inguinal sentinel lymph node dissection between 2001 and 2007 were evaluated in the present study. **RESULTS:** Out of 44 patients, 3 had a false-negative intraoperative frozen section result due to micrometastasis. No false-positive result of the intraoperative frozen section analysis was obtained. We identified two studies, which exclusively examined the false-negative rate of frozen section analysis of the sentinel lymph node. Data of these 3 studies were pooled, yielding an overall underdiagnosis of frozen section analysis in 6/128 4.7% patients, resulting in sensitivity, specificity and positive and negative predictive values of 88.5%, 100%, 100% and 93.2%, respectively. **CONCLUSION:** Intraoperative frozen section analysis of the inguinal sentinel lymph nodes exhibits good sensitivity/specificity characteristics for the assessment of inguinal lymph node involvement in patients with vulvar cancer.

Burke, T. W., C. Levenback, et al. 1995. "Surgical therapy of T1 and T2 vulvar carcinoma: further experience with radical wide excision and selective inguinal lymphadenectomy." *Gynecol Oncol* **57**: 215 -220.

Radical wide excision and selective inguinal node dissection provide a more conservative and less morbid surgical option for women with vulvar carcinoma than en bloc radical vulvectomy with bilateral inguinofemoral lymphadenectomy. We have expanded our initial experience with this approach to 76 patients with T1 n = 33 and T2 n = 43 squamous carcinomas with invasion > 1 mm and clinically negative groin nodes treated between 1978 and 1994. Lateral tumors n = 53 were more frequent than midline lesions n = 23. Tumors were excised with a measured gross margin of 2 cm, and dissection was carried to the deep perineal fascia. The mean largest tumor dimension was 26 mm; the mean depth of invasion was 4.4 mm. Superficial inguinal lymphadenectomy, unilateral or bilateral depending on lesion location, was performed. Perioperative complications occurred on the vulva in 8% of cases and in the groin in 11%. Delayed complications, all related to groin treatment, were seen in 29%. The median follow-up interval was 38 months. Seven patients 9% had inguinal lymph node metastases identified at their primary operation. Most received additional therapy; one has died of disease. Nine women 12% developed recurrent disease in the vulva: all were controlled by additional resection. Four 5% developed recurrence in a previously negative groin: three of these are dead of disease. Actuarial 4-year survival is 81%. Radical wide excision and selective inguinal lymphadenectomy can be safely offered to women with T1 and T2 vulvar cancers. Patients with known positive nodes or vulvar failure can be salvaged by further therapy. Women with unanticipated groin failure usually die of disease. These experiences are similar to those observed in more radically resected patients.

Butler, J. S., D. A. Milliken, et al. 2010. "Isolated groin recurrence in vulval squamous cell cancer VSCC. The importance of node count." *Eur J Gynaecol Oncol* **31**: 510 -513.

OBJECTIVE: To determine whether there is a node count which can define an adequate inguinofemoral lymphadenectomy IFL in primary VSCC. **METHODS:** A retrospective and prospective review of patients with node negative VSCC who had a full staging IFL. Detection of isolated groin recurrences IGR would allow groins with higher risk of groin recurrence to be identified. **RESULTS:** The median node count of 228 IFLs in 139 patients was eight 0 -24. There were six IGR 4.3%. Increased rate of IGR was present in patients with increased age, tumour diameter and depth of invasion, lymphovascular space invasion, unilateral IFL, and moderate/poor tumour grade. In the 138 groins with node counts of eight or greater there were no IGRs compared to six in the patients with either undissected groins or groin node counts less than eight p = 0.030 Interval to IGR was significantly shorter than other sites of recurrence. Both disease-specific and overall survival were significantly reduced in IGR. **CONCLUSIONS:** An inadequate IFL is a nodal count of less than eight per groin; both these groins and undissected groins are at increased risk of IGR and should have close surveillance.

Camara, O., H. Gonnert, et al. 2009. "Sentinel lymph node biopsy in vulvar cancer: a pilot study." *Eur J Gynaecol Oncol* **30**: 622 -624.

BACKGROUND: The aim of the pilot study was to assess the feasibility, efficacy, and accuracy of the sentinel lymph node biopsy SLNB procedure in vulvar cancer. **PATIENTS AND METHODS:** From February 2003 to March 2007, 17 patients with vulvar cancer, clinical Stages I and II, underwent SLN sentinel lymph node detection, followed by a complete inguinal -femoral lymphadenectomy. Demographic, surgical, and pathologic data on all patients were reviewed. **RESULTS:** 17 patients underwent the SLNB procedure. Sixteen had vulvar carcinoma and one patient suffered from melanoma of the vulva. Midline localisation was done in 11 patients 64.7%. A total of 371 lymph nodes were resected. The median number of removed lymph nodes was 15 range 2 to 81. Nineteen lymph nodes were positive with a maximum of six in one patient. Overall the detection rate for the sentinel lymph node was 88.2% 15 out of 17. One of the two patients with a non detectable sentinel node had positive lymph nodes. Eighty lymph nodes were detected as the sentinel node. The median number of sentinel nodes was five range 0 to 11. Seventeen sentinel nodes were involved. The sentinel node was negative in nine patients; one of these had involved lymph nodes. **CONCLUSIONS:** SLNB is feasible and safe to perform in vulvar cancer. Further evaluation is needed until new guidelines allow the use in early-stage vulvar cancer.

Canlorbe, G., R. Rouzier, et al. 2012. "[Impact of sentinel node technique on the survival in patients with vulvar cancer: analysis of the Surveillance, Epidemiology, and End Results SEER database]." *Gynecol Obstet Fertil* **40**11: 647 -651.

OBJECTIVES: Vulvar cancer is usually treated with vulvectomy and bilateral groin lymphadenectomy, which result in serious morbidities while only 30% of patients have positive nodes. The sentinel node technique has good sensitivity and specificity for detecting lymph node involvement while minimizing postoperative morbidity. The aim of this study was to evaluate the specific and overall survival impact of sentinel lymph node procedure versus inguinofemoral lymphadenectomy in patients with vulvar cancer. **PATIENTS AND METHODS:** This is a retrospective study from the Surveillance, Epidemiology, and End Results SEER database on patients with vulvar squamous cell carcinoma, T1 or T2 stage, metastasis-free, followed between 2004 and 2008. **RESULTS:** One thousand and thirty eight patients had a systematic groin lymphadenectomy and 56 a sentinel node technique including 22 with an associated lymphadenectomy because of a positive sentinel node. There is no significant difference in overall or specific survival between the two groups. In multivariate analysis, age, T stage and nodal status are prognostic factors for overall and specific mortality $P < 0.05$. **DISCUSSION AND CONCLUSION:** Sentinel node technique is not associated with an excess risk of mortality or recurrence.

Carcopino, X., G. Houvenaeghel, et al. 2005. "[Feasibility and morbidity of sentinel lymph node detection in patients with vulvar carcinoma]." *Bull Cancer* **92**5: 489 -497.

The aim of this study was to investigate the feasibility and the morbidity of sentinel lymph node detection in patients with vulvar carcinoma. In 15 patients with vulvar squamous cell carcinoma, the inguinal sentinel lymph nodes was detected using both peritumoral injection of technetium-99m sulfur colloid and isosulfan blue before the surgical time. The detection of the inguinal sentinel lymph node was never completed by an inguinal lymphadenectomy. In case of metastatic lymph node, patients were treated by complementary inguinal irradiation. A total of 19 inguinal node dissection were performed. The sentinel lymph node was identified in 18/19 94.7% groin dissections. A total of 38 sentinel lymph nodes were removed. 4 patients were found to have metastatic lymph node 26.7% with a total of 6 metastatic lymph nodes. The postoperative morbidity was minimal, with only one patient presenting a permanent edema of the extremity 6.7% after complementary inguinal irradiation. We confirm the results of previous studies that sentinel node dissection appears to be technically feasible in patients with vulvar carcinoma. This may reduce the morbidity of usual inguinal lymphadenectomy without under-evaluate the nodal status. This procedure could be implemented in future therapy concepts.

Carlino, G., S. Parisi, et al. 1984. "Interstitial radiotherapy with Ir192 in vulvar cancer." *Eur J Gynaecol Oncol* **53**: 183 -185.

Radical surgical intervention is not always possible in vulvar tumours, particularly in infiltrating forms of paraurethral locations. In our case-series, the supplementary performance of Curietherapy, particularly with Radium substitutes Iridium 192 and following the afterloading method, has enabled us not only to obtain long disease-free periods but also, coupled with the "large volume" of External Radiotherapy, to master forms exceeding the surgical action scope.

Carlson, J. W., J. Kauderer, et al. 2008. "A randomized phase III trial of VH fibrin sealant to reduce lymphedema after inguinal lymph node dissection: a Gynecologic Oncology Group study." *Gynecol Oncol* **110**: 76 -82.

OBJECTIVES: To evaluate VH fibrin sealant's influence on lower extremity lymphedema after inguinal lymphadenectomy in vulvar cancer patients. **METHODS:** Patients undergoing an inguinal lymphadenectomy during the management of vulvar malignancy were randomized to receive sutured closure SC vs VH fibrin sealant sprayed into the groin followed by sutured closure FS. Leg measurements were taken preoperatively and during postoperative encounters when surgical outcomes were assessed. Grade 2 or 3 lymphedema was defined as circumferential measurement increases of 3-5 cm and >5 cm, respectively. **RESULTS:** 150 patients were enrolled. 137 patients were evaluable for lymphedema analysis with 67 and 70 patients in the SC arm and FS arm, respectively. The incidence of grade 2 and 3 lymphedema was 67%45/67 in the SC arm, and 60% 42/70 FS arm $p=0.4779$. The incidence of lymphedema was strongly associated with inguinal infection $p=0.0165$. Lymphedema was not statistically increased in those who received adjuvant radiation. 139 patients remained evaluable for a descriptive analysis of their surgical complications. The overall incidence of complications was 61%43/70 and 59% 41/69 for SC and FS arms, respectively. There was no statistically significant difference in duration of drains, drain output or incidence of inguinal infections, wound breakdowns or seromas. There was an increased incidence of vulvar infections in the FS arm 23/ 69 vs 10/70 $p=0.0098$. The utilization of a Blake drain was associated with an increase in vulvar $p=0.0157$ and inguinal wound breakdown $p=0.0456$. **CONCLUSION:** VH fibrin sealant in inguinal lymphadenectomies does not reduce leg lymphedema and may increase the risk for complications in the vulvar wound.

Carson, L. F., L. B. Twiggs, et al. 1990. "Multimodality therapy for advanced and recurrent vulvar squamous cell carcinoma. A pilot project." *J Reprod Med* **35**: 1029 -1032.

From 1985 to 1989 eight women with advanced or recurrent vulvar carcinoma were treated at the Women's Cancer Center of the University of Minnesota Hospital and Clinic. Each received a combination of 5-fluorouracil, mitomycin C and cisplatin during radiotherapy. Five of the eight women who underwent posttreatment radical vulvectomy had acceptable operative morbidity. Six patients experienced a complete clinical response. Of them, one had microscopic residual disease in the surgical specimen. One patient with recurrent vulvar carcinoma experienced progression of disease on therapy. One death was attributable to chemotherapy toxicity, and two patients died of intercurrent disease. The overall survival rate at 27 months was 33%. This multimodality approach to the treatment of advanced vulvar carcinoma should be considered when designing a therapeutic approach to treating extensive or resistant vulvar carcinoma.

CCO 2014. "Sentinel Lymph Node Biopsy in Vulvar Cancer." <https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=313084>.

Chafe, S., L. Honore, et al. 2000. "An analysis of the impact of pathology review in gynecologic cancer." *Int J Radiat Oncol Biol Phys* **48**: 1433 -1438.

PURPOSE: To analyze the impact of pathology review in gynecologic malignancies. **METHODS AND MATERIALS:** For all new gynecologic patients seen between December 2, 1993 and January 4, 1996, we conducted a retrospective chart review to determine if a pathology review by the institute's consultant pathologist changed the diagnosis, and if so whether the change altered patient management.

A total of 514 patients were seen, of whom 120 had cervical cancer, 226 had endometrial cancer, 122 had a primary ovarian or peritoneal malignancy, 9 had a vaginal malignancy, 28 had vulvar cancer, and 9 had a miscellaneous gynecologic malignancy. **RESULTS:** On pathology review the diagnosis changed for 200 of 599 specimens 33%. This altered management for 63 of 514 patients 12%. For patients with cervical cancer, the grade of tumor was the main change in pathologic diagnosis, with occasional change in the presence of lymph vascular invasion. These did not translate into patient management alterations. Eight patients 1.5% had management alterations. The changes in depth of invasion and vascular invasion altered management for 3 patients. Changes in pap smears resulted in two management alterations, and changes in histologic diagnoses altered management for 3 cases. For endometrial primaries the changes in pathologic diagnosis included grade, depth of invasion, and the presence of cervical involvement. This did alter management in 40 cases 8%. For the ovarian malignancies, the main changes were grade, extent of disease, or histologic classification, some of which 10 patients, 2% resulted in altered management. One patient with a vaginal lesion had the diagnosis changed, which did alter management. Of the patients diagnosed with vulvar cancer, the pathologic diagnosis changed for 11 patients. This included changes in grade and depth of invasion. This altered management of 2 patients. The remaining miscellaneous gynecologic malignancies had only two diagnosis changes that altered management. **CONCLUSIONS:** Pathologic review of gynecologic malignancies is justified as it can alter patient management. In addition, the process facilitates cooperation of the multidisciplinary team and provides a valuable educational forum to enhance patient care.

Chan, Y. M., A. N. Cheung, et al. 1999. "Pathology slide review in gynecologic oncology: routine or selective?" *Gynecol Oncol* **75**: 267 -271.

OBJECTIVE: The aims of this study were to assess the cost/benefit ratio for interinstitution pathology consultation IPC and to identify the types of specimens with little or no risk of diagnostic error in order to reduce the cost. **METHODS:** All gynecologic oncology referrals having IPC from 1993 to 1998 were reviewed. Each case was evaluated by comparing both the original and the consulted pathology reports. A discrepancy was major if it led to treatment alteration. A minor discrepancy was defined as differences without clinical consequences. Consultation error was determined by comparison with the final diagnosis and clinical data obtained from the records. The cost per review was adjusted to 1998 dollars for all cases over the 5-year study period. Statistical data were obtained by Fisher's exact test and Pearson's correlation test. **RESULTS:** Five hundred sixty-nine pathology specimens from 498 patients were analyzed in this study. The major discrepancy rate was 6.5% and the minor discrepancy rate was 12.5%. Cytological specimens accounted for no major discrepancy and 13 minor discrepancies compared to 37 major and 58 minor discrepancies in histological specimens. The difference was statistically significant $P = 0.003$. Consultation errors occurred in 5 cases with no alteration of clinical care. By excluding cervical and vaginal smears and cervical biopsy specimens in cases with clinically gross tumors, the cost can be reduced by 25% with no detriment to the clinical management. **CONCLUSIONS:** The types of specimens that do not need consultative pathology review include 1 cervical biopsy specimens in those patients with gross tumors and 2 cervical and vaginal smears.

Cohn, D. E., F. Dehdashti, et al. 2002. "Prospective evaluation of positron emission tomography for the detection of groin node metastases from vulvar cancer." *Gynecol Oncol* **85**: 179 -184.

OBJECTIVE: We set out to determine the ability of positron emission tomography with fluorodeoxyglucose to detect groin lymph node metastases from vulvar cancer. **METHODS:** From January 2000 to August 2001, patients with squamous cell cancer of the vulva undergoing radical excision and lymphadenectomy were offered preoperative positron emission tomography. The imaging and pathologic status of each patient and groin were compared, and the sensitivity, specificity, and predictive value of positron emission tomography in predicting nodal metastasis were determined. **RESULTS:** Fifteen patients underwent positron emission tomography prior to exploration of 29 groins. Six patients had positive scans, suggesting metastases in 8 groins. Pathologically, 5 patients had metastases in 9 groins, with positron emission tomography demonstrating metastases in 4 of 5 patients

and 6 of 9 groins with disease. On a patient-by-patients basis, positron emission tomography had a sensitivity of 80%, specificity of 90%, positive predictive value of 80%, and negative predictive value of 90% in demonstrating metastases. On a groin-by-groin basis, positron emission tomography had a sensitivity of 67%, specificity of 95%, positive predictive value of 86%, and negative predictive value of 86%. Positron emission tomography was more accurate in detecting extranodal metastases than disease confined within the groin nodes $P = 0.048$. **CONCLUSIONS:** Positron emission tomography is relatively insensitive in predicting lymph node metastasis, and a negative study is not a reliable surrogate for a pathologically negative groin. However, the high specificity suggests that positron emission tomography is useful in planning radiation therapy and as an adjunct to lymphatic mapping and sentinel lymph node dissection.

Coleman, R. L., S. Ali, et al. 2011. "When is bilateral lymphadenectomy for midline squamous cell carcinoma of the vulva necessary? An ancillary analysis from GOG-173." *Int J Gynecol Cancer* **21**: S50.

Coleman, R. L., S. Ali, et al. 2013. "Is bilateral lymphadenectomy for midline squamous carcinoma of the vulva always necessary? An analysis from Gynecologic Oncology Group GOG) 173." *Gynecol Oncol* **128**: 155-159.

OBJECTIVE: To determine which patients with near midline lesions may safely undergo unilateral groin dissection based on clinical exam and lymphoscintigraphy (LSG) results. **METHODS:** Patients participating in GOG-173 underwent sentinel lymph node (SLN) localization with blue dye, and radiocolloid with optional LSG before definitive inguinal-femoral lymphadenectomy (LND). This analysis interrogates the reliability of LSG alone relative to primary tumor location in those patients who had an interpretable LSG and at least one SLN identified. Primary tumor location was categorized as lateral >2cm from midline, midline, or lateral ambiguous (LA) if located within 2cm, but not involving the midline. **RESULTS:** Two-hundred-thirty-four patients met eligibility criteria. Sixty-four had lateral lesions, and underwent unilateral LND. All patients with LA ($N=65$) and midline ($N=105$) tumors underwent bilateral LND. Bilateral drainage by LSG was identified in 14/64 (22%) patients with lateral tumors, 38/65 (58%) with LA tumors and in 73/105 (70%) with midline tumors. At mapping, no SLNs were found in contralateral groins among those patients with LA and midline tumors who had unilateral-only LSGs. However, in these patients groin metastases were found in 4/32 patients with midline tumors undergoing contralateral dissection; none were found in 27 patients with LA tumors. **CONCLUSION:** The likelihood of detectable bilateral drainage using preoperative LSG decreases as a function of distance from midline. Patients with LA primaries and unilateral drainage on LSG may safely undergo unilateral SLN.

Cormio, G., V. Loizzi, et al. 2009. "Cisplatin and vinorelbine chemotherapy in recurrent vulvar carcinoma." *Oncology* **77**: 281 -284.

PURPOSE: To evaluate the activity and toxicity of the combination of cisplatin and vinorelbine in patients with recurrent carcinoma of the vulva that has not been previously treated with chemotherapy. **PATIENTS AND METHODS:** Sixteen women with a median age of 65 years (range 43 -79) with recurrent vulvar carcinoma were enrolled in the study. Nine patients had local recurrent disease (perineum, vagina and/or vulva), whereas 7 had disease in the groin; 9 patients had received prior radiotherapy. Cisplatin was administered intravenously on day 1 and vinorelbine was given on day 1 immediately after cisplatin and on day 8. **RESULTS:** A total of 68 cycles of chemotherapy were administered. Fifteen women were assessed for response. Objective responses were recorded in 6 patients (40%) - with 4 patients (27%) achieving a complete response and 2 (13%) achieving a partial response -, whereas 4 patients (27%) had stable disease and 5 had progressive disease. The median progression-free survival was 10 months (range 3 -17), whereas the overall survival from the beginning of the chemotherapy was 19 months (range 1 -30). Due to the small number of patients, no significant correlation with site of recurrence could be found. **CONCLUSION:** The combination of cisplatin and vinorelbine is a well-tolerated and active regimen in the treatment of patients with recurrent vulvar carcinoma.

Corusic, A., D. Babic, et al. 2011. "Safety of sentinel node biopsy in vulvar cancer FIGO staging IB and II." *Int J Gynecol Cancer* **21**: S900.

Covens, A., E. T. Vella, et al. 2015. "Sentinel lymph node biopsy in vulvar cancer: Systematic review, meta-analysis and guideline recommendations." *Gynecol Oncol* **137**: 351 -361.

OBJECTIVES: Traditionally, treatment for early stage vulvar cancer has included removal of the primary tumor and inguinofemoral lymph node dissection (IFLD). Sentinel lymph node biopsy (SLNB) has been proposed as an alternative to IFLD for early stage vulvar cancer patients. The aim of this project was to systematically review and assess the potential for harms and benefits with the SLNB procedure in order to make recommendations regarding the adoption of the procedure, selection of patients and appropriate technique and procedures. **METHODS:** A working group with expertise in gynecologic oncology and health research methodology was formed to lead the systematic review and process of guideline development. MEDLINE, Embase and The Cochrane Database of Systematic Reviews were searched for relevant articles published up to September 2014. Outcomes of interest included detection, false negative, complication and recurrence rates and indicators related to pathology. Meta-analyses were conducted where appropriate. **RESULTS:** The evidence-base of a previously published health technology assessment was adopted. An additional search to update the HTA's evidence base located three systematic reviews, and eleven individual studies that met the inclusion criteria. According to a meta-analysis, per groin detection rate for SLNB using radiocolloid tracer and blue dye was 87% [82-92]. The false negative rate with SLNB was 6.4% [4.4-8.8], and the recurrence rates with SLNB and IFLD were 2.8% [1.5-4.4] and 1.4% [0.5-2.6], respectively. An internal and external review process elicited concerns about the necessity of performing this procedure in an appropriate organizational context. **CONCLUSION:** SLNB is recommended for women with unifocal tumors <4 cm and clinically non-suspicious nodes in the groin, provided that specific infrastructure and human resource needs are met. Some recommendations for appropriate techniques and procedures are also provided.

Crane, L. M., G. Themelis, et al. 2011. "Intraoperative near-infrared fluorescence imaging for sentinel lymph node detection in vulvar cancer: first clinical results." *Gynecol Oncol* **120**: 291 -295.

OBJECTIVE: Disadvantages of the combined sentinel lymph node (SLN) procedure with radiocolloid and blue dye in vulvar cancer are the preoperative injections of radioactive tracer in the vulva, posing a painful burden on the patient. Intraoperative transcutaneous imaging of a peritumorally injected fluorescent tracer may lead to a one-step procedure, while maintaining high sensitivity. Aim of this pilot study was to investigate the applicability of intraoperative fluorescence imaging for SLN detection and transcutaneous lymphatic mapping in vulvar cancer. **METHODS:** Ten patients with early stage squamous cell carcinoma of the vulva underwent the standard SLN procedure. Additionally, a mixture of 1 mL patent blue and 1 mL indocyanin green (ICG; 0.5 mg/mL) was injected immediately prior to surgery, with the patient under anesthesia. Color and fluorescence images and videos of lymph flow were acquired using a custom-made intraoperative fluorescence camera system. The distance between skin and femoral artery was determined on preoperative CT-scan as a measure for subcutaneous adipose tissue. **RESULTS:** In 10 patients, SLNs were detected in 16 groins (4 unilateral; 6 midline tumors). Transcutaneous lymphatic mapping was possible in five patients (5 of 16 groins), and was limited to lean patients, with a maximal distance between femoral artery and skin of 24 mm, as determined on CT. In total, 29 SLNs were detected by radiocolloid, of which 26 were also detected by fluorescence and 21 were blue. **CONCLUSIONS:** These first clinical results indicate that intraoperative transcutaneous lymphatic mapping using fluorescence is technically feasible in a subgroup of lean vulvar cancer patients.

Crosbie, E. J., B. Winter-Roach, et al. 2010. "The accuracy of the sentinel node procedure after excision biopsy in squamous cell carcinoma of the vulva." *Surg Oncol* **19**: e150 -154.

INTRODUCTION: Restricting inguinofemoral lymphadenectomy to patients with malignant nodes would reduce treatment-related morbidity in vulval cancer patients. A prospective study was conducted to determine the diagnostic accuracy of the Sentinel Lymph Node (SLN) procedure in vulval cancer patients referred following either diagnostic or excision biopsy. **METHODS:** Patients with clinical stage I and II squamous cell carcinoma of the vulva underwent SLN identification with peri-scar/lesional injection of ^{99m}Techneium -labelled nanocolloid pre-operative lymphoscintigraphy and intra-operative use of a hand-held probe and intra-operative blue dye. Radical excision of the vulval tumour or scar and formal inguinofemoral lymphadenectomy was then performed as necessary. SLN were processed separately and further examined at multiple levels to exclude micrometastases H&E/cytokeratin staining if negative on routine analysis. Clinical follow-up was carried out to identify and treat recurrences or treatment-related morbidity. **RESULTS:** Thirty-two women took part. Fifteen were referred following excision biopsy and seventeen following diagnostic biopsy of their primary vulval tumour. One or more SLN was successfully detected intra-operatively in 31 patients (97%) and 45 groins. An SLN could not be identified intra-operatively in one case (re-excision of scar). On average, more SLN were identified in patients with their primary vulval lesion in situ compared with those whose tumour had previously been excised (2.6 vs. 1.8, $p = 0.03$). Midline tumours were more likely (15/17) than lateral tumours (1/15) to have bilateral SLN identified pre-operatively. Two patients with midline tumours previously excised had unilateral SLN. Seven patients (23%) and ten groins had inguinofemoral lymph node metastases. The SLN procedure correctly identified inguinofemoral metastases in six patients (nine groins). In one case (midline tumour, re-excision of scar) the sentinel node was positive on one side but false negative on the other. **CONCLUSIONS:** The SLN procedure may be used to identify malignant groins in selected patients with vulval cancer. The extent to which previous vulval surgery might influence the accuracy of the SLN procedure deserves further investigation.

Cunningham, M. J., R. P. Goyer, et al. 1997. "Primary radiation, cisplatin, and 5-fluorouracil for advanced squamous carcinoma of the vulva." *Gynecol Oncol* **66**: 258-261.

OBJECTIVE: To evaluate a regimen of radiation and chemotherapy as an alternative for those patients in whom the location and extent of advanced vulvar carcinoma make pelvic exenteration the only surgical option. **METHODS:** Between December 1988 and March 1995, 14 patients with primary squamous carcinoma of the vulva who were not candidates for standard radical vulvectomy were treated with radiation therapy in combination with cisplatin and 5-fluorouracil (5-FU) chemotherapy at the Albany Medical Center. Patients ranged in age from 40 to 90 years, mean 68. Tumors were stage III in 9 patients and stage IV in 5 patients. Treatment included two cycles of chemotherapy with cisplatin 50 mg/m² and 5-FU 1000 mg/m²/24 x 96 hr in addition to radiation therapy. Total radiation doses to the vulva and groins ranged from 50 to 65 Gray Gy, with pelvic doses of 45 to 50 Gy. Surgical excision of the primary site was not performed in patients who had complete clinical response. **RESULTS:** Acute complications included desquamation requiring treatment interruptions in 5 patients and deep venous thrombosis in 1 patient. Delayed complications were limited to small bowel obstruction and colonic stricture in one patient. There was a 92% response rate with complete responses in 9 patients (64%). Among patients with complete clinical response, there has been only one recurrence with follow-up of 7-81 months, mean 36.5. All patients with partial responses died, with survival of 8-25 months, mean 15.7. **CONCLUSIONS:** This combination of chemoradiation was found to be effective therapy for locally advanced vulvar carcinoma, with acceptable morbidity even in an elderly population. Surgical excision of the primary site is not necessary in patients with complete response.

Curry, S. L., J. T. Wharton, et al. 1980. "Positive lymph nodes in vulvar squamous carcinoma." *Gynecol Oncol* **9**: 63-67.

Dardarian, T. S., H. J. Gray, et al. 2006. "Saphenous vein sparing during inguinal lymphadenectomy to reduce morbidity in patients with vulvar carcinoma." *Gynecol Oncol* **101**: 140-142.

OBJECTIVES: To compare short- and long-term morbidity associated with saphenous vein sparing versus ligation during inguinal lymphadenectomy for vulvar carcinoma. **METHODS:** A retrospective evaluation of patients with carcinoma of the vulva that underwent inguinal lymphadenectomy was performed. Operative reports were evaluated and patients were divided into those who had sparing of the saphenous vein versus ligation. Postoperative short- and long-term complications were compared between the two groups using Pearson chi squared analysis. **RESULTS:** There were a total of 49 inguinal lymphadenectomies performed on 29 patients. The saphenous vein was spared in 18 37% groin dissections compared to 31 63% in which the saphenous vein was ligated. The two groups were similar in regards to clinical characteristics. All patients received closed suction drains and prophylactic antibiotics. Median number of nodes dissected was similar. Cellulitis was more common in the vein-ligated group compared to the vein-spared group 45% vs. 0%; $P < 0.001$. Wound breakdown occurred in 25% of dissections where the saphenous vein was ligated versus 0% in dissections where the vein was spared $P = 0.02$. Short-term edema ≤ 6 months was similar between vein-ligated and vein-spared groups 67% vs. 72%, $P = 1.0$. Subsequently, chronic lymphedema > 6 months persisted in 38% of the vein-ligated group compared to 11% in the vein-spared group $P < 0.05$. The incidence of recurrent disease was similar in both groups 19.3 % vs. 22.2% $P < 0.1$. **CONCLUSIONS:** Routine preservation of the saphenous vein during inguinal lymphadenectomy for vulvar carcinoma may reduce the incidence of wound cellulitis, wound breakdown, and chronic lymphedema.

De Cicco, C., M. Sideri, et al. 2000. "Sentinel node biopsy in early vulvar cancer." *Br J Cancer* **822**: 295 -299.

Lymph node pathologic status is the most important prognostic factor in vulvar cancer; however, complete inguinofemoral node dissection is associated with significant morbidity. Lymphoscintigraphy associated with gamma-probe guided surgery reliably detects sentinel nodes in melanoma and breast cancer patients. This study evaluates the feasibility of the surgical identification of sentinel groin nodes using lymphoscintigraphy and a gamma-detecting probe in patients with early vulvar cancer. Technetium-99m-labelled colloid human albumin was administered perilesionally in 37 patients with invasive epidermoid vulvar cancer T1 -T2 and lymphoscintigraphy performed the day before surgery. An intraoperative gamma-detecting probe was used to identify sentinel nodes during surgery. A complete inguinofemoral node dissection was then performed. Sentinel nodes were submitted separately to pathologic evaluation. A total of 55 groins were dissected in 37 patients. Localization of the SN was successful in all cases. Eight cases had positive nodes: in all the sentinel node was positive; the sentinel node was the only positive node in five cases. Twenty-nine patients showed negative sentinel nodes: all of them were negative for lymph node metastases. Lymphoscintigraphy and sentinel-node biopsy under gamma-detecting probe guidance proved to be an easy and reliable method for the detection of sentinel node in early vulvar cancer. This technique may represent a true advance in the direction of less aggressive treatments in patients with vulvar cancer.

de Gregorio, N., F. Ebner, et al. 2013. "The role of preoperative ultrasound evaluation of inguinal lymph nodes in patients with vulvar malignancy." *Gynecol Oncol* **1311**: 113 -117.

OBJECTIVES: Inguinal lymphadenectomy in vulvar malignancies is associated with significant morbidity, especially in patients over 70 years old. Under certain conditions, surgical guidelines recommend biopsy and evaluation of the sentinel node in early vulvar cancer. The purpose of our study is to evaluate ultrasonography as a predictor of inguinal lymph node involvement. **METHODS:** A retrospective study was performed with 60 patients who had vulvar malignancies 92% of which were squamous cell carcinomas and who were treated at our hospital between 2002 and 2012. The patients ranged in age from 35 to 89 years, with a median age of 76 years. In total, 118 groin scans were retrospectively evaluated for sonographic evidence of lymph node involvement i.e., absence of fatty hilum, irregular shape, cortical region diameter and vascularization pattern. The results were then compared with histopathologically confirmed lymph node status. **RESULTS:** Histopathologically confirmed lymph node status was available for 107 of the inguinal nodes examined by ultrasound, and lymph node metastases were found in 38 35.5% cases. The presence or absence of inguinal lymph node metastases was correctly identified by sonography in 92 86.0% of the scanned areas. Sensitivity

was 76.3%, specificity was 91.3%, and positive and negative predictive values were 82.9% and 87.5%, respectively. **CONCLUSIONS:** Ultrasonography of the inguinal lymph nodes showed a relatively high sensitivity and specificity for predicting inguinal tumor metastases. However, our results indicate that surgical lymph node staging is still needed to precisely determine inguinal lymph node status in vulvar cancer, especially because a missed lymph node-metastasis is often fatal.

de Hullu, J. A., A. C. Ansink, et al. 2001. "What doctors and patients think about false -negative sentinel lymph nodes in vulvar cancer." *J Psychosom Obstet Gynaecol* **224**: 199 -203.

The sentinel lymph node procedure is a relatively new, minimally-invasive method for the assessment of nodal status in malignancies such as breast cancer, cutaneous melanoma and vulvar cancer. Although highly accurate, this new method is inevitably associated with a certain false-negative rate, possibly leading to worse survival in a small subset of patients. The clinical implementation of the sentinel lymph node procedure is therefore a matter of ongoing debate, especially among doctors. The aim of this study was to assess opinions on the acceptable false-negative rate of the sentinel lymph node procedure in patients with vulvar cancer, who in the past had undergone standard routine radical vulvectomy and complete inguinofemoral lymphadenectomy and frequently experienced complications, and in gynecologists treating patients with vulvar cancer. Structured questionnaires were sent to both patients and gynecologists. The patients had been treated for vulvar cancer between 1985 and 1993, and were all in complete remission with a median follow-up of 118 months range: 76 - 185. Questions to the patients dealt with experienced side-effects of the standard treatment and opinion on the acceptable false-negative rate of the sentinel lymph node procedure. The response rate among patients was 91% 106/117. Forty per cent of the patients experienced one or more infections in the legs cellulitis and 49% of the patients still experience either severe pain and/or severe lymphedema in the legs. Sixty-six per cent of the patients preferred complete inguinofemoral lymphadenectomy in preference to a 5% false-negative rate of the sentinel lymph node procedure of 5%. Their preference was not related to age or the side-effects they had experienced. The response rate among gynecologists was 80% 80/100, of whom 60% were willing to accept a 5 -20% false-negative rate of the sentinel lymph node procedure. While gynecologists may consider the sentinel lymph node procedure to be a promising diagnostic tool, the majority of vulvar cancer patients, who have undergone complete inguinofemoral lymphadenectomy in the past and have frequently experienced complications, would not advise introduction of this technique because they do not want to take any risk of missing a lymph node metastasis.

De Hullu, J. A., E. Doting, et al. 1998. "Sentinel lymph node identification with technetium-99m-labeled nanocolloid in squamous cell cancer of the vulva." *J Nucl Med* **39**: 1851-1855.

de Hullu, J. A., H. Hollema, et al. 2002. "Vulvar melanoma: is there a role for sentinel lymph node biopsy?" *Cancer* **942**: 486 -491.

BACKGROUND: The objective of this study was to evaluate the author's recent, preliminary experience with the sentinel lymph node procedure in patients with vulvar melanoma and to compare this experience with treatment and follow-up of patients with vulvar melanomas who were treated previously at their institution. **METHODS:** From 1997, sentinel lymph node procedure with the combined technique 99mTechnetium -labeled nanocolloid and Patente Blue-V) was performed as a standard staging procedure for patients with vulvar melanoma with a thickness > 1 mm and no clinically suspicious inguinofemoral lymph nodes. For the current study, clinicopathologic data from all 33 patients with vulvar melanoma who were treated between 1978 and 2000 at the University Hospital Groningen were reviewed and analyzed. **RESULTS:** From January 1997 until December 2000, identification of sentinel lymph nodes was successful in all nine patients who were referred for treatment of vulvar melanoma. Three patients underwent subsequent complete inguinofemoral lymphadenectomy because of metastatic sentinel lymph nodes. In follow-up, groin recurrences in -transit metastases occurred in two of nine patients, both 12 months after primary treatment. Both patients had melanomas with a thickness > 4 mm and previously had negative sentinel lymph nodes.

There was a trend toward more frequent groin recurrences in patients after undergoing the sentinel lymph node procedure 2 of 9 patients compared with 24 historic control patients 0 of 24 patients; $P = 0.06$. Five of 33 patients developed local recurrences: Two patients had groin recurrences, and 11 patients developed distant metastases. Twelve patients died of vulvar melanoma. Seventeen patients with a median follow-up of 66 months range, 9 -123 months are currently alive overall survival rate, 52%. **CONCLUSIONS:** Although the numbers were small, this study showed that the sentinel lymph node procedure is capable of identifying patients who have occult lymph node metastases and who may benefit from lymphadenectomy for locoregional control and prevention of distant metastases. However, the data also suggest that the sentinel lymph node procedure may increase the risk of locoregional recurrences in -transit metastases, especially in patients with thick melanomas. The potential role of the sentinel lymph node procedure as an alternative method of lymph node staging in patients with vulvar melanoma needs further investigation only within the protection of clinical trials and probably should be restricted to patients with melanomas with intermediate thickness 1 -4 mm.

de Hullu, J. A., H. Hollema, et al. 2002. "Vulvar carcinoma. The price of less radical surgery." *Cancer* **95**11: 2331-2338.

BACKGROUND: The objective of this study was to determine whether modifications in the treatment of patients with vulvar carcinoma influence the rates of recurrence and survival. **METHODS:** Between 1982 and 1997, 253 patients with T1 and T2 invasive squamous cell carcinoma of the vulva were treated by essentially the same team of gynecologic oncologists, and 168 patients Group I underwent radical vulvectomy with en bloc inguinofemoral lymphadenectomy. Standard therapy was changed in 1993, and 85 patients Group II underwent wide local excision with inguinofemoral lymphadenectomy through separate incisions. The rates of recurrence and survival were compared between both groups. **RESULTS:** In Group II, the overall recurrence rate 33.3% within 4 years was increased compared with Group I 19.9%; $P = 0.03$. In Group II, 5 of 79 patients 6.3% developed fatal groin or skin bridge recurrences compared with 2 of 159 patients 1.3% in Group I $P = 0.029$; this did not result in a difference in overall survival. In Group II, 40 of 79 patients had tumor free margins measuring ≤ 8 mm, resulting in 9 local recurrences; whereas 39 of 79 patients had tumor free margins measuring > 8 mm, resulting in no local recurrences $P = 0.002$. **CONCLUSIONS:** The current study showed that fatal recurrences in either the groin or the skin bridge were more frequent after wide local excision and inguinofemoral lymphadenectomy through separate incisions; however, probably due to lack of power, this did not result in shorter survival. In 40 of 79 patients, the histologic margins measured ≤ 8 mm, resulting in a high risk of local recurrences. Therefore, the authors recommend obtaining surgical margins of 2 cm for the local treatment of patients with vulvar carcinoma.

de Hullu, J. A., H. Hollema, et al. 2000. "Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva." *J Clin Oncol* **18**15: 2811 -2816.

PURPOSE: To determine the diagnostic accuracy of the sentinel lymph node procedure in patients with squamous cell carcinoma of the vulva and to investigate whether step sectioning and immunohistochemistry of sentinel lymph nodes increase the sensitivity for detection of metastases. **PATIENTS AND METHODS:** Between July 1996 and July 1999, 59 patients with primary vulvar cancer were entered onto a two-center prospective study. All patients underwent sentinel lymph node procedure with the combined technique preoperative lymphoscintigraphy with technetium -99m-labeled nanocolloid and intraoperative blue dye. Radical excision of the primary tumor with uni - or bilateral inguinofemoral lymphadenectomy was performed subsequently. Sentinel lymph nodes and lymphadenectomy specimens were sent for histopathologic examination separately. Sentinel lymph nodes, negative at the time of routine pathologic examination, were re-examined with step sectioning and immunohistochemistry. **RESULTS:** In 59 patients, 107 inguinofemoral lymphadenectomies were performed (11 unilateral and 48 bilateral). All sentinel lymph nodes, as observed on preoperative lymphoscintigram, were identified successfully intraoperatively. Routine histopathologic examination showed lymph node metastases in 27 groins, all of which were detected by the sentinel lymph node procedure. The negative predictive value for a negative sentinel lymph node was 100% 97.5%

confidence interval [CI], 95% to 100%. Step sectioning and immunohistochemistry showed four additional metastases in 102 sentinel lymph nodes 4%; 95% CI, 1% to 9% that were negative at the time of routine histopathologic examination. **CONCLUSION:** Sentinel lymph node procedure with the combined technique is highly accurate in predicting the inguinofemoral lymph node status in patients with early-stage vulvar cancer. Future trials should focus on the safe clinical implementation of the sentinel lymph node procedure in these patients. Step sectioning and immunohistochemistry slightly increase the sensitivity of detecting metastases in sentinel lymph nodes and should be included in these trials.

de Hullu, J. A., M. H. Oonk, et al. 2004. "Pitfalls in the sentinel lymph node procedure in vulvar cancer." *Gynecol Oncol* **94**: 10 -15.

OBJECTIVES: There is an increasing interest among gynecologic oncologists to implement the sentinel lymph node (SLN) procedure in vulvar cancer patients in clinical practice. However, the safety of this promising method of staging still has to be proven in a randomized trial. **MATERIALS AND METHODS:** Two vulvar cancer patients are reported to illustrate pitfalls in the sentinel lymph node procedure. **RESULTS:** The phenomena of bypassing the sentinel lymph node and confusion about the number of removed sentinel lymph nodes are presented and discussed. **CONCLUSION:** Gynecological oncologists who perform the sentinel lymph node procedure in vulvar cancer patients should perform this technique by following a strict protocol and within the protection of a clinical trial.

de Hullu, J. A., J. Pruim, et al. 1999. "Noninvasive detection of inguinofemoral lymph node metastases in squamous cell cancer of the vulva by L." *Int J Gynecol Cancer* **9**: 141 -146.

In the majority of patients with early stage squamous cell cancer (SCC) of the vulva, an inguinofemoral lymphadenectomy is performed (in retrospect) for diagnostic reasons: exclusion of inguinofemoral lymph node metastases. The morbidity of this procedure, however, is significant. The aim of the present study was to evaluate noninvasive detection of inguinofemoral lymph node metastases by positron emission tomography (PET) using L-[1-¹¹C]-tyrosine (TYR) as tracer. In patients with SCC of the vulva, scheduled for resection of the primary tumor and uni- or bilateral inguinofemoral lymphadenectomy, results of preoperative palpation of the groins and TYR-PET imaging were compared with histopathology. PET imaging was performed using two different methods. In a first group n = 16, nonattenuation corrected 'whole body' scans were performed, and in a second group n = 9, attenuation corrected static emission scans. Sensitivity, specificity, accuracy, and positive and negative predictive value for palpation were 62%, 89%, 82%, 67%, and 87% per groin. Sensitivity, specificity, accuracy, and positive and negative predictive value for TYR-PET were calculated for the two methodologies separately and overall. There were no significant differences. Overall values were 53%, 95%, 94%, 33%, and 98% per lymph node and 75%, 62%, 65%, 41% and 88% per groin. Detection of inguinofemoral lymph node metastases by TYR-PET is not superior to palpation. Neither palpation nor TYR-PET is able to adequately predict or exclude presence of inguinofemoral lymph node metastases in patients with SCC of the vulva.

Decesare, S. L., J. V. Fiorica, et al. 1997. "A pilot study utilizing intraoperative lymphoscintigraphy for identification of the sentinel lymph nodes in vulvar cancer." *Gynecol Oncol* **66**: 425 -428.

OBJECTIVE: To identify sentinel lymph nodes using intraoperative lymphoscintigraphy. **METHODS:** Technetium-99-labeled sulfur colloid was injected at the site of primary vulvar carcinoma. An intraoperative gamma counter was used to identify one or more sentinel lymph nodes. **RESULTS:** Ten patients underwent bilateral inguinal and femoral lymphadenectomy. The clinical stages are as follows: T1 in 6, T2 in 2, and T3 in 2. A total of four groins 3 patients were positive for metastases. In one patient only the sentinel node was positive for disease. In a second patient, two unilateral nodes were positive for disease and both were identified with the gamma counter as sentinel nodes. In the third patient, a single sentinel node was positive for malignancy in each groin. Multiple nonsentinel lymph nodes were positive in each groin in this patient. In no case was the sentinel node negative when other

nonsentinel nodes were positive. **CONCLUSION:** Intraoperative lymphoscintigraphy quantitatively identifies one or more sentinel lymph nodes. Since sentinel lymph nodes can be localized transcutaneously, this technique may be useful for selective lymphadenectomy. Larger patient accrual is necessary to verify this technique.

DeSimone, C. P., J. S. Van Ness, et al. 2007. "The treatment of lateral T1 and T2 squamous cell carcinomas of the vulva confined to the labium majus or minus." *Gynecol Oncol* **104**: 390 -395.

OBJECTIVE: To determine the pattern of lymph node metastases, recurrence rate, and survival of patients with lateral T1 and T2 squamous cell cancer SCC of the vulva treated by radical vulvectomy or hemivulvectomy and inguinal lymphadenectomy. **METHODS:** An institutional review was performed to identify lateral T1 and T2 SCC of the vulva confined to the labium majus and minus. **RESULTS:** Sixty-one patients with lateral T1 and 61 patients with lateral T2 SCC of the vulva were treated from 1963 to 2003. Radical vulvectomy (RV) was performed in 60 patients, and radical hemivulvectomy (RHV) in 62 patients. Seven of 61 patients (11%) with T1 lesions had ipsilateral superficial inguinal lymph node (SIL) metastases, but none had deep inguinal lymph node (DIL) metastases. Nineteen of 61 patients (31%) with T2 lesions had ipsilateral SIL metastases, and 8 had ipsilateral DIL metastases. No patient had contralateral SIL or DIL metastases. Six patients (10%) with T1 lesions and seven patients (11%) with T2 lesions developed recurrence to the ipsilateral vulva and were treated by re-excision. All patients are alive with no evidence of disease 10-195 months after treatment. One patient with T1 and three patients with T2 SCC developed distant recurrence and died of disease (DOD) 10 -15 months after surgery. Disease-free survival of patients with T1 lesions was 98% at 2 years and 98% at 5 years, and with T2 lesions was 95% at 2 years and 93% at 5 years. Local or distant recurrence was not more common in patients treated by RHV than in those treated by RV. **CONCLUSION:** Lateral T1 and T2 squamous cell cancers of the vulva spread to the ipsilateral inguinal lymph nodes and can be treated effectively with RHV and ipsilateral SIL dissection. Deep inguinal lymphadenectomy is indicated only when the SIL are positive.

Devaja, O., G. Mehra, et al. 2011. "A prospective study of sentinel lymph node detection in vulval carcinoma: is it time for a change in clinical practice?" *Int J Gynecol Cancer* **21**: 559 -564.

OBJECTIVES: To determine the accuracy of sentinel lymph node (SLN) detection in vulval carcinoma and to report the reliability and safety of this procedure. **METHODS/MATERIALS:** For a period of 6 years, we recruited women undergoing surgery for vulval carcinoma. All women had a preoperative biopsy confirming the depth of invasion greater than 1 mm. Sentinel lymph node detection was performed using the combined method Tc-99m and methylene-blue dye. The standard management included complete inguinofemoral lymphadenectomy. When inguinofemoral lymph nodes were found grossly to be enlarged, these nodes were debulked, and the women subsequently treated with radiotherapy with or without chemotherapy. During the last 2 years of the study, a selected group of women had an SLN dissection alone. The SLNs were ultrastaged when they were negative on routine hematoxylin and eosin examination. **RESULTS:** Among 60 women undergoing SLN detection, SLN was detected in 59 women (98.3%) with combined method. Blue dye did not detect an SLN in 3 women resulting in a 93.3% detection rate. The median SLN count was 2 nodes (range, 1 -9). Of the 60 women, 41 had inguinofemoral lymphadenectomy, 4 had only enlarged inguinofemoral nodes debulked, and 15 had the SLN only removed. The non-SLN count was 9 nodes (range, 3 -17). There were no false-negative SLNs. Twenty-one women (35%) had positive nodes on final histology. Ultrastaging increased detection of metastases in 6.9% of nodes relative to routine hematoxylin and eosin examination and upstaged 12% of women. The median follow-up was 24 months (range, 2 -66 months). **CONCLUSIONS:** Sentinel lymph node detection is safe and accurate in assessing lymph node status in women with vulval cancer undergoing staging. The combined method using Tc-99m and methylene blue dye injection for SLN detection has the best detection rate. Routine ultrastaging of negative SLN improves the detection of nodal metastases.

DiSaia, P. J., W. T. Creasman, et al. 1979. "An alternate approach to early cancer of the vulva." *Am J Obstet Gynecol* **133**: 825 -832.

Early invasive squamous cell carcinoma of the vulva has emerged as a controversial issue in recent literature. Reports illustrating metastatic disease in the inguinal lymph nodes have conflicted with other reports suggesting local treatment only. The morbidity produced by radical vulvectomy to both body image and sexual function make this issue worthy of serious consideration. This report deals with an alternate approach to this disease entity which attempts to preserve vulvar tissue without sacrificing curability where possible metastatic disease exists. The concept is proposed of utilizing the superficial inguinal nodes as sentinel nodes in the treatment planning. The results of 20 patients treated in this manner are presented.

Domingues, A. P., F. Mota, et al. 2010. "Neoadjuvant chemotherapy in advanced vulvar cancer." *Int J Gynecol Cancer* **20**: 294 -298.

INTRODUCTION: Locally advanced tumors of the vulva represent approximately one third of all vulvar cancers. Therapeutic options include chemoradiation, radiotherapy, and neoadjuvant chemotherapy NACT. **MATERIALS AND METHODS:** Analysis of 3 NACT schemes, bleomycin, paclitaxel, and 5-fluorouracil/cisplatin, used in patients with locally advanced vulvar tumors in a 12-year period. The following parameters were evaluated and compared between regimens: age, initial tumor size, inguinal involvement, histological type, toxicities, response to treatment, surgery performed after NACT, and overall survival. **RESULTS:** Of the 25 patients included, 10 underwent an NACT regimen with bleomycin Group A; 5, with paclitaxel Group B; and 10, with a combination of 5 - fluorouracil/cisplatin Group C. In Group A, there was a 60% response rate. Mortality was 70%, with an overall survival rate of 70%, 40%, and 30% at 12, 24, and 60 months, respectively. The mean (SD) survival was 46.7 15.4 months. In Group B, the response rate was 40 %, with an 80% mortality rate and a survival rate of 60% and 20% at 12 and 24 months, respectively. The mean (SD) survival was 17.0 3.8 months. In Group C, 20% of the responses were observed and the mortality was 90%, with an overall survival rate of 10% at 12 and 24 months and a mean (SD) survival of 7.6 2.0 months. **CONCLUSION:** The best response and overall survival rates were achieved in Group A with the NACT scheme of bleomycin.

Durrant, K. R., C. Mangioni, et al. 1990. "Bleomycin, methotrexate, and CCNU in advanced inoperable squamous cell carcinoma of the vulva: a phase II study of the EORTC Gynaecological Cancer Cooperative Group GCCG)." *Gynecol Oncol* **37**: 359 -362.

Echt, M. L., M. A. Finan, et al. 1999. "Detection of sentinel lymph nodes with lymphazurin in cervical, uterine, and vulvar malignancies." *South Med J* **92**: 204 -208.

BACKGROUND: Identification of sentinel lymph nodes may allow prediction of metastatic disease in cancer patients. We did a prospective study to determine whether lymphazurin dye could identify sentinel lymph nodes in patients with cervical, uterine, and vulvar cancer. **METHODS:** In 33 patients having surgery for either uterine, cervical, or vulvar carcinoma, lymphazurin dye was injected into the respective organs before the tumor and node dissection began. Sentinel lymph nodes were identified and dissected in situ. **RESULTS:** The identification rate of sentinel lymph nodes was 0/8 0% for uterine cancer patients, 2/13 15.4% for cervical cancer patients, and 9/12 for vulvar cancer patients 75%. **CONCLUSIONS:** In a limited number of patients, lymphazurin dye may be useful in identifying or assessing the sentinel nodes draining vulvar and cervical cancers. The role of this procedure in treatment planning for patients with gynecologic malignancies is yet to be determined.

Eifel, P. J., M. Morris, et al. 1995. "Prolonged continuous infusion cisplatin and 5 -fluorouracil with radiation for locally advanced carcinoma of the vulva." *Gynecol Oncol* **59**: 51 -56.

Twelve patients ages 37-85 years mean, 59 years with locoregionally advanced vulvar carcinoma were treated with a combination of irradiation and chemotherapy using prolonged continuous infusions

of 5-fluorouracil 5 -FU) and cisplatin. Eleven patients had advanced vulvar disease with tumors 5-18 cm in maximum diameter mean, 8.7 cm, eight had palpable inguinal nodes with biopsy -proven metastatic carcinoma, and five had fixed nodes. Patients received weekly 96-hr infusions of cisplatin 4 mg/m²/day and 5 -FU 250 mg/m²/day for a total of 64 mg/m² of cisplatin and 4 g/m² of 5 -FU in 4 weeks. Concurrent radiation therapy was delivered to the lower pelvis, vulva, and inguinal nodes to a total dose of 40-50 Gy at 2 Gy per fraction in 11 patients. One patient who had been previously treated for cervical cancer received radiation only to the vulva with an appositional electron beam field. Chemoradiation was well tolerated with virtually no hematologic toxicity and no unscheduled breaks in treatment. Eleven of 12 patients had at least a partial clinical response; one patient had a minimal response of unresectable vulvar disease. Of eight patients who underwent vulvar resection 6 weeks after chemoradiation, four had no residual disease in the resected vulvar specimen and remain disease-free 17, 20, 25, and 37 months, respectively, after surgery. Another patient is disease-free 28 months after a complete clinical response without vulvar resection. However, of four patients who had residual disease in the vulvar surgical specimen, disease has recurred within the irradiation field in three. Overall, 6 of 12 patients treated with this chemoradiation regimen remain disease-free 17-30 months after treatment. This is a well-tolerated outpatient regimen that yields a high response rate in patients with massive vulvar carcinomas.

Ennik, T. A., D. G. Allen, et al. 2011. "Effects of previous surgery on the detection of sentinel nodes in women with vulvar cancer." *Int J Gynecol Cancer* **21**: 1679 -1683.

BACKGROUND: There is a growing interest to apply the sentinel node (SN) procedure in the treatment of vulvar cancer. Previous vulvar surgery might disrupt lymphatic patterns and thereby decrease SN detection rates, lengthen scintigraphic appearance time SAT, and increase SN false -negative rate. The aims of this study were to evaluate the SN detection rates at the Mercy Hospital for Women in Melbourne and to investigate whether previous vulvar surgery affects SN detection rates, SAT, and SN false-negative rate. **METHODS:** Data on all patients with vulvar cancer who underwent an SN procedure blue dye, technetium, or combined technique from November 2000 to July 2010 were retrospectively collected. **RESULTS:** Sixty-five SN procedures were performed. Overall detection rate was 94% per person and 80% per groin. Detection rates in the group of patients who underwent previous excision of the primary tumor were not lower compared with the group without previous surgery or with just an incisional biopsy. There was no statistical significant difference in SAT between the previous excision group and the other patients. None of the patients with a false-negative SN had undergone previous excision. **CONCLUSIONS:** Results indicate that previous excision of a primary vulvar malignancy does not decrease SN detection rates or increase SN false-negative rate. Therefore, the SN procedure appears to be a reliable technique in patients who have previously undergone vulvar surgery. Previous excision did not significantly lengthen SAT, but the sample size in this subgroup analysis was small.

Evans, L. S., C. R. Kersh, et al. 1988. "Concomitant 5 -fluorouracil, mitomycin-C, and radiotherapy for advanced gynecologic malignancies." *Int J Radiat Oncol Biol Phys* **15**: 901 -906.

Advanced gynecologic neoplasms continue to pose major therapeutic problems; 22,500 deaths were estimated for 1987. Between December 1983 and October 1985, there were 25 patients evaluated at our institution who on joint evaluation by the radiation oncologist and gynecologic oncologists were found to have extensive disease not amenable to standard therapy. Patients were to be treated by a combined modality approach with Mitomycin-C and 5-Fluorouracil given concomitantly with radiotherapy. Nineteen patients were treated definitively and six patients were treated with palliative intent (4 primary, 1 recurrent). The patients ranged in age from 27 to 90 years with a mean of 57.3 and a median of 57. Primary sites at presentation were: cervix--14 patients, vagina--7 patients, and vulva--4 patients. The initial FIGO stages at time of the initial diagnosis were: Stage I--1 recurrent), Stage II --4, Stage III--15, and Stage IV--5. Chemotherapy consisted of 5-fluorouracil 1 gm/m² given continuous infusion for 4 days with Mitomycin-C 10 mg/m² IV push on day 1. Radiation therapy was started on day 1. Only 2 of 25 patients 8% required chemotherapy reductions. All 25 patients received mega -voltage

irradiation. The external beam dose range was 2000-6500 cGy and 14/25 patients received intracavitary or interstitial therapy. In the definitive patient group, there was no reduction in the therapeutic dose. Only four patients underwent surgical therapy. With a minimum follow-up of 8 months and a median follow-up of 28 months, the survival for the entire population was 56%. Fourteen of the 19 patients 74% treated definitively are surviving with 12 patients having no evidence of disease. Survival by site in the definitive therapy group was cervix--70%, vulva--100%, and vagina--66%. The overall response rate was 84% at 3 and 9 months 3 months; CR --36%, PR--48%, and 9 months; CR--60%, PR--24%. There were no local recurrences in the 12 patients who achieved a complete response. Three patients died of metastatic disease alone and the overall local control was 60%. Evaluation of therapeutic side effects was performed. Hematologic analysis by the Southeastern Oncology Group criteria showed neutropenia in 14 patients 1 --life-threatening, 2--severe, and 11 patients--mild/moderate and thrombocytopenia was observed in 11 patients all mild or moderate. All hematologic complications resolved. Acute complications did not appear increased except for the addition of mild oral mucositis 12 patients. Six patients demonstrated late effects with only 2 patients felt to have severe complications.ABSTRACT TRUNCATED AT 400 WORDS

Fairey, R. N., P. A. MacKay, et al. 1985. "Radiation treatment of carcinoma of the vulva, 1950 -1980." *Am J Obstet Gynecol* **151**5: 591 -597.

A retrospective study of all patients with carcinoma of the vulva treated by radiation therapy at the A. Maxwell Evans Clinic of the Cancer Control Agency of British Columbia, between 1950 and 1980, is reported. Sixty-eight patients, representing 30% of all referred patients with vulvar cancer, were analyzed for survival, recurrence patterns, complications, and clinical features. This group is companion to a series of patients treated with operation reported in 1979. The data confirm a major role for radiation therapy both in palliation and in combined radiotherapy-operation. For 13 cases, radiotherapy with curative intent was used in combination with operation resulting in a 5-year actuarial survival of 92%, with acceptable posttreatment morbidity. The advantages of preoperative radiotherapy, particularly for posterior vulvar lesions, are suggested by the data, and the need for a reappraisal of the role of radiotherapy in vulvar carcinoma is stressed.

Fambrini, M., F. Sorbi, et al. 2014. "Two -team simultaneous total radical vulvectomy and inguino-femoral lymphadenectomy via separate incisions for locally advanced FIGO stages IB \geq 4 cm -III squamous vulvar cancer." *Anticancer Res* **34**12: 7345 -7350.

AIM: To describe the feasibility, safety, and oncological outcomes of a modified triple-incision total radical vulvectomy and inguino-femoral lymphadenectomy in patients with locally advanced squamous vulvar cancer. **PATIENTS AND METHODS:** A modified triple-incision technique performed by two surgical teams operating simultaneously under regional anesthesia was performed on a consecutive series of 57 patients with Federation Internationale de Gynecologie Ostetrique (FIGO) stages IB \geq 4 cm to III squamous vulvar cancer. Adjuvant radiation therapy was delivered according to margin status and groin involvement. Surgical outcomes and follow-up data were retrospectively analyzed. **RESULTS:** The mean age of patients was 75.5 \pm 10.7 years and 54 94.7% had at least one comorbidity. Fifteen 26.3% had disease of clinical FIGO stage I \geq 4 cm, 7 12.3% had stage II, and 35 61.4% had a stage III . All surgical procedures were completed as planned. The mean surgical duration was 108 \pm 37 min. Major intraoperative complications were observed in two cases 3.5%. Twenty-one 36.8% patients received adjuvant radiation therapy. During a mean follow -up of 51.6 \pm 50.5 months, 29 50.9% patients developed local, regional or distant recurrence. The disease -free survival was 39.5 \pm 20.9 months. Nineteen 33.3% patients died of primary disease. Overall survival for the entire cohort was 65.4%, with 3-year and 5-year overall survival of 60.5% and 48.6%, respectively. **CONCLUSION:** Our results seem to reveal that the procedure is safe, with surgical and oncological outcomes comparable to classic sequential triple-incision technique. The shortening of surgical duration along with the use of regional anesthesia can have significant advantages for perioperative care, reducing the global burden of treatment and increasing the number of patients eligible for therapeutic surgery.

Farias-Eisner, R., F. D. Cirisano, et al. 1994. "Conservative and individualized surgery for early squamous carcinoma of the vulva: the treatment of choice for stage I and II T1 -2N0-1M0 disease." *Gynecol Oncol* **53**: 55-58.

We studied the outcome of patients undergoing radical local excision modified radical vulvectomy with inguinal-femoral lymphadenectomy through separate groin incisions for stage I and II invasive squamous carcinoma of the vulva. The purpose was to determine whether less radical and more individualized surgery is consistent with local control and cure. We have reported previously our experience using radical local excision and modified radical vulvectomy in stage I disease *Obstet. Gynecol.* 63, 155 1984 and with separate groin incisions *Obstet. Gynecol.* 58, 57 4 1981. This current report expands our experience with stage I and adds stage II patients treated over the past decade. Seventy-four patients were studied retrospectively over the 5-year period ending in January 1990. Reviews of both patient charts and histopathology reports were correlated with recurrence and survival. Factors analyzed included FIGO stage and grade, histology, lesion size and depth of invasion, surgical procedure, radiotherapy, lymph node status, interval to and site of recurrence, and survival. Thirty-nine patients had stage I disease and 35 had stage II. The primary operation was a radical local excision modified radical vulvectomy in 56 patients and radical vulvectomy in 18 patients; 13 underwent ipsilateral inguinal-femoral lymphadenectomy and 58 bilateral lymphadenectomy, each through separate groin incisions. The survival of those treated conservatively 97 and 90% for stages I and II, respectively is the same as those undergoing a radical vulvectomy 100 and 75% for stages I and II, respectively with only the presence of inguinal -femoral lymph node metastases impacting negatively on survival. In the entire group, the survival for negative and positive nodes was 98 and 45%, respectively. In conclusion, conservative, modified, and individualized vulvectomy in both stage I and II disease is associated with the same outcome and survival as radical vulvectomy, and lymph node status is the most important prognostic factor.

Farrell, R., V. Gebiski, et al. 2014. "Quality of life after complete lymphadenectomy for vulvar cancer: do women prefer sentinel lymph node biopsy?" *Int J Gynecol Cancer* **24**: 813 -819.

OBJECTIVES: Leg lymphoedema occurs in up to 60% of women after a complete inguinal-femoral lymphadenectomy for vulvar cancer. To avoid lymphoedema, sentinel lymph node biopsy has become the preferred method of staging. However, false-negative results may influence survival, making the sentinel node procedure unacceptable to many fully informed women. The aims of this study were to measure the quality of life QoL in women after a complete lymphadenectomy for vulvar cancer and to quantify the risk to survival these women would be prepared to take with sentinel node biopsy. **MATERIALS AND METHODS:** Sixty women who had a complete lymphadenectomy for early-stage vulvar cancer participated in structured interviews. The severity of lymphoedema symptoms was recorded. The QoL-adjusted survival was measured using the Utility-Based Questionnaire-Cancer, a cancer-specific validated QoL instrument. The women stated their preference for sentinel node biopsy or complete lymphadenectomy. A "standard-gamble" preference table was used to quantify the degree of risk to survival they would take to avoid lymphoedema. **RESULTS:** Seventy-three percent of women reported lymphoedema after complete lymphadenectomy. Women with lymphoedema or leg pain had significantly worse scores for QoL in terms of social activity as well as physical and sexual function. Overall, 80% of women would choose complete lymphadenectomy rather than sentinel node biopsy if the risk of missing a positive lymph node was higher than 1 in 100, but if the risk of missing a positive lymph node was lower than 1 in 100, almost one third of the women would prefer sentinel node biopsy. **CONCLUSIONS:** Although women treated for early-stage vulvar cancer report reduced QoL after complete lymphadenectomy, most would choose complete lymphadenectomy over sentinel node biopsy. However, there is an individual level of risk that each woman can define with regard to her preference for the sentinel node procedure. Women with early-stage vulvar cancer should be offered an informed choice between complete lymphadenectomy or sentinel node biopsy.

Faul, C. M., D. Mirmow, et al. 1997. "Adjuvant radiation for vulvar carcinoma: improved local control." *Int J Radiat Oncol Biol Phys* **38**: 381 -389.

PURPOSE: Local recurrence is a significant problem following primary surgery for advanced vulva carcinoma. The objectives of this study were to evaluate the impact of adjuvant vulvar radiation on local control in high risk patients and the impact of local recurrence on overall survival. **METHODS AND MATERIALS:** From 1980-1994, 62 patients with invasive vulva carcinoma and either positive or close less 8 mm margins of excision were retrospectively studied. Thirty-one patients were treated with adjuvant radiation therapy to the vulva and 31 patients were observed after surgery. Kaplan-Meier estimates and the Cox proportional hazard regression model were used to evaluate the effect of adjuvant radiation therapy on local recurrence and overall survival. Independent prognostic factors for local recurrence and survival were also assessed. **RESULTS:** Local recurrence occurred in 58% of observed patients and 16% in patients treated with adjuvant radiation therapy. Adjuvant radiation therapy significantly reduced local recurrence rates in both the close margin and positive margin groups $p = 0.036$, $p = 0.0048$. On both univariate and multivariate analysis adjuvant radiation and margins of excision were significant prognostic predictors for local control. Significant determinants of actuarial survival included International Federation of Gynecologists and Obstetricians (FIGO) stage, percentage of pathologically positive inguinal nodes and margins of excision. The positive margin observed group had a significantly poorer actuarial 5 year survival than the other groups $p = 0.0016$ and adjuvant radiation significantly improved survival for this group. The 2 year actuarial survival after developing local recurrence was 25%. Local recurrence was a significant predictor for death from vulva carcinoma risk ratio 3.54. **CONCLUSION:** Local recurrence is a common occurrence in high risk patients. In this study adjuvant radiation therapy significantly reduced local recurrence rates and may improve overall survival in certain subgroups. As salvage rates after developing local recurrence are poor adjuvant vulvar radiation should be considered for patients at risk after primary surgery.

Fons, G., S. M. Groenen, et al. 2009. "Adjuvant radiotherapy in patients with vulvar cancer and one intra capsular lymph node metastasis is not beneficial." *Gynecol Oncol* **114**: 343 -345.

AIM OF THE STUDY: The aim of the study was to analyze the benefit from adjuvant radiotherapy in patients with vulvar cancer and a single positive node without extra capsular spread. **MATERIALS AND METHODS:** The study population comprised data of 75 patients with vulvar cancer and one lymph node metastasis. The patients were treated in three different university centers in Amsterdam, Groningen and Rotterdam between 1984 and 2005. **RESULTS:** Out of 75 patients, 31 (41%) were treated with adjuvant radiotherapy. Both disease-free survival (DFS) and disease -specific survival (DSS) were comparable between the groups who did and who did not receive adjuvant radiotherapy HR 0.98, 95% CI 0.45 -2.14, $p=0.97$ and HR=1.02, 95% CI 0.42-2.47, $p=0.96$. **CONCLUSION:** We could not demonstrate any beneficial effect of adjuvant radiotherapy in the group of patients with one intra capsular metastasis.

Forner, D. M., R. Dakhil, et al. 2015. "Quality of life and sexual function after surgery in early stage vulvar cancer." *Eur J Surg Oncol* **41**: 40 -45.

OBJECTIVES AND METHODS: Vulvar carcinomas are rare genital malignancies. In a retrospective study on 21 patients factors influencing the quality of life and sexual function were investigated. All patients were interviewed according to the Female Sexual Function Index questionnaire (FSFI) and the Short Form 12R questionnaire (SF12). **RESULTS:** We identified 21 patients that had been operated for vulvar carcinoma FIGO stage I or IIIa in the years 2006-2008. Patients that had adjuvant radiotherapy were excluded. 14 patients had been treated by a wide excision, the other 7 by a vulvectomy. 10 patients had undergone a total inguinal lymphadenectomy, 5 patients a sentinel node biopsy. In a multivariate analysis lymphadenectomy was the only factor influencing the patients' sexual function: Patients without lymphadenectomy or with sentinel node biopsy scored better in terms of sexual function, neither age nor the extent of the surgery resulted in a significant difference. **CONCLUSION:** The lymphadenectomy has a negative influence on the patients' sexual function after surgical treatment for vulvar carcinoma. The indication for lymphadenectomy should hence be seen critically.

Fotiou, S. K., A. J. Tserkezoglou, et al. 1996. "'Butterfly' operation vs triple incision technique in vulvar cancer. a comparison of morbidity and clinical outcome." *Eur J Gynaecol Oncol* **171**: 67 -73.

Two groups group A = 25 cases and group B = 34 cases of vulvar cancer patients, treated with a modified "butterfly" operation MBO = group A and a triple incision TI = group B technique, were evaluated retrospectively. The aim was to compare the two operative methods, regarding perioperative morbidity and clinical outcome. The histopathologic and clinical characteristics of the patients were comparable, in the two groups. The hospitalization period was significantly shorter in group B TI, both when primary 22 vs 34 days, $p < 0.01$ or secondary 41 vs 55 days, $p < 0.05$ healing occurred. Local recurrences were quite similar in number A = 5/25, B = 6/34 and were successfully treated. No relapses in the remaining skin bridges were observed in group B. The overall survival was similar in the two groups A = 64%, B = 63%. However, LN positive cases had a better $p < 0.05$ survival when treated by MBO 48% vs 23%.

Frumovitz, M., P. T. Ramirez, et al. 2004. "Characteristics of recurrence in patients who underwent lymphatic mapping for vulvar cancer." *Gynecol Oncol* **921**: 205 -210.

OBJECTIVE: To evaluate patients with vulvar cancer who experienced a recurrence after undergoing lymphatic mapping and sentinel lymph node (SLN) biopsy. **METHODS:** We reviewed the records of 52 patients who underwent vulvectomy and lymphatic mapping with blue dye for treatment of vulvar cancer at our institution from 1993 to 1999 and identified patients who experienced recurrent disease. **RESULTS:** Fourteen 27% of 52 patients experienced a recurrence. The patients' median age was 60 years range 35 -84 years. Nine patients had squamous lesions, four patients had melanoma, and one patient had Paget's disease with stromal invasion. Four tumors were stage T1, seven were T2, and three were T3. Eight lesions were located at the midline and six were lateral. Thirteen patients underwent superficial inguinal lymphadenectomy while one patient underwent SLN biopsy only. Postoperatively, seven patients underwent no further treatment, six underwent radiation therapy, and one patient underwent chemotherapy. The median follow-up was 46 months and the median disease-free interval was 21 months. Primary recurrence was in the vulva in eight patients 57% , in the groin in three patients 21%, and distant in three patients 21%. Nine of 32 22% squamous lesions recurred, four 57% of seven melanomas recurred, and the sole patient with invasive Paget's recurred. Patient weight was found to be significantly different between patients who experienced a recurrence and those who did not $P = 0.05$. At least one SLN was identified in 46 88% of the 52 patients. One 17% of six patients in whom no SLN was identified experienced a recurrence, and 13 28% of 46 patients in whom a SLN was identified experienced a recurrence $P = 0.5$. In the 41 patients with negative SLNs and negative non-SLNs, the recurrence rate was 24%; in the six patients with positive SLNs and negative non-SLNs, the recurrence rate was 40%; and in the five patients with positive SLNs and positive non-SLNs, the recurrence rate was 40% $P = 0.6$. No patients had a negative SLN and positive non-SLN. Of the three patients who experienced a recurrence in the groin, one had a negative SLN and negative non-SLN, one had a positive SLN and positive non-SLN, and one had no SLN identified and a negative non-SLN. **CONCLUSIONS:** . This heterogeneous group of patients who underwent lymphatic mapping with blue dye had similar patterns of recurrence to reported series of patients who did not undergo lymphatic mapping. Groin relapse following a negative SLN biopsy is of concern and suggests that long-term follow-up data are required before lymphatic mapping and SLN biopsy alone can be considered standard treatment for patients with vulvar cancer.

Gaarenstroom, K. N., G. G. Kenter, et al. 2003. "Postoperative complications after vulvectomy and inguinofemoral lymphadenectomy using separate groin incisions." *Int J Gynecol Cancer* **134**: 522 -527.

The focus of this study was to document postoperative complications after vulvectomy and inguinofemoral lymphadenectomy using separate incisions. Data from 172 consecutive patients with newly diagnosed carcinoma of the vulva were studied. One hundred and one patients primarily treated with modified radical vulvectomy and complete inguinofemoral lymphadenectomy using separate groin incisions $n = 187$ were included in this study. One or more complications were documented in 77 of

the 101 76% patients. Complications after groin dissection were observed in 66% of the patients. The main complications were wound breakdown 17% and/or infection 39% of the groin, lymphocyst formation 40%, and lymphedema 28%. In 98 of 187 52% groin dissections, one or more complications were documented. The presence of lymph node metastases, postoperative radiation, age older than 65 years, and removal of the vena saphena magna were not significant risk factors for the occurrence of complications. The occurrence of early complications after groin dissection was significantly related to the late-complication lymphedema $P = 0.002$. Our results confirm relatively high rates of wound breakdown, infection, lymphocyst formation, and lymphedema even with separate groin incisions. The occurrence of early complications was related to lymphedema. No other risk factors could be identified.

Garcia, J. D., G. R. Altolaguirre, et al. 2009. "First results in the sentinel lymph node procedure in vulvar squamous cell carcinoma." *Prog Obstet Ginecol* **52**: 675-680.

Garcia-Iglesias, A., M. O. Rodriguez-Martin, et al. 2012. "Sentinel node dissection in the treatment of early stages of vulvar cancer." *Eur J Gynaecol Oncol* **332**: 151 -154.

OBJECTIVES: To assess the results of sentinel lymph node (SLN) detection in the initial stages of vulvar cancer and the recurrences that may appear. **STUDY DESIGN:** 76 patients with vulvar carcinoma, Stage I and II. Between 2000 and 2010, identification of the SLN was performed with a perilesional injection of Tc99m and vital dye. Ninety sentinel lymph nodes were found. They were removed separately, and lymphadenectomy was performed depending on the involved areas. Vulvar tumour was also removed. **RESULTS:** 76 patients were included in the study; 20 22.22% out of 90 SLNs presented metastases and 70 77.77% did not. There were no false negatives, and the sensitivity and negative predictive value reached 100%. Thirty-six months after treatment, one patient presented recurrence with a negative SLN, and two with positive SLNs. **CONCLUSION:** Biopsy of the SLN is a reasonable alternative to lymphadenectomy in patients with vulvar cancer Stage I and II.

Gaudineau, A., D. Weitbruch, et al. 2012. "Neoadjuvant chemoradiotherapy followed by surgery in locally advanced squamous cell carcinoma of the vulva." *Oncol Lett* **44**: 719 -722.

Alternative therapies have been sought to alleviate mutilation and morbidity associated with surgery for vulvar neoplasms. Our prime objective was to assess tumor absence in pathological vulvar and nodal specimens following neoadjuvant chemoradiotherapy in locally advanced vulvar neoplasms. Data were retrospectively collected from January 2001 to May 2009 from 22 patients treated with neoadjuvant therapy for locally advanced squamous cell carcinoma of the vulva. Neoadjuvant treatment consisted of inguino-pelvic radiotherapy 50 Gy in association with chemotherapy when possible. Surgery occurred at intervals of between 5 to 8 weeks. The median age of patients at diagnosis was 74.1 years. All patients were primarily treated with radiotherapy and 15 received a concomitant chemotherapy. Additionally, all patients underwent radical vulvectomy and bilateral inguino-femoral lymphadenectomy. Tumor absence in the vulvar and nodal pathological specimens was achieved for 6 27% patients, while absence in the vulvar pathological specimens was only achieved for 10 45.4% patients. Postoperative follow-up revealed breakdown of groin wounds, vulvar wounds and chronic lymphedema in 3 14.3%, 7 31.8% and 14 cases 63.6%, respectively. Within a median follow-up time of 2.3 years [interquartile range IQR, 0.6 -4.6], 12 54.6% patients experienced complete remission and 6 cases succumbed to metastatic evolution within a median of 2.2 years IQR, 0.6 -4.6, with 1 case also experiencing perineal recurrence. Median survival time, estimated using the Kaplan-Meier method, was 5.1 years IQR, 1.0 -6.8. We suggest that neoadjuvant chemoradiotherapy may represent a reliable and promising strategy in locally advanced squamous cell carcinoma of the vulva.

Geisler, J. P., K. J. Manahan, et al. 2006. "Neoadjuvant chemotherapy in vulvar cancer: avoiding primary exenteration." *Gynecol Oncol* **1001**: 53 -57.

OBJECTIVE: To determine whether neoadjuvant cisplatin and 5-fluorouracil chemotherapy can be used to preserve the anal sphincter and/or urethra in patients with advanced vulvar cancer involving these sites. **METHODS:** Fourteen patients with advanced vulvar cancer 1997 -2003 involving the anal sphincter and/or urethra were given 3-4 cycles of neoadjuvant chemotherapy to attempt preservation of these pelvic structures rather than undergoing a primary pelvic exenteration. Following 3 cycles, a radical vulvectomy and groin lymph node dissection were planned. All patients had lesion size documented by measurement and photograph prior to and following chemotherapy. **RESULTS:** The median age was 63 years range 39 -88. Thirteen patients received a median of 3 cycles range 2 -4 of neoadjuvant chemotherapy. Ten patients received cisplatin and 5-fluorouracil, while three received cisplatin alone. The median time from diagnosis to surgery was 77 days range 54 -143. All patients with cisplatin and 5-fluorouracil chemotherapy underwent surgery except one patient who had a synchronous renal cell carcinoma and died prior to surgery. Patients receiving cisplatin alone showed no measurable response, while all patients receiving cisplatin and 5-fluorouracil demonstrated at least a partial response. Two patients had no residual invasive carcinoma on final pathology. All patients receiving cisplatin and 5-fluorouracil followed by surgery are disease-free, while two of three receiving cisplatin have progressive disease. The anal sphincter and urethra were conserved in all patients receiving cisplatin and 5-fluorouracil. **CONCLUSION:** Neoadjuvant cisplatin and 5-fluorouracil in advanced vulvar cancer demonstrated a response rate of 100%. The anal sphincter and urethra were conserved in all patients receiving cisplatin and 5-fluorouracil. Responders are disease-free at this time. This response rate demonstrates superior activity of 5-fluorouracil in vulvar cancer and spares these patients the morbidity of exenteration or radiation.

Gerszten, K., R. N. Selvaraj, et al. 2005. "Preoperative chemoradiation for locally advanced carcinoma of the vulva." *Gynecol Oncol* **99**: 640 -644.

OBJECTIVE: A twice daily BID) radiation treatment schedule interval of 4 -6 h delivered concurrent with chemotherapy for advanced or critically located carcinoma of the vulva was modeled on the schema developed by the Gynecology Oncology Group (GOG). Inguinal nodes were included in the treatment fields even if clinically negative. This review analyzed the outcomes using this approach. **METHODS:** A retrospective review was conducted of the records of 18 patients with vulvar cancer. Patients were treated with a modified GOG schema using 5-fluorouracil (5FU) and cisplatin with BID radiation treatments during the first and last weeks of treatment and seven daily radiation treatments in between. The regional nodes and primary tumor were prescribed 44.6 Gy. Resection of the primary tumor bed and inguinal dissection was planned at 4-6 weeks post-treatment. Clinical and pathological responses as well as locoregional control and toxicity were assessed. **RESULTS:** All patients responded. There were 13/18 complete clinical responses (cCR), of whom 12 remained NED at 25 months. Of the five partial clinical response (cPR) patients, two have suffered local recurrences, despite surgical resection in one and electron boost in the other. All patients developed a desquamative perineal skin reaction necessitating a mean treatment break of 15 days. No severe hematological toxicity was encountered, and only one patient had grade 3 small bowel toxicity. One patient required surgical debridement for groin wound breakdown. **CONCLUSION:** The use of BID chemoradiation resulted in complete or partial responses in all cases. Post-treatment groin dissection can be performed without significant post-operative complications.

Gill, B. S., M. E. Bernard, et al. 2015. "Impact of adjuvant chemotherapy with radiation for node -positive vulvar cancer: A National Cancer Data Base (NCDB) analysis." *Gynecol Oncol* **137**: 365 -372.

BACKGROUND: For node-positive vulvar cancer, adjuvant radiotherapy has an established benefit, whereas the impact of chemotherapy is unknown. A National Cancer Data Base (NCDB) analysis was conducted to determine patterns of care and evaluate the survival impact of adjuvant chemotherapy. **METHODS:** The NCDB was queried for vulvar cancer patients diagnosed from 1998-2011 who underwent extirpative surgery with confirmed inguinal nodal involvement treated with adjuvant radiotherapy. Patients with inadequate follow-up or non-squamous histologies were excluded. Chi-square test, logistic regression analysis, log-rank test and multivariable Cox proportional regression

modeling with adjustment using propensity score with inverse probability of treatment weights IPTW were conducted to establish factors associated with utilization and survival. RESULTS: A total of 1797 patients were identified: 26.3% received adjuvant chemotherapy and 76.6% had 1-3 involved lymph nodes. Adoption of adjuvant chemotherapy significantly increased over time, from 10.8% in 1998 to 41.0% in 2006 $p<0.001$. Lower utilization was seen in older patients, Northeast or Southern facilities, and patients with more extensive nodal dissection, whereas greater number of involved nodes, stage IVA disease and positive surgical margins led to a higher probability of receiving chemotherapy. Unadjusted median survival without and with adjuvant chemotherapy was 29.7 months and 44.0 months $p=0.001$. On IPTW -adjusted Cox proportional regression modeling, delivery of adjuvant chemotherapy resulted in a 38% reduction in the risk of death HR 0.62, 95% CI 0.48 -0.79, $p<0.001$. CONCLUSION: In a large population-based analysis, adjuvant chemotherapy resulted in a significant reduction in mortality risk for node-positive vulvar cancer patients who received adjuvant radiotherapy.

GMCT 2009 . "Gynaecological Cancer Guidelines." http://www.aci.health.nsw.gov.au/data/assets/pdf_file/0010/154549/go_clinical_guidelines.pdf.

Goni, E., C. Estebanez, et al. 2011. "Sentinel lymph node biopsy in vulvar cancer: our experience." *Eur J Nucl Med Mol Imaging* 38: S368-369.

Gonzalez Bosquet, J., J. F. Magrina, et al. 2005. "Long -term survival and disease recurrence in patients with primary squamous cell carcinoma of the vulva." *Gynecol Oncol* 973: 828 -833.

OBJECTIVES: To assess time to failure and sites of failure with extended follow-up of patients with squamous cell carcinoma SCC of the vulva. METHODS: A retrospective analysis of 330 patients with primary SCC of the vulva treated at Mayo Clinic between 1955 and 1990 was conducted. The main outcome measures were the rates of treatment failure. The Kaplan-Meier method and the log-rank test were used to estimate the rates of overall survival, disease-free survival, and recurrence. The Cox proportional hazards model was used to assess independent variables as prognostic factors for treatment failure. RESULTS: All 330 patients in the cohort underwent lymphadenectomy; 113 patients 34.2% had involvement of the inguinofemoral nodes and 88 patients 26.7% had treatment failure. Treatment failures occurred more frequently in patients who presented with inguinal metastasis at the primary surgery and during the first 2 years of follow-up. After 2 years, both groups, with or without positive inguinal nodes, had similar treatment failure rates. Most patients with disease recurrence in the groin died within the first 2 years of follow-up. Involvement of the inguinal nodes was the main independent predictive factor for survival, disease recurrence, and metastasis. CONCLUSIONS: Most treatment failures occurred during the 2 years after initial surgical management. However, in 35% of patients, disease reoccurred 5 years or more after diagnosis, which demonstrates the need for long-term follow-up. Complete ipsilateral or bilateral inguinofemoral lymph node dissection ensures a thorough evaluation and treatment of the groin.

Gordinier, M. E., A. Malpica, et al. 2003. "Groin recurrence in patients with vulvar cancer with negative nodes on superficial inguinal lymphadenectomy." *Gynecol Oncol* 903: 625 -628.

OBJECTIVE: The objective of this study was to investigate the cause of groin recurrence in patients with vulvar cancer who had negative nodes in their superficial inguinal lymphadenectomy SIL specimens. METHODS: The records of patients with vulvar cancer treated at M. D. Anderson Cancer Center between 1986 and 1997 were reviewed to identify patients with squamous histology, clinical and surgical stage I or II, depth of invasion greater than 1 mm, and primary treatment consisting of radical wide excision and SIL. One hundred four patients met these criteria. Among these, nine experienced recurrent disease that involved one or both of the groins. All of the original hematoxylin and eosin H&E -stained slides were reviewed by one pathologist AM. Then, each paraffin block containing nodal tissue was recut at 40 microm intervals to obtain five sections for H&E staining and two unstained sections to be used for cytokeratin immunostaining if necessary. RESULTS: The median age at diagnosis and primary surgery was 65 years and the median depth of invasion was 4 mm. Seven

patients underwent bilateral, and two underwent unilateral, groin dissections. The median number of lymph nodes removed per groin was seven. The median time to recurrence was 22 months. A total of 785 additional H&E-stained slides were prepared and examined at 100x and 400x magnification. No micrometastases were identified, and there were no other suspicious findings. Therefore, immunohistochemical staining was not performed. At recurrence, one patient had a biopsy only, and eight had attempted surgical resection. In two patients, tumor was identified in fibroadipose tissue only; no lymph nodes were identified. Among the other six patients, the median number of lymph nodes resected at the time of the recurrence was five range 1 to 10. At last report, six patients had died and three were alive and free of disease. Median follow-up for survivors was 63 months range 42 to 71. CONCLUSION: These data strongly suggest that groin relapse in patients with negative nodes on SIL is caused by metastatic disease in unresected inguinal nodes. SIL as performed on the patients in this study did not eliminate all sites of nodal metastasis.

Gori, J. R., H. W. Fritsches, et al. 2002. "Ipsilateral superficial inguinal lymphadenectomy for the treatment of early cancer of the vulva." *J Low Genit Tract Dis* 63: 150 -154.

OBJECTIVE: This study compared the rates of survival, recurrence, and the occurrence of complications after surgery for vulvar cancer in selected patients treated by simple vulvectomy or wide local excision WLE and ipsilateral superficial inguinal lymphadenectomies ISIL and who were in a representative group of previous patients treated by standard radical surgery control). MATERIALS AND METHODS: Superficial inguinal lymphadenectomies were performed in 32 patients with laterally localized squamous cell tumors of 1 to 3 cm in size and without palpable lymph nodes. Eight cases, which showed histological evidence of lymph node metastasis, were submitted to conventional radical treatment and excluded from the study. Of the remaining 24 patients, 12 underwent vulvectomy, 7 hemivulvectomy, and 5 WLE. The results of this group were compared with those of 21 historical controls who previously had tumors of 1 to 3 cm and had been treated by radical vulvectomy with superficial and deep bilateral inguinal lymphadenectomy. RESULTS: Dehiscence of the flaps occurred in 66.6% of the control patients and in 8.3% of the ISIL group chi , $p < .0001$. There was lymphedema in 13.8% of the controls and none in the ISIL group Fisher exact test, $p < .02$. Upon follow -up 3 to 8 years, results are reported for 3 years of follow-up, there were 9.5% vulvar recurrences in the controls and 12.5% in the ISIL group Fisher exact test, $p < .652$ not significant). CONCLUSIONS: WLE and deep local excision of the primary lesion and ISIL in selected patients with early vulvar cancer seems to be a safe alternative to the traditional radical method.

Gould, N., S. Kamelle, et al. 2001. "Predictors of complications after inguinal lymphadenectomy." *Gynecol Oncol* 822: 329 -332.

OBJECTIVE: The aim of this study was to identify predictors of complications in patients undergoing inguinal lymphadenectomy (LND) in the treatment of vulvar carcinoma. METHODS: Clinical information was abstracted from records of patients with invasive vulvar cancer. All patients underwent LND. Closed suction drains were placed in groin incisions and removed when output was less than 30 ml/24 h. Associations between variables were studied by chi(2 and t tests. RESULTS: Sixty -seven patients undergoing 112 LND were evaluated. Eighty-eight percent of patients underwent radical vulvar surgery and LND while 12% underwent LND alone. Patients were treated with either unilateral 22 or bilateral 45 LND. Seventy -three percent received extended postoperative prophylactic antibiotics. The median duration of suction drainage was 15 days for one drain and 14 days for two drains. Early postoperative cellulitis <30 days after surgery developed in 35.4%, early wound breakdown in 19.4%, early lymphedema in 4.8%, and early lymphocyst formation in 13.1%. Late cellulitis >30 days after surgery developed in 22.2%, late wound breakdown in 3.2%, late lymphedema in 29.5%, and late lymphocysts in 5%. Patients developing early cellulitis were more likely to have early wound breakdown $P = < 0.001$, RR 14.2 or early lymphocyst formation $P = 0.016$, RR 7.6. Type of procedure, antibiotic use, need for adjuvant therapy, and duration of suction drainage did not influence early complications. Early complications and management strategies did not predict late complications. CONCLUSIONS: Chronic lymphedema occurs in nearly 30% of patients after LND. Late

complications after LND were not predicted by early complications. New strategies for prevention of chronic lymphedema are needed.

Grimshaw, R. N., J. B. Murdoch, et al. 1993. "Radical vulvectomy and bilateral inguinal -femoral lymphadenectomy through separate incisions-experience with 100 cases." *Int J Gynecol Cancer* 31: 18 -23.

Over a 6-year period 100 patients with vulvar cancer were treated by radical vulvectomy and bilateral inguinal femoral lymphadenectomy performed through separate incisions. The average age of the patients was 68.8 years. Ninety patients had squamous carcinoma, six had melanoma and four had other vulvar malignancies. FIGO staging was stage I-46, stage II-25, and stage III-23, and stage IVa-6. Twenty-seven patients were found to have spread of tumor to groin nodes, 21 unilateral and six bilateral. For patients with squamous carcinomas, groin nodes were positive in four of 45 8.9% with tumor diameter < 2 cm vs. 17 of 42 40.5% with tumors > 2 cm. In 60 patients with unilateral squamous tumors, no isolated contralateral node metastases were found, however two of 13 patients 15.4% with positive ipsilateral nodes had positive contralateral nodes also. One patient with negative nodes developed bilateral recurrent tumor in the skin bridges and subsequently died. Overall 5-year survival corrected for death from intercurrent illness was 74.6%. Corrected survival by stage for squamous carcinomas was as follows: stage I-96.7%, stage II-85%, stage III-45.8% and stage IV-50%.

Guedec-Ghelfi, R., D. Papathanassiou, et al. 2011. "Impact of the SPECT/ CT in the sentinel lymph node detection. Apropos of 32 cases." *Med Nucl* 35: 208-218.

Gunther, V., B. Malchow, et al. 2014. "Impact of radical operative treatment on the quality of life in women with vulvar cancer--a retrospective study." *Eur J Surg Oncol* 407: 875 -882.

OBJECTIVES: For patients undergoing vulva surgery the quality of life QoL is generally accepted as an important outcome parameter in addition to long-term survival, mortality and complication rates. Less radical operative treatment can reduce morbidity and thereby improve quality of life. This study focuses on outcome in terms of QoL in patients comparing wide local excision WLE with radical vulvectomy and waiver of lymphonodectomy LNE with inguinofemoral lymphonodectomy. **METHODS:** In a retrospective single-center study from 2000 to 2010, 199 patients underwent surgery for vulvar cancer. To assess QoL, the EORTC QLQ-C30 and a tumor-specific module questionnaire were sent to all patients in the follow-up period. **RESULTS:** Women who underwent WLE have a superior QoL with regard to global health status and physical, role, emotional and cognitive functioning than those who underwent radical vulvectomy. Less radical surgery also implies less fatigue, nausea/vomiting, pain, insomnia, appetite loss, diarrhea and financial difficulties. After radical vulvectomy 89% of patients have sexual complications. **CONCLUSION:** Radical operative treatment, such as radical vulvectomy, causes deterioration in the QoL of these patients. An individualized, less radical surgery must be the aim in the treatment of vulvar cancer.

Hacker, N. F., J. S. Berek, et al. 1984. "Preoperative radiation therapy for locally advanced vulvar cancer." *Cancer* 5410: 2056 -2061.

Eight patients with locally advanced vulvar cancer that would have necessitated pelvic exenteration to encompass the primary tumor were given preoperative radiation therapy in an attempt to shrink the primary tumor and allow more conservative surgery. From 4400 to 5400 rad of external radiation were delivered to the primary tumor, and one patient received an additional 2400 rad from intracavitary therapy. Satisfactory shrinkage of tumor occurred in seven of the eight patients 87.5%, thus allowing conservative surgical excision. In four patients 50%, there was no viable tumor in the surgical specimen. Moist desquamation of the vulva occurred in all patients and was of sufficient severity to require temporary cessation of radiation in four patients 50%. Five received groin radiation, and one 20% subsequently developed bilateral hip fractures. No other major morbidity occurred. Five of the eight patients 62.5% are alive without evidence of disease at intervals ranging from 15 months to 10

years. Preoperative radiation in this group obviated the need for pelvic exenteration, resulting in significantly less morbidity without compromising survival.

Hacker, N. F., J. S. Berek, et al. 1983. "Management of regional lymph nodes and their prognostic influence in vulvar cancer." *Obstet Gynecol* **61**: 408 -412.

One hundred thirteen patients with invasive carcinoma of the vulva underwent radical vulvectomy and bilateral inguinal-femoral lymphadenectomy between 1957 and 1978. Eighteen had unilateral pelvic lymphadenectomy. Thirty-one patients 27.4% had positive lymph nodes. The corrected actuarial five-year survival for patients with negative nodes was 96%, whereas it was 94% for patients with one positive node, 80% for those with two positive nodes, and 12% for those with three or more positive nodes. All patients with positive pelvic nodes or pelvic recurrence had three or more positive unilateral groin nodes, and all had palpably suspicious groin nodes preoperatively. Groin and systemic recurrences occurred in 2.9 and 3.8%, respectively, of patients with fewer than three positive unilateral inguinal-femoral nodes, as compared to 33 and 66%, respectively, of patients with three or more positive nodes. These data do not support routine pelvic lymphadenectomy in patients who have no clinically suspicious groin nodes and fewer than three positive nodes on histologic examination.

Hacker, N. F., J. S. Berek, et al. 1984. "Individualization of treatment for stage I squamous cell vulvar carcinoma." *Obstet Gynecol* **63**: 155 -162.

Of 177 cases of invasive squamous cell vulvar cancer seen at the University of California at Los Angeles and the City of Hope National Medical Center from 1957 to 1980, 84 47.5% had stage I disease. Seventy-seven patients with stage I disease 91.7% had stromal invasion of 5 mm or less. Correlation between lymph node status and depth of invasion was as follows: 1 mm or less, none of 34 0%; 1.1 to 2 mm, two of 19 10.5%; 2.1 to 3 mm, two of 17 11.8%; 3 to 5 mm, one of seven 14.3%; more than 5 mm, three of seven 42.9%. Fifty-six patients had radical vulvectomy for the primary lesion, and 28 had more conservative excision, but the incidence of local invasive recurrence 4% was the same in each group. None of 58 patients treated with inguinal-femoral lymphadenectomy developed a groin recurrence, but three of 26 patients 11.5% who had omission or modification of inguinal-femoral lymphadenectomy died with groin recurrence within 12 months. These data suggest that although some modification of the standard radical vulvectomy is appropriate for the primary lesion in patients with stage I disease, patients with greater than 1 mm of stromal invasion require at least an ipsilateral inguinal-femoral lymphadenectomy.

Hacker, N. F., R. S. Leuchter, et al. 1981. "Radical vulvectomy and bilateral inguinal lymphadenectomy through separate groin incisions." *Obstet Gynecol* **58**: 574 -579.

One hundred patients underwent radical vulvectomy and bilateral inguinal lymphadenectomy using separate groin incisions. Forty-nine had stage I disease, 37 stage II, and 14 stage III. Corrected actuarial 5-year survival for each stage was 97.4, 86, and 49.2%, respectively. Inguinal lymph nodes were positive in 25% of cases: 10.2% of stage I, 27% of stage II, and 71.4% of stage III cases. Major complications occurred in 21 patients, including major groin breakdown in 14. Thirty patients experienced no acute postoperative morbidity. The mean postoperative hospital stay was 19 days, and mean operative blood loss was 620 ml. No patients developed isolated metastases in either the groin or the inguinal skin bridge, but 2 stage III patients developed simultaneous metastases in the skin bridge and elsewhere. For appropriately selected patients, separate groin incisions for inguinal lymphadenectomy appear to result in lower morbidity than traditional methods, without compromising survival.

Hakam, A., A. Nasir, et al. 2004. "Value of multilevel sectioning for improved detection of micrometastases in sentinel lymph nodes in invasive squamous cell carcinoma of the vulva." *Anticancer Res* **24**: 1281 -1286.

Clinical usefulness of sentinel lymph node (SLN) biopsy has been demonstrated in the management of early vulvar cancer. However, what constitutes a negative SLN has not been well defined. Furthermore,

to what extent the SLNs should be sectioned for the greatest likelihood of detection of micrometastases and whether multilevel sectioning will further increase this detection rate in this setting have not been well studied. We analyzed 280 groin lymph nodes SLNs=45, non-sentinel [NSLNs]=235 in 14 patients with invasive squamous cell carcinoma ISCC of the vulva treated with vulvectomy and inguinal SLN and NSLN dissection at the H. Lee Moffitt Cancer Center HLMCC between 1996 and 2001. Each SNL was evaluated for micrometastases by H&E and pancytokeratin AE1/3 CKAE1/3 immunohistochemical staining. All negative SNLs N=40 were sectioned times 3 x3 at 50 -micron intervals and independently reviewed by two pathologists in order to assess the utility of this inexpensive and logical approach to identifying additional micrometastases. Also, the Wilcoxon Rank Sum Test was used to determine if there was an association between tumor size, depth of invasion and SNL status. The patient age ranged from 35 to 81 years mean 59 yrs; size of invasive tumor from 1.0 to 7.0 cm mean 3.4 cm; depth of invasion from 3 to 25 mm mean 10.8 mm. Of 45 SLNs examined from 14 patients, 11% 5/45 SNLs were positive for micrometastases on initial H&E and/or CKAE1/3 stains. Eighty-nine per cent 40/45 SNLs were negative in the remaining 9 patients. None of the latter 40 SNLs showed micrometastases on additional multilevel sectioning. Instead 3 of 135 NSLNs examined in these 9 patients revealed micrometastases on H&E skip-micrometastases. Mean tumor size cm and depth of invasion cm were 4.06 s.d. 1.89 and 1.20 s.d. 0.35 for SLN + and 3.02 s.d. 2.12 and 1.01 s.d. 0.86 for SLN - tumor subsets p values 0.385 and 0.348, respectively. CONCLUSION: Following routine H&E and CK AE1/3 stains, multilevel sectioning does not appear to detect additional micrometastases in sentinel lymph nodes in squamous cell carcinoma of the vulva. Even though mean tumor size and depth of invasion were greater in SNL + as compared to SLN - tumor subsets in our series, this difference did not reach statistical significance.

Hall, T. B., D. P. Barton, et al. 2003. "The role of ultrasound-guided cytology of groin lymph nodes in the management of squamous cell carcinoma of the vulva: 5-year experience in 44 patients." *Clin Radiol* **58**: 367 - 371.

AIM: To assess the accuracy of ultrasound combined with fine-needle aspiration cytology FNAC in the detection of lymph node metastasis in patients with squamous cell carcinoma of the vulva. MATERIALS AND METHODS: The groin nodes of 44 consecutive patients with primary squamous cell carcinoma of the vulva undergoing groin node dissection were assessed with ultrasound and FNAC. The results were compared with histology from subsequent inguinofemoral lymph node dissection. Twenty-nine patients underwent bilateral groin node dissections and 15 unilateral providing comparable data for 73 groins. RESULTS: Histology demonstrated metastatic disease in 28 groins and no evidence of metastatic disease in 45. Ultrasound agreed with the histology in 67 of the 73 groins 92%, with two false-positives, four false-negatives and two indeterminate appearances. Cytology agreed with the histology in 65 of 72 FNAC samples obtained 90%, with six false-negatives, and one indeterminate result. No false-positive cytology results were seen. Ultrasound and FNAC together failed to detect metastatic disease in four groins, one with an indeterminate ultrasound appearance, another with indeterminate cytology, the two others each having a single positive inguinal node despite a negative ultrasound and FNAC. CONCLUSION: The combination of ultrasound and FNAC provides a sensitive and specific tool for pre-operative assessment and may prevent unnecessary groin dissection and the attendant morbidity in selected patients with vulval cancer.

Hampl, M., P. Hantschmann, et al. 2008. "Validation of the accuracy of the sentinel lymph node procedure in patients with vulvar cancer: results of a multicenter study in Germany." *Gynecol Oncol* **111**: 282 -288.

OBJECTIVE: To investigate the diagnostic accuracy of the sentinel node procedure in patients with vulvar cancer, a multicenter study was launched in Germany in 2003 involving 7 oncology centers. PATIENTS AND METHODS: Between 2003 and 2006, 127 women with primary T1-T3 vulvar cancer were entered in the study and treated with sentinel node removal after application of 99mTechnetium labeled nanocolloid and/or blue dye. Subsequently, in all women a complete inguinofemoral lymphadenectomy and the adequate vulvar operation were performed. Sentinel lymph nodes were examined by routine pathologic examination H&E, followed by step-sectioning and

immunohistochemistry if negative. **RESULTS:** The sentinel node procedure was successful in 125 out of 127 cases, in 2 cases no sentinel nodes were detected. 21 patients received unilateral lymphadenectomy, 103 women were operated on both groins. In 39 women out of 127, positive lymph nodes in one or both groins were identified 30.7%. In 36 women, the sentinel nodes were also positive sensitivity 92.3%. We had three cases with a false negative sentinel node false negative rate: 7.7%, all of these women presenting with tumors in midline position. One tumor was a T1 tumor 10 mm, 2 tumors being classified as T2 40 and 56 mm, respectively. In one additional case 18 mm T1 tumor, midline position, the sentinel was positive in the right groin, but false negative on the left side. **CONCLUSIONS:** This study shows that identification of SLN in squamous cell cancer of the vulva is feasible, however not highly accurate depending on tumor localization and size. The false negative rate seems to be acceptable if the procedure is restricted to stage 1 tumors with clinically negative lymph node status. Tumors situated in or close to the midline seem to be less suitable for this procedure. Implementation of SLNB into clinical practice should be performed with care and only by experienced teams as to avoid preventable groin relapses.

Han, S. C., D. H. Kim, et al. 2000. "Chemoradiation as primary or adjuvant treatment for locally advanced carcinoma of the vulva." *Int J Radiat Oncol Biol Phys* **475**: 1235 -1244.

PURPOSE: To determine the impact of primary or adjuvant chemotherapy and radiation CRT on the survival rates of patients with locally advanced vulvar carcinoma. **METHODS AND MATERIALS:** Between 1973 and 1998, 54 patients with vulvar cancer were treated with radiation therapy, among which 20 received CRT, while 34 patients received radiation therapy RT alone. Of the 20 patients, 14 were treated for primary or recurrent disease pCRT, and 6 after radical vulvectomy for high -risk disease aCRT. Of the 34 patients, 12 were treated primarily pRT and 22 received adjuvant treatment aRT. Chemotherapy consisted of 2 courses of 5 -fluorouracil 5 -FU) and mitomycin C administered during RT. Six patients received cisplatin in place of mitomycin C. In CRT groups, radiation was administered to the vulva, pelvic, and inguinal lymph nodes to a median dose of 45 Gy with additional 6-17 Gy to gross disease. In RT groups, the median dose to the microscopic diseases was 45 Gy. Nine patients received external beam boost and 16 patients received supplementary brachytherapy in the forms of 226Ra or 241Am plaques to sites of macroscopic disease. **RESULTS:** Over all survival was superior in the patients treated with pCRT versus pRT with statistical significance $p = 0.04$. There was also a statistically significant improvement in disease-specific $p = 0.03$ and relapse -free survival $p = 0.01$ favoring pCRT. No statistically significant trends of improved survival rates favoring aCRT over aRT were observed. **CONCLUSION:** Concurrent radiation therapy and chemotherapy decreases local relapse rate, improves disease-specific and overall survival over RT alone as primary treatment for locally advanced vulvar cancer.

Han, S. N., I. Vergote, et al. 2012. "Weekly paclitaxel/carboplatin in the treatment of locally advanced, recurrent, or metastatic vulvar cancer." *Int J Gynecol Cancer* **225**: 865 -868.

OBJECTIVE: To evaluate efficacy of weekly paclitaxel/carboplatin chemotherapy in patients with locally advanced, metastatic, or recurrent vulvar squamous cell carcinoma. **METHOD:** A prospective, single-arm, single-center pilot study was initiated to study response rate of 9 weekly courses of paclitaxel 60 mg/m and carboplatin area under the curve, 2.7. We used this regimen in the neoadjuvant or metastatic setting when surgery would cause serious morbidity or was not an option owing to distant metastases. Primary outcome was response rate, measured according to Response Criteria in Solid Tumors criteria. Treatment toxicity, surgical morbidity, and type of surgery were also evaluated. **RESULTS:** We treated 6 patients in the period between May 2009 and May 2011, of which 4 patients had a diagnosis of locally advanced disease and 2 patients had a diagnosis of recurrent disease. A median number of 7.5 cycles of paclitaxel/carboplatin weekly was administered range, 3 -9. No objective response was observed. Paclitaxel/carboplatin weekly was discontinued after a mean of 4.3 weekly cycles in 3 patients owing to local disease progression. After a median follow-up of 4.2 months range, 1 -29 months, 3 patients died owing to progressive disease and 1 patient died owing to intercurrent disease. The 2 remaining patients underwent radical vulvectomy + bilateral inguinofemoral

lymphadenectomy after neoadjuvant chemotherapy. The main chemotherapy-related toxicity was anemia and could be managed conservatively with erythropoietin and intravenous iron therapy. **CONCLUSION:** Weekly administration of paclitaxel-carboplatin has limited clinical benefit in the treatment of vulvar squamous cell carcinoma.

Hassanzade, M., M. Attaran, et al. 2013. "Lymphatic mapping and sentinel node biopsy in squamous cell carcinoma of the vulva: systematic review and meta-analysis of the literature." *Gynecol Oncol* **130**1: 237 -245.

OBJECTIVES: We reviewed the available literature on the accuracy of sentinel node (SN) mapping in the inguinal lymph node staging of vulvar squamous cell carcinoma (SCC). **METHODS:** Medline and SCOPUS were searched by using "sentinel AND vulv*" as key words. Studies evaluating the accuracy of SN mapping in the inguinal lymph node staging of vulvar SCC were included if enough data could be extracted for calculation of detection rate and/or sensitivity. Only studies validated by inguinal lymph node dissection were included for sensitivity meta-analysis. **RESULTS:** Forty-nine studies were included in the systematic review. Pooled patient and groin basis SN detection rates were 94.4% [92.4-95.9] and 84.6% [80.5-88], respectively. Pooled patient and groin basis sensitivity were 92% [90-95] and 92% [89-94], respectively or 8% [5 -10] and 8% [6-11] false negative rates. Pooled negative predictive values were 97% [96-98] and 98% [97-99] for patient and groin basis analyses respectively. SN detection rate and sensitivity were related to mapping method blue dye, radiotracer, or both and location of the tumor midline vs. lateral tumors. Patients with palpable inguinal nodes had lower detection rate and sensitivity. **CONCLUSION:** SN mapping is an accurate method for inguinal node staging in vulvar SCC. Combining radiotracer and blue dye methods and excluding patients with palpable inguinal nodes result in the highest detection rate and sensitivity. For midline tumors possible false negative results of SN mapping should be taken into account.

Hauspy, J., M. Beiner, et al. 2007. "Sentinel lymph node in vulvar cancer." *Cancer* **110**5: 1015 -1023.

BACKGROUND: The aim of the study was to assess the feasibility, efficacy, and accuracy of the sentinel lymph node (SLN) procedure in vulvar cancer. **METHODS:** From April 2004 to September 2006, all patients with vulvar cancer, clinical stages I and II, underwent SLN detection, followed by a complete inguinofemoral lymphadenectomy. Demographic, surgical, and pathologic data on all patients were prospectively entered in a database. **RESULTS:** Forty-two patients underwent the SLN procedure. One patient was excluded from further analysis due to metastases to the vulva. The detection rate for at least 1 SLN per patient was 95%, with bilateral SLNs detected in 46% of patients. There was a trend toward improved ability to detect bilateral SLNs and proximity of the cancer to the midline $r = 0.996$; $P = .057$. No contralateral SLNs were identified in patients with lateral vulvar lesions >1 cm from the midline. For 'close -to-midline' ≤ 1 cm from the midline lesions, SLNs were detected in 93% of ipsilateral groins and bilateral SLNs were found in 46% of patients, whereas lesions abutting the midline had unilateral and bilateral SLN detected in 100% and 93%, respectively. Sixteen of 41 patients 39% and 18 of 68 groins 26% revealed metastatic disease in the lymph nodes; all were correctly identified by the SLN procedure. There were no false-negative SLN results. **CONCLUSIONS:** SLN dissection is feasible and safe to perform in vulvar cancer. The ability to identify bilateral sentinel inguinal lymph nodes appears to be related to the proximity of the vulvar cancer to the midline.

Hawnaur, J. M., K. Reynolds, et al. 2002. "Identification of inguinal lymph node metastases from vulval carcinoma by magnetic resonance imaging: an initial report." *Clin Radiol* **57**11: 995 -1000.

AIM: Magnetic Resonance Imaging (MRI) has the potential to assess inguinal lymph nodes more accurately than palpation and less invasively than surgical exploration. The objective of this study was to measure the accuracy of MRI in identifying inguinal metastases by demonstrating abnormal lymph node morphology. **MATERIALS AND METHODS:** 10 women with vulval malignancy underwent T1- and fat-suppressed T2-weighted surface coil MRI of both groins before surgery. Each groin was prospectively categorised as normal or as having metastatic lymphadenopathy using criteria established in normal volunteers. Histopathological findings in patients undergoing groin dissection for invasive

vulval carcinoma were used as validation. **RESULTS:** MRI had a positive predictive value of 89%, negative predictive value of 91%, sensitivity of 89%, specificity of 91% and accuracy of 90%. The most useful observations on MRI to identify metastatic lymphadenopathy were those of lymph node contour irregularity, cystic change in a lymph node, short axis diameter exceeding 10mm and abnormal long: short axis diameter ratio. **CONCLUSION:** High resolution MRI of the inguinal regions has potential to screen for lymph node metastases in patients with vulval cancer, with the aim of reducing the number of women who have to undergo groin dissection.

Heaps, J. M., Y. S. Fu, et al. 1990. "Surgical -pathologic variables predictive of local recurrence in squamous cell carcinoma of the vulva." *Gynecol Oncol* **38**3: 309 -314.

One hundred and thirty-five patients with squamous carcinoma of the vulva were treated at UCLA and City of Hope Medical Centers between 1957 and 1985. Sixty-two cases were stage I, 48 stage II, 18 stage III, and 7 stage IV. Twenty-one patients developed a local vulvar recurrence after primary radical resection. Ninety-one patients had a surgical tumor-free margin greater than or equal to 8 mm on tissue section and none had a local vulvar recurrence. Forty-four patients had a margin less than 8 mm; 21 had a local recurrence and 23 did not P less than 0.0001. Of the 23 patients with a margin less than 8 mm who did not recur locally, 14 remained free of disease, and 9 had either advanced disease, declining health, or short follow-up. Depth of invasion is associated with local recurrence, with a 9.1-mm reference value correctly predicting outcome in 81.5% of cases. Increasing tumor thickness is associated with local recurrence, with a 10-mm reference value predictive of 90% non-recurrence and 33% recurrences. A pushing border pattern is less likely to recur than an infiltrative growth pattern. Lymph-vascular space invasion has a combined predictive accuracy of 81.5%. Increasing keratin and greater than 10 mitoses per 10 high-power fields correlate with local recurrence. Neither clinical tumor size nor coexisting benign vulvar pathology correlates with local recurrence. Fourteen of twenty-one patients with vulvar recurrence died of metastatic disease, four died of intercurrent disease, and three were alive at 32, 68, and 157 months, with 16 recurring in less than 1 year. Surgical margin is the most powerful predictor of local vulvar recurrence. Combining factors in a stepwise logistical regression does not significantly improve this predictive value. Accounting for specimen preparation and fixation, a 1-cm tumor-free surgical margin on the vulva results in a high rate of local control, whereas a margin less than 8 mm is associated with a 50% chance of recurrence.

Hefler, L. A., C. Grimm, et al. 2008. "Inguinal sentinel lymph node dissection vs. complete inguinal lymph node dissection in patients with vulvar cancer." *Anticancer Res* **28**1B: 515 -517.

BACKGROUND: The aim of this retrospective study was to ascertain the postoperative morbidity in patients with vulvar cancer undergoing sentinel lymph node vs. complete inguinal lymph node dissection. **PATIENTS AND METHODS:** In total 29 and 46 patients with vulvar cancer, were treated by the technique of inguinal sentinel lymph node dissection or complete inguinal lymph node dissection, respectively. **RESULTS:** Inguinal sentinel lymph node dissection was associated with a shorter operation time, a reduced rate of inguinal seromas, wound breakdown and wound infection, fewer days of inguinal drainage, and reduced postoperative lymphatic secretion. **CONCLUSION:** Evidence of reduced peri- and postoperative morbidity with the sentinel lymph node technique for inguinal lymph node dissection in patients with vulvar cancer was demonstrated.

Helm, C. W., K. Hatch, et al. 1992. "A matched comparison of single and triple incision techniques for the surgical treatment of carcinoma of the vulva." *Gynecol Oncol* **46**2: 150 -156.

Thirty-two patients with invasive squamous cell carcinoma of the vulva SCC undergoing radical vulvectomy or radical local excision with bilateral superficial groin node dissection using a triple incision technique TI were matched for new FIGO stage, lymph node status, size of lesion, and site of lesion with patients with SCC undergoing traditional radical vulvectomy with en bloc bilateral groin but not pelvic node dissection using a single incision SI technique. Average operative time 134 min: 191 min, blood loss 424 ml: 733 ml), and hospital stay 9.7 days: 17.2 days were significantly

less in the TI group. After SI 6/32 19% patients and after TI 1/32 3% patients experienced complete breakdown of the groin wounds. There was no significant difference in overall survival $P = 0.56$ or disease-free survival $P = 0.53$ between the two groups. There was no significant difference in survival between the two groups by lesion size or by FIGO 1989 stage. Disease recurred in six patients after SI compared with seven after TI $P = 0.75$. There were no skin bridge recurrences in the TI group. Two patients in each group had isolated vulvar recurrences and all four were successfully treated by local excision. These data indicate that outcome following TI surgery is essentially equal to that of SI in early-stage disease but major morbidity is much reduced.

Hicks, M. L., R. E. Hempling, et al. 1993. "Vulvar carcinoma with 0.5 mm of invasion and associated inguinal lymph node metastasis." *J Surg Oncol* **54**: 271 -273.

A case of vulvar carcinoma with 0.5 mm of invasion treated by radical wide local excision only, which later developed ipsilateral inguinal lymph node recurrence, is presented. This represents the least amount of invasion reported resulting in inguinal lymph node metastasis. Review of the literature of stage I vulvar carcinoma with less than 1 mm of invasion indicates that this phenomenon occurs in only 1.6% of all patients who have undergone inguinal lymphadenectomy. Although this represents the second report of ipsilateral inguinal nodal metastasis associated with less than 1 mm of invasion, we continue to perform radical wide local excision without ipsilateral inguinal lymphadenectomy until more cases demonstrate a higher incidence of lymph node involvement.

Hoffman, J. S., N. B. Kumar, et al. 1983. "Microinvasive squamous carcinoma of the vulva: search for a definition." *Obstet Gynecol* **61**: 615 -618.

All cases of stage I squamous cell carcinoma of the vulva from the University of Michigan Tumor Registry from 1935 to 1981 were reviewed. Seventeen of 90 19% patients had nodal metastases. All had a depth of invasion of more than 2 mm and all exhibited histologic confluence. The risk of nodal metastases varied with depth of invasion, size of lesion, and histologic grade, although the association with grade was not statistically significant. The size of the lesion influenced the incidence of nodal metastases only in that it was associated with the depth of invasion. Lymphovascular invasion was present in only four patients, but three of them had nodal metastases, including one patient with only 3 mm depth of invasion.

Homesley, H. D., B. N. Bundy, et al. 1986. " Radiation therapy versus pelvic node resection for carcinoma of the vulva with positive groin nodes." *Obstet Gynecol* **68**: 733 -740.

From 1977 to 1984, 114 eligible patients with invasive squamous cell carcinoma of the vulva and positive groin nodes after radical vulvectomy and bilateral groin lymphadenectomy were randomized to receive either radiation therapy or pelvic node resection. Fifty-three of the 59 patients randomized to radiation therapy received a 4500- to 5000-rad tumor dose in five to 6.5 weeks bilaterally to the groins and to the midplane of the pelvis even if only unilateral positive groin nodes had been detected; no radiation was given to the central vulvar area. Fifty-three of the 55 patients randomized to further surgery had pelvic node resection performed on the side containing positive groin nodes either unilaterally or bilaterally. Acute and chronic morbidity was similar for both regimens. The two major poor prognostic factors were clinically suspicious or fixed ulcerated groin nodes and two or more positive groin nodes. The difference in survival for the 114 evaluable patients was significant, favoring the adjunctive radiation therapy group $P = .03$. The estimated two -year survival rates were 68% for the radiation therapy group and 54% for pelvic node resection group. The most dramatic survival advantage for radiation therapy was in patients who had either of the two major poor prognostic factors present; at this time, the benefit of radiation therapy for the remaining patients is uncertain. In this randomized prospective study, the addition of adjunctive groin and pelvic irradiation therapy after radical vulvectomy and inguinal lymphadenectomy proved superior to pelvic node resection.

Horowitz, N. S., A. B. Olawaiye, et al. 2012. "Phase II trial of erlotinib in women with squamous cell carcinoma of the vulva." *Gynecol Oncol* **127**: 141 -146.

OBJECTIVE: To evaluate the efficacy and toxicity of erlotinib in the management of squamous cell carcinoma SCC of the vulva. **METHODS:** Patients with vulvar lesions amenable to surgery or chemoradiation cohort 1 or those with metastatic measurable disease cohort 2 received erlotinib 150 mg daily. Patients were monitored for toxicity. Responses were determined by digital photography or RECIST 1.1. Cohort 1 underwent pre and post treatment biopsies. EGFR immunohistochemistry IHC, fluorescence in-situ hybridization FISH), and mutational analysis were performed. **RESULTS:** 41 patients were enrolled: 17 in cohort 1 and 24 in cohort 2. Notable grade 3 or 4 toxicities included allergic reaction 1, diarrhea/electrolyte abnormalities 3, ischemic colitis 1, and renal failure 3 and electrolyte abnormalities n=2. Mean number of cycles for cohort 2 was 3.3. Overall clinical benefit rate was 67.5% with 11 27.5% partial responses PR, 16 40.0% stable disease SD), and 7 17.5% progressive disease. Responses were of short duration. All pre and post treatment biopsies exhibited 2-3+ EGFR staining. 5 of 14 patients 35% were found to have EGFR amplification n=3 or high polysomy/trisomy n=2. These five patients had either a PR n=3 or SD n=2. Gain of function mutations were not been identified. **CONCLUSIONS:** This is the first reported controlled trial evaluating erlotinib for the management of vulvar carcinoma. Toxicities were acceptable given the lack of treatment options for these patients. Given the observed clinical benefits erlotinib may represent one of the most active agents available to treat vulvar SCC.

Hutteman, M., J. R. van der Vorst, et al. 2012. "Optimization of near -infrared fluorescent sentinel lymph node mapping for vulvar cancer." *Am J Obstet Gynecol* **206**: 89 e81 -85.

OBJECTIVES: Near-infrared fluorescence imaging has the potential to improve sentinel lymph node mapping in vulvar cancer, which was assessed in the current study. Furthermore, dose optimization of indocyanine green adsorbed to human serum albumin was performed. **STUDY DESIGN:** Nine vulvar cancer patients underwent the standard sentinel lymph node procedure using ^{99m}Tc-antibody and patent blue. In addition, intraoperative imaging was performed after peritumoral injection of 1.6 mL of 500, 750, or 1000 µM of indocyanine green adsorbed to human serum albumin. **RESULTS:** Near-infrared fluorescence sentinel lymph node mapping was successful in all patients. A total of 14 sentinel lymph nodes average, 1.6; range, 1 -4 were detected: 14 radioactive 100%, 11 blue 79%, and 14 near -infrared fluorescent 100%. **CONCLUSION:** This study demonstrates feasibility and accuracy of sentinel lymph node mapping using indocyanine green adsorbed to human serum albumin. Considering safety, cost, and pharmacy preferences, an indocyanine green adsorbed to human serum albumin concentration of 500 µM appears optimal for sentinel lymph node mapping in vulvar cancer.

Iversen, T. 1981. "The value of groin palpation in epidermoid carcinoma of the vulva." *Gynecol Oncol* **123**: 291-295.

Iversen, T. 1982. "Irradiation and bleomycin in the treatment of inoperable vulval carcinoma." *Acta Obstet Gynecol Scand* **613**: 195 -197.

Fifteen patients with inoperable squamous cell carcinoma of the vulva were treated with Bleomycin and irradiation. Only 2 patients were also treated with vulvectomy and bilateral lymphadenectomy 2 weeks later. One patients survived more than 4 years without signs of recurrence, another survived 2 1/2 years and 2 more 18 and 12 months respectively. The rest died less than 6 months after the treatment. Three patients developed signs of lung fibrosis. Bleomycin and irradiation may render a tumor operable, but in most cases this regime merely aims at palliation.

Iversen, T., V. Abeler, et al. 1981. "Individualized treatment of stage I carcinoma of the vulva." *Obstet Gynecol* **57**: 85 -89.

A series of 117 patients with stage I squamous cell carcinoma of the vulva was followed for 3 to 21 years. Twenty recurrences 17.1% were found, 12 in the vulva or vagina, 7 in the groin, and 1 in a patient who developed distant metastases. Invasion of tumor cells in lymph or blood vessels was found in operative specimens from 19 patients 16.2%, 8 of whom 42.1% developed local recurrences of metastases. Of 76 patients who underwent lymphadenectomy, 7 had ipsilateral and 1 had bilateral metastases to the inguinal lymph nodes. Five-year crude survival rate for the whole series was 79%, but only 52% for the group of patients with vessel invasion. Treatment should in most cases be hemivulvectomy with ipsilateral inguinal lymphadenectomy.

Jackson, K. S., N. Das, et al. 2003. "Contralateral groin node metastasis following ipsilateral groin node dissection in vulvar cancer: a case report." *Gynecol Oncol* **89**: 529 -531.

BACKGROUND: The majority of vulvar cancers are of the squamous cell type. Current operative management strategies are based on modifications of radical vulvectomy and groin node dissection, enabling a more individualised and conservative approach to surgery. This has led to interesting dilemmas regarding the most appropriate management in certain individuals. **CASE:** We describe a case of a contralateral recurrence following unilateral groin node dissection for vulvar cancer, with an initial single microscopically positive node. The patient did not receive adjuvant treatment. Evidence regarding the safety of this approach is discussed. **CONCLUSION:** The subject remains controversial, and further such cases should be recorded in the literature in order to gather more information on this difficult problem.

Jafari, K., F. Magalotti, et al. 1981. "Radiation therapy in carcinoma of the vulva." *Cancer* **47**: 686 -691.

Sixteen patients who had malignant lesions of the vulva and were treated at Cook County Hospital from July 1957 to June 1976 are presented. Nine patients received irradiation as a primary treatment, four received preoperative irradiation, and three received postoperative irradiation. External irradiation was employed for all patients, and tele-cobalt or tele-caesium therapy was utilized to deliver 3000 to 6000 rad to the vulvar and/or inguinal area. The number of patients in this study is small; however, the response to radiation therapy was remarkable in all patients. There was no residual cancer in vulvectomy specimens of four patients with invasive squamous cell carcinoma who received 3000--4200 rad external irradiation prior to surgery. This study suggests that further investigation of radiation therapy in the management of vulvar cancer seems justified.

Johann, S., B. Klaeser, et al. 2008. "Comparison of outcome and recurrence-free survival after sentinel lymph node biopsy and lymphadenectomy in vulvar cancer." *Gynecol Oncol* **110**: 324 -328.

OBJECTIVES: Lymph node status is an important prognostic factor in patients with squamous cell carcinoma SCC of the vulva. Complete inguinofemoral lymph node dissection (ILND) is accompanied by a high morbidity. Sentinel lymph node biopsy (SLNB) was established for less invasive lymph node (LN) staging. The aim of this study was to evaluate safety of SLNB in terms of accuracy and outcome in a clinical routine setting. **METHODS:** We retrospectively reviewed the data of patients who underwent SLNB and/or ILND for vulvar SCC in the years 1990-2007. Clinical follow-up was evaluated for histological nodal-negative patients with tumor stage T1 or T2. The false negative rate of SLNB was determined in patients who underwent both SLNB and ILND. **RESULTS:** Preoperative sentinel lymph node (SLN) visualization by scintigraphy was successful in 95% of all patients. SLNB was false negative in 1/45 inguinae 2.2%. All SLN were detected intraoperatively. During the follow-up period median 24 months for SLNB and 111 months for ILND, no groin recurrences in initially nodal negative patients occurred n=34, 59 inguinae. Transient lymph edema occurred in 7/18 patients after ILND 39% and 2/16 patients 13% after SLNB. No persistent edemas were found after SLNB and ILND. **CONCLUSION:** According to our experience SLNB is feasible and accurately predicts LN status of vulvar SCC under clinical routine conditions. SLNB in vulvar cancer seems to be a safe alternative to ILND in order to reduce morbidity of surgical treatment.

Judson, P. L., A. L. Jonson, et al. 2004. "A prospective, randomized study analyzing sartorius transposition following inguinal-femoral lymphadenectomy." *Gynecol Oncol* **95**: 226 -230.

OBJECTIVES: Based on the reduced morbidity seen in our retrospective study, we undertook a prospective, randomized trial to determine whether transposition of the sartorius muscle improves post-operative morbidity in women with squamous cell carcinoma of the vulva undergoing inguinal-femoral lymphadenectomy. **METHODS:** Patients with squamous carcinoma of the vulva requiring inguinal-femoral lymphadenectomy were randomized to undergo sartorius transposition or not. All patients received perioperative antibiotics, DVT prophylaxis, and closed suction surgical site drainage. Outcomes assessed include wound cellulitis, wound breakdown, lymphocyst formation, lymphedema, and/or rehospitalization. Cohorts were compared using Fisher's exact test. Baseline characteristics were compared using Student's t test or Fischer's exact test as appropriate. Logistic regression was used to assess the impact of sartorius transposition, after adjusting for other factors. **RESULTS:** From June 1996 to December 2002, 61 patients underwent 99 inguinal-femoral lymphadenectomies, 28 with sartorius transposition, and 33 without. The mean (SD) age for controls and patients undergoing sartorius transposition was 63.5 (15.2) and 73.8 (13.7) years, respectively $P < 0.05$. There were no statistically significant differences in BSA, tobacco use, co-morbid medical conditions, past surgical history, medication use, size of incision, duration of surgery, number of positive lymph nodes, pathologic stage, pathologic grade, pre- or postoperative hemoglobin, or length of hospitalization. There were no statistically significant differences in the incidence of wound cellulitis, wound breakdown, lymphedema, or rehospitalization. The incidence of lymphocyst formation was increased in the sartorius transposition group. After adjusting for age, however, the groups appeared similar. **CONCLUSIONS:** Sartorius transposition after inguinal-femoral lymphadenectomy does not reduce postoperative wound morbidity.

Kalra, J., E. Cortes, et al. 1985. "Effective multimodality treatment for advanced epidermoid carcinoma of the female genital tract." *J Clin Oncol* **3**: 917 -924.

Fifteen patients with advanced or recurrent squamous-cell carcinoma of the cervix, vulva, vagina, and urethra were treated with simultaneous combination chemotherapy 5-fluorouracil infusion and mitomycin C and radiotherapy 3,000 rad for a period of three weeks. Three to four weeks after completion of radiotherapy, 13 of 15 patients achieved partial or complete tumor shrinkage. Nine of 15 patients are alive, eight of whom at a median follow-up time of 24 months have no evidence of disease. The longest survival time was 45 + months. There was minimal toxicity associated with this therapy. The results of this pilot study suggest that the simultaneous administration of radiation and chemotherapy is an effective method of treatment of advanced female genital tract carcinoma.

Kamran, M. W., F. O'Toole, et al. 2014. "Whole -body [18F]fluoro-2-deoxyglucose positron emission tomography scan as combined PET-CT staging prior to planned radical vulvectomy and inguinofemoral lymphadenectomy for squamous vulvar cancer: a correlation with groin node metastasis." *Eur J Gynaecol Oncol* **35**: 230 -235.

Surgery is the mainstay of treatment for vulvar cancer. FIGO staging requires histopathological detail of the primary tumor and inguinofemoral lymph nodes but groin node dissection carries a substantial risk of short and long-term morbidity. The trend in current practice is towards sentinel lymphadenectomy for cancers with a low risk of metastases. Full lymphadenectomy is undertaken if the sentinel lymph node contains metastasis. The predictive value of 18F-FDG-PET in preoperative assessment of the groin in vulvar squamous cancer was assessed in retrospect at a single institution. A period of three years prior to the introduction of sentinel lymph node mapping was chosen in order to have full histopathological assessment of inguinal and femoral lymph nodes available as the gold standard for correlation with positron emission tomography-computerized tomography PET -CT to determine the accuracy of the enhanced radiological technique. In patients with histologically proven metastases to groin nodes, comparisons between PET-CT positive True-positive/TP and negative False -negative/FN) groups vis-a-vis histology showed a tendency towards higher FDG avidity in the vulvar

lesions, more bilateral nodes, multiple metastases, larger metastases and more extra-capsular extension in the TP group. Calculations per patient for PET-CT yielded a sensitivity of 50% and specificity at 100%. The positive predictive value (PPV) was 100% and the negative predictive value (NPV) was 57.1%. The test accuracy was 70% per patient. The high positive predictive value of PET-CT can be used to advance treatment planning prior to surgical staging of patients identified with Stage III disease. The poor sensitivity makes it unsuitable as a substitute for staging lymphadenectomy.

Kataoka, M. Y., E. Sala, et al. 2010. "The accuracy of magnetic resonance imaging in staging of vulvar cancer: a retrospective multi-centre study." *Gynecol Oncol* **117**: 82–87.

OBJECTIVE: To retrospectively evaluate the diagnostic accuracy and clinical relevance of magnetic resonance imaging (MRI) in the management of primary and recurrent vulvar cancer and to examine the added value of contrast-enhanced MRI (CE-MRI). **METHODS:** The research ethics committee waived informed consent for this study of 49 patients with vulvar cancer (36 primary and 13 recurrent) who underwent MRI before surgery at three major cancer centers from December 2003 to January 2008. CE-MRI was available for 31 patients (20 primary and 11 recurrent). MR images were retrospectively evaluated by three radiologists for tumor size and stage. Lymph nodes with a short axis >5 mm were measured and scored for contour, presence of necrosis, loss of fatty hilum, signal intensity relative to the vulvar lesion, and reader's diagnosis of lymph node metastasis. Scoring was repeated for CE-MRI. Histopathology constituted the reference standard. **RESULTS:** The size of the vulvar lesion was accurately characterized on MRI in 83% of patients. Accuracy in staging of primary vulvar cancers on unenhanced MRI was 69.4% ($n=36$). Adding CE-MRI increased lesion detection and raised staging accuracy from 75% to 85% ($n=20$). For groin lymph node metastasis prediction, the ratio of the short- to the long-axis diameter and the reader's diagnosis of lymph node metastasis yielded accuracy of 85% and 87%, respectively, in groin-by-groin analysis. **CONCLUSION:** MRI can be useful in accurately assessing the size of vulvar lesion and groin lymph node metastasis. CE-MRI may be of help in improving local staging.

Katz, A., P. J. Eifel, et al. 2003. "The role of radiation therapy in preventing regional recurrences of invasive squamous cell carcinoma of the vulva." *Int J Radiat Oncol Biol Phys* **57**: 409–418.

PURPOSE: To evaluate treatment of the inguinal nodes for patients with squamous cell carcinoma of the vulva. **METHODS AND MATERIALS:** We reviewed the records of 227 patients who had treatment of the inguinal lymph nodes between 1980 and 1998 for squamous cell carcinoma of the vulva. The inguinal nodes were clinically suspicious in 67 patients and clinically negative in 160. Regional treatment was as follows: lymph node dissection (LND) alone in 119 patients, LND plus radiation therapy (RT) in 57, and RT alone in 51. The extent of LND ranged from node excision to radical inguinal LND; all patients treated with LND alone had at least a superficial inguinal LND. Median follow-up of surviving patients was 98 months. Rates of inguinal node recurrence (INR) at 5 years were calculated using the Kaplan-Meier method. **RESULTS:** Thirty-two patients had INRs (5-year INR rate, 15.4%). Patients who received RT alone or RT + LND were significantly more likely than those treated with LND alone to have T3-4 tumors, tumors >5 cm, or lymph node involvement. However, 5-year INR rates were similar for the three groups (16%, 13%, and 16%, respectively). For patients who had LND only, the risk of INR was greater if the primary tumor was more than 2 cm ($p = 0.056$) or poorly differentiated ($p = 0.04$). For patients who had postoperative RT, INR was significantly greater if the time from LND to RT was greater than 50 days ($p = 0.03$). Ten patients had severe groin or lower-extremity complications after LND. Two patients died of postoperative cardiopulmonary complications. Six patients who were treated with RT had hip fractures or hip replacements after treatment. **CONCLUSION:** RT alone or in combination with LND is highly effective in preventing INR in patients with squamous cell carcinoma of the vulva and is associated with a low risk of major late complications.

Kelley, J. L., 3rd, T. W. Burke, et al. 1992. "Minimally invasive vulvar carcinoma: an indication for conservative surgical therapy." *Gynecol Oncol* **44**: 240–244.

It has been proposed that squamous carcinoma of the vulva with 1 mm or less of stromal invasion can be treated with local resection without inguinal node dissection. A retrospective review of 255 cases of stages I and II vulvar carcinoma demonstrated 24 cases of minimally invasive carcinoma. All cases were subjected to detailed chart review and pathologic confirmation. Mean age at diagnosis was 60 years. Seven patients had a preoperative diagnosis of preinvasive disease, ten had stage I disease, and seven had stage II disease. Fifteen cases had associated vulvar carcinoma in situ. Treatment consisted of local excision in 2 patients, radical wide excision in 11, hemivulvectomy in 5, and radical vulvectomy in 6. Eleven patients had either unilateral or bilateral inguinal node dissection. Five-year life-table survival was 89%. Four patients 17% developed recurrent dysplasia and four 17% developed invasive recurrences. One invasive recurrence was in an inguinal node in a patient previously treated with a hemivulvectomy and negative ipsilateral superficial node dissection. Univariate analysis revealed no statistically significant associations between recurrence and age, symptom duration, margin status, location, FIGO stage, or coexisting VIN. Large areas of coexisting dysplasia and variable gross appearance make meaningful application of FIGO staging criteria difficult in lesions with minimal focal invasion. Wide excision or radical wide excision of lesions with "high-risk" VIN or those showing less than or equal to 1 mm of stromal invasion on biopsy is adequate therapy. If final pathologic review demonstrates deeper invasion, a selective lymph node dissection can be performed as a second procedure. Careful surveillance with liberal use of colposcopy and biopsies is indicated in these patients.

Khalifa, M. A., J. Dodge, et al. 2003. "Slide review in gynecologic oncology ensures completeness of reporting and diagnostic accuracy." *Gynecol Oncol* **90**: 425 -430.

OBJECTIVE: We reviewed patient records in our tertiary care teaching hospital to assess the value of the mandatory slide review policy in gynecologic oncology with emphasis on completeness of reports. **METHODS:** Cases reviewed between October 2001 to September 2002 were studied. Clinical information was gathered from discussions at the weekly tumor board and from chart review. The standardized reporting guidelines in benchmark surgical pathology textbooks were used to assess the completeness of original pathology reports of excisional specimens. Diagnostic discrepancies were classified as major if the resultant change led to alteration of management or minor if it did not. **RESULTS:** Three hundred fifty-one cases were reviewed; 173 biopsies and 178 excisional specimens. Only 140 78.7% of the original pathology reports of the latter group conformed to standardized reporting guidelines. Of the 38 incomplete reports, 18 were missing critical information necessary for planning of further therapy, representing 10.1% of reports of all excisional specimens. We agreed with the original diagnosis in 252 cases 71.8%. Minor discrepancies were noted in 70 19.9% and major discrepancies in 29 cases 8.3%. No major discrepancy resulted from reviewing any of the vulvar specimens or cases that were already reviewed by gynecologic pathologists of other academic institutes. **CONCLUSION:** Mandatory slide review in gynecologic oncology is an important component in the management of gynecologic cancer patients because it completes reporting on missing parameters required for planning subsequent therapy in 10.1% of cases and recognizes discrepancies altering management in 8.3% of patients.

Kidd, E., D. Moore, et al. 2013. "ACR Appropriateness Criteria for management of locoregionally advanced squamous cell carcinoma of the vulva." *Am J Clin Oncol* **36**: 415 -422.

OBJECTIVES: Locoregionally advanced vulvar cancer LRAVC is a rare disease that presents many challenging medical decisions. An expert panel was convened to reach consensus on the most appropriate pretreatment assessment and therapeutic interventions in LRAVC patients. **METHODS:** The American College of Radiology Appropriateness Criteria are evidenced-based guidelines for specific clinical conditions that are reviewed every 2 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer-reviewed journal and the application of a well-established consensus methodology modified Delphi) to rate appropriateness of imaging and treatment procedures by the panel. In those instances where evidence is lacking or not definitive, expert opinion may be used to formulate recommendations.

RESULTS: Three clinical variants were developed to address common scenarios in the management of LRAVC. Group members reached consensus on the appropriateness of specific evaluation and treatment approaches, with numerical ratings and descriptive commentary. **CONCLUSIONS:** In combining available medical literature and expert opinion, this manuscript may serve as an aid for other practitioners in the appropriate management of patients with LRAVC.

Kirby, T. O., R. P. Rocconi, et al. 2005. "Outcomes of Stage I/II vulvar cancer patients after negative superficial inguinal lymphadenectomy." *Gynecol Oncol* **98**: 309 -312.

OBJECTIVES: To investigate the patterns of recurrence associated with superficial inguinal lymphadenectomy and vulvectomy for patients with Stage I/II vulvar cancer. **METHODS:** A retrospective chart review identified patients from 1990-2001 with Stage I/II vulvar cancer that underwent SupIL and vulvectomy. Survival was analyzed using the Kaplan-Meier method with Fisher Exact and Chi-square tests for comparisons between groups. **RESULTS:** 65 patients with Stage I/II vulvar cancer with a pathologically negative SupIL were identified 30 Stage I, 35 Stage II. Three patients recurred in the inguinal region, 4.6% and 11 patients 16.9% recurred on the vulva. Two of the 11 patients died of disease, six patients are alive without evidence of disease after additional therapy. Five-year disease-free survival and overall survival were 66% and 97%, respectively. Risk of recurrence was not associated with smoking status, stage, or margin status. **CONCLUSIONS:** SupIL and vulvectomy for Stage I/II vulvar cancer have a low recurrence rate in the inguinal region when nodes are negative. The local recurrence rate 17% is acceptable, and overall survival is good using this conservative approach.

Klar, M., M. Bossart, et al. 2011. "Sentinel lymph node detection in patients with vulvar carcinoma; Feasibility of intra-operative mapping with technetium-99m-labeled nanocolloid." *Eur J Surg Oncol* **37**: 818 -823.

AIMS: Sentinel lymph node (SLN) mapping appears to be feasible in patients with primary vulvar cancer. Previous protocols describe the injection of the technetium-99m-nanocolloid at least 3 h before surgery which involves two invasive procedures for the patient. In this study, we assessed the feasibility, safety, and accuracy of an intra-operative rather than preoperative SLN mapping in patients with primary vulvar cancer. **METHODS:** Patients with histologically confirmed squamous cell vulvar cancer and clinically FIGO stage Ib disease underwent intra-operative SLN mapping by intradermal injection of the nanocolloid around the tumor. SLN were identified and removed before a complete inguinofemoral lymphnode dissection was performed. Surgical and pathologic data on all patients were prospectively entered into a database. **RESULTS:** An SLN procedure was performed in 16 patients; 3 patients received unilateral lymphadenectomy, and 13 women underwent surgery on both groins. In all groins but 4 at least one SLN was clearly identified detection rate 25/29, 86%. A median number of 2 SLN and 4 non-SLN per groin were removed. 3 of 16 patients 19% had metastatic disease in the lymph nodes. There was no false negative SLN result. **CONCLUSION:** Intra-operative SLN detection seems feasible in patients with early stage vulvar cancer. More patients need to be enrolled in this ongoing study before this more convenient technique can be considered safe.

Klat, J., L. Sevcik, et al. 2009. "Characteristics of sentinel lymph nodes' metastatic involvement in early stage of vulvar cancer." *Aust N Z J Obstet Gynaecol* **49**: 672 -676.

BACKGROUND: Nodal involvement is one of the most significant prognostic factors in early-stage vulvar cancer. **AIMS:** To determine the diagnostic accuracy of sentinel lymph node (SLN) detection in early-stage vulvar cancer and to describe the characteristics of metastatic lymph node involvement. **METHODS:** Of 23 women with early-stage squamous cell vulvar cancer included in the study, five had lateral lesions and 18 had midline lesions. SLN detection was performed by using a radioactive tracer and blue dye, followed by radical vulvectomy or radical wide excision with uni/bilateral inguinofemoral lymphadenectomy, depending on tumour size and localization. SLNs were subsequently examined with haematoxylin-eosin and immunohistochemistry. **RESULTS:** The SLN detection was successful in all 23 women 100% and in 38 of 41 groins 92.3% tested. The total number of SLNs was 67, with an

average of 1.76 per groin. In total, 20 positive SLNs were detected in 14 of 23 patients. From a total of 20 positive SLNs, micrometastases were found in five SLNs and isolated tumour cells in one SLN. We experienced one case with a false negativity of SLN. Sensitivity, negative predictive value, accuracy and false negativity of SLN detection were 93.3%, 88.8%, 95.6% and 7.1% respectively. **CONCLUSION:** The SLN biopsy performed by an experienced team is a feasible method, with high accuracy in patients with early-stage vulvar cancer. Prognostic value of micrometastases should be confirmed in further studies.

Koh, W. J., M. Chiu, et al. 1993. "Femoral vessel depth and the implications for groin node radiation." *Int J Radiat Oncol Biol Phys* **274**: 969 -974.

PURPOSE: To quantify, based on pretreatment computer tomographic measurements, potential groin node depths, which will aid in optimal treatment planning for patients requiring groin node radiation. **METHODS AND MATERIALS:** The pretreatment computer tomographic scans of 50 gynecologic cancer patients were reviewed to determine the distance of each femoral vessel beneath the overlying skin surface, as an indicator of potential groin node depth. Correlative data regarding height and weight were obtained from patient medical records, and were used to calculate the Quetelet index, defined as weight in kg/(height in m)². Treatment parameters of 5 patients who failed prophylactic groin radiation in a recently published study were assessed to determine if underdosage represented a possible cause of failure. **RESULTS:** Individual femoral vessel depths ranged from 2.0 to 18.5 cm. When the depths of all four femoral vessels were averaged in each patient, the mean "4-vessel average" depth for this patient population was 6.1 cm. The median Quetelet index for the group was 25.6, and there was a strong correlation between femoral vessel depth and patient Quetelet index. Recalculation of doses provided to the 5 patients failing prophylactic groin radiation in the Gynecologic Oncology Group study showed that all had received potential tumor doses < 4700 cGy, with 3 patients being underdosed by > 30%. **CONCLUSION:** While surgery is often indicated in the management of patients with potential groin node metastases, the role of prophylactic groin radiation should not be rejected. Data from this study may aid in the optimal design and implementation of groin node radiotherapy.

Koh, W. J., H. J. Wallace, 3rd, et al. 1993. "Combined radiotherapy and chemotherapy in the management of local-regionally advanced vulvar cancer." *Int J Radiat Oncol Biol Phys* **265**: 80 9-816.

PURPOSE: To determine, in a retrospective single institutional study, the role of concurrent radiotherapy and chemotherapy in the treatment of local-regionally advanced vulvar cancer. **METHODS AND MATERIALS:** From 1984 to 1991, 20 patients with locally extensive primary or recurrent carcinoma of the vulva were treated with initial combined radiotherapy and chemotherapy. Seven patients had Federation Internationale de Gynecologie et d'Obstretrique Stage III disease, 10 had Stage IV disease, and three were treated for recurrent disease. None of these patients were considered candidates for primary radical vulvectomy and groin node dissection. Median radiation doses to regions of microscopic disease and gross tumor were 40 Gy range 30 -54 Gy and 54 Gy 3 4-70.4 Gy, respectively. All patients received 2 or 3 cycles of 5-Fluorouracil concurrently with radiotherapy. In addition, five patients received Cis-platinum, and one Mitomycin-C. Median at-risk follow-up interval was 37 months. **RESULTS:** Ten patients had complete resolution of tumor to initial chemoradiotherapy, and eight of these have remained free of tumor relapse. Eight other patients had partial responses, with tumor bulk reduced by > 50%, while the remaining two patients had local-regionally progressive disease. Six of the patients with partial responses had residual tumor successfully resected, although four subsequently recurred. For the entire group of 20 patients, the actuarial 3- and 5-year local control rates were 48% each, and the corresponding disease-specific survival rates were 59% and 49%. There was a suggestion that better local control was obtained in patients who received gross tumor radiation doses > or = 50 Gy. Skin reaction was the major acute toxicity and responded well to conservative management. Long-term sequelae were limited to skin and subcutaneous atrophy. **CONCLUSION:** These results indicate that initial combined radiotherapy and chemotherapy is effective in the management of advanced vulvar cancer.

Kunos, C., F. Simpkins, et al. 2009. "Radiation therapy compared with pelvic node resection for node -positive vulvar cancer: a randomized controlled trial." *Obstet Gynecol* **114**: 537 -546.

OBJECTIVES: To report long-term survival and toxicity of radiation compared with pelvic node resection for patients with groin node-positive vulvar cancer. **METHODS:** A Gynecologic Oncology Group protocol enrolled 114 patients randomly allocated to postoperative pelvic and groin radiation 45 -50 Gy, n=59 or to ipsilateral pelvic node resection n=55 after radical vulvectomy and inguinal lymphadenectomy. Retrospective analyses for 114 enrolled patients included both risk of progression and death after treatment and assessment of toxicity. **RESULTS:** Median age was 70 years. Median survivor follow-up was 74 months. The relative risk of progression was 39% in radiation patients 95% confidence interval [CI] 0.17-0.88, P=.02. Fourteen intercurrent deaths occurred after radiation as compared with only two after pelvic node resection, narrowing 6-year overall survival 51% compared with 41%, hazard ratio 0.61 [95% CI 0.30-1.3], P=.18. However, the cancer -related death rate was significantly higher for pelvic node resection compared with radiation 51% compared with 29% at 6 years, hazard ratio 0.49 [95% CI 0.28-0.87], P=.015. Six -year overall survival benefit for radiation in patients with clinically suspected or fixed ulcerated groin nodes P=.004 and two or more positive groin nodes P<.001 persisted. A ratio of more than 20% positive ipsilateral groin nodes number positive/number resected was significantly associated with contralateral lymph node metastasis, relapse, and cancer-related death. Late chronic lymphedema 16% compared with 22% and cutaneous desquamation 19% compared with 15% were balanced after radiation and pelvic node resection. **CONCLUSION:** Radiation after radical vulvectomy and inguinal lymphadenectomy significantly reduces local relapses and decreases cancer-related deaths. Late toxicities remained similar after radiation or pelvic node resection. **LEVEL OF EVIDENCE:** I.

Landoni, F., A. Maneo, et al. 1996. "Concurrent preoperative chemotherapy with 5 -fluorouracil and mitomycin C and radiotherapy FUMIR followed by limited surgery in locally advanced and recurrent vulvar carcinoma." *Gynecol Oncol* **61**: 321 -327.

To prospectively evaluate the feasibility and efficacy of neoadjuvant chemoradiotherapy locally advanced or recurrent vulvar carcinoma, 58 patients referring for primary 41 or recurrent 17 disease received preoperative external radiotherapy to a dose of 54 Gy, divided into two courses with an interval of 2 weeks. 5-Fluorouracil 750 mg/m² daily for 5 days and mitomycin -C 15 mg/m² single bolus were given at the start of each cycle. Wide local excision and inguinal lymphadenectomy were planned after treatment. Eighty-nine percent of patients completed the chemoradiotherapeutic treatment, whereas 72% underwent surgery. Objective responses were observed in 80% of vulvar diseases and in 79% of groin metastases. Pathologic complete response of both the vulvar and inguinal disease was confirmed in 13 patients 31%. Early severe toxicity was recorded in 3 patients and severe worsening of performance status in 3. Three deaths occurred shortly after treatment and at least one is directly related to toxic effects. This treatment allows good control of locally advanced and recurrent vulvar cancer with acceptable side effects. Further follow-up is required to determine the long-term outcome and the effectiveness of the surgical procedure.

Landrum, L. M., V. Skaggs, et al. 2008. "Comparison of outcome measures in patients with advanced squamous cell carcinoma of the vulva treated with surgery or primary chemoradiation." *Gynecol Oncol* **108**: 584-590.

OBJECTIVE: To review outcome measures including overall survival OS, progression free survival PFS, and patterns of recurrence in patients with advanced vulvar cancer managed by primary surgery PS or primary chemoradiation PCRT as well as population characteristics for the two groups. **METHODS:** Patients diagnosed with stage III and IV squamous cell carcinoma of the vulva from 1990 to 2006 were identified for retrospective analysis at a single institution. Charts were abstracted for clinical and pathologic findings, treatment modalities, complications, recurrence, and follow-up. Kaplan-Meier method was used to determine PFS and OS. **RESULTS:** Sixty-three patients with stage III n=47 and IV n=16 carcinoma of the vulva were identified; 30 patients were treated with PS, and

33 patients had tumor that was unresectable by vulvectomy and underwent PCRT. Patients treated with PCRT were younger 61 vs. 72 years; $p=0.09$, had less metastasis to lymph nodes 54% vs. 83%, $p=0.01$, and larger tumors 6 vs. 3.5 cm, $p=0.0001$ compared to patients treated with PS. Despite these differences, OS for the PS and PCRT groups was 69% and 76% NS, respectively, with median follow-up at 31 months. There were no differences in PFS or recurrence rates between the two groups. By multivariate analysis, age was the only significant predictor of OS or PFS. **CONCLUSIONS:** Patients with advanced vulvar cancer that are managed with PS tend to be older patients that have smaller lesions but positive lymph nodes, whereas patients requiring PCRT are younger and have larger volume disease but fewer lymph node metastases. Despite these differences, patients treated with PS and PCRT have no differences in OS, PFS, or recurrence rates. Age is the most powerful predictor of survival when size, lymph node status, stage and treatment are accounted for.

Lawrie, T. A., A. Patel, et al. 2014. "Sentinel node assessment for diagnosis of groin lymph node involvement in vulval cancer." *Cochrane Database Syst Rev* 6: CD010409.

BACKGROUND: Vulval cancer is usually treated by wide local excision with removal of groin lymph nodes inguinofemoral lymphadenectomy from one or both sides, depending on the tumour location. However, this procedure is associated with significant morbidity. As lymph node metastasis occurs in about 30% of women with early vulval cancer, accurate prediction of lymph node metastases could reduce the extent of surgery in many women, thereby reducing morbidity. Sentinel node assessment is a diagnostic technique that uses traceable agents to identify the spread of cancer cells to the lymph nodes draining affected tissue. Once the sentinel nodes are identified, they are removed and submitted to histological examination. This technique has been found to be useful in diagnosing the nodal involvement of other types of tumours. Sentinel node assessment in vulval cancer has been evaluated with various tracing agents. It is unclear which tracing agent or combination of agents is most accurate. **OBJECTIVES:** To assess the diagnostic test accuracy of various techniques using traceable agents for sentinel lymph node assessment to diagnose groin lymph node metastasis in women with FIGO stage IB or higher vulval cancer and to investigate sources of heterogeneity. **SEARCH METHODS:** We searched MEDLINE 1946 to February 2013, EMBASE 1974 to March 2013 and the relevant Cochrane trial registers. **SELECTION CRITERIA:** Studies that evaluated the diagnostic accuracy of traceable agents for sentinel node assessment involving the identification of a sentinel node plus histological examination compared with histological examination of removed groin lymph nodes following complete inguinofemoral lymphadenectomy IFL in women with vulval cancer, provided there were sufficient data for the construction of two-by-two tables. **DATA COLLECTION AND ANALYSIS:** Two authors TAL, AP independently screened titles and abstracts for relevance, classified studies for inclusion/exclusion and extracted data. We assessed the methodological quality of studies using the QUADAS-2 tool. We used univariate meta-analytical methods to estimate pooled sensitivity estimates. **MAIN RESULTS:** We included 34 studies evaluating 1614 women and approximately 2396 groins. The overall methodological quality of included studies was moderate. The studies included in this review used the following traceable techniques to identify sentinel nodes in their participants: blue dye only three studies, technetium only eight studies, blue dye plus technetium combined combined tests; 13 studies and various inconsistent combinations of these three techniques mixed tests; 10 studies. For studies of mixed tests, we obtained separate test data where possible. Most studies used haematoxylin and eosin H&E stains for the histological examination. Additionally an immunohistochemical IHC stain with and without ultrastaging was employed by 14 and eight studies, respectively. One study used reverse transcriptase polymerase chain reaction analysis CA9 RT-PCR, whilst three studies did not describe the histological methods used. The pooled sensitivity estimate for studies using blue dye only was 0.94 68 women; 95% confidence interval CI 0.69 to 0.99, for mixed tests was 0.91 679 women; 95% CI 0.71 to 0.98, for technetium only was 0.93 149 women; 95% CI 0.89 to 0.96 and for combined tests was 0.95 390 women; 95% CI 0.89 to 0.97. Negative predictive values NPVs for all index tests were > 95%. Most studies also reported sentinel node detection rates the ability of the test to identify a sentinel node of the index test. The mean detection rate for blue dye alone was 82%, compared with 95%, 96% and 98% for mixed tests, technetium only and combined

tests, respectively. We estimated the clinical consequences of the various tests for 100 women undergoing the sentinel node procedure, assuming the prevalence of groin metastases to be 30%. For the combined or technetium only tests, one and two women with groin metastases might be 'missed', respectively 95% CI 1 to 3; and for mixed tests, three women with groin metastases might be 'missed' 95% CI 1 to 9. The wide CIs associated with the pooled sensitivity estimates for blue dye and mixed tests increased the potential for these tests to 'miss' women with groin metastases. **AUTHORS' CONCLUSIONS:** There is little difference in diagnostic test accuracy between the technetium and combined tests. The combined test may reduce the number of women with 'missed' groin node metastases compared with technetium only. Blue dye alone may be associated with more 'missed' cases compared with tests using technetium. Sentinel node assessment with technetium-based tests will reduce the need for IFL by 70% in women with early vulvar cancer. It is not yet clear how the survival of women with negative sentinel nodes compares to those undergoing standard surgery IFL. A randomised controlled trial of sentinel node dissection and IFL has methodological and ethical issues, therefore more observational data on the survival of women with early vulvar cancer are needed.

Leiserowitz, G. S., A. H. Russell, et al. 1997. "Prophylactic chemoradiation of inguinofemoral lymph nodes in patients with locally extensive vulvar cancer." *Gynecol Oncol* **66**: 509 -514.

OBJECTIVE: Primary surgical resection of locally advanced squamous cancer of the vulva may compromise the integrity of important midline structures such as the anus, clitoris, urethra, and vagina. Chemoradiation synchronous radiation and cytotoxic chemotherapy has been used as alternative initial treatment which may serve as definitive management for some patients, or may reduce the scope and functional sequelae of subsequent surgery in others. Inguinofemoral node dissection is associated with substantial risk of both acute and late morbidity, prompting consideration of elective inclusion of groin nodes within the irradiated volume and deletion of subsequent groin surgery. Concern that disease relapse in the groins is potentially fatal suggested the prudence of formal outcome assessment of our recent experience with prophylactic treatment of clinically uninvolved groin nodes in the context of concurrent chemoradiation for locally advanced primary vulvar cancer. **METHODS:** A review was conducted of 23 previously untreated patients with locally advanced squamous cancer of the vulva 2 T2, 20 T3, 1 T4 and clinically uninvolved groin nodes 1969 FIGO stages 14 N0, 4 N1, and 5 N2 with negative node biopsies who were treated since 1987 with chemoradiation administered to a volume electively including bilateral inguinofemoral nodes. These patients did not undergo subsequent groin surgery. **RESULTS:** With follow-up from 6 to 98 months mean, 45.3 months; median, 42 months, no patient has failed in the prophylactically irradiated inguinofemoral nodes. No patient has developed lymphedema, vascular insufficiency, or neurological injury in a lower extremity, and no patient has experienced aseptic necrosis of a femur. **CONCLUSIONS:** Elective irradiation of the groin nodes in the context of initial chemoradiation for locally advanced vulvar cancer is an effective therapy associated with acceptable acute toxicity and minimal late sequelae. It constitutes a sensible alternative to groin dissection in this patient population.

Leminen, A., M. Forss, et al. 2000. "Wound complications in patients with carcinoma of the vulva. Comparison between radical and modified vulvectomies." *Eur J Obstet Gynecol Reprod Biol* **93**: 193 -197.

OBJECTIVE: To evaluate complications after different vulvectomies performed because of vulvar cancer. **STUDY DESIGN:** Retrospective analysis of 149 patients who underwent vulvectomy. **RESULTS:** Wound infections was found in 58%. Overweight, central or bilateral location of the tumor, and non-radical surgery were significant predictors of wound infections. Patients with a wound infection had more often wound breakdown $P<0.001$, prolonged healing time $P<0.000$, and lymphedema $P<0.001$ than patients without infection. Antimicrobial prophylaxis did not prevent wound infection. Wound infections were found in 75% after radical en bloc vulvectomy (RV) and in 47% after modified vulvectomies (MV) $P<0.001$. Also wound breakdown 47 versus 20% $P<0.001$ and lymphedema 48 versus 12% $P<0.0001$ were more common in RV group than in MV group. Lymphocysts were found in 7%, and showed no association with wound infection or type of operation. The mean hospital stay was 26 days in patients with wound infection and 12 days in patients without

infection, 31 days in RV group and 12 days in MV group, respectively. **CONCLUSIONS:** Wound infections are major determinants for both acute and late complications. Postoperative complications reduce with increasing use of modified vulvectomies.

Levenback, C., T. W. Burke, et al. 1994. "Intraoperative lymphatic mapping for vulvar cancer." *Obstet Gynecol* **84**: 163 -167.

OBJECTIVE: To determine the feasibility of intraoperative lymphatic mapping in patients with vulvar cancer. **METHODS:** Isosulfan blue was injected intradermally at the junction of tumor and normal skin in nine patients. We then attempted to identify the dye in the superficial lymphatic channels and in a superficial groin lymph node. **RESULTS:** The sentinel node was identified in seven of 12 groins in seven of the nine subjects studied. Six of the successful cases had unilateral lesions. The cases in which a sentinel node was not identified were both patients with midline lesions, including one whose scar was injected following a prior wide local excision of a perineal tumor and one who appeared to have direct drainage to the deep pelvic nodes. There were no technique-related complications. In no case was there a positive non-sentinel node in the presence of a negative sentinel node. **CONCLUSION:** Intraoperative lymphatic mapping is technically feasible in patients with vulvar cancer, particularly those with unilateral disease. Further experience is needed to evaluate the reliability of the technique in identification of groin node metastases.

Levenback, C., T. W. Burke, et al. 1995. "Potential applications of intraoperative lymphatic mapping in vulvar cancer." *Gynecol Oncol* **59**: 216 -220.

OBJECTIVE: We describe early results of and potentially important anatomic findings with intraoperative lymphatic mapping in patients with vulvar cancer. **METHODS:** Isosulfan blue was injected into the dermis at the leading edge of the vulvar lesion in 21 patients. One to five minutes later a standard groin incision was made and carried to the superficial fascia. After gentle dissection, the afferent lymphatic channel and/or sentinel lymph node was identified by its bright blue color. The sentinel node was removed and then the superficial inguinal lymphadenectomy was completed. **RESULTS:** The 21 patients, ranging in age from 23 to 85 years median, 52 years, underwent intraoperative lymphatic mapping. The clinical stages were as follows: T1 in 9, T2 in 10, T3 in 1, and unknown in 1 patient with a prior wide local excision. Two patients had palpably suspicious nodes. Ten patients had lateral lesions, and 11 had midline tumors. Eight of the 11 patients had bilateral groin dissections, making a total of 29 groins dissected. The sentinel node was identified in 18 patients 86% and in 19 groins 66%. Five patients had unilateral node metastases, and one patient had bilateral node metastases. A sentinel node was found in five of these seven groins. A total of 238 nodes were removed median , 8.2 nodes per groin. In no case was a nonsentinel node positive if the sentinel node was negative. In one patient the only metastasis was microscopic tumor in the sentinel lymph node. In one case, the sentinel node was found below the cribriform fascia. The sentinel node could not be identified in either groin in one patient with a clitoral primary; however, dye was seen in lymphatic channels passing under the symphysis pubis. The sentinel node was identified in various sites within the superficial compartment including lateral to the femoral artery and at the extreme medial border of the dissection. No complication related to the injection of isosulfan blue was seen. **CONCLUSION:** Intraoperative lymphatic mapping is safe and simple to perform and may help identify the sentinel node, define the extent of superficial inguinal lymphadenectomy, and identify uncommon anatomic variations.

Levenback, C., R. L. Coleman, et al. 2001. "Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer." *Gynecol Oncol* **83**: 276 -281.

OBJECTIVE: To determine the effectiveness of intraoperative lymphatic with blue dye alone as a means of localizing sentinel nodes in patients with vulvar cancer. **METHODS:** All patients undergoing primary surgical treatment for vulvar cancer were eligible for this prospective study. Isosulfan blue dye was injected intradermally at the edge of the primary tumor closest to the adjacent groin. Bilateral dye

injections and groin dissections were performed if the tumor was within 2 cm of the midline. RESULTS: Fifty-two patients were enrolled in the study between 1993 and 1999. The median age was 58 years. Eighty-seven percent of the patients had T1 or T2 lesions, and 92% had nonsuspicious lymph nodes on palpation. Sixty-seven percent of the patients had squamous cell carcinoma; the remaining patients had melanoma or adenocarcinoma. The sentinel node was identified in 46 of the 52 patients 88%, comprising 22 of the 25 patients with lateral tumors and 24 of the 27 patients with midline lesions. The sentinel node was successfully identified in 57 of the 76 75% dissected groins. Sentinel node identification in the groin was hampered by the effects of prior excisional biopsy vs punch biopsy 11 of 25 vs 8 of 51, $P = 0.007$ and by the lateral vs midline location of the tumor 22 of 25 groins vs 35 of 51 groins, $P = 0.067$. During the first 2 years 1993–1994, a sentinel node could not be identified in 4 of the 25 16% patients and 13 of the 36 36% groins dissected, compared with 2 of the 27 7% of patients treated and 6 of the 40 15% groins dissected from 1995 through 1999 $P = 0.034$. A total of 556 nodes were removed median, 7 per groin, of which 83 median, 1 per groin were sentinel. The sentinel node was not identified in 2 of the 12 groins that proved to have metastatic disease. Both events occurred in the first 2 years of the study. There were no false-negative sentinel nodes. Since 1995, we have successfully identified the sentinel node in 16 of the 16 patients 25 of 25 groins with T1 or T2 primary lesions, squamous histology, and nonsuspicious groin nodes on physical examination. CONCLUSIONS: Experience and careful patient selection can permit sentinel node identification with blue dye injection alone in more than 95% of patients with vulvar cancer.

Levenback, C. F., S. Ali, et al. 2012. "Lymphatic mapping and sentinel lymph node biopsy in women with squamous cell carcinoma of the vulva: a gynecologic oncology group study." *J Clin Oncol* **30**31: 3786–3791.

PURPOSE: To determine the safety of sentinel lymph node biopsy as a replacement for inguinal femoral lymphadenectomy in selected women with vulvar cancer. PATIENTS AND METHODS: Eligible women had squamous cell carcinoma, at least 1-mm invasion, and tumor size ≥ 2 cm and ≤ 6 cm. The primary tumor was limited to the vulva, and there were no groin lymph nodes that were clinically suggestive of cancer. All women underwent intraoperative lymphatic mapping, sentinel lymph node biopsy, and inguinal femoral lymphadenectomy. Histologic ultra staging of the sentinel lymph node was prescribed. RESULTS: In all, 452 women underwent the planned procedures, and 418 had at least one sentinel lymph node identified. There were 132 node-positive women, including 11 8.3% with false-negative nodes. Twenty-three percent of the true-positive patients were detected by immunohistochemical analysis of the sentinel lymph node. The sensitivity was 91.7% 90% lower confidence bound, 86.7% and the false-negative predictive value 1-negative predictive value was 3.7% 90% upper confidence bound, 6.1%. In women with tumor less than 4 cm, the false-negative predictive value was 2.0% 90% upper confidence bound, 4.5%. CONCLUSION: Sentinel lymph node biopsy is a reasonable alternative to inguinal femoral lymphadenectomy in selected women with squamous cell carcinoma of the vulva.

Levenback, C. F., C. Tian, et al. 2009. "Sentinel node (SN) biopsy in patients with vulvar cancer: a Gynecologic Oncology Group (GOG) study." *J Clin Oncol* **27**: 5505.

Levenback, C. F., A. G. van der Zee, et al. 2009. "Sentinel lymph node biopsy in patients with gynecologic cancers Expert panel statement from the International Sentinel Node Society Meeting, February 21, 2008." *Gynecol Oncol* **114**2: 151–156.

An expert panel was formed for the 6th biennial International Sentinel Node Society to review the status of sentinel lymph node biopsy (SLNB) in gynecologic oncology. This paper presents the opinion of the experts who participated regarding indications for SLNB, technical considerations, and directions for future investigation.

Levin, W., G. Goldberg, et al. 1986. "The use of concomitant chemotherapy and radiotherapy prior to surgery in advanced stage carcinoma of the vulva." *Gynecol Oncol* **25**1: 20–25.

Six cases of primary advanced squamous carcinoma of the vulva were treated with concomitant chemotherapy and radiotherapy C + RT. In five patients it was given in preparation for surgery. The radiation was delivered to the whole pelvis in 10 equal daily fractions of either 2.0 or 2.5 Gy. Mitomycin C 10 mg/m² was given on Day 1, and 5 -fluorouracil 1,000 mg/m² was given daily from Days 1 to 4, inclusive. All six patients had satisfactory early tumor response. Three patients received one course of C + RT and three were given two courses. One patient died suddenly of unknown causes 6 days after completing the C + RT. One patient with fixed groin nodes was treated with palliative intent. She maintained a complete local response but died 6 months later of liver metastases. The remaining four patients underwent surgery without healing complications and are alive with no evidence of disease at 1, 4, 14, and 26 months. In our experience vulval carcinomas can be reduced in size and extent by prior chemotherapy and radiotherapy and require less extensive surgery.

Li, B., L. Y. Wu, et al. 2009. "[An initial experience of the use of sentinel lymph node biopsy in squamous cell cancer of the vulva]." *Zhonghua Fu Chan Ke Za Zhi* 445: 364 -368.

OBJECTIVE: To evaluate the feasibility of sentinel lymph node biopsy SLNB in patients with vulvar cancer. **METHODS:** Twenty-one patients with vulvar squamous cancer undergoing radical surgery admitted in Cancer Hospital of Chinese Academy of Medical Sciences from Oct. 2004 to Apr. 2008, were enrolled in the study. SLNB procedure was performed with blue dye alone in the first eleven patients, while the later ten patients, a combination procedure with radioactive tracer and blue dye was used to detect sentinel lymph node (SLN). All resected nodes were submitted to the pathological examination, which was considered as the gold standard to determine the efficacy of SLNB. The complications related to SLNB were also observed during the study. **RESULTS:** The sentinel node was identified in 20 patients 95%, included 8 cases with unilateral SLNs and 12 cases with bilateral SLN. A total of 83 SLN were identified with a mean number of 4.2 per patient range, 1 - 9 or 2.6 per groin range, 1 - 6. Difference between the mean number of SLN 4.4 per patient, 2.5 per groin identified by blue dye or by combined procedure 3.9 per patient, 2.7 per groin was not statistically significant $t = 0.459$, $P = 0.652$; $t = -0.421$, $P = 0.717$. Twenty patients were detected to positively superficial inguinal SLN and one of them also positively bilateral deep femoral SLN, 8 10 groins of them were detected positively nodal metastases. Among of eight patients, 7 9 groins of them were detected more than one SLN involved, while 1 of them were detected false-negative node involved. The false negative rate of was 10% 1/10, negative predictive value was 96% 22/23. No complications were attributed to the study. **CONCLUSIONS:** SLNB procedure in vulvar cancer is feasible and safe. SLN identification appears to be highly accurate for detecting metastases in the ipsilateral inguinal lymphatic basins.

Lin, J. Y., B. DuBeshter, et al. 1992. "Morbidity and recurrence with modifications of radical vulvectomy and groin dissection." *Gynecol Oncol* 471: 80 -86.

Vulvar carcinoma has been managed in recent years with modifications of radical vulvectomy and groin dissection. Separate groin incisions, superficial inguinal lymphadenectomy, unilateral groin dissection, and wide excision have been utilized to reduce the morbidity of treatment. In this study, the surgical management of 82 patients with vulvar squamous cell carcinoma was reviewed in order to assess morbidity and risk of recurrence. A modification of radical vulvectomy and groin dissection was employed in 67 patients, while 15 patients underwent classical en-bloc vulvar and groin dissection. Wound complications of the vulva occurred in 1 of 12 patients undergoing hemivulvectomy, in 8 of 55 undergoing radical vulvectomy, and in 7 of 15 who had en-bloc vulvar resection and groin dissection $P = 0.01$. Among the 46 patients undergoing bilateral groin dissection through separate incisions, groin breakdown, lymphocyst, and lymphedema occurred in 10 22%, 7 15%, and 7 15%, versus 0, 1 7%, and 2 13% of the 15 who had unilateral groin dissection. Modification of vulvar resection did not increase the risk of local recurrence. Groin recurrence developed in 2 of 15 patients who underwent en-bloc groin dissection and in 1 of 46 who underwent bilateral groin dissection through separate incisions. Two of 15 who had a unilateral groin dissection recurred in the contralateral groin. The risk of recurrence as well as morbidity following modifications of radical vulvectomy with groin dissection should be considered when planning treatment.

Lindell, G., C. Jonsson, et al. 2010. "Evaluation of preoperative lymphoscintigraphy and sentinel node procedure in vulvar cancer." *Eur J Obstet Gynecol Reprod Biol* **152**: 91 -95.

OBJECTIVE: To assess the value of preoperative lymphoscintigraphy, and to evaluate the validity and feasibility of the sentinel node (SN) procedure in vulvar carcinoma. **STUDY DESIGN:** Retrospective clinical and histopathological review of 77 patients with invasive squamous cell carcinoma in vulva who were treated at Karolinska University Hospital Stockholm, Sweden, from 2000 to 2007. The patients underwent SN mapping preoperatively with radioactive tracer and blue dye n=60 or only blue dye n=17. The SN was removed separately followed by complete inguinofemoral lymphadenectomy. **RESULTS:** The relation between SNs detected on the scintigram and those found during surgery showed good agreement using weighted kappa. The detection rate of SN was 98% for radioisotope plus blue dye, and 94% for blue dye alone. Two cases of false negative SN false negative rate 2.7% were found, both with large midline tumors. **CONCLUSION:** Preoperative scintigram is a valuable help to identify and localize the SNs and gives the best estimate of the accurate number but cannot determine if unilateral or bilateral groins should be explored in cases of midline tumors. Our results are in favor of using radioisotope and blue dye to identify the SNs. This study supports previous reports that the method is not recommended for tumors larger than 40 mm to optimize detection of SN and minimize the false negative detection rate.

Louis-Sylvestre, C., E. Evangelista, et al. 2005. "Sentinel node localization should be interpreted with caution in midline vulvar cancer." *Gynecol Oncol* **97**: 151 -154.

OBJECTIVE: Carcinomas of the vulva situated on the midline or close to it, are supposed to have a bilateral lymphatic drainage. The aim of this study was to evaluate sentinel node identification in these tumors. **METHODS:** Between April 2002 and February 2004, 17 patients with operable vulvar cancer situated on, or close to the midline were entered in a prospective study. All patients underwent sentinel node identification with ^{99m}Tc -labelled nanocolloid preoperative lymphoscintigraphy and intraoperative use of a handheld probe. Depending on the surgeon, intraoperative blue dye was associated. Radical excision of the tumor and routine bilateral lymphadenectomy were then performed. Sentinel nodes were sent separately for histologic examination. Negative sentinel nodes on hematoxylin/eosine were further examined with immunohistochemistry. **RESULTS:** One or more sentinel nodes were identified in the 17 patients and in 21 of the 34 groins. In 5 patients, the sentinel nodes were metastatic. There was no false negative negative sentinel node and metastatic non-sentinel node. In 13 patients, lymphoscintigraphy and then intraoperative identification suggested a unilateral drainage of the tumor with sentinel nodes localized in only one groin. Among these 13 patients, 3 groins with no sentinel node identified contained in fact massively metastatic nodes. **CONCLUSION:** Unilateral finding of a sentinel node in tumors of the midline does not preclude a metastatic node in the other groin. Lymph node assessment should remain bilateral in these lesions.

Louis-Sylvestre, C., E. Evangelista, et al. 2006. "[Interpretation of sentinel node identification in vulvar cancer]." *Gynecol Obstet Fertil* **34**: 706 -710.

OBJECTIVE: Sentinel node (SN) identification in vulvar carcinoma would avoid groin dissection and its complications in early stages, but we first have to validate the method, as an unrecognized node metastasis is detrimental to survival. **PATIENTS AND METHODS:** Since June 2002, 38 patients with T1 or T2 lesions underwent SN identification by radioactive tracer injection and scintigraphy with, on the following day, per operative use of a handheld probe +/- patent blue dye. In case of a midline lesion, a bilateral inguinal dissection was performed whatever the result of SN identification. SN free from disease were ultrastaged with immunohistochemistry. **RESULTS:** 1 or more SN were identified in 36 out of 38 patients. 64 groins were analysed, 15 with node metastases. In 9 out of these 15 cases the SN was metastatic, in 5 it had not been identified, and in 1 it was a false negative. In these last 6 cases, there were massively metastatic nodes in the groin. In 19 out of the 26 midline lesions the surgeon identified only unilateral SN. The side without SN contained metastatic nodes in 5 cases. **DISCUSSION AND CONCLUSION:** Failure in SN identification is sometimes related to a massively invaded node.

This should be taken into account especially in the management of midline tumors where a seemingly unilateral drainage at scintigraphy warrants nevertheless a surgical assessment of the mute groin.

Lupi, G., F. Raspagliesi, et al. 1996. "Combined preoperative chemoradiotherapy followed by radical surgery in locally advanced vulvar carcinoma. A pilot study." *Cancer* **77**: 1472 -1478.

BACKGROUND: Although for decades exenterative surgery has represented the standard treatment for patients with locally advanced vulvar cancer, combined approaches, including preoperative radiation with or without chemotherapy, are now considered the treatment of choice. We report the results of a pilot study on concurrent chemoradiotherapy followed by radical surgery for patients with locally advanced squamous cell carcinomas of the vulva. **METHODS:** Thirty-one patients with squamous cell carcinoma of the vulva were treated with two courses of combination chemotherapy mitomycin C, 15 mg/m² intravenously i.v. on Day 1, and 5 -fluorouracil, 750 mg/m² i.v., in continuous 24-hour infusion on Days 1 to 5. Inguinal and pelvic lymph node chains and the vulva were irradiated starting on the same day as the chemotherapy up to a total dose of 36 Gy. After a 2 -week interval, a second course of chemoradiotherapy was given 18 Gy on the vulvar region only. After 2 weeks, patients underwent radical surgery. **RESULTS:** An objective response was observed in 22 of 24 primary cases 91.6% and in 7 of 7 recurrent cases. All but two unresponsive patients underwent radical surgery. The postoperative morbidity rate was 65% 19 of 29 patients, and the mortality rate was 13.8% 4 of 29 patients. Five of nine patients 55% with biopsy -proven inguinal lymph node metastases showed no residual lymph node disease in the surgical specimen. The recurrence rate was 31.8% and the median follow-up time was 34 months. **CONCLUSIONS:** Chemoradiotherapy seems to be effective for squamous cell carcinoma of the vulva. If treatment-related morbidity could be decreased, such a combined approach might offer a new perspectives for a conservative treatment of locally advanced vulvar cancer.

Magrina, J. F., J. Gonzalez-Bosquet, et al. 2000. "Squamous cell carcinoma of the vulva stage IA: long -term results." *Gynecol Oncol* **76**: 24 -27.

OBJECTIVE: The aim of this study was to evaluate the risk of metastases to lymph nodes and long-term results of radical and modified radical surgery in patients with a T1 squamous cell carcinoma of the vulva and ≤ 1 mm of invasion. **METHODS:** A retrospective review of 40 patients with T1 squamous cell carcinoma of the vulva and ≤ 1 mm of invasion was performed. The clinical, pathologic, surgical, and follow-up data were abstracted from the patients' records. All slides were reviewed by two pathologists according to previously established guidelines. The overall mean follow-up was 7.6 years. **RESULTS:** Vulvar recurrence developed in 2 patients 5 -year rate, 5.9%. There were no groin recurrences among 10 patients undergoing groin lymphadenectomy. One of the 30 patients 10 -year rate, 6.7% without groin dissection developed groin metastases at 7.5 years, subsequent to an invasive vulvar recurrence. The 5- and 10-year cause-specific survivals were 100 and 94.7%, respectively. **CONCLUSIONS:** T1 squamous cell carcinoma of the vulva with ≤ 1 mm of invasion was associated with a low risk of vulvar recurrence and no groin node metastases. A low risk of subsequent groin node metastasis exists in patients developing an invasive vulvar recurrence. Long-term follow-up of these patients is recommended. Lesser forms of vulvar excision, such as wide local excision, were equally effective as radical vulvectomy for the prevention of vulvar recurrences. Patients treated by radical vulvar surgery experienced increased postoperative complications compared with patients treated by less radical surgery.

Magrina, J. F., J. Gonzalez-Bosquet, et al. 1998 . "Primary squamous cell cancer of the vulva: radical versus modified radical vulvar surgery." *Gynecol Oncol* **71**: 116 -121.

OBJECTIVE: To evaluate the results of surgical therapy and to specifically compare radical and modified radical vulvar surgery relative to survival, recurrence, metastasis, and complications. **METHODS:** A retrospective review of 225 patients with primary squamous cell cancer of the vulva was performed. Clinical, pathologic, surgical, and follow-up data were collected from the patient records.

All pathology slides were reviewed with a pathologist. Radical surgery included 134 patients treated by the Basset operation. Modified radical surgery accounted for 91 patients with vulvar excision alone 65 or with lymphadenectomy 26 via separate groin incisions. **RESULTS:** The 5-year recurrence rate was 14%. The overall and disease-free survival rates at 5 years were 76.1 and 83.4%, respectively. There were no statistically significant differences between the two procedures regarding overall survival, disease-free survival, or the development of recurrence, even after adjusting for stage $P > 0.05$. Patients undergoing radical vulvar surgery were more likely to develop surgical complications and sequelae than patients having modified radical surgery, even after adjusting for stage. **CONCLUSIONS:** Modified radical vulvar surgery is associated with decreased complications and 5-year overall and disease-free survival and recurrence rates similar to those of radical vulvar surgery.

Mahner, S., J. Jueckstock, et al. 2015. "Adjuvant therapy in lymph node -positive vulvar cancer: the AGO-CaRE-1 study." *J Natl Cancer Inst* **107**3.

BACKGROUND: Women with node-positive vulvar cancer have a high risk for disease recurrence. Indication criteria for adjuvant radiotherapy are controversial. This study was designed to further understand the role of adjuvant therapy in node-positive disease. **METHODS:** Patients with primary squamous-cell vulvar cancer treated at 29 gynecologic cancer centers in Germany from 1998 through 2008 were included in this retrospective exploratory multicenter cohort study. Of 1618 documented patients, 1249 had surgical groin staging and known lymph node status and were further analyzed. All statistical tests were two-sided. **RESULTS:** Four hundred forty-seven of 1249 patients 35.8% had lymph node metastases N+. The majority of N+ patients had one 172 [38.5%] or two 102 [22.8%] positive nodes. The three-year progression-free survival PFS rate of N+ patients was 35.2%, and the overall survival OS rate 56.2% compared with 75.2% and 90.2% in node -negative patients N-. Two hundred forty-four 54.6% N+ patients had adjuvant therapy, of which 183 40.9% had radiotherapy directed at the groins +/- other fields. Three -year PFS and OS rates in these patients were better compared with N+ patients without adjuvant treatment PFS: 39.6% vs 25.9%, hazard ratio [HR] = 0.67, 95% confidence interval [CI] = 0.51 to 0.88, $P = .004$; OS: 57.7% vs 51.4%, HR = 0.79, 95% CI = 0.56 to 1.11, $P = .17$. This effect was statistically significant in multivariable analysis adjusted for age, Eastern Cooperative Oncology Group, Union internationale contre le cancer stage, grade, invasion depth, and number of positive nodes PFS: HR = 0.58, 95% CI = 0.43 to 0.78, $P < .001$; OS: HR = 0.63, 95% CI = 0.43 to 0.91, $P = .01$. **CONCLUSION:** This large multicenter study in vulvar cancer observed that adjuvant radiotherapy was associated with improved prognosis in node-positive patients and will hopefully help to overcome concerns regarding adjuvant treatment. However, outcome after adjuvant radiotherapy remains poor compared with node-negative patients. Adjuvant chemoradiation could be a possible strategy to improve therapy because it is superior to radiotherapy alone in other squamous cell carcinomas.

Mak, R. H., L. M. Halasz, et al. 2011. "Outcomes after radiation therapy with concurrent weekly platinum -based chemotherapy or every-3-4-week 5-fluorouracil-containing regimens for squamous cell carcinoma of the vulva." *Gynecol Oncol* **120**1: 101 -107.

OBJECTIVE: To compare outcomes in patients with squamous cell carcinoma SCC of the vulva treated with radiation RT and concurrent weekly platinum -based or every-3-4-week regimens containing 5-fluorouracil 5 -FU). **METHODS:** Records of 44 patients with vulvar SCC treated with concurrent chemotherapy and radiation chemoRT from 1988 to 2008 were reviewed. Rates of disease -free survival DFS, overall survival OS, locoregional recurrence LRR, and distant metastases DM were estimated using the Kaplan-Meier method. **RESULTS:** The median age was 63 years range, 44 -90, 84.1% of patients had ECOG performance status 0 -1, and patients had FIGO Stage II n=6, III n=31, or IVA n=7 disease. Patients were treated preoperatively n=10, postoperatively n=10, or without surgery n=24. The median RT dose to the vulva was 50.2 Gray range, 22 -75. Concurrent chemotherapy regimens included weekly platinum n=16 or every 3 -4 week regimens with 5-FU as the backbone n=28. With a median follow-up of 31.5 months, there was no significant difference in 2-year OS 74.5% vs. 70.0%; $p=0.65$, DFS 61.9% vs. 56.0%; $p=0.85$, LRR 31.3% vs. 32.9%; $p=0.93$,

or DM 6.3% vs. 10.6%; $p=0.81$ between the weekly platinum and every -3-4-week 5-FU regimens. Twenty patients 45.4% recurred: 16 LRR, 2 DM, and 2 with both. The clinical and pathologic complete response rates were 58.8% 20/34, and 53.8% 14/26, respectively. There was a higher proportion of grade 3 or higher acute non-skin toxicities in patients receiving every-3-4-week 5-FU 46.1% vs. 13.3%; $p=0.07$, but more grade 3 or higher skin toxicity in patients receiving weekly platinum 62.5% vs. 32.0%; $p=0.01$. **CONCLUSION:** OS, response rates, and recurrence rates were not significantly different after RT with concurrent weekly platinum-based versus every-3-4-week regimens containing 5-FU for vulvar SCC.

Makela, P. J., A. Leminen, et al. 1993. "Pretreatment sonographic evaluation of inguinal lymph nodes in patients with vulvar malignancy." *J Ultrasound Med* **125**: 255 -258.

The state of the inguinal nodes is a major prognostic factor in vulvar carcinoma. Because of new surgical trends with selective inguinal lymphadenectomy, the preoperative evaluation of inguinal lymph nodes is essential for adequate treatment of vulvar carcinoma. To evaluate the adequacy of clinical examination and high-frequency transducer sonography in detecting metastatic inguinal lymph nodes, we studied 25 patients with vulvar malignancy who underwent operation. Histopathologically proved lymph node metastases were found in 11 22% of 50 inguinal areas studied. All of the suspected metastases were in patients with stage III-IV disease. The inguinal lymph node metastases were found by sonography in nine 82%, by preoperative palpation in one 9%, and by operative palpation in six 55% of 11 areas. The difference between sonography and palpation was statistically significant $P < 0.01$. The sensitivity and specificity were 82% and 87% for sonography, 9% and 100% for preoperative palpation, and 55% and 90% for operative palpation.

Manavi, M., A. Berger, et al. 1997. "Does T1, N0 -1 vulvar cancer treated by vulvectomy but not lymphadenectomy need inguinofemoral radiation?" *Int J Radiat Oncol Biol Phys* **384**: 749 -753.

PURPOSE: The objective of our study was to demonstrate differences in relapse rates, total survival times, and complication rates between inguinofemoral radiation and its absence in cases of invasive vulvar carcinoma without lymph node involvement FIGO Stages T1, N0 -1. **METHODS AND MATERIALS:** From 1974 to 1990, 135 patients with invasive vulvar carcinoma in Stage T1 without clinical evidence of inguinal lymph node involvement underwent simple vulvectomy performed by hot-knife resection without lymphadenectomy. Although 65 patients Group 1 received postoperative inguinofemoral radiation therapy, 70 patients Group 2 did not, and none received local vulva irradiation. **RESULTS:** The 5-year survival rates were 93.7% in Group 1 and 91.4% in Group 2 $p = \text{NS}$. Although clitoris involvement was significantly more prevalent in the irradiation group $p = 0.04$, inguinal relapse was found less frequently in Group 1 4.6% or 3 out of 65 patients than in group 2 10% or 7 out of 70 patients $p = 0.32$. The complication rates were, 7 .7% in Group 1 and 2.9% in Group 2, 2.7% for vaginal stenosis two patients in each group, 1.5% for inguinal pain one patient in Group 1, 1.5% for rectovaginal fistula one patient in Group 1, 1.5% for vulvar infection one patient in Group 1. **CONCLUSION:** No statistically significant differences in the relapse rates and survival times were found. Risk factors were equally distributed in both study groups except for clitoris involvement. The 5-year survival rates in both groups were similar to those reported in the literature for radical vulvectomy and inguinal lymph-node dissection 83 -96%. Morbidity in our study was low. Although our data showed similar results in both groups, we are not recommending at this time to omit groin radiation in general, but it may be justified in low-risk cases.

Manci, N., C. Marchetti, et al. 2009. "Inguinofemoral lymphadenectomy: randomized trial comparing inguinal skin access above or below the inguinal ligament." *Ann Surg Oncol* **163**: 721 -728.

BACKGROUND: Groin wound breakdown, lymphoceles, cellulitis, and chronic leg edema are the most frequent complications of inguinal lymphadenectomy, resulting in severe patient discomfort and significant lengthening of postoperative stay. Despite all innovations, complication rates are still high and inevitable. Our experience suggests that cutaneous flap preparation, identification of the Camper

fascia, and preservation of the most lateral lymphatics decrease associated morbidity. The aim of this study is to analyze whether different cutaneous skin flap preparations and their different devascularization above or below the inguinal ligament), resecting all the lymphofatty tissue, reduce groin wound complications, and whether the same therapeutic approach and number of lymph nodes removed are comparable. **METHODS:** This prospective randomized clinical trial of 62 consecutive patients affected by vulvar carcinoma requiring inguinal lymphadenectomy compared skin inguinal incision carried out 3-4 cm above the inguinal ligament group A or below it group B. **RESULTS:** Inguinal dehiscence was present in 17 of 53 32.1% patients in group B and in 9 of 54 16.7% in group A $P=0.10$. Lymphocele was observed in 10 of 53 lymphadenectomies 18.9% in group B and in 3 of 54 dissections 5.6% in group A $P=0.07$. Upper incision allows more precise identification of the Camper fascia, is less painful, and gives better cosmetic results. Moreover, there may be advantage, albeit not statistically significant, regarding flap length, wound dehiscence rate, and speed of wound healing. There was no difference in chronic leg edema, number of nodes removed, or hospital stay.

Maneo, A., F. Landoni, et al. 2003. "Randomised study between neoadjuvant chemoradiotherapy and primary surgery for the treatment of advanced vulvar cancer." *Int J Gynecol Cancer* **13 Suppl 1** 6: Abstract PL 19.

Martinez-Palones, J. M., M. A. Perez-Benavente, et al. 2007. "Comparison of recurrence after vulvectomy and lymphadenectomy with and without sentinel node biopsy in early stage vulvar cancer: Commentary." *Obstet Gynecol Surv* **62**: 240-242.

Martinez-Palones, J. M., M. A. Perez-Benavente, et al. 2006. "Comparison of recurrence after vulvectomy and lymphadenectomy with and without sentinel node biopsy in early stage vulvar cancer." *Gynecol Oncol* **103**: 865-870.

OBJECTIVES: To determine the usefulness of sentinel lymph node biopsy in early stage vulvar cancer and to assess recurrences after surgical treatment with sentinel node identification or surgical treatment without sentinel node identification. **METHODS:** We reviewed the records of 55 patients with early stage vulvar cancer operated on between 1995 and 2005. A prospective series of 28 patients who underwent vulvectomy and lymphadenectomy with intraoperative sentinel lymph node identification between 2000 and 2005 SLN group was compared with a retrospective series of 27 patients who underwent vulvectomy and lymphadenectomy without sentinel node procedure between 1995 and 2000 non-SLN group. Patients in the sentinel node identification group underwent preoperative lymphoscintigraphy technetium -99 colloid albumin injection around the tumor and intraoperative mapping with isosulfan blue dye. **RESULTS:** In the SLN group, 9 tumors were T1 and 19 were T2, with a total of 40 groins dissected and 9 positive nodes in 7 patients. Sixty-two sentinel lymph nodes were detected with a mean of 2.2 sentinel nodes per patient range 0 -4. A false negative case was found. In the non-SLN group, 7 tumors were T1 and 20 were T2, with a total of 49 groins dissected and 9 positive nodes in 6 patients. Recurrence occurred in 8 patients 28.6% in the SLN group and in 6 26.9% in the non-SLN group $P=0.8$. **CONCLUSIONS:** Sentinel lymph node identification in early stage vulvar cancer is a feasible. Analysis of recurrence may allow considering this procedure as a possible alternative to inguino-femoral lymphadenectomy.

McCall, A. R., M. C. Olson, et al. 1995. "The variation of inguinal lymph node depth in adult women and its importance in planning elective irradiation for vulvar cancer." *Cancer* **75**: 2286 -2288.

BACKGROUND: The Gynecologic Oncology Group (GOG) protocol #88 reported an 18.5% failure in inguinal lymph nodes of patients with vulvar cancer whose groins were treated with radiation alone. This high failure rate may be due to the study design. **METHODS:** In this study, the depths of inguinal lymph nodes were evaluated with computed tomography CT scans in 100 adult women without inguinal adenopathy or prior inguinal surgery. The dose that would have been delivered to the inguinal lymph nodes of these patients was determined using isodose curves constructed according to the guidelines in GOG protocol #88. **RESULTS:** Only 18% of women had all inguinal lymph nodes measured at a depth of 3 cm or less. **CONCLUSIONS:** More than one-half of all women in this study

would have received less than 60% of the prescribed radiation dose because their inguinal lymph nodes were deeper than 5 cm, if the depth of their inguinal lymph nodes had not been measured before therapy.

Meads, C., A. J. Sutton, et al. 2014. "Sentinel lymph node biopsy in vulval cancer: systematic review and meta-analysis." *Br J Cancer* **110**12: 2837 -2846.

BACKGROUND: The purpose of this study was to determine the accuracy of sentinel lymph node (SLN) biopsy with technetium 99 99mTc and/or blue dye -enhanced lymphoscintigraphy in vulval cancer. **METHODS:** Sensitive searches of databases were performed upto October 2013. Studies with at least 75% of women with FIGO stage IB or II vulval cancer evaluating SLN biopsy with 99mTc, blue dye or both with reference standard of inguinofemoral lymphadenectomy IFL or clinical follow-up were included. Meta-analyses were performed using Meta-Disc version 1.4. **RESULTS:** Of the 2950 references, 29 studies 1779 women were included; most of them evaluated 99mTc combined with blue dye. Of these, 24 studies reported results for SLN followed by IFL, and 5 reported clinical follow-up only for SLN negatives. Pooling of all studies was inappropriate because of heterogeneity. Mean SLN detection rates were 94.0% for 99mTc, 68.7% for blue dye and 97.7% for both. SLN biopsy had pooled sensitivity of 95% 95% CI 92 -98% with negative predictive value (NPV) of 97.9% in studies using 99mTc/blue dye, ultrastaging and immunohistochemistry with IFL as reference. Pooled sensitivity for SLN with clinical follow-up for SLN-negatives was 91% 85 -95% with NPV 95.6%. Patients undergoing SLN biopsy experienced less morbidity than those undergoing IFL. **CONCLUSIONS:** Sentinel lymph node biopsy using 99mTc, blue dye and ultrastaging with immunohistochemistry is highly accurate when restricted to carefully selected patients, within a rigorous protocol, with close follow-up and where sufficient numbers for learning curve optimisation exist. Patients must make an informed choice between the slightly higher groin recurrence rates of SLN biopsy vs the greater morbidity of IFL.

Merisio, C., R. Berretta, et al. 2005. "Radioguided sentinel lymph node detection in vulvar cancer." *Int J Gynecol Cancer* **15**3: 493 -497.

Lymph node status is the most important prognostic factor in vulvar cancer. Histologically, sentinel nodes may be representative of the status of the other regional nodes. Identification and histopathologic evaluation of sentinel nodes could then have a significant impact on clinical management and surgery. The aim of this study was to evaluate the feasibility and diagnostic accuracy of sentinel lymph node detection by preoperative lymphoscintigraphy with technetium-99 m-labeled nanocolloid, followed by radioguided intraoperative detection. Nine patients with stage T1, N0, M0, and 11 patients with stage T2, N0, M0 squamous cell carcinoma of the vulva were included in the study. Only three cases had lesions exceeding 3.5 cm in diameter. Sentinel nodes were detected in 100% of cases. A total of 30 inguinofemoral lymphadenectomies were performed, with a mean of 10 surgically removed nodes. Histological examination revealed 17 true negative sentinel nodes, 2 true positive, and 1 false negative. In our case series, sentinel lymph node detection had a 95% diagnostic accuracy, with only one false negative. Based on literature evidence, the sentinel node procedure is feasible and reliable in vulvar cancer; however, the value of sentinel node dissection in the treatment of early-stage vulvar cancer still needs to be confirmed.

Molpus, K. L., M. C. Kelley, et al. 2001. "Sentinel lymph node detection and microstaging in vulvar carcinoma." *J Reprod Med* **46**10: 863 -869.

OBJECTIVE: To determine the efficacy of using complementary techniques for detecting sentinel lymph nodes (SLNs) in vulvar carcinoma and to evaluate the utility of microstaging techniques. **STUDY DESIGN:** Patients with invasive vulvar carcinoma underwent sentinel lymph node detection (SLN D) using preoperative lymphoscintigraphy, intraoperative isosulfan blue dye injection and an intraoperative hand-held gamma-detecting probe. Eleven patients were included and a total of 16 groins evaluated. Sentinel nodes identified were excised, bisected and examined in surgical pathology using

hematoxylin and eosin H&E staining. Pathologically negative SLNs were subjected to additional microstaging via serial sectioning and immunohistochemical staining for cytokeratin. Surgical management of the vulvar cancer and extent of inguinal-femoral lymphadenectomy were individualized based on clinicopathologic parameters, including depth of invasion, location of the tumor and patient performance status. **RESULTS:** Lymphoscintigraphy, dye and gamma-detector methods led to the total detection of 16, 19 and 17 SLNs, respectively. In two cases the isosulfan blue dye assisted in the isolation of an additional sentinel node over that of the gamma probe. Each method individually identified SLNs in 10/11 patients 91%. A total of 19 sentinel nodes were isolated. One SLN 5% was positive for metastatic disease using H&E staining. Of the 18 negative SLNs, 2 11% had micrometastases < 0.2 mm upon serial sectioning and immunohistochemical staining. **CONCLUSION:** Combined-modality mapping enhances detection of SLNs in vulvar carcinoma. Histologic microstaging improves the detection of micrometastases within SLNs.

Montana, G. S., G. M. Thomas, et al. 2000. "Preoperative chemo -radiation for carcinoma of the vulva with N2/N3 nodes: a gynecologic oncology group study." *Int J Radiat Oncol Biol Phys* **484**: 1007 -1013.

PURPOSE: To determine if patients with carcinoma of the vulva, with N2/N3 lymph nodes, could undergo resection of the lymph nodes and primary tumor following preoperative chemo-radiation. **METHODS AND MATERILAS:** Fifty-two patients were entered in the study, but six patients did not meet the criteria of the protocol and were excluded. The remaining 46 patients are the subject of this report. Patients underwent a split course of radiation, 4760 cGy to the primary and lymph nodes, with concurrent chemotherapy, cisplatin/5-FU, followed by surgery. **RESULTS:** Four patients did not complete the chemo-radiation, because three expired and one refused to complete the treatment. Four patients who completed chemo-radiation did not undergo surgery, because two of them died of non-cancer-related causes, and in the other two patients, the nodes remained unresectable. Following chemo-radiation, the disease in the lymph nodes became resectable in 38/40 patients. Two patients who completed the course of chemo-radiation did not undergo surgery as per protocol because of pulmonary metastasis. One underwent radical vulvectomy and unilateral node dissection and the other radical vulvectomy only. The specimen of the lymph nodes was histologically negative in 15/37 patients. Nineteen patients developed recurrent and/or metastatic disease. The sites of failure were as follows: primary area only, 9; lymph node area only, 1; primary area and distant metastasis, 1; distant metastasis only, 8. Local control of the disease in the lymph nodes was achieved in 36/37 and in the primary area in 29/38 of the patients. Twenty patients are alive and disease-free, and five have expired without evidence of recurrence or metastasis. Two patients died of treatment-related complications. **CONCLUSION:** High resectability and local control rates of the lymph nodes were obtained in patients with carcinoma of the vulva with N2/N3 nodes treated preoperatively with chemo-radiation.

Moore, D. H., S. Ali, et al. 2012. "A phase II trial of radiation therapy and weekly cisplatin chemotherapy for the treatment of locally-advanced squamous cell carcinoma of the vulva: a gynecologic oncology group study." *Gynecol Oncol* **1243**: 529 -533.

OBJECTIVES: To determine the efficacy and toxicity of radiation therapy and concurrent weekly cisplatin chemotherapy in achieving a complete clinical and pathologic response when used for the primary treatment of locally-advanced vulvar carcinoma. **METHODS:** Patients with locally-advanced T3 or T4 tumors not amenable to surgical resection via radical vulvectomy, previously untreated squamous cell carcinoma of the vulva were treated with radiation 1.8 Gy daily x 32 fractions=57.6 Gy plus weekly cisplatin 40 mg/m² followed by surgical resection of residual tumor or biopsy to confirm complete clinical response. Management of the groin lymph nodes was standardized and was not a statistical endpoint. Primary endpoints were complete clinical and pathologic response rates of the primary vulvar tumor. **RESULTS:** A planned interim analysis indicated sufficient activity to reopen the study to a second stage of accrual. Among 58 evaluable patients, there were 40 69% who completed study treatment. Reasons for prematurely discontinuing treatment included: patient refusal N=4, toxicity N=9, death N=2, other N=3. There were 37 patients with a complete clinical response 37/58; 64%. Among these women there were 34 who underwent surgical biopsy and 29 78% who

also had a complete pathological response. Common adverse effects included leukopenia, pain, radiation dermatitis, pain, or metabolic changes. **CONCLUSIONS:** This combination of radiation therapy plus weekly cisplatin successfully yielded high complete clinical and pathologic response rates with acceptable toxicity.

Moore, D. H., G. M. Thomas, et al. 1998. "Preoperative chemoradiation for advanced vulvar cancer: a phase II study of the Gynecologic Oncology Group." *Int J Radiat Oncol Biol Phys* **42**: 7 9-85.

PURPOSE: To determine the feasibility of using preoperative chemoradiotherapy to avert the need for more radical surgery for patients with T3 primary tumors, or the need for pelvic exenteration for patients with T4 primary tumors, not amenable to resection by standard radical vulvectomy. **METHODS AND MATERIALS:** Seventy-three evaluable patients with clinical Stage III-IV squamous cell vulvar carcinoma were enrolled in this prospective, multi-institutional trial. Treatment consisted of a planned split course of concurrent cisplatin/5-fluorouracil and radiation therapy followed by surgical excision of the residual primary tumor plus bilateral inguinal-femoral lymph node dissection. Radiation therapy was delivered to the primary tumor volume via anterior-posterior-posterior-anterior AP -PA fields in 170-cGy fractions to a dose of 4760 cGy. Patients with inoperable groin nodes received chemoradiation to the primary vulvar tumor, inguinal-femoral and lower pelvic lymph nodes. **RESULTS:** Seven patients did not undergo a post-treatment surgical procedure: deteriorating medical condition 2 patients; other medical condition 1 patient); unresectable residual tumor 2 patients; patient refusal 2 patients. Following chemoradiotherapy, 33/71 46.5% patients had no visible vulvar cancer at the time of planned surgery and 38/71 53.5% had gross residual cancer at the time of operation. Five of the latter 38 patients had positive resection margins and underwent: further radiation therapy to the vulva 3 patients; wide local excision and vaginectomy necessitating colostomy 1 patient); no further therapy 1 patient). Using this strategy of preoperative, split -course, twice-daily radiation combined with cisplatin plus 5-fluorouracil chemotherapy, only 2/71 2.8% had residual unresectable disease. In only three patients was it not possible to preserve urinary and/or gastrointestinal continence. Toxicity was acceptable, with acute cutaneous reactions to chemoradiotherapy and surgical wound complications being the most common adverse effects. **CONCLUSION:** Preoperative chemoradiotherapy in advanced squamous cell carcinoma of the vulva is feasible, and may reduce the need for more radical surgery including primary pelvic exenteration.

Moore, R. G., S. E. DePasquale, et al. 2003. "Sentinel node identification and the ability to detect metastatic tumor to inguinal lymph nodes in squamous cell cancer of the vulva." *Gynecol Oncol* **89**: 475 -479.

OBJECTIVES: The goal of this study was to identify one or more inguinal sentinel nodes in patients with primary squamous cell carcinoma of the vulva and to determine the ability of the sentinel node to predict metastasis to the inguinal lymphatic basin. **METHODS:** Techniques employing technetium-99m Tc -99m sulfur colloid and isosulfan blue dye were utilized to identify sentinel nodes in the inguinal lymphatic beds. Technetium-99m sulfur colloid was injected intradermally at the tumor margins 90-180 min preoperatively followed by a similar injection of isosulfan blue dye 5-10 min before the groin dissection. A handheld collimated gamma counter was employed to identify Tc-99m-labeled sentinel nodes. Lymphatic tracts that had taken up blue dye and their corresponding sentinel node were also identified and retrieved. A completion inguinal dissection was then performed. Each sentinel node was labeled as hot and blue, hot and nonblue, or cold and blue. The sentinel nodes were subjected to pathologic examination with step sections and nonsentinel nodes were evaluated in the standard fashion. **RESULTS:** Twenty-one patients with a median age of 79 were entered onto protocol and a total of 31 inguinal node dissections were performed. A sentinel node was identified in 31/31 100% groin dissections with the use of Tc-99m. Isosulfan blue dye identified a sentinel node in 19/31 61% groin dissections. Surgical staging revealed 7 patients with stage I disease, 5 with stage II disease, 5 with stage III disease, and 4 with stage IV disease. Lymph nodes in 9 groin dissections were found to have metastatic disease, and in 4 of these dissections, the sentinel node was the only positive node. Lymph nodes in 22 groin dissections had no evidence of metastasis. No false-negative sentinel lymph nodes were obtained sentinel node negative and a nonsentinel node positive. **CONCLUSION:** Tc -99m

sulfur colloid is superior to isosulfan blue dye in the detection of sentinel nodes in inguinal dissections of patients with vulvar cancer. A sentinel node dissection utilizing Tc-99m alone can identify a sentinel node in all inguinal dissections. Pathologic examination with step sections has shown the sentinel node to be an accurate predictor of metastatic disease to the inguinal nodal chain.

Moore, R. G., C. O. Granai, et al. 2003. "Pathologic evaluation of inguinal sentinel lymph nodes in vulvar cancer patients: a comparison of immunohistochemical staining versus ultrastaging with hematoxylin and eosin staining." *Gynecol Oncol* **91**: 378 -382.

OBJECTIVES: To evaluate the value of immunohistochemical IHC staining of inguinal sentinel lymph nodes (SLN) found to be negative for metastatic disease by ultrastaging with hematoxylin and eosin H&E staining. **METHODS:** An IRB approved study identified 29 patients who had undergone an inguinal sentinel lymph node dissection for squamous cell carcinoma of the vulva. All sentinel lymph nodes found to be negative for metastatic disease based on ultrastaging with H&E staining were reevaluated with pancytokeratin antibody AE1/AE3 immunohistochemical IHC staining to detect micrometastasis. **RESULTS:** Twenty-nine patients with squamous cell carcinoma of the vulva underwent an inguinal sentinel node dissection. Nineteen patients had inguinal dissections negative for metastatic disease, 2 patients had bilateral inguinal metastasis, and 8 patients had unilateral inguinal metastasis. A total of 42 groin dissections with SLN biopsies were performed; 12 groins were positive for metastatic disease and 30 were negative based on ultrastaging with eosin and hematoxylin staining. A total of 107 sentinel lymph nodes 2.5 SLN per groin were obtained, of which 18 SLN contained metastatic disease identified by ultrastaging and staining with H&E. Two SLN contained micrometastasis less than 0.3mm in size and 16 SLN contained metastasis greater than 2mm in size. Eighty-nine SLN found to be negative for metastasis by ultrastaging with H&E staining were also negative for micrometastasis on evaluation with pancytokeratin antibody AE1/AE3 IHC staining. **CONCLUSIONS:** The addition of immunohistochemical staining to ultrastaging with H&E staining in the pathologic evaluation of inguinal sentinel lymph nodes does not increase the detection of micrometastasis in patients with primary squamous cell carcinoma of the vulva.

Moore, R. G., K. Robison, et al. 2008. "Isolated sentinel lymph node dissection with conservative management in patients with squamous cell carcinoma of the vulva: a prospective trial." *Gynecol Oncol* **109**: 65 -70.

OBJECTIVES: Sentinel lymph node (SLN) dissections have a high sensitivity and negative predictive value for the detection of metastatic disease. The objective of this study was to examine the inguinal recurrence rate along with complication rates for patients undergoing inguinal SLN dissection alone for vulvar carcinoma. **METHODS:** An IRB approved prospective study enrolled patients with biopsy proven squamous cell carcinoma of the vulva. Peritumoral injection of Tc-99 sulfur colloid and methylene blue dye was used to identify SLNs intraoperatively. Patients with SLNs negative for metastatic disease were followed clinically. Patients with metastasis detected in a SLN subsequently underwent a full groin node dissection followed by standard treatment protocols. **RESULTS:** Thirty-six patients were enrolled onto study with 35 undergoing a SLN dissection. All SLN dissections were successful with a mean of 2 SLN obtained per groin. There were 24 patients with stage I disease, 8 stage II, 3 stage III and 1 stage IV. A total of 56 SLN dissections were performed with 4 patients found to have inguinal metastasis by SLN dissection. There were 31 patients with a total of 46 SLN dissections found to be negative for metastatic disease. The median follow-up has been 29 months range 8 to 51 with 2 groin recurrences for a groin recurrence rate of 4.3% and a recurrence rate per patient of 6.4%. There have been no reports of groin breakdown, extremity cellulitis or lymphedema. **CONCLUSIONS:** The recurrence rate for patients undergoing inguinal sentinel node dissection alone is low. These patients did not experience any complications as seen with complete groin node dissections. Sentinel lymph node dissection should be considered as an option for evaluation of inguinal nodes for metastatic disease.

Morotti, M., M. Valenzano Menada, et al. 2011. "Role of routine preoperative lymphoscintigraphy in sentinel node biopsy for vulvar cancer." *Int J Gynecol Cancer* **21**: S917.

Moskovic, E. C., J. H. Shepherd, et al. 1999. "The role of high resolution ultrasound with guided cytology of groin lymph nodes in the management of squamous cell carcinoma of the vulva: a pilot study." *Br J Obstet Gynaecol* **106**: 863 -867.

The accuracy of high resolution ultrasound with guided fine needle aspiration cytology in detecting inguinal lymph node involvement was assessed in 24 women undergoing radical vulvectomy and groin node dissection for squamous cell vulval cancer. Of the 43 groins dissected, ultrasound correctly diagnosed the lymph node status in 36, with five false positive and two false negative results. Cytology in 40 groins showed no false positive and five false negative results. The sensitivity and specificity for the combined techniques were 83% and 82% respectively. Assessed together, the combined technique failed to detect metastatic disease in two groins; in both cases the extent of nodal metastatic involvement was a solitary focus < 3 mm in diameter. The ultrasound and fine needle aspiration procedure is safe and well tolerated and can be repeated as needed for surveillance. The authors suggest that this procedure should be evaluated further to determine whether a policy of individual selection for lymphadenectomy can be implemented based on this technique.

Mulayim, N., D. Foster Silver, et al. 2004. "Chemoradiation with 5 -fluorouracil and mitomycin C in the treatment of vulvar squamous cell carcinoma." *Gynecol Oncol* **93**: 659 -666.

OBJECTIVE: To investigate the acute and late toxicities associated with the use of chemoradiation therapy CRT with 5 -fluorouracil 5 -FU) and mitomycin C or mitomycin C alone for primary, adjuvant, and salvage therapy for vulvar cancer. **METHODS:** Medical charts of 17 patients who received CRT with this regimen were reviewed. Toxicity was scored by 1998 standardized common toxicity criteria, Version 2.0, for acute toxicity and the RTOG/EORT Late Radiation Morbidity Scoring Schema for late toxicity. Median follow-up was 20 months range: 5 -74 months. **RESULTS:** Six patients had grade 4 neutropenia. In three patients, life-threatening neutropenic sepsis developed after the second cycle of chemotherapy. Severe enterocolitis was a direct cause of death in two patients. In four patients, the second cycle of chemotherapy was cancelled because of severe toxicity associated with the first cycle. One patient had grade 4 skin toxicity in the vulvar-perineal area. Six patients had grade 3 and seven patients had grade 2 acute skin toxicity. Skin toxicity necessitated the interruption of CRT in nine patients at a median dose of 32.4 Gy range: 16.2 -48 Gy. One patient developed bowel perforation and colovaginal fistula 1.5 years after completion of CRT. **CONCLUSION:** Chemoradiation therapy utilizing 5-FU and mitomycin C or mitomycin C alone in the treatment of vulvar cancer can be associated with a high incidence of morbidity and mortality. Strict attention to indications for treatment interruptions or chemotherapy dose adjustments is obligatory for safe delivery of CRT to these patients.

Muss, H. B., B. N. Bundy, et al. 1989. "Mitoxantrone in the treatment of advanced vulvar and vaginal carcinoma. A gynecologic oncology group study." *Am J Clin Oncol* **12**: 142 -144.

Nineteen evaluable patients with advanced carcinoma of the vulva or vagina were treated with mitoxantrone, 12 mg/m², every 3 weeks. All patients had good performance status and measurable disease and only nine had received prior chemotherapy. No complete or partial responses were noted. The major toxicity was myelosuppression; other toxicity was mild, and no cardiac toxicity or drug deaths occurred. The median progression-free interval was 1.3 months for patients with vulvar cancer and 1.6 months for patients with vaginal cancer. Median survival was 3.2 months for patients with vulvar cancer and 2.7 months for patients with vaginal cancer. Mitoxantrone displays no activity in patients with advanced carcinoma of the vulva or vagina.

NCCN 2016. "Vulvar Cancer Squamous Cell Carcinoma. Version 1." http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

NHS 2015. "Medical Protocol - Oncological Management of Vulvar Cancer " http://www.cmscnsenate.nhs.uk/index.php/download_file/view/415/1178/.

Novackova, M., M. J. Halaska, et al. 2015. "A prospective study in the evaluation of quality of life after vulvar cancer surgery." *Int J Gynecol Cancer* **25**: 166 -173.

OBJECTIVE: The aim of this study was to prospectively monitor the patients' quality of life QoL after vulvar cancer surgery. **DESIGN:** The design was prospective clinical study. **SETTING:** The study was set in the Department of Obstetrics and Gynecology, 2nd Medical Faculty of the Charles University and University Hospital Motol, Prague, Czech Republic. **METHODS:** A group of 36 patients underwent vulvar cancer surgery: 24 patients were subject to inguinofemoral lymphadenectomy (RAD) and 12 to sentinel lymph node biopsy. To evaluate QoL, the European Organisation for Research and Treatment of Cancer, QoL questionnaires QLQ -C30 and QLQ-CX24 were administered to patients before and 6 and 12 months after surgery. **RESULTS:** In patients with vulvar cancer after inguinofemoral lymphadenectomy, increased fatigue and impaired lymphedema were observed. In the group of patients after sentinel lymph node biopsy, none of the QoL variables worsened postoperatively. Comparing both groups 12 months after surgery, the RAD group had significantly worse outcomes in body image and cognitive functioning than the sentinel lymph node biopsy group. Patients in the RAD group, who received adjuvant radiotherapy $n = 13$, had worse QoL in symptom experience $P < 0.05$ at 6 and 12 months after the surgery than patients without radiotherapy $n = 11$. **CONCLUSIONS:** Less radical surgery showed objectively better QoL results.

Nyberg, R. H., M. Iivonen, et al. 2007. "Sentinel node and vulvar cancer: a series of 47 patients." *Acta Obstet Gynecol Scand* **86**: 615 -619.

BACKGROUND: There is growing interest to apply the sentinel node technique in the treatment of vulvar cancer. **METHODS:** All charts of the patients operated on for vulvar cancer at Tampere University Hospital from January 1, 2001 through June 30, 2005 were retrospectively reviewed. Demographic, clinical, and histopathological information was collected from each patient. The sentinel lymph node mapping was done intraoperatively either with a combination of the radioisotope and dye techniques 40 patients or with the dye technique alone 7 patients. The sentinel lymph node was dissected separately for histopathological evaluation, and then a routine inguinal lymphadenectomy was performed. **RESULTS:** The final FIGO surgical Stage distribution was: Stage I, 11 23%; Stage II, 14 30%; Stage III, 21 45%; and Stage IV, 1 2%. Sentinel lymph node was identified in 46 98% women with either one or both of the methods. In Stage I-II, the sentinel lymph node identification rate was 25/25 100% with the combined method. The only patient with unidentified sentinel lymph node had lymphatic spread beyond inguinal area or Stage IV disease. Eighteen of the sentinel lymph nodes 39% were positive for tumor cells, and in 5 cases additional metastatic nodes were found. One patient with macroscopically enlarged metastatic inguinal nodes and Stage III disease had a negative sentinel lymph node. In the 25 patients with Stage I-II disease, the false-negative rate of the sentinel lymph node method was 0/4, giving a negative predictive value of 1.00. **CONCLUSIONS:** A sentinel node identification rate of 98% with a false-negative rate of 0% in the patients with Stage I-II disease is an encouraging finding.

Oonk, M. H., B. M. van Hemel, et al. 2010. "Size of sentinel node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study." *Lancet Oncol* **11**: 646 -652.

BACKGROUND: Currently, all patients with vulvar cancer with a positive sentinel node undergo inguinofemoral lymphadenectomy, irrespective of the size of sentinel-node metastases. Our study aimed to assess the association between size of sentinel-node metastasis and risk of metastases in non-sentinel nodes, and risk of disease-specific survival in early stage vulvar cancer. **METHODS:** In the Groningen International Study on Sentinel nodes in Vulvar cancer GROINSS -V), sentinel-node detection was done in patients with T1-T2 <4 cm squamous cell vulvar cancer, followed by inguinofemoral lymphadenectomy if metastatic disease was identified in the sentinel node, either by routine examination or pathological ultrastaging. For the present study, sentinel nodes were independently reviewed by two pathologists. **FINDINGS:** Metastatic disease was identified in one or more sentinel

nodes in 135 33% of 403 patients, and 115 85% of these patients had inguino-femoral lymphadenectomy. The risk of non-sentinel-node metastases was higher when the sentinel node was found to be positive with routine pathology than with ultrastaging 23 of 85 groins vs three of 56 groins, $p=0.001$. For this study, 723 sentinel nodes in 260 patients (2.8 sentinel nodes per patient) were reviewed. The proportion of patients with non-sentinel-node metastases increased with size of sentinel-node metastasis: one of 24 patients with individual tumour cells had a non-sentinel-node metastasis; two of 19 with metastases 2 mm or smaller; two of 15 with metastases larger than 2 mm to 5 mm; and ten of 21 with metastases larger than 5 mm. Disease-specific survival for patients with sentinel-node metastases larger than 2 mm was lower than for those with sentinel-node metastases 2 mm or smaller 69.5% vs 94.4%, $p=0.001$. **INTERPRETATION:** Our data show that the risk of non-sentinel-node metastases increases with size of sentinel-node metastasis. No size cutoff seems to exist below which chances of non-sentinel-node metastases are close to zero. Therefore, all patients with sentinel-node metastases should have additional groin treatment. The prognosis for patients with sentinel-node metastasis larger than 2 mm is poor, and novel treatment regimens should be explored for these patients.

Oonk, M. H., M. A. van Os, et al. 2009. "A comparison of quality of life between vulvar cancer patients after sentinel lymph node procedure only and inguino-femoral lymphadenectomy." *Gynecol Oncol* 113: 301 -305.

OBJECTIVES: The SLN-procedure has been introduced in vulvar cancer treatment to reduce morbidity and thereby improve quality of life. Aim of this study was to compare quality of life in vulvar cancer patients who were treated with a SLN-procedure only to those who underwent inguino-femoral lymphadenectomy. Moreover, it was evaluated what patients would advise relatives on the application of the SLN-procedure in light of possible false negative results. **METHODS:** Patients who participated in the Groningen International Study on Sentinel nodes in Vulvar cancer (GROINSS -V) were invited to fill out three questionnaires: the EORTC QLQ-C30, a vulvar specific questionnaire and a questionnaire about the opinion of patients on new treatment options. Patients who only underwent SLN-procedure were compared to those who subsequently underwent inguino-femoral lymphadenectomy because of a positive SLN. **RESULTS:** With a response rate of 85%, 35 patients after the SLN-procedure and 27 patients after inguino-femoral lymphadenectomy filled out the questionnaires. No difference in overall quality of life was observed between the two groups. The major difference was the increase in complaints of lymphedema of the legs after inguino-femoral lymphadenectomy. The majority of patients would advise the SLN-procedure to relatives. Patients after inguino-femoral lymphadenectomy were more reserved concerning the acceptable false negative rate of a new diagnostic procedure. **CONCLUSIONS:** Patients who underwent the SLN-procedure report less treatment related morbidity compared to those who underwent inguino-femoral lymphadenectomy. However, this did not influence overall quality of life. Furthermore, patients who underwent inguino-femoral lymphadenectomy are more reserved in advising the SLN-procedure to relatives.

Paley, P. J., P. R. Johnson, et al. 1997. "The effect of sartorius transposition on wound morbidity following inguinal-femoral lymphadenectomy." *Gynecol Oncol* 64: 237 -241.

In spite of efforts to reduce complications associated with inguinal-femoral lymphadenectomy (IFL), morbidity continues to be substantial. We sought to assess the efficacy of sartorius transposition (ST) in reducing groin wound complications following IFL, in patients with vulvar malignancy. The records of 101 patients with vulvar cancer undergoing IFL through separate incisions between March 1975 and December 1994 were examined. Sixty-two patients undergoing ST group 1 were compared to 38 who did not group 2. The groups were similar with respect to age, weight, tobacco/alcohol use, prior abdominal/vulvar surgery, prevalence of diabetes, hypertension, or peripheral vascular disease, and previous exposure to irradiation or chemotherapy. Additionally, there was no significant difference with respect to extent of disease, incidence of macro-/microscopic groin metastases, use of groin drains, and use of perioperative antibiotics or deep venous thrombosis prophylaxis. Groin wound complications were less frequent in patients undergoing ST group 1. The incidence of groin cellulitis was 30% in group 1 compared with an incidence of 58% in group 2 $P = 0.011$. Significant groin wound morbidity,

defined as either wound breakdown or cellulitis, was seen less frequently in group 1 41% vs 66%; $P = 0.029$. Employing a multivariate analysis, only patient weight < 150 lbs and performance of ST were established as independently associated with a reduction in groin morbidity following IFL $P = 0.0281$ and $P = 0.0075$, respectively. In conclusion, despite waning enthusiasm for its performance, ST appeared to significantly reduce the incidence of wound morbidity after IFL. Our data confirmed that separate incisions, and improved perioperative antibiotics, have not eliminated the value inherent in this surgical modification. We suggest a prospective trial to further establish the benefit of sartorius transposition during IFL.

Pao, W. M., C. A. Perez, et al. 1988. "Radiation therapy and conservation surgery for primary and recurrent carcinoma of the vulva: report of 40 patients and a review of the literature." *Int J Radiat Oncol Biol Phys* **14**: 1123-1132.

Forty patients with histologically confirmed primary or recurrent vulvar carcinoma were treated with radiation therapy for loco-regional disease. Nineteen of the patients with primary tumors received postoperative radiotherapy 5000 cGy in 6 weeks. Fifteen of the 19 exhibited local tumor control. Five patients with Stage III or IV disease were managed with radiotherapy alone. Four had a complete response with two currently NED. Two patients who received preoperative radiotherapy with local excision are also currently free of disease. The 4-year NED survival for the study population is 100%, 28%, 50%, 0% and 10% for Stage I, II, III, IV and recurrent tumors respectively. The poor results obtained in Stage II tumors is likely due to selection criteria since four of seven patients developed distant metastases. Two of the 14 patients treated for recurrent disease remain NED after local excision of their tumors prior to irradiation. Even though the number of patients is small no dose response for subclinical disease could be found between 4500 and 7000 cGy. Treatment morbidity was acceptable with two patients developing severe long-term complications requiring surgical intervention.

Parthasarathy, A., M. K. Cheung, et al. 2006. "The benefit of adjuvant radiation therapy in single node-positive squamous cell vulvar carcinoma." *Gynecol Oncol* **103**: 1095 -1099.

OBJECTIVE: To determine if adjuvant radiotherapy improves the survival of women with invasive squamous cell carcinoma of the vulva involving one inguinal node. **METHODS:** Demographic, pathologic, and treatment information was obtained on patients with vulvar cancers from the Surveillance, Epidemiology, and End Results database between 1988 and 2001. Kaplan-Meier estimates and Cox-proportional hazards model were used for analyses. **RESULTS:** Of the 490 patients with stage III, node-positive vulvar cancers, 208 had a single positive inguinal node. The median age of this group was 71 years range: 29 -100. 82.2% of patients were White, 7.2% were Hispanic, 7.7% were Black, 1.4% were Asian, and 1.4% were Others. 91.8% of patients underwent a radical vulvectomy with a unilateral or bilateral inguinal lymphadenectomy. The median number of lymph nodes resected was 13 range: 1 -34. 102 women underwent adjuvant radiotherapy, while 106 did not receive any radiation treatment. Women who received adjuvant radiotherapy had a 5-year disease-specific survival of 77.0% compared to 61.2% in those without radiotherapy $p=0.02$. After stratifying the study group based on the extent of lymphadenectomy, we found that radiation treatment improved the survival of those with ≤ 12 lymph nodes removed 76.6% versus 55.1%, $p=0.035$. In those with more than 12 nodes resected, radiotherapy increased the survival from 66.7% to 77.3%, though this difference was not statistically significant $p=0.23$. In multivariate analysis, younger age $p=0.01$ remained as a significant prognostic factor for improved survival; however, adjuvant radiotherapy had a borderline significance $p=0.06$. **CONCLUSION:** Our data suggest that adjuvant radiotherapy may improve the disease-specific survival of patients with single-node-positive vulvar cancer who underwent a less extensive lymph node resection ≤ 12 nodes removed.

Pecorelli, S. 2009. "Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium." *Int J Gynaecol Obstet* **105**: 103 -104.

Perez, C. A., P. W. Grigsby, et al. 1998. "Irradiation in carcinoma of the vulva: factors affecting outcome." *Int J Radiat Oncol Biol Phys* **422**: 335 -344.

PURPOSE: This report reviews the increasing role of radiation therapy in the management of patients with histologically confirmed vulvar carcinoma, based on a retrospective analysis of 68 patients with primary disease 2 in situ and 66 invasive and 18 patients with recurrent tumor treated with irradiation alone or combined with surgery. **METHODS AND MATERIALS:** Of the patients with primary tumors, 14 were treated with wide local excision plus irradiation, 19 received irradiation alone after biopsy, 24 were treated with radical vulvectomy followed by irradiation to the operative fields and inguinal-femoral/pelvic lymph nodes, and 11 received postoperative irradiation after partial or simple vulvectomy. The 18 patients with recurrent tumors were treated with irradiation alone. Indications and techniques of irradiation are discussed in detail. **RESULTS:** In patients treated with biopsy/local excision and irradiation, local tumor control was 92% to 100% in Stages T1-3N0, 40% in similar stages with N1-3, and 27% in recurrent tumors. In patients treated with partial/radical vulvectomy and irradiation, primary tumor control was 90% in patients with T1-3 tumors and any nodal stage, 33% in patients with any T stage and N3 lymph nodes, and 66% with recurrent tumors. The actuarial 5-year disease-free survival rates were 87% for T1N0, 62% for T2-3N0, 30% for T1-3N1 disease, and 11 % for patients with recurrent tumors; there were no long-term survivors with T4 or N2-3 tumors. Four of 18 patients 22% treated for postvulvectomy recurrent disease remain disease -free after local tumor excision and irradiation. In patients with T1-2 tumors treated with biopsy/wide tumor excision and irradiation with doses under 50 Gy, local tumor control was 75% 3 of 4, in contrast to 100% 13 of 13 with 50.1 to 65 Gy. In patients with T3 -4 tumors treated with local wide excision and irradiation, tumor control was 0% with doses below 50 Gy 3 patients and 63% 7 of 11 with 50.1 to 65 Gy. In patients with T1-2 tumors treated with partial/radical vulvectomy and irradiation, local tumor control was 83% 14 of 17, regardless of dose level, and in T3 -4 tumors, it was 62% 5 of 8 with 50 to 60 Gy and 80% 8 of 10 with doses higher than 60 Gy. The differences are not statistically significant. There was no significant dose response for tumor control in the inguinal-femoral lymph nodes; doses of 50 Gy were adequate for elective treatment of nonpalpable lymph nodes, and 60 to 70 Gy controlled tumor growth in 75% to 80% of patients with N2-3 nodes when administered postoperatively after partial or radical lymph node dissection. Significant treatment morbidity included one rectovaginal fistula, one case of proctitis, one rectal stricture, four bone/skin necroses, four vaginal necroses, and one groin abscess. **CONCLUSIONS:** Irradiation is playing a greater role in the management of patients with carcinoma of the vulva; combined with wide local tumor excision or used alone in T1-2 tumors, it is an alternative treatment to radical vulvectomy, with significantly less morbidity. Postradical vulvectomy irradiation in locally advanced tumors improves tumor control at the primary site and the regional lymphatics in comparison with reports of surgery alone.

Petru, E., H. J. Luck, et al. 2009. "Gynecologic Cancer Intergroup GCIG) proposals for changes of the current FIGO staging system." *Eur J Obstet Gynecol Reprod Biol* **143** 2: 69 -74.

The FIGO has invited the GCIG to make contributions for possible changes of the FIGO staging system. We report on the consensus within the GCIG committee to propose the following changes in the current FIGO classification. Cervical cancer: Since fertility-preserving surgery is increasingly used in early disease, stage IB1-A may include tumors of up to 2 cm in diameter. Endometrial cancer: Positive peritoneal cytology alone should not classify this patient to be allotted to stage IIIA disease. Lymphadenectomy should be recommended in high-risk clinical stage I patients and in those with adverse histologies. Ovarian cancer: In early stage disease, grading and in advanced disease, the amount of residual disease should be reported. Vulvar cancer: The lymph node status should always be reported. In the case of enlarged inguinal nodes, histology should be obtained by any means. Vaginal cancer: Besides bladder and rectal tumor involvement urethral mucosal involvement should be added. Gestational trophoblastic disease: The modified WHO scoring system which is widely accepted should be adopted.

Pitynski, K., A. Basta, et al. 2003. "[Lymph node mapping and sentinel node detection in carcinoma of the cervix, endometrium and vulva]." *Ginekol Pol* **749**: 830 -835.

OBJECTIVES: Validity of the sentinel node concept in patients with cervical, endometrial and vulvar cancer. **MATERIAL AND METHODS:** 47 cases of FIGO stage I and II cervical cancer, 33 cases of first clinical stage of endometrial cancer and 37 patients with FIGO stage I and II of vulvar cancer. In cervical and vulvar cancer preoperative lymphoscintygraphy and intraoperative lymphatic mapping with blue dye and handheld gamma probe were performed. In patients with endometrial cancer intraoperative lymphatic mapping with blue dye injected into the cervix and into the uterine corpus subserously were done. In the last 10 cases radiolabeled nannocolloid were administered and the patients underwent preoperative lymphoscintygraphy and intraoperative radio detection of sentinel node. Sentinel nodes were labeled as blue, radioactive, or blue/radioactive. **RESULTS:** In cervical cancer sensitivity of the dye and radiocolloid methods was 94%, specificity 100% and negative predictive value 97%. Out of 33 cases of endometrial cancer sentinel node was identified in 29 87.87% patients. None of women with histological negative sentinel node had metastases in the rest of lymph nodes resected. Sentinel node was detected in all cases of vulvar cancer. The status of sentinel nodes were representative for all lymph node resected. **CONCLUSIONS:** Concept of sentinel node may be applied first of all for vulvar cancer and also for cervical and endometrial cancer.

Piura, B., A. Rabinovich, et al. 1998. "Squamous cell carcinoma of the vulva in the south of Israel: a study of 50 cases." *J Surg Oncol* **673**: 174 -181.

BACKGROUND AND OBJECTIVES: Vulvar carcinoma accounts for 4.9% of all female genital tract malignancies in the south of Israel. The most common histologic type is squamous cell carcinoma 82%. The purpose of this study was to investigate the clinical findings, treatment, and outcome of patients with vulvar squamous cell carcinoma in the south of Israel. **METHODS:** Data from the files of 50 patients with vulvar squamous cell carcinoma who were managed at the Soroka Medical Center between January 1961 and December 1996 were evaluated. **RESULTS:** Mean age at diagnosis was 67.1 years. The most prevailing presenting symptoms were vulvar lump, ulcer, and itching. Mean patient delay in seeking medical help was 48.2 months. Clinical palpation as a test for detecting groin lymph node metastases had a sensitivity and specificity of 57.1% and 61.5%, respectively. The 5-year survival rate was 60.3% overall. By means of univariate analysis, a significant worsening in survival was demonstrated with advancing stage of disease $P < 0.001$, tumor >4 cm $P < 0.001$, and positivity of surgical margins $P < 0.0001$. In a multivariate analysis Cox proportional hazards model) in a group of 45 patients, stage of disease was the strongest and the only significant predictor of survival $P = 0.0098$. **CONCLUSIONS:** Vulvar squamous cell carcinoma predominantly affects older women. Stage of disease, tumor size, and status of surgical margins are sensitive predictors of survival. The treatment of choice for most patients is surgery consisting of radical vulvectomy and bilateral groin lymphadenectomy.

Podratz, K. C., R. E. Symmonds, et al. 1983. "Carcinoma of the vulva: analysis of treatment and survival." *Obstet Gynecol* **611**: 63 -74.

The treatment of 224 patients with invasive squamous cell carcinoma of the vulva over a 20-year interval at the Mayo Clinic resulted in an overall survival rate of 75%, compared with 89% for age-matched controls. For patients with stage I disease, 5-year survival was 90%; for those with stages II, III, and IV, it was 81, 68, and 20%, respectively. A precipitous decline in survival rates was noted when metastases to regional nodes were encountered, when lesion size was more than 3 cm, and when histologic dedifferentiation exceeded grade 2. Incorrect clinical staging efforts were observed in 25% of the cases, so the necessity for surgical staging was apparent.

Puig-Tintore, L. M., J. Ordi, et al. 2003. "Further data on the usefulness of sentinel lymph node identification and ultrastaging in vulvar squamous cell carcinoma." *Gynecol Oncol* **881**: 29 -34.

OBJECTIVE: The aim was to determine the feasibility of surgical identification and pathological ultrastaging of sentinel nodes SNs in vulvar carcinoma and to evaluate whether SN negativity rules out the possibility of metastasis in other nodes and can therefore avoid conventional lymphadenectomy. **MATERIAL AND METHODS:** In 26 patients with vulvar squamous cell carcinoma the SNs were detected using both peritumoral injection of 99mTc and blue dye isosulfan or methylene before the surgical procedure. Dissection of the SNs was followed by standard lymphadenectomy and vulvar exeresis. For pathological ultrastaging at least eight histological sections of every node separated 400 microm were evaluated using hematoxylin & eosin and immunostaining against cytokeratin. **RESULTS:** We identified the SNs in 25/26 patients 96%. In 19 patients 76% the SN was unilateral and in 6 24% it was bilateral. A total of 46 SNs were isolated. Metastatic carcinoma was identified in 9 SNs from 8 patients 30.8%. Thirty -eight percent 3 of 8 patients with metastatic SNs presented micrometastasis detected only in ultrastaging. Seven 3.3% of 239 nonsentinel nodes non -SNs showed metastasis. No metastatic implant was detected in non-SNs when SNs were negative in patients without clinical suspicious adenopathy 100% negative predictive value. **CONCLUSION:** Inguinofemoral lymph nodes can be confidently avoided when sentinel node metastases are excluded by histological ultrastaging. This may reduce the surgical morbidity of conventional inguinofemoral lymphadenectomy, without worsening vulvar cancer prognosis.

Radziszewski, J., M. Bidzinski, et al. 2003. "Sentinel lymph node in vulvar cancer-a pilot study to identify and assess the diagnostic value." *NOWOTWORY* **53**: 268-274.

Radziszewski, J., M. Kowalewska, et al. 2010. "The accuracy of the sentinel lymph node concept in early stage squamous cell vulvar carcinoma." *Gynecol Oncol* **116**: 473 -477.

OBJECTIVE: The purpose of the study was to determine the feasibility and accuracy of the sentinel lymph node (SLN) identification in vulvar carcinoma patients. **METHODS:** Sixty -two patients with clinical early stage vulvar cancer underwent SLN detection procedure, followed by a complete inguinofemoral lymphadenectomy. The SLN was identified intraoperatively using lymphoscintigraphy with technetium-99m as well as patent blue V staining. The resected lymph nodes (LN) were submitted for histological examination by hematoxylin-eosin staining (H-E) and cytokeratin immunohistochemistry (IHC) and examined by the reverse transcriptase -polymerase chain reaction (RT -PCR) assay. **RESULTS:** A total of 109 inguinal LN were dissected in 56 patients. SLNs were identified in 76% groins with patent blue V and in 99% with the use of Tc-99m. The accuracy differed significantly $p < 0.0001$. An H-E examination combined with IHC revealed 7 false-negative SLNs. The sensitivity of this method was 73% 95% CI, 64% to 81% and the negative predictive value for a negative SLN finding was 92% 95% CI, 87% to 97%. The RT -PCR assay showed 8 false-negative SLNs. The sensitivity of the RT-PCR-based assay was 83% 95% CI, 75% to 90% and the negative predictive value for a negative SLN was 88% 95% CI, 82% to 94%. The two diagnostic methods were found not to differ significantly. **CONCLUSIONS:** In SLN mapping, the Tc-99m colloid lymphoscintigraphy is superior to the blue dye staining. Our data do not support the concept of the SLN identification as a highly accurate procedure in predicting the inguinofemoral LN status in patients with early stage vulvar cancer.

RCOG 2014. "Guidelines for the Diagnosis and Management of Vulval Carcinoma." <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/vulval-carcinoma-guidelines-for-the-diagnosis-and-management-of/>.

Reade, C. J., W. Jimenez, et al. 2012. "Sentinel lymph node biopsy in vulvar cancer: a health technology assessment for the canadian health care context." *J Obstet Gynaecol Can* **34**: 1053 -1065.

OBJECTIVES: Inguinofemoral lymphadenectomy for vulvar cancer is associated with a high incidence of groin wound complications and lymphedema. Sentinel lymph node biopsy (SLNB) is a morbidity -reducing alternative to lymphadenectomy. The objective of this health technology assessment was to determine the clinical effectiveness, cost-effectiveness, and organizational feasibility of SLNB in the

Canadian health care system. **METHODS:** A review of the English-language literature published from January 1992 to October 2011 was performed across five databases and six grey-literature sources. Predetermined eligibility criteria were used to select studies, and results in the clinical, economic, and organizational domains were summarized. Included studies were evaluated for methodologic quality using the Newcastle-Ottawa Scale. **RESULTS:** Of 825 reports identified, 88 observational studies met the eligibility criteria. Overall study quality was poor, with a median Newcastle-Ottawa Scale score of 2 out of 9 stars. Across all studies, the detection rate of the sentinel lymph node was 82.2% per groin and the false-negative rate was 6.3%. The groin recurrence rate after negative SLNB was 3.6% compared with 4.3% after negative lymphadenectomy, and complications were reduced after SLNB. No economic evaluations were identified comparing SLNB to lymphadenectomy. Safe implementation of SLNB requires appropriate patient selection, detection technique, and attention to the learning curve. **CONCLUSIONS:** Although study quality is poor, the available data suggest implementation of SLNB may be safe and feasible in Canadian centres with adequate procedural volumes, assuming that implementation includes careful patient selection, careful technique, and ongoing quality assessment. Cost-effectiveness has yet to be determined.

Rob, L., H. Robova, et al. 2006. "[Sentinel lymph nodes identification in vulvar cancer --methods and technique]." *Ceska Gynekol* **714**: 298 -301.

OBJECTIVE: To evaluate detection of sentinel lymph nodes (SLN) in squamous vulvar cancer with blue dye and ^{99m}Tc. The study describes technique of application, timing, management, detection rate DR, specific side detection rate SSDR and false negative rate. **DESIGN:** Prospective clinical study. **SETTING:** Department of Obstetrics and Gynecology, Charles University Prague, 2nd Medical Faculty, Teaching Hospital Motol. **PATIENTS AND METHODS:** 46 women with squamous cell carcinoma tumors stage I or II, <4 cm with no clinical suspect lymph nodes were included. Blue dye alone was used in 16 women and the combination of ^{99m}Tc and blue dye was used in 30 women. Radiocolloid ^{99m}Tc was applied 3-5 hours and blue dye 3-5 minutes prior to inguinal incision. **RESULTS:** We detected 88 SLN in 61 inguinal spaces. The detection rate in the blue dye group was 68.8 % 11 cases. One false negative SLN 6.3 % appeared in this group. In blue dye+ ^{99m}Tc group detection rate was 100 % with no false negative SLN. **CONCLUSION:** Detection of SLN in squamous vulvar cancer with the combination of ^{99m}Tc and blue dye was statistically significantly more effective than using the blue dye alone.

Rob, L., H. Robova, et al. 2007. "Further data on sentinel lymph node mapping in vulvar cancer by blue dye and radiocolloid Tc99." *Int J Gynecol Cancer* **171**: 147 -153.

We studied the distribution of sentinel lymph nodes (SLNs) in vulvar cancer using blue dye and ^{99m}Tc radiocolloid and evaluated the techniques used, including the optimum timing of preoperative scintigraphy scans and its contribution to ^{99m}Tc SLN detection over that of the intraoperative handheld gamma probe. Fifty-nine women with squamous cell cancers <4 cm treated at our institution between December 2001 and December 2005 were included in this study. Blue dye alone was used in the first 16 women group A and the combination of ^{99m}Tc and blue dye was used on 43 women group B. Of the 118 SLN detected in 82 groins, 83.9% 99 were sited in the superficial medial and intermediate inguinal chain, none were in superficial lateral groin, 16.1% 19 were deep femoral. The patient-specific SLN detection and false-negative rate in group B was 100% and 0%, compared to 68.8% 11/16 cases and 6.3% 1/16 in group A. The optimum timing for preoperative lymphoscintigraphy scans was 45 min postinjection, but intraoperative use of the handheld gamma probe yielded 15% more "hot" nodes and allowed tailored placement of the lymphadenectomy incision. Eighty-four percent of SLNs were in the medial and intermediate region of the superficial inguinal chain, 16.1% were deep femoral. The combined use of ^{99m}Tc radiocolloid and blue dye was significantly superior at SLN detection than blue dye alone. ^{99m}Tc SLN detection using the intraoperative handheld probes was not enhanced by preoperative scintigraphy scans.

Rodier, J. F., J. C. Janser, et al. 1999. "Sentinel node biopsy in vulvar malignancies: a preliminary feasibility study." *Oncol Rep* **66**: 1249 -1252.

Sentinel lymph node biopsies SLNB were investigated in 8 cases 6 squamous cell carcinomas, 2 melanomas of vulvar malignancy. The sentinel node was detected by patent blue dye injection 1 case, pre operative lymphoscintigraphy with intra-operative gamma hand-held probe 2 cases, and combined techniques 5 cases. The procedure was successful in all cases but one 1 invasive squamous cell carcinoma in which there was medial groin recurrence at 6 months. Nodal invasion was observed in only one case and was confined to the sentinel node. No specific morbidity related to the SLNB procedure occurred. SLNB appears to be a feasible and promising technique, however, requiring further evaluation before being considered as a reliable method to spare inguinofemoral lymphadenectomy in early-stage patients free of sentinel node metastasis, or to be substituted in screening elderly clinically node-negative females.

Rodolakis, A., E. Diakomanolis, et al. 2000. "Squamous vulvar cancer: a clinically based individualization of treatment." *Gynecol Oncol* **783 Pt 1**: 346 -351.

OBJECTIVE: The aim of the study was to evaluate treatment results in 211 patients with previously untreated squamous cell vulvar cancer who were primary managed by surgery at the Gynecologic Oncology Unit of Alexandra Hospital, in terms of en bloc radical vulvectomy N = 105 , modified radical vulvectomy with three different incisions technique N = 60, and radical hemivulvectomy N = 46 with inguinofemoral lymphadenectomy. **METHODS:** The surgical stage of disease, nodal status, lesion location and focality, marginal status, tumor size, physical and performance status, surgical modality used, and finally complications and recurrence rates were the analyzed factors for both survival and disease remission. **RESULTS:** The overall 5-year survival was 70.1%. The 5-year survival for node-positive patients was 53.8% versus 79.7% for node-negative patients. Unifocal lesions had a 5-year survival of 76% compared with 50% of multifocal lesions. Posterolateral lesions had a better 5-year survival than that of anterior central lesions 79.5% vs 54.4%. The marginal status of the surgical specimen was a significant predictor of both survival and recurrence. There was a significant difference in complications related to the en bloc radical vulvectomy in terms of wound breakdown, infection, and wound cellulitis. **CONCLUSIONS:** Modified radical procedures are equally effective with the en bloc radical vulvectomy for the management of early stage I/II vulvar cancer. In advanced disease conservative surgery in an individualized approach could also effectively be applied.

Ross, M. J. and R. L. Ehrmann 1987. "Histologic prognosticators in stage I squamous cell carcinoma of the vulva." *Obstet Gynecol* **705**: 774 -784.

Sixty-four cases of stage I vulvar squamous cell carcinoma were analyzed histologically to define a patient subset at minimum risk for recurrence or nodal metastases. Three patterns of invasion were predefined: carcinoma in situ with early stromal invasion 33%, pushing 8%, and infiltrative 59%. Infiltrative pattern and invasion deeper than 1.5 mm equally predicted nodal metastases P = .045, although depth measurement in biopsy specimens was subject to sampling error. Confluence and absence of carcinoma in situ each predicted extranodal recurrence P = .011. Local recurrence appeared more related to inadequate surgical margins than failure to perform radical vulvectomy. Carcinoma in situ with early stromal invasion represents a group at zero risk for nodal metastases. We recommend wide local excision for all stage I lesions. In general, omission of lymphadenectomy should be reserved for cases of carcinoma in situ with early stromal invasion.

Rotmensch, J., S. J. Rubin, et al. 1990. "Preoperative radiotherapy followed by radical vulvectomy with inguinal lymphadenectomy for advanced vulvar carcinomas." *Gynecol Oncol* **362**: 181 -184.

A therapeutic alternative to exenteration for large locally advanced vulvar carcinoma involving the rectum, anus, or vagina is the use of preoperative radiation followed by radical surgery. Between 1980 and 1988, 13 patients with Stage III and 3 with Stage IV vulvar carcinoma involving the rectum/anus,

urethra, or vagina were treated with 4000 rad to the vulva and 4500 rad to the inguinal and pelvic nodes followed by a radical vulvectomy and inguinal lymphadenectomy 4 weeks later. The overall 5 year cumulative survival was 45%. Twelve tumors regressed after radiation with 62.5% of the patients having visceral preservation while in 4 patients there was no major response to radiation and urinary or fecal diversion was required. Of the 6 recurrences 4 were central and 2 distant. Three patients with central recurrences had tumor within 1 cm of the vulvectomy margin. Complications included wet desquamation, inguinal wound separation, lymphedema, and urethral strictures. There were no operative deaths. It is concluded that the use of preoperative radiation followed by radical vulvectomy may be an alternative to pelvic exenteration in selected patients with advanced vulvar lesions.

Rouzier, R., B. Haddad, et al. 2003. "Inguinofemoral dissection for carcinoma of the vulva: effect of modifications of extent and technique on morbidity and survival." *J Am Coll Surg* **196**: 442 -450.

BACKGROUND: The aim of this study was to evaluate the impact of modifications of extent medial inguinal and medial femoral lymphadenectomy, inguinal lymphadenectomy, inguinal and medial femoral lymphadenectomy, and inguinofemoral lymphadenectomy and surgical technique of lymphadenectomy including sartorius transposition, preservation of the fascia lata, and preservation of the saphenous vein on morbidity, groin recurrence, and survival in patients with vulvar carcinoma. **STUDY DESIGN:** A retrospective review of 194 patients with primary squamous cell cancer of the vulva was conducted. Clinical, surgical, histopathologic, postoperative short- and longterm complications, and followup data were collected from patient records. **RESULTS:** Inguinal lymphadenectomy and medial inguinal and medial femoral lymphadenectomy produced about half fewer nodes than did other surgical procedures. On the other hand, number of lymph nodes removed did not differ notably between inguinofemoral lymphadenectomy and inguinal and medial femoral lymphadenectomy. Logistic regression showed that obesity was associated with increased risk of cellulitis. Age greater than 70, obesity, and extent of lymphadenectomy increased wound breakdown risk. Factors associated with leg edema persisting for more than 6 months were: extent of lymphadenectomy, sartorius transposition, and adjuvant irradiation of groin area. With a mean followup time of 38 months, neither groin recurrence rate nor disease-specific survival markedly differed according to technique of lymphadenectomy. **CONCLUSION:** Techniques of lymphadenectomy with preservation of fascia lata and saphenous vein are associated with a decreased risk of postoperative morbidity without jeopardizing outcomes.

Russell, A. H., J. B. Mesic, et al. 1992. "Synchronous radiation and cytotoxic chemotherapy for locally advanced or recurrent squamous cancer of the vulva." *Gynecol Oncol* **47**: 14 -20.

Between July 1987 and September 1991 a program of external beam radiation and synchronous, radiopotentiating chemotherapy was employed to treat 25 women with locoregionally advanced or locoregionally recurrent squamous cancer of the vulva. Of 18 previously untreated patients, 1 was Stage II, 10 were Stage III, 6 were Stage IVA, and 1 was Stage IVB. Reasons for patient referral for nonsurgical management included the presence of initially unresectable disease 5 patients, disease extent which would have necessitated partial or total exenteration if treated surgically 9 patients, disease extent predictive of inadequate surgical margins less than 1 cm gross margin if treated by less than exenterative surgery 8 patients, and severe comorbid illness precluding surgical management 3 patients. Complete clinical response was obtained in 16 of 18 previously untreated patients 89% and in 4 of 7 patients with recurrent disease following vulvar surgery 57%. Of 20 patients achieving a complete clinical response, 3 patients have relapsed within the irradiated volume at 11, 38, and 48 months following completion of treatment. Fourteen patients remain alive and continuously cancer free from 2-52 months after completion of treatment median follow-up 24 months. This experience suggests that initial management with radiation and chemotherapy may offer some patients with locally advanced squamous cancer of the vulva an alternative to exenterative surgery and may hold curative potential for some patients with surgically unresectable or medically inoperable disease.

Rutledge, F. N., M. F. Mitchell, et al. 1991. "Prognostic indicators for invasive carcinoma of the vulva." *Gynecol Oncol* **42**: 239 -244.

Three hundred sixty-five patients with invasive squamous cell carcinoma of the vulva have been treated at M.D. Anderson Cancer Center between 1944 and 1990. We undertook a rigorous review of the medical records, and a Cox proportional hazards model was applied to examine predictors of both failure to survive and recurrence. Significant predictors of both failure to survive and recurrence included tumor size, clinical stage, therapy aim, pelvic or inguinal nodal metastases, and positive margins. We then undertook an analysis of Stage I and II lesions treated with a curative aim to see if there was a difference in survival or in disease-free interval between those patients treated with radical vulvectomy and those treated with radical wide local excision. There was no survival advantage from the radical vulvectomy procedure. We conclude that careful selection may allow us to choose some patients for less radical procedures.

Salani, R., F. J. Backes, et al. 2011. "Posttreatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations." *Am J Obstet Gynecol* **204**: 466 -478.

Although gynecologic cancers account for only 10% of all new cancer cases in women, these cancers account for 20% of all female cancer survivors. Improvements in cancer care have resulted in almost 10 million cancer survivors, and this number is expected to grow. Therefore, determining the most cost-effective clinical surveillance for detection of recurrence is critical. Unfortunately, there has been a paucity of research in what are the most cost-effective strategies for surveillance once patients have achieved a complete response. Currently, most recommendations are based on retrospective studies and expert opinion. Taking a thorough history, performing a thorough examination, and educating cancer survivors about concerning symptoms is the most effective method for the detection of most gynecologic cancer recurrences. There is very little evidence that routine cytologic procedures or imaging improves the ability to detect gynecologic cancer recurrence at a stage that will impact cure or response rates to salvage therapy. This article will review the most recent data on surveillance for gynecologic cancer recurrence in women who have had a complete response to primary cancer therapy.

Santos, J. T., R. L. Coleman, et al. 1998. "Pathology slide review in gynecologic oncology." *Obstet Gynecol* **91** Pt 1: 730 -734.

OBJECTIVE: To analyze the diagnostic accuracy and alteration in treatment planning from interinstitution different institution pathologic consultation. **METHODS:** We reviewed pathologic reports from 720 referred patients. The diagnosis rendered from a gynecologic pathologist was compared with the original diagnosis. Discrepancies were coded as none, minor, or major. A discrepancy was major if it led to treatment alteration. A discrepancy was minor if it did not lead to treatment alteration. The judgment to declare a discrepancy was made by a gynecologic pathologist, a gynecologist, and three gynecologic oncologists. The review cost was \$150 per case. The Cochran-Mantel-Haenszel test evaluated any systematic pattern in discrepancies. **RESULTS:** Seven hundred twenty specimens consisted of 113 vulvar, 170 uterine, 289 cervical, 105 ovarian, and 43 vaginal tissues. Six hundred one 84% pathologic diagnoses showed no discrepancy. There were 104 14% minor and 15 2% major discrepancies. After reviewing 15 major discrepancies, six surgeries were canceled, two surgeries were modified, one adjuvant radiation treatment was added, one chemotherapy treatment was modified, and five adjuvant chemotherapy treatments were cancelled. No systematic error was identified with regard to the sources tissue origin or methods of obtaining the specimen $P = .675$. The cost of reviewing 720 specimens was \$108,000. The cost of identifying each major discrepancy was \$7200. **CONCLUSION:** Reviewing pathology slides before definitive treatment reveals notable discrepancies in diagnoses. The cost of pathology review is globally expensive but has consequential impact on proper treatment planning for the individual patient.

Sawan, S., R. Mugnai, et al. 2009. "Lower -limb lymphedema and vulval cancer: feasibility of prophylactic compression garments and validation of leg volume measurement." *Int J Gynecol Cancer* **19**: 1649 -1654.

OBJECTIVES: Leg lymphedema remains a significant health problem after treatment of vulval cancer. This pilot study explored the feasibility of conducting a larger trial to investigate whether the early use of compression stockings is effective in preventing leg lymphedema. **METHODS:** Fourteen patients undergoing inguofemoral lymphadenectomy for vulval cancer were randomized to either best supportive care or best supportive care plus the use of graduated compression stockings for 6 months. **RESULTS:** Six of 7 patients in the treatment group complied with the study protocol. The incidence of clinically significant lymphedema was not different between both groups; however, there was a greater increase in mean leg volume in the control group 953 vs 607 mL, $P = 0.010$. Furthermore, patients in the treatment group showed better performance as judged by leg symptoms $P = 0.031$, at 3 months and clinical examination $P = 0.039$ at 4 weeks and $P = 0.004$ at 6 months. There was no difference in the incidence of groin wound dehiscence, infection, or lymphocyst formation. We detected no difference between both groups' scores when using a validated quality-of-life questionnaire. Intraobserver and interobserver variabilities of leg-volume measurement technique were investigated using the principles of repeatability and reproducibility statistics. Intraobserver variability was estimated at 270 mL, whereas interobserver variability was 1000 mL. **CONCLUSIONS:** The prophylactic use of stockings in this population is feasible, and further larger studies are justified to investigate its role in reducing the incidence of leg lymphedema. The design of these studies should take into account the observer-related variability in measuring leg volume or consider alternative methods.

Sawicki, S., J. Kobierski, et al. 2011. "Sentinel lymph node detection in early vulvar cancer." *Int J Gynecol Cancer* **21**: S935.

Sawicki, S., G. Romanowicz, et al. 2010. "The usefulness of sentinel lymph node detection in vulvar cancer - a short communication." *Nucl Med Rev Cent East Eur* **132**: 81 -83.

BACKGROUND: The sentinel lymph node (SLN) biopsy is a solution for decreasing the extent of surgery with a significant reduction of the incidence of complications without influencing treatment results. **MATERIAL AND METHODS:** We performed the sentinel lymph node procedure in 24 women with vulvar cancer. In 14 cases, only the blue dye technique was applied, and in 10 cases ^{99m}Tc -labelled nanocolloid with blue dye was administered simultaneously. The extent of the surgery included radical vulvectomy in 23 patients and a wide local excision in 1 patient. In 15 patients unilateral inguofemoral lymphadenectomy was performed and in 9 cases bilateral lymphadenectomy. The total number of operated groins was 39. **RESULTS:** SLNs were detected in 34/39 of operated groins 87.2%. In 4 cases 16.6% tumour metastases to the lymph nodes were found. In total, 10 metastatic lymph nodes were detected in 9 sentinel-nodes and in 1 non-sentinel node. In three patients the nodal metastases were found only in the sentinel nodes. In one patient the metastases were found in the contralateral groin in two SLNs. There were no false negative sentinel lymph nodes. With the sole use of blue dye, SLNs were found in 79.5% of groins. The additional administration of the radiocolloid improved SLN detection to 88.9% of groins. **CONCLUSIONS:** The parallel use of the ^{99m}Tc labelled radiocolloid and blue dye enables high sentinel node detection rates by adequately trained surgeons.

Schaafsma, B. E., F. P. Verbeek, et al. 2013. "Near -infrared fluorescence sentinel lymph node biopsy in vulvar cancer: a randomised comparison of lymphatic tracers." *BJOG* **120**: 758 -764.

This study aims to confirm the feasibility of near-infrared (NIR) fluorescence imaging for sentinel lymph node (SLN) biopsy in vulvar cancer and to compare the tracer indocyanine green (ICG) bound to human serum albumin (HSA) versus ICG alone. Women received ^{99m}Tc -nanocolloid and patent blue for SLN detection. Subsequently, women randomly received ICG:HSA or ICG alone. In 24 women, 35 SLNs were intraoperatively detected. All SLNs detected were radioactive and NIR fluorescent and 27

77% were blue. No significant difference was found between ICG:HSA and ICG alone. This trial confirms the feasibility of NIR fluorescence imaging for SLN mapping in vulvar cancer.

Scheistroen, M. and C. Trope 1993. "Combined bleomycin and irradiation in preoperative treatment of advanced squamous cell carcinoma of the vulva." *Acta Oncol* **326**: 657 -661.

Forty-two patients with advanced squamous cell carcinoma of the vulva were treated with a combination regimen of bleomycin 180 mg and external irradiation 30-45 Gy. Twenty patients had primary lesions, and 22 patients had recurrent disease. Fifteen 75% of the patients with primary disease showed objective response five complete and ten partial response. Four underwent surgery. Of these, one is alive after 60 months with no evidence of disease. Two have died of unrelated causes without signs of recurrence. Seventeen relapsed and died of carcinoma of the vulva. Median survival for patients treated for primary disease was 8.0 months. Thirteen 59% of 22 patients treated for recurrence showed objective response two complete and eleven partial responses. None underwent surgery. All these patients died of carcinoma of the vulva. Median survival was 6.4 months. Toxicity was acceptable, and there were no treatment-related deaths. Even taking into account that our patients had very advanced disease, the results are disappointing. An increase of the radiation dose beyond the maximum of 45 Gy given, and more aggressive surgery, might have improved the results.

Schmidt, E., K. Zambo, et al. 2003. "Preliminary experiences with sentinel node detection in cases of vulvar malignancy." *Magyar Noorvosok Lapja* **66**: 177-180.

Sebag-Montefiore, D. J., C. McLean, et al. 1994. "Treatment of advanced carcinoma of the vulva with chemoradiotherapy - can exenterative surgery be avoided?" *Int J Gynecol Cancer* **43**: 150 -155.

Thirty-seven patients with advanced FIGO stage 17 stage III, 20 stage IV) carcinoma of the vulva whose extent of disease would have required extenterative surgery were treated with chemoradiotherapy CRT. Radiotherapy was given as a split course 2500 cGy mid -plane dose in 10 daily fractions, repeated 1 month later to the first seven patients. Subsequently radiotherapy was given as a continuous course 4500 cGy mid -plane dose in 20-25 daily fractions. Chemotherapy included mitomycin c as an intravenous bolus and 5 fluorouracil as a continuous intra-venous infusion over 4-5 days, with variations in timing and dose according to the type of radiotherapy course. Fifteen 47% complete and 11 34 % partial responses were seen at 3 months after completion of treatment. Of the 15 patients with complete response, 10 remained disease-free for a median of 24 months range 6 -36 months. The median survival for complete and partial responding patients was 15 and 11 months, respectively range 2 -37 months. Acute toxicity included moist perineal desquamation, diarrhea and myelosuppression. One death secondary to neutropaenic sepsis occurred in the split course group. WHO grade 3 radiation enteritis occurred in one patient 14% in the split course and two patients 6% in the continuous CRT groups. Using CRT, very high response rates have been obtained with relatively low toxicity. There is a useful role for CRT in the treatment of patients with locally advanced recurrent disease although its place in the management of extensive primary disease requires further evaluation.

Selman, A. E., T. H. Niemann, et al. 1999. "Quality assurance of second opinion pathology in gynecologic oncology." *Obstet Gynecol* **942** : 302 -306.

OBJECTIVE: To determine the effect of routine second review of pathologic material that was sent to Ohio State University before initiation of therapy. **METHODS:** All the gynecologic-oncologic histopathology review diagnoses made during a 1-year period were compared with original pathologic diagnoses. When there was a discrepant diagnosis with the second interpretation, the case was reviewed by at least two pathologists. Discrepancies were coded as no diagnostic disagreement, no diagnostic disagreement but pertinent information not included, diagnostic disagreement without clinical consequences, diagnostic disagreement with minor clinical significance, or diagnostic disagreement with major clinical significance. Proportions and confidence intervals were calculated. **RESULTS:** Pathology reports from 295 referred patients were reviewed. Two hundred forty-five 83.1% showed

no discrepancy. Discrepancies were found in 50 cases 16.9%. There was significant information missing in four cases 1.4%, diagnostic disagreement with no clinical significance in 22 cases 7.5%, and diagnostic disagreement with minor clinical significance in 10 cases 3.4%. In 14 cases 4.7%, 95% confidence interval 2.28, 7.12 the changes in diagnoses had major therapeutic or prognostic implications that included changes from malignant or low malignant potential to benign seven cases, malignant to low malignant potential three cases, change in tumor type two cases, and assessment of invasion two cases. The cost of reviewing 295 specimens was approximately \$39,235. The cost of identifying each major discrepancy was about \$2802. **CONCLUSION:** Routine pathology review of gynecologic-oncologic cases before definite treatment revealed notable discrepancies in diagnoses. In 4.7% of cases, the change in diagnosis had a major effect on proper treatment planning or a significant prognostic implication.

Selman, T. J., D. M. Luesley, et al. 2005. "A systematic review of the accuracy of diagnostic tests for inguinal lymph node status in vulvar cancer." *Gynecol Oncol* **99**: 206 -214.

OBJECTIVE: To determine the accuracy of minimally and non-invasive tests to assess the groin node status in squamous cell vulvar cancer. **METHODS:** A systematic review of published research from 1979 to 2004 that compares the results of tests to determine groin node status with histology at inguinofemoral lymphadenectomy was made. Studies included in the review were those that compared the index test to the standard surgical intervention of inguinofemoral lymphadenectomy and allowed the construction of two-by-two tables. From these tables, sensitivity, specificity, and the likelihood ratios with 95% confidence intervals were reported and, where feasible, meta-analysis was used to pool results for each test separately. Sentinel node biopsy using technetium-99m-labelled nanocolloid 99mTc had a pooled sensitivity and negative LR of 97% 91 -100 95% CI and 0.12 0.053 -0.28 95% CI, respectively, and was the most accurate test reviewed. **CONCLUSION:** Five diagnostic tests were identified in a total of 29 studies 961 groins. Although the studies were small and the design often poor, this represents the best summary of the data to date. Sentinel node identification using 99mTc appeared to be the most promising test for accurately excluding lymph node metastases in squamous cell vulvar cancer and potentially reducing the radicality of surgery. Its efficacy as a tool in reducing the need for radical surgery and associated patient morbidity without reducing survival needs further assessment probably in a randomised control trial.

Shylasree, T. S., A. Bryant, et al. 2011. "Chemoradiation for advanced primary vulvar cancer." *Cochrane Database Syst Rev*4: CD003752.

BACKGROUND: Vulvar cancer is a rare gynaecological cancer. There is no standard approach for treating locally advanced primary vulvar cancer FIGO stage III and IV). Combined treatment modalities have been developed using radiotherapy, chemotherapy and surgery. The advantages and disadvantages of such treatment is not well evaluated. **OBJECTIVES:** To evaluate the effectiveness and safety of neoadjuvant and primary chemoradiation for women with locally advanced primary vulvar cancer compared to other primary modalities of treatment such as primary surgery or primary radiation. **SEARCH STRATEGY:** We searched the Cochrane Central Register of Controlled Trials CENTRAL The Cochrane Library 2009, Issue 3, Cochrane Gynaecological Cancer Group Trials Register, MEDLINE and EMBASE to July 2009. We also searched registers of clinical trials, abstracts of scientific meetings, reference lists of included studies and contacted experts in the field. **SELECTION CRITERIA:** Randomised controlled trials RCTs or non-randomised studies that included multivariate analyses of chemoradiation in women with locally advanced, primary squamous cell carcinoma of the vulva. **DATA COLLECTION AND ANALYSIS:** Two review authors independently abstracted data and assessed risk of bias. An adjusted hazard ratio HR for overall survival was calculated for one non-randomised study and risk ratios RRs were used in an RCT to compare five-year death rates and adverse events in women who received neoadjuvant, primary chemoradiation or primary surgery. Adverse events were also reported more extensively in a further non-randomised study. All results were displayed in single study analyses. **MAIN RESULTS:** One RCT and two non-randomised studies that allowed for multivariate analyses met the inclusion criteria and included a total of 141 women. One

RCT found that neoadjuvant chemoradiation did not appear to offer longer survival compared to primary surgery in advanced vulval tumours RR = 1.29, 95% confidence interval CI 0.87 to 1.91. There was also no statistically significant difference in survival between primary chemoradiation and primary surgery in a study that included 63 women pooled adjusted HR= 1.09, 95% CI 0.37 to 3.17 and in another study that only included 12 eligible women and compared the same interventions HR was non-informative when statistical adjustment was made. Adverse events were extensively reported in only one study, which found no statistically significant difference in risk of adverse events between primary chemoradiation and primary surgery due to the very small numbers in each group. In the RCT there was no observed statistically significant difference between neoadjuvant chemoradiation and primary surgery. Adverse events were not reported in the largest study of 63 women. Quality of life QoL was not reported in any of the included studies. All studies were at high risk of bias. **AUTHORS' CONCLUSIONS:** Women with advanced vulval tumours showed no significant difference in overall survival or treatment-related adverse events when chemoradiation primary or neoadjuvant) was compared with primary surgery. The retrospective studies had a high risk of bias as the entry criteria for primary chemoradiation was based on inoperability or tumour requiring exenteration. The radiochemotherapy regimens varied widely. There was no data on QoL. There is no standard terminology for 'operable and inoperable vulval cancer', and for 'primary and neoadjuvant chemoradiation'. Stratification according to unresectability of the primary tumour and/or lymph nodes is needed, for good quality comparison.

Sideri, M., C. De Cicco, et al. 2000. "Detection of sentinel nodes by lymphoscintigraphy and gamma probe guided surgery in vulvar neoplasia." *Tumori* **86**: 359 -363.

BACKGROUND: Pathologic lymph node status is the most important prognostic factor in vulvar cancer; however, complete inguinofemoral node dissection is associated with significant morbidity. Intraoperative lymphoscintigraphy associated with gamma detecting probe-guided surgery has proved to be reliable in the detection of sentinel node (SN) involvement in melanoma and breast cancer patients. The present study evaluates the feasibility of the surgical identification of inguinal sentinel nodes using lymphoscintigraphy and a gamma detecting probe in patients with early vulvar cancer. **METHODS:** Technetium-99-labeled colloid human albumin was administered perilesionally in 44 patients. Twenty patients had T1 and 23 had T2 invasive epidermoid vulvar cancer; one patient had a lower-third vaginal cancer. An intraoperative gamma detecting probe was used to identify SNs during surgery. Complete inguinofemoral node dissection was subsequently performed. SNs underwent separate pathologic evaluation. **RESULTS:** A total of 77 groins were dissected in 44 patients. SNs were identified in all the studied groins. Thirteen cases had positive nodes: the SN was positive in all of them; in 10 cases the SN was the only positive node. Thirty-one patients showed negative SNs: all of them were negative for lymph node metastasis. **CONCLUSIONS:** Lymphoscintigraphy and SN biopsy under gamma detecting probe guidance proved to be an easy and reliable method for detection of SNs in early vulvar cancer. If these preliminary data will be confirmed, the technique would represent a real progress towards less aggressive treatment in patients with vulvar cancer.

Sidor, J., R. Diallo-Danebrock, et al. 2006. "Challenging the concept of microinvasive carcinoma of the vulva: report of a case with regional lymph node recurrence and review of the literature." *BMC Cancer* **6**: 157.

BACKGROUND: It is widely accepted that vulvar carcinoma with a depth of invasion of less than one millimeter is sufficiently treated by vulvectomy or wide local excision without inguinal lymphadenectomy. **CASE PRESENTATION:** However, a patient with inguinal lymph node recurrence 21 months after radical vulvectomy for stage IA squamous cell carcinoma was observed. **CONCLUSION:** According to a review of the literature, there are five additional cases of metastasizing vulvar cancer with a depth of invasion of less than one millimeter. Therefore, the definition of microinvasive carcinoma of the vulva based on depth of invasion alone may not be as reliable as previously thought and does not rule out inguinal lymph node involvement or recurrence. Consequently, the necessity of inguinal node dissection for microinvasive carcinoma needs to be discussed on an

individual basis taking into account the age of the patient as well as the potential morbidity of extended surgery.

Siller, B. S., R. D. Alvarez, et al. 1995. "T2/3 vulva cancer: a case -control study of triple incision versus en bloc radical vulvectomy and inguinal lymphadenectomy." *Gynecol Oncol* **57**: 335 -339.

The purpose of this case-control study was to compare outcome in T2/3 vulvar cancer patients treated with radical vulvectomy and inguinal lymphadenectomy using either a triple incision or en bloc technique. All T2/3 vulvar cancer patients treated by the triple incision technique were identified and compared to a control group consisting of similar T2/3 patients treated with an en bloc procedure at the same institution. Survival by surgical stage, lesion diameter, nodal status, and margin status was analyzed and compared between the two groups. Twenty-seven vulvar cancer patients with a T2/3 lesion underwent radical vulvectomy and inguinal lymphadenectomy using the triple incision technique; the control group consisted of 20 T2/3 vulvar cancer patients treated by en bloc resection. The two groups were matched for age, surgical stage, grade, lesion diameter, margin status, nodal status, and adjuvant treatment. The recurrence rate in the triple incision group was 37% compared to 35% in the en bloc group. OR, 1.092, 95% CI, [0.327, 3.649], P = 0.9. There was no difference in the local recurrence rate between the two groups 80% in the triple incision group and 72% in the en bloc group P = 0.5. Five -year survival for the triple incision and the en bloc groups was similar, 64 and 82%, respectively P = 0.15. Survival between the groups was not statistically different when analyzed according to surgical stage, lesion diameter, nodal status, and negative margin status. These data indicate that the triple incision technique provides survival outcomes similar to the standard en bloc radical vulvectomy in patients with T2/3 vulva cancer. Due to the significant morbidity that has been associated with the en bloc radical vulvectomy and inguinal lymphadenectomy, the triple incision technique should be considered as the preferred method of treatment for most vulvar cancer patients.

Singh, K., C. O. Orakwue, et al. 2006. "Accuracy of magnetic resonance imaging of inguinofemoral lymph nodes in vulval cancer." *Int J Gynecol Cancer* **16**: 1179 -1183.

Inguinofemoral lymphadenectomy contributes to the high morbidity related to surgical treatment of vulval cancer. The objective of this study was to assess the accuracy of magnetic resonance imaging MRI in predicting inguinofemoral lymph nodes metastasis in women with vulval cancer. We reviewed the clinical, MRI, surgical, and pathologic findings of 59 women with vulval cancer who were treated at our institution from January 2000 to June 2004. Histology was available for 39 women who had undergone inguinofemoral lymphadenectomy. Clinical and MRI findings were compared with histology result to assess test accuracy. MRI had a positive likelihood ratio LR+ of 4.8 95% confidence interval of 2.7-8.6 and negative likelihood ratio LR - of 0.17 0.06 -0.49. It had a sensitivity of 85.7% 63.7 - 97, specificity of 82.1% 69.6 -91.1, positive predictive value PPV) of 64.3% 44.1 -81.4, and negative predictive value NPV) of 93.9% 83.1 -98.7. Clinical examination had an LR+ of 6.1 1.8 - 21.6 and LR - of 0.69 0.5 -0.96. It had a sensitivity of 35% 15.3 -59.4, specificity of 94.3% 84.3 - 98.8, PPV of 70% 34.7 -93.3, and NPV of 79.4% 67.3 -88.5. Kappa statistics for interobserver and intraobserver agreement were 0.9091 and 0.8475, respectively. MRI assessment was accurate in predicting negative nodal status that is clinically useful in identifying women who can be spared inguinofemoral lymphadenectomy. It is noninvasive and is superior to clinical assessment. In clinical practice, this should encourage toward nodal sparing surgery, thus lowering surgical-related patient morbidity.

Sliutz, G., A. Reinthaller, et al. 2002. "Lymphatic mapping of sentinel nodes in early vulvar cancer." *Gynecol Oncol* **84**: 449 -452.

OBJECTIVE: The aim of the study was to determine the diagnostic accuracy and feasibility of sentinel lymph node (SLN) detection using a gamma probe in patients suffering from vulvar cancer. **METHODS:** From May 1998 to November 2000, 26 patients with early vulvar cancer, planned for local wide excision or vulvectomy including groin dissection, were eligible for the study. Two to 3 h before

the planned procedure we injected technetium99 m -labeled microcolloid intradermally at four locations around the tumor. Dynamic and static images were recorded using a gamma camera. SLN locations were marked on the overlying skin. In the operating theater SLNs were identified at the beginning of the procedure using a handheld gamma-detection probe. After resection of suspected SLNs a standard unilateral or bilateral groin dissection was performed, subsequently followed by local wide excision or, if indicated, radical vulvectomy. Sentinel node detection using technetium99 m -labeled microcolloid was compared with final histopathological and immunohistochemical results. RESULTS: Scintigraphy showed focal uptake in all 26 patients. Intraoperatively we detected all sentinel nodes by handheld gamma probe. In 20 patients, one sentinel node was identified unilaterally, while in 6 patients two or more nodes were identified bilaterally. Histologically positive SLNs were found in 9 patients. In our preliminary series we did not find any false-negative SLN. CONCLUSION: Identification of sentinel nodes in vulvar cancer is feasible with preoperatively administered technetium99m -labeled microcolloid. We confirm the results of previous studies and improve the evidence that the SLN procedure could be implemented in future therapy concepts.

Sobin, L. H., M. K. Gospodarowicz, et al. 2009. "TNM classification of malignant tumours. 7th edition." Oxford: Wiley-Blackwell.

SOGC 2006. "Management of Squamous Cell Cancer of the Vulva." <http://sogc.org/fr/guidelines/prise-en-charge-du-cancer-spinocellulaire-de-la-vulve-remplace-2-mai-1993/>.

Sohaib, S. A., P. S. Richards, et al. 2002. "MR imaging of carcinoma of the vulva." *AJR Am J Roentgenol* **178**: 373 -377.

OBJECTIVE: The aim of this study was to describe the MR imaging features of cancer of the vulva and to determine the accuracy of MR imaging in staging the disease. MATERIALS AND METHODS: We reviewed the MR images of 22 patients range, 21 -85 years; median, 74 years with cancer of the vulva who were treated at our institution between 1995 and 2000. Note was made of the primary tumor size, site, signal characteristics, enhancement, and local extension and of lymph node number, size, and position. The MR imaging features were correlated with surgical and pathologic findings. RESULTS: The tumors were isointense to muscle on T1-weighted images and showed intermediate-to-high signal intensity on T2-weighted scans. After IV gadolinium was administered to four patients, tumor enhancement was seen in two 50%. MR imaging correctly staged the primary site in 14 70% of the 20 patients. If superficial inguinal nodes 10 mm or greater in short-axis diameter are considered abnormal, then the sensitivity for detection of malignant nodes was 40% and the specificity, 97%. If deep inguinal nodes 8 mm or greater in short-axis diameter are considered abnormal, then the sensitivity for detection of malignant nodes was 50% and the specificity, 100%. CONCLUSION: MR imaging is highly specific for the detection of nodal involvement in patients with cancer of the vulva but correlates only moderately with clinicopathologic staging of the primary tumor.

Soliman, A. A., M. Heubner, et al. 2012. "Morbidity of inguinofemoral lymphadenectomy in vulval cancer." *ScientificWorldJournal* **2012**: 341253.

BACKGROUND: The aim of this study is to detect possible risk factors for development of short- and long-term local complications after inguinofemoral lymphadenectomy for vulval cancer. METHODS: This retrospective cohort study included 34 vulval cancer patients that received inguinofemoral lymphadenectomy. The detected complications were wound cellulitis, wound seroma formation, wound breakdown, wound infection, and limb lymphoedema. Followup of the patient ran up to 84 months after surgery. RESULTS: Within a total of 64 inguinofemoral lymphadenectomies, 24% of the inguinal wounds were affected with cellulitis, 13% developed a seroma, 10% suffered wound breakdown, 5% showed lower limb edema within a month of the operation, and 21.4% showed lower limb edema during the long-term followup. No significant correlation could be found between saphenous vein ligation and the development of any of the local complications. The 3-year survival rate in our cohort was 89.3%. CONCLUSIONS: Local complications after inguino-femoral lymphadenectomy are still

very high, with no single pre-, intra-, or postoperative factor that could be incriminated. Saphenous vein sparing provided no significant difference in decreasing the rate of local complications. More trials should be done to study the sentinel lymph node detection technique.

Stehman, F. B., B. N. Bundy, et al. 1992. "Early stage I carcinoma of the vulva treated with ipsilateral superficial inguinal lymphadenectomy and modified radical hemivulvectomy: a prospective study of the Gynecologic Oncology Group." *Obstet Gynecol* **79**4: 490 -497.

Although cure rates are high, the morbidity of radical operation for carcinoma of the vulva is substantial. Between 1983-1989, member institutions of the Gynecologic Oncology Group entered 155 patients in a prospective evaluation of modified radical hemivulvectomy and ipsilateral inguinal lymphadenectomy for clinical stage I vulvar cancer. Only patients with neoplastic thickness of 5 mm or less, without vascular space invasion, and negative inguinal lymph nodes were eligible for this study. There have been 19 recurrences and seven deaths from disease among the 121 eligible and evaluable patients. Patients whose disease recurred on the vulva were frequently eight of ten patients salvaged by further operation. Five of the seven deaths due to cancer occurred among patients whose first recurrence was in the groin. Acute and long-term morbidity as well as hospital stay were each less than in the Group's previous experience in a comparable patient population treated with radical vulvectomy and bilateral inguinal-femoral lymphadenectomy. There was a significantly increased risk of recurrence but not death when compared with these same historic controls. Modified radical hemivulvectomy and ipsilateral inguinal lymphadenectomy is an alternative to traditional radical operation for these selected patients with stage I carcinoma of the vulva. The number of patients who experienced recurrence in the operated groin is of concern and may be attributable to the decision to leave the femoral nodes intact.

Stehman, F. B., B. N. Bundy, et al. 1992. "Groin dissection versus groin radiation in carcinoma of the vulva: a Gynecologic Oncology Group study." *Int J Radiat Oncol Biol Phys* **24**2: 389 -396.

PURPOSE: The objective of this study was to determine if groin radiation was superior to and less morbid than groin dissection. **METHODS AND MATERIALS:** Members of the Gynecologic Oncology Group randomized 58 patients with squamous carcinoma of the vulva and nonsuspicious N0 -1 inguinal nodes to receive either groin dissection or groin radiation, each in conjunction with radical vulvectomy. Radiation therapy consisted of a dose of 50 Gray given in daily 200 centigray fractions to a depth of 3 cm below the anterior skin surface. **RESULTS:** The study was closed prematurely when interim monitoring revealed an excessive number of groin relapses on the groin radiation regimen. Metastatic involvement of the groin nodes was projected to occur in 24% of patients based on this Group's previous experience. On the groin dissection regimen, there were 5/25 20.0% patients with positive groin nodes. These patients received post-operative radiation. There were five groin relapses among the 27 18.5% patients on the groin radiation regimen and none on the groin dissection regimen. The groin dissection regimen had significantly better progression-free interval $p = 0.03$ and survival $p = 0.04$. **CONCLUSION:** Radiation of the intact groins as given in this study is significantly inferior to groin dissection in patients with squamous carcinoma of the vulva and N0-1 nodes.

Stuckey, A., M. Schutzer, et al. 2013. "Locally advanced vulvar cancer in elderly women: is chemoradiation beneficial?" *Am J Clin Oncol* **36** 3: 279 -282.

OBJECTIVES: There is a higher incidence of invasive vulvar cancer in the elderly population. With multiple medical comorbidities, radiation with sensitizing chemotherapy in the elderly can be complicated, yet the risks and benefits of chemoradiation have not been studied in this population. We investigate whether elderly patients are more likely to die of intercurrent disease (ICD) or of treatment complications. **METHODS:** A meta-analysis was performed to compare remission rates, death from ICD or treatment complications, and rates of surgery in elderly and nonelderly patients with vulvar cancer treated with chemoradiation. Data were searched in the Cochrane Review. Eligibility criteria included: woman with advanced primary squamous cell carcinoma of the vulva, women receiving preoperative or primary chemoradiation treatment with curative intent, and prospective studies that

reported the necessary data of interest. Data collected included: age elderly, defined as 65 years and above, stage, treatment, and mortality. RESULTS: Seventy subjects were identified from 7 studies that met eligibility criteria. Seventy-eight percent 25/32 of patients younger than 65 years were without evidence of disease after treatment versus 66% 25/38 of patients aged 65 years and above $P=0.30$. Three percent 1/32 of patients younger than 65 years of age died of ICD or treatment complications versus 11% 4/38 of patients 65 years and above $P=0.37$. CONCLUSIONS: We noticed a trend demonstrating death from ICD or treatment complications was higher for elderly patients. Future research should focus on treatment with chemoradiation in the elderly population with regard to survival benefit, toxicity, and death from ICD or treatment complications.

Sznurkowski, J. J. and J. Emerich 2010. "Characteristic features of recurrences of squamous cell carcinoma of the vulva." *Ginekol Pol* **81**: 12 -19.

AIM: The objective of this study was to find prognostic factors for the development of recurrences in patients who had undergone surgical treatment of vulvar cancer. METHODS: The records of patients with primary vulvar cancer $n=104$ treated at the Department of Gynaecological Oncology of the Medical University of Gdansk between 1998 and 2001 were reviewed to identify those with squamous histology. Of the 93 thus identified 27 were excluded because of lack of standard treatment and 7 because of lack of radical surgery. A total number of 59 patients with squamous cell carcinoma were finally analyzed. For each record the age of the patient, size of the lesion, depth of invasion, margins of resection and lymph node status were analyzed. All patients were staged according to FIGO 1996. Recurrences were recorded by localization, whether local, groin or distant, and compared with a group of patients without any recurrences after radical surgery $n=59$. RESULTS: Recurrence was recorded in 19 cases 28.8%. A local vulvar/perineal recurrence was diagnosed in 10 patients 10/59, 16.9%, while 5 5/59, 8.5% developed groin recurrence and 4 4/59, 6.8% had distant recurrences. Multifocality of the primary tumour is an independent risk factor for local recurrence HR: 3.12; 95% CI: 0.84-11.6. A metastatic node was the only independent prognostic risk factor for groin or distant recurrence HR: 3.16; 95% CI: 0.94 -10.2. CONCLUSION: Close follow-up of patients treated for vulvar cancer is recommended to detect recurrences at an early and potentially curable stage. Deep inguinal-femoral lymphadenectomy could be replaced with superficial inguinal groin dissection.

Tabbaa, Z. M., J. Gonzalez, et al. 2012. "Impact of the new FIGO 2009 staging classification for vulvar cancer on prognosis and stage distribution." *Gynecol Oncol* **127**: 147 -152.

OBJECTIVE: In 2009, FIGO modified staging of vulvar cancer--the performance of the new classification relative to the prior system has not been assessed. We sought to investigate the impact of the 2009 FIGO vulvar cancer staging system on stage distribution and prognostic ability of the 2009 sub-stage classifications in a large cohort of uniformly staged cases with long-term followup. METHODS: Patients undergoing surgery for vulvar cancer were identified from 2 institutions Mayo Clinic and Medical University, Gdansk, Poland using a similar surgical approach. Inclusion criteria required primary surgery for invasive vulvar cancer for cases with >1 mm invasion with complete inguinal/femoral lymphadenectomy. The technique of inguinofemoral node dissection used in both institutions was designed to remove both superficial and deep inguinofemoral nodes. A retrospective review was performed and all cases were assigned stage using the 1988 and 2009 FIGO systems after reviewing pathology slides. Cause-specific survival CSS, death due to cancer was estimated using the Kaplan-Meier method and compared using the Cox proportional hazards model for the first 10 years after surgery. RESULT: A total of 468 patients met inclusion criteria. Thirty-one percent $n=155$ were down-staged, and 1 case up-staged using 2009 staging. The new system fails to effectively separate 10-yr CSS for stage I and II cases $p=0.52$, while FIGO 1988 failed to separate stages II and III $p=0.41$. We observed a difference in survival for stage I and II cases based on tumor diameter. For smaller stage II lesion ≤ 4 cm vs. >4 cm we observed no difference in survival compared to all stage IB cases $p=0.25$. Considering node positive disease, patients with 2009 FIGO stages IotaIotaA, IotaIotaB, and IotaIotaC were not significantly different in terms of CSS $p=0.17$. However, CSS approached significance between patients with extracapsular vs. intracapsular disease $p=0.072$.

For stages IIIA and IIIB excluding extracapsular spread, IIIC, we observed that the number of positive nodes and diameter of lymph node metastasis were not significantly associated with CSS. When comparing bilateral nodal involvement vs. unilateral cases with at least 2 involved nodes, we found no statistical difference in CSS $p=0.30$. **CONCLUSION:** This is the largest cohort study to evaluate the effect and prognostic performance of the new FIGO vulvar cancer staging system. The new staging does not stratify survival between stages I and II and reduces CSS in stage I cases. Our results suggest that lesion size in node negative cases is an important prognostic variable that could be addressed in future staging classifications. Among the node positive cases, the current classification results in slight differences in CSS, primarily between intra- and extra-capsular disease and not according to the number of positive nodes and lymph node metastasis diameter. Finally we observe that bilateral nodal disease does not appear to impact CSS, justifying it being omitted from the 2009 staging system and that separating node positive 2009 stage III from node negative 2009 stage II cases is justified.

Tan, J., N. Chetty, et al. 2012. "Validation of the FIGO 2009 staging system for carcinoma of the vulva." *Int J Gynecol Cancer* **22**: 498 -502.

BACKGROUND: The previous 1988 International Federation of Gynecology and Obstetrics (FIGO) vulvar cancer staging system failed in 3 important areas: 1 stage 1 and 2 disease showed similar survival; 2 stage 3 represented a most heterogeneous group of patients with a wide survival range; and 3 the number and morphology of positive nodes were not taken into account. **OBJECTIVE:** To compare the 1988 FIGO vulvar carcinoma staging system with that of 2009 with regard to stage migration and prognostication. **METHODS:** Information on all patients treated for vulvar cancer at the Queensland Centre for Gynecological Cancers, Australia, between 1988 to the present was obtained. Data included patients' characteristics as well as details on histopathology, treatments, and follow-up. We recorded the original 1988 FIGO stage, reviewed all patients' histopathology information, and restaged all patients to the 2009 FIGO staging system. Data were analyzed using the Kaplan-Meier method to compare relapse-free survival and overall survival. **RESULTS:** Data from 394 patients with primary vulvar carcinoma were eligible for analysis. Patients with stage IA disease remained unchanged. Tumors formerly classified as stage II are now classified as stage IB. Therefore, FIGO 2009 stage II has become rare, with only 6 of 394 patients allocated to stage II. Stage III has been broken down into 3 substages, thus creating distinct differences in relapse-free survival and overall survival. Prognosis of patients with stage IIIC disease is remarkably poor. **CONCLUSION:** The FIGO 2009 staging system for vulvar carcinoma successfully addresses some concerns of the 1988 system. Especially, it identifies high-risk patients within the heterogeneous group of lymph node-positive patients.

Tans, L., A. C. Ansink, et al. 2011. "The role of concurrent chemo-radiotherapy in the management of locally advanced carcinoma of the vulva: single institutional experience and review of literature." *Am J Clin Oncol* **34**: 22 -26.

OBJECTIVE: To retrospectively investigate the outcome and toxicity of concurrent chemo-radiotherapy in the treatment of locally advanced vulvar cancer (LAVC). **PATIENTS AND METHODS:** Between 1996 and 2007, 28 consecutive patients with LAVC were treated with chemoradiation 20 primary tumors and 8 loco-regional recurrences. Treatment consists of 2 separate courses of external-beam radiotherapy 40 Gy -2 weeks split-20 Gy. During each course of radiotherapy, 5-fluorouracil 1000 mg/m²/d, was given as a continuous intravenous infusion over the first 4 days, and mitomycin-C 10 mg/m² on day 1, as a bolus intravenous injection. Outcome measures were rates of complete and partial response, loco-regional control, progression-free survival, overall survival, and toxicity. **RESULTS:** The median follow-up was 42 months and the median age of patients was 68 years. Twenty patients 72% achieved complete remission, 4 patients 14% partial remission, for an overall response rate of 86%. Four patients 14% had progressive disease directly after chemo-radiotherapy. The actuarial rates of loco-regional control, progression-free survival and overall survival at 4 years were 75%, 71%, and 65%, respectively. There was no treatment break for acute toxicity. Vulvar desquamation was the main acute treatment-related side effect 93%. Three patients developed transient grade 2 neutropenia or thrombocytopenia. Mild skin fibrosis and atrophy n = 6, 21%,

radiation ulcer n = 4, 14%, in one patient treatment was needed, telangiectasia n = 3, 11%, and lymphoedema n = 2, 7% were the most common late toxicity of chemoradiation. **CONCLUSION:** These data support the use of concurrent chemoradiotherapy as an effective alternative to primary ultra-radical surgery to treat LAVC with an acceptable toxicity profile.

Tantipalakorn, C., G. Robertson, et al. 2009. "Outcome and patterns of recurrence for International Federation of Gynecology and Obstetrics (FIGO) stages I and II squamous cell vulvar cancer." *Obstet Gynecol* **113**: 895 - 901.

OBJECTIVE: To study patterns of recurrence, to evaluate pathologic features correlating with recurrence, and to estimate the prognostic implications for each different pattern of recurrence in the International Federation of Gynecology and Obstetrics (FIGO) stages I and II squamous cell vulvar cancer. **METHODS:** This was a retrospective study of 121 cases of vulvar cancer managed at our institution from 1987 to 2005. Time to recurrence, sites of local and distant recurrence, and the type of surgery were recorded. Relapse-free and overall survival were calculated. **RESULTS:** There was no difference in recurrence rates, time to recurrence, or survival between patients with FIGO stages I or II disease. The 5-year actuarial survival corrected for competing risks for stage I disease was 97% compared with 95% for stage II $P=.83$. Progression-free survival at 5 years was 86% for stage I and 94% for stage II. In this study, 95.9% of patients were treated with vulvar-conserving surgery without detriment with respect to recurrence or survival. **CONCLUSION:** Vulvar-conserving surgery, even for large tumors, results in excellent outcomes. Vulvar recurrences have an excellent prognosis, but primary site and remote site vulvar recurrences are biologically different. There is no justification for the FIGO differentiation of node-negative cancers confined to the vulva on the basis of tumor size. **LEVEL OF EVIDENCE:** III.

Tavares, M. G., M. T. Sapienza, et al. 2001. "The use of ^{99m}Tc -phytate for sentinel node mapping in melanoma, breast cancer and vulvar cancer: a study of 100 cases." *Eur J Nucl Med* **28**: 1597 -1604.

Sentinel node mapping reduces surgical morbidity and allows the use of more accurate tumour staging techniques. Radionuclide studies are preferentially performed using small colloids, which have limited availability in our country. The possibility of using phytate for sentinel node mapping was raised because of the similarity between its biodistribution and that of nanocolloids in the reticulo-endothelial system. In this paper we evaluated the use of ^{99m}Tc -phytate for sentinel node mapping, correlating the histopathological results with the status of the rest of the lymph node chain in different malignant tumours. A total of 100 patients were studied. group 1 consisted of 62 patients with breast cancer, group 2 of 20 patients with melanoma and group 3 of 18 patients with vulvar carcinoma. Lymph node scintigraphy was carried out after injecting ^{99m}Tc -phytate subdermally, and the sentinel node projection was marked on the skin. After 18-24 h, intraoperative sentinel node localisation was performed using a gamma probe combined with visual localisation using patent blue dye in 75 patients, and lymph node dissection was then carried out. Radionuclide scintigraphy identified the sentinel node in 98% of all studies. Intraoperative detection using the gamma probe was equally efficient: group 1=93% 38/41, group 2=95% 18/19 and group 3=100% 15/15. The sentinel node was involved in 41%, 31% and 20% of cases in groups 1, 2 and 3, respectively. Among the patients with positive nodes, the sentinel node was the only one affected in 53% of group 1, 50% of group 2 and 67% of group 3 cases. The method's negative predictive value was 91% in group 1 and 100% in the other groups. One false-negative study occurred in a patient who had a multifocal tumour and an intraparenchymatous lymph node; another occurred in a patient with a macroscopically affected node found during surgery. There were no side-effects related to the ^{99m}Tc -phytate. It is concluded that scintigraphic and intraoperative sentinel node identification was satisfactorily performed using ^{99m}Tc -phytate. The results were comparable to those previously described in the literature using other radiopharmaceuticals. Easy availability and low cost justify the use of phytate in our practice.

Te Grootenhuis, N. C., A. G. van der Zee, et al. 2015. "Sentinel nodes in vulvar cancer: Long-term follow-up of the GROningen International Study on Sentinel nodes in Vulvar cancer (GROINSS -V) I." *Gynecol Oncol*.

Terada, K. Y., M. N. Coel, et al. 1998. "Combined use of intraoperative lymphatic mapping and lymphoscintigraphy in the management of squamous cell cancer of the vulva." *Gynecol Oncol* **70**1: 65 -69.

BACKGROUND: The standard care of the patient with squamous cell cancer of the vulva is radical vulvectomy along with inguinal-femoral node dissection. We explored the feasibility of sentinel lymphadenectomy in patients with squamous cell cancer of the vulva. **METHODS:** Patients with biopsy proven squamous cell cancer of the vulva were studied with preoperative lymphoscintigraphy, intraoperative lymphatic mapping with isosulfan blue combined with intraoperative lymphoscintigraphy utilizing a hand-held gamma counter. **RESULTS:** Five patients with invasive squamous cell cancer were studied. Sentinel nodes were identified in six lymphatic basins. One lymphatic basins had two sentinel nodes. Six of seven sentinel nodes were blue and all retained radioactivity at a ratio of at least 3:1 above the background levels in the regional node basin. One patient was found to have metastatic tumor which was confined to a sentinel lymph node. There was minimal morbidity associated with the procedure. **CONCLUSIONS:** Lymphatic mapping is feasible in patients with squamous cell cancer of the vulva. These initial results suggests further study is warranted.

Terada, K. Y., D. M. Shimizu, et al. 2006. "Outcomes for patients with T1 squamous cell cancer of the vulva undergoing sentinel node biopsy." *Gynecol Oncol* **102**2: 200 -203.

OBJECTIVE: This retrospective review was undertaken to evaluate survival in patients with T1 squamous cell carcinoma of the vulva treated with radical local excision and sentinel node dissection. **METHODS:** Patients with T1 cancers underwent pre-operative lymphoscintigraphy and sentinel lymph node dissection using technetium sulfur colloid and isosulfan blue dye. The primary tumor was removed with radical local excision. Patients with negative sentinel nodes did not receive any additional treatment. Survival was calculated using life table analysis. **RESULTS:** There were 21 patients who underwent 27 sentinel node dissections. Three patients were found to have positive sentinel nodes. At a median follow-up of 4.6 years, two patients have died of cancer, and three patients have died of intercurrent illness. None of the patients with negative sentinel nodes has died of cancer. There were no groin or distant recurrences in patients with negative sentinel nodes. Three-year disease-free survival for all patients and for patients with negative sentinel nodes were 90% and 100% respectively. **CONCLUSION:** The survival for patients with early vulvar cancer treated with sentinel node dissection and radical local excision appears excellent.

Tham, K. F., J. H. Shepherd, et al. 1993. "Early vulval cancer: the place of conservative management." *Eur J Surg Oncol* **19**4: 361 -367.

There is a trend towards conservative surgery for early vulval cancer, which is increasingly being diagnosed in younger women. In this series there were 21 patients who had lesions which had invaded to a depth of 3 mm or less. Nine patients were treated by wide local excision without any form of lymphadenectomy, and eight patients had wide local excision with ipsilateral groin dissection. In the remaining four patients, radical surgery was carried out, consisting of radical vulvectomy and bilateral lymphadenectomy. None of the 12 patients who had some form of lymphadenectomy was shown to have nodal involvement. None of the patients suffered from local recurrence or recurrence in the groin nodes. No patient died from vulval cancer, and all but one of the patients are still alive with a mean follow-up period of 54.8 months. Though there is as yet no universal agreement on the criteria for early vulval cancer, with superficial invasion there is a place for individualized treatment, when patients will benefit from less than radical surgery.

Thangavelu, A., A. Andrew, et al. 2006. "Groin recurrence following Stage 1A squamous cell carcinoma of the vulva." *Gynecol Oncol* **101**1: 172 -174.

BACKGROUND: It has been well established that stage 1 squamous cell carcinomas of the vulva with a depth of stromal invasion less than 1 mm have a <1% risk of lymph node involvement. The treatment for these stage 1A tumours has therefore been to perform radical wide local excision without removal of

groin nodes. CASE: We present two cases of stage 1A microinvasive cancer of the vulva that presented with groin recurrence 3 months and 3 years following their primary surgery respectively. CONCLUSION: The current management of stage 1A tumours may need to be re-evaluated to include some form of lymph node assessment in view of these rare but nonetheless aggressive tumours.

Thigpen, J. T., J. A. Blessing, et al. 1986. "Phase II trials of cisplatin and piperazinedione in advanced or recurrent squamous cell carcinoma of the vulva: a Gynecologic Oncology Group Study." *Gynecol Oncol* **233**: 358-363.

Thirty-eight patients with advanced or recurrent squamous cell carcinoma of the vulva no longer amenable to control with surgery and/or radiotherapy were entered onto one of two phase II studies. One was deemed ineligible because of a primary site of origin other than vulva. Of the remaining 37, 13 patients received piperazinedione 9 mg/m² iv every 3 weeks. No objective regressions were observed. Five patients were judged to have had stable disease, while eight demonstrated increasing disease. The other 24 patients received cisplatin 50 mg/m² iv every 3 weeks. Of the 22 who were evaluable for response because of the presence of measurable disease, no objective regression of disease was observed. Ten had stable disease, while the remaining 12 had increasing disease. Adverse effects were tolerable for each study agent and were essentially those reported in other series for these two drugs. These results suggest that neither agent is active in advanced or recurrent squamous cell carcinoma of the vulva at least at the dose and schedule tested.

Thomas, G., A. Dembo, et al. 1989. "Concurrent radiation and chemotherapy in vulvar carcinoma." *Gynecol Oncol* **343**: 263 -267.

Between June 1984 and February 1988 the role of radiation with concurrent infusional 5-fluorouracil with or without mitomycin C CT-RT was examined in 33 patients with vulvar cancer. The median duration of follow-up is 16 months range 5 to 45 months. Nine received adjuvant postsurgical CT-RT and none has relapsed in the radiation field. Seven are alive disease free. Two have died of distant metastases. Of the 9 receiving definitive primary CT-RT, 6 had initial complete response with subsequent vulvar relapse developing in 3. Seven of the 9 remain disease free after CT-RT alone in 3 or with the addition of a local excision of residual or recurrent disease in 6. One patient did not respond to CT-RT and required a radical vulvectomy and groin node dissection. Fifteen received CT-RT for disease recurrence following primary surgery. Disease was present in the vulva only in 11, vulva and inguinal nodes in 1 and nodes only in 3. Eight of the 15 had a complete response and no relapses occurred in the treated sites. Four of the 8 dying of disease developed pulmonary metastases. Serious late complications developed in 2 patients, 1 avascular hip necrosis and 1 proctitis requiring a defunctioning colostomy. CT-RT appears tolerable and may contribute to enhanced locoregional control in recurrent or advanced disease. As initial therapy it may allow lesser surgery with preservation of normal anatomy in selected primary vulvar cancers.

Trifiro, G., L. L. Travaini, et al. 2010. "Sentinel node detection by lymphoscintigraphy and sentinel lymph node biopsy in vulvar melanoma." *Eur J Nucl Med Mol Imaging* **374**: 736 -741.

PURPOSE: Vulvar melanoma is a rare malignant tumour. Its surgical excision is the mainstay of treatment whilst the surgical management of regional lymph nodes remains controversial; on the contrary elective inguinofemoral lymphadenectomy causes considerable morbidity. Lymphoscintigraphy LS and sentinel lymph node biopsy SLNB are accurate staging procedures of lymph node status in breast cancer and cutaneous melanoma patients. In this retrospective paper we report our experience of LS and SLNB in vulvar melanoma patients. METHODS: Twenty-two consecutive patients with a diagnosis of vulvar melanoma were treated at our institute: patients with clinically positive groin nodes or with previous surgery on the primary tumour were excluded. Twelve were selected for our analysis. All patients underwent sentinel lymph node localization with LS the day before surgery and the surgical procedure of SLNB associated with radical surgery. RESULTS: Six patients had metastatic SLNB and in five of six 83.3% it was the only positive node. In the other six

patients SLNB was negative for metastatic disease. No skip metastases were observed. In SLNB negative patients the mean Breslow thickness was 2.06 mm range: 0.60 -7.10 and only one patient showed a high Breslow thickness patient 8. In SLNB positive patients the mean Breslow thickness was 4.33 mm 1.8 -6.0. CONCLUSION: Our data indicate that, even in vulvar melanoma, the sentinel lymph node pathological status predicts the pathological status of the remaining groin nodes and suggests that elective groin dissection can be spared in cases of a negative SLNB. Breslow thickness <1 mm was not predictive of negative nodes.

Trope, C., M. Scheistroen, et al. 2001. "[Surgery and sentinel node examination in early vulvar cancer]." Tidsskr Nor Laegeforen **121**23: 2723 -2727.

BACKGROUND: Less than radical vulvectomy for primary vulvar cancer has been controversial. Less mutilating surgery without sacrificing benefits in prognosis is warranted. MATERIAL AND METHODS: Based on relevant literature and our own experience, we give a review of surgery and sentinel node examination in early vulvar cancer. RESULTS: Regional lymph node metastasis rarely occurs when tumour thickness is less than 1 mm. Smaller lesions < 2 cm in diameter should therefore be treated by wide excision only and without lymph node dissection. Other T1 lesions with deeper invasion should be radically excised with at least 2 cm margins and extend deep to the inferior fascia of the urogenital diaphragm. Complete inguinal-femoral lymphadenectomy should be performed in patients without groin metastases to avoid a small, but definite risk of recurrence, although the incidence of lymph node metastases for all clinical stage I patients is less than 10%. Lymphatic mapping with 99mTechnetium and patent blue technique is a potentially valuable intraoperative tool for assuring removal of the sentinel node most likely to have metastasis, defining the extent of the superficial inguinal lymphadenectomy and identifying uncommon anatomic variations. INTERPRETATION: Until reliable data on the benefits of selective lymphadenectomy using intraoperative lymphoscintigraphy are available, the procedure should only be performed in an approved research setting.

UHN 2015. "Princess Margaret Cancer Centre - Clinical Practice Guidelines - Gynecologic Cancer." http://www.uhn.ca/PrincessMargaret/Health_Professionals/Programs_Departments/Gynecologic/Pages/clinical_practice_guidelines.aspx.

Vakselj, A. and S. Bebar 2007. "The role of sentinel lymph node detection in vulvar carcinoma and the experiences at the Institute of Oncology Ljubljana." Radiol Oncol **41**: 167-173.

Van den Eynden, J., L. Lannoo, et al. 2003. "Sentinel node biopsy in the treatment of vulvar cancer." Tijdschr voor Geneeskunde **59**: 1169-1178.

van der Steen, S., H. P. de Nieuwenhof, et al. 2010. "New FIGO staging system of vulvar cancer indeed provides a better reflection of prognosis." Gynecol Oncol **119**3: 520 -525.

OBJECTIVE: To find out whether the new FIGO staging system introduced 2009 indeed leads to a more specific prediction of the survival for patients with vulvar SCC. METHODS: A retrospective study of 269 patients with vulvar SCC from 1988 to 2009. All patients were staged according the old and revised FIGO staging system by histopathological data. Overall survival OS and disease specific survival DSS were calculated. RESULTS: Of all 269 patients, a total number of 113 patients 4 2.4% was restaged according to the new FIGO staging, mainly downstaged. In patients with negative nodes, tumor size was not predictive for OS $p = 0.475$ and DSS $p = 0.915$. Patients of old FIGO stage III and negative node status showed no difference in survival with the group mentioned above OS $p = 0.105$ and DSS $p = 0.743$, respectively. An increasing number of positive lymph nodes range 1 -9 led to a decrease in survival in OS and DSS $p = 0.022$ and $p = 0.004$ respectively. When corrected for the number of positive nodes, there was no difference in survival between patients with unilateral or bilateral lymph nodes. In patients with positive nodes, extranodal growth showed a significant worse survival compared to patients without extranodal growth OS $p < 0.001$ and DSS $p = 0.004$.

CONCLUSION: The new FIGO staging system provides indeed a better reflection of prognosis for patients with vulvar SCC. An accurate description of clinical and histopathological data combined with information about which FIGO classification has been used is necessary to interpret the literature correctly and to keep the possibility to compare data of different studies.

Van der Velden, J. 1996. "Some aspects of the management of squamous cell carcinoma of the vulva." Thesis. Amsterdam, The Netherlands.

van der Velden, J. 2000. "Surgical interventions for early squamous cell carcinoma of the vulva." Cochrane Database Syst Rev2: CD002036.

BACKGROUND: Radical surgery has been standard treatment for patients with early vulvar cancer since mid century. Survival figures are excellent, but complication rates are high. Over the last two decades, surgical treatment has become more individualised in order to decrease complications in patients with limited disease. **OBJECTIVES:** To determine whether the effectiveness and safety of individualised treatment is comparable with that of more extensive non-individualised surgery. **SEARCH STRATEGY:** The criteria set by the Cochrane Gynaecological Cancer Group were used. We searched Medline and Embase last search on 16 November 1999. We used our own publication archives, based on a prospective handsearch of six leading relevant journals which was started in December 1986. Reference lists of identified studies, gynaecological cancer handbooks and conference abstracts were also used. **SELECTION CRITERIA:** Types of study: RCT's, case control and observational studies on the effectiveness of surgical treatment of vulvar cancer. **TYPES OF PARTICIPANTS:** patients with cT1N0M0 squamous cell carcinoma of the vulva. Types of interventions: local surgical treatment as well as regional lymph node dissection. Types of outcome measurements: overall, disease specific and disease free survival; treatment complications; quality of life issues. **DATA COLLECTION AND ANALYSIS:** The two reviewers independently assessed study quality and extracted data. **MAIN RESULTS:** Only two studies with a total of 94 participants were included in the review. Both were observational studies. None of the other eleven considered studies met the minimum criteria as set by the Cochrane Collaboration. From these two studies, it can be concluded that: 1. radical local excision is as safe as a radical vulvectomy; 2. An ipsilateral lymph node dissection is safe in patients with a well lateralised tumour, and 3. A superficial groin node dissection is not as safe as a full femoro-inguinal groin node dissection. The fourth question we intended to answer is of great clinical importance: is the triple incision technique as safe as an en bloc dissection? This question could only be answered by using some of the unselected studies. From these studies, the triple incision technique appears to be as safe as the en bloc technique. **REVIEWER'S CONCLUSIONS:** The available evidence regarding surgical treatment of early vulvar cancer is generally of poor quality. From the evidence with sufficient quality we conclude that radical local excision, ipsilateral lymph node dissection in lateral tumors and triple incision technique are safe treatment options for early vulvar cancer. However, superficial groin node dissection results in an excess of groin recurrences compared to a full femoro-inguinal groin node dissection.

van der Velden, J., G. Fons, et al. 2011. "Primary groin irradiation versus primary groin surgery for early vulvar cancer." Cochrane Database Syst Rev5: CD002224.

BACKGROUND: Despite changes in technique, morbidity after surgery for vulvar cancer is high and mainly related to the groin dissection. Primary radiotherapy to the groin is expected to result in lower morbidity. However, studies on the efficacy of primary radiotherapy to the groin in terms of groin recurrences and survival show conflicting results. **OBJECTIVES:** To determine whether the effectiveness and safety of primary radiotherapy to the inguinofemoral lymph nodes in early vulvar cancer is comparable with surgery. **SEARCH STRATEGY:** We searched The Cochrane Gynaecological Cancer Group Specialised Register, Cochrane Central Register of Controlled Trials CENTRAL, MEDLINE and EMBASE from 1966 to July 2010. **SELECTION CRITERIA:** We selected randomised clinical trials RCTs comparing inguinofemoral lymph node dissection and primary radiotherapy of the inguinofemoral lymph nodes for patients with early squamous cell cancer of the vulva. **DATA**

COLLECTION AND ANALYSIS: Two reviewers independently assessed study quality and extracted results. Primary outcome measures were the incidence of groin recurrences, patient survival and morbidity. **MAIN RESULTS:** No new RCTs were identified by the updated search. Out of twelve identified papers only one met the selection criteria. From this one small RCT of 52 women, there was a trend towards increased groin recurrence rates relative risk RR 10.21, 95% confidence interval CI 0.59 to 175.78, lower disease-specific survival rates RR 3.70, 95% CI 0.87 to 15.80, less lymphoedema RR 0.06, 95% CI 0.00 to 1.03 and fewer life-threatening cardiovascular complications RR 0.08, 95% CI 0.00 to 1.45 in the radiotherapy group. Primary surgery was associated with a longer hospital stay than primary groin irradiation RR 0.28, 95% CI 0.13 to 0.58. **AUTHORS' CONCLUSIONS:** Primary radiotherapy to the groin results in less morbidity but may be associated with a higher risk of groin recurrence and decreased survival when compared with surgery. Due to the small numbers in this trial and criticisms regarding the depth of radiotherapy applied, corroboration of these findings by larger RCTs using a standardised radiotherapy method, is desirable. However, until better evidence is available, surgery should be considered the first choice treatment for the groin nodes in women with vulvar cancer. Individual patients not physically able to withstand surgery may be treated with primary radiotherapy.

van der Velden, J., C. D. Kooyman, et al. 1992. "A stage Ia vulvar carcinoma with an inguinal lymph node recurrence after local excision. A case report and literature review." *Int J Gynecol Cancer* 23: 157 -159.

A patient with a stage Ia vulvar squamous cell carcinoma < 1 mm invasion is reported in which an inguinal recurrence one and a half years after partial radical vulvectomy and superficial inguinal lymph node sampling was noted. After the initial biopsy showing a tumor invading 0.3 mm into the stroma, residual tumor could not be shown in the vulvectomy specimen nor in the superficial lymph nodes. A review of the literature indicates that this is only the second reported case of stage Ia vulvar carcinoma with lymph node metastases.

van der Velden, J., M. S. Schilthuis, et al. 2004. "Squamous cell cancer of the vulva with occult lymph node metastases in the groin: the impact of surgical technique on recurrence pattern and survival." *Int J Gynecol Cancer* 144: 633 -638.

OBJECTIVE: The triple incision technique is an established surgical method of management for early vulvar cancer. There is only limited data available on the efficacy of this form of treatment for patients with occult inguinofemoral lymph node metastases. It was the objective of this study to obtain more insight into the efficacy of this treatment compared with the en bloc resection, when utilized in surgical pathological advanced disease. **METHODS:** A retrospective review was performed in patients with vulvar cancer in the presence of occult inguinofemoral lymph node metastases. Tumor diameter, extracapsular nodal spread, FIGO stage, number of positive lymph nodes, and type of treatment were analyzed in relation to recurrence pattern and survival in both univariate and multivariate analyses. **RESULTS:** There was no significant impact of surgical technique on disease-specific and overall survival. When corrected for other prognostic variables in a multivariate analysis, the type of surgical treatment was an independent predictor for vulvar recurrence HR 0.10, 95% CI 0.02 -0.44, P = 0.002 but not for inguinal/pelvic recurrence. **CONCLUSION:** The type of surgical technique did not influence disease-specific and overall survival in patients with occult inguinofemoral lymph node metastases. The triple incision technique is an independent poor prognostic variable for vulvar recurrence.

van der Zee, A. G., M. H. Oonk, et al. 2008. "Sentinel node dissection is safe in the treatment of early-stage vulvar cancer." *J Clin Oncol* 266: 884 -889.

PURPOSE: To investigate the safety and clinical utility of the sentinel node procedure in early-stage vulvar cancer patients. **PATIENTS AND METHODS:** A multicenter observational study on sentinel node detection using radioactive tracer and blue dye was performed in patients with T1/2 < 4 cm squamous cell cancer of the vulva. When the sentinel node was found to be negative at pathologic ultrastaging, inguinofemoral lymphadenectomy was omitted, and the patient was observed with follow-

up for 2 years at intervals of every 2 months. Stopping rules were defined for the occurrence of groin recurrences. RESULTS: From March 2000 until June 2006, a sentinel node procedure was performed in 623 groins of 403 assessable patients. In 259 patients with unifocal vulvar disease and a negative sentinel node median follow-up time, 35 months, six groin recurrences were diagnosed 2.3%; 95% CI, 0.6% to 5%, and 3-year survival rate was 97% 95% CI, 91% to 99%. Short-term morbidity was decreased in patients after sentinel node dissection only when compared with patients with a positive sentinel node who underwent inguinofemoral lymphadenectomy wound breakdown in groin: 11.7% v 34.0%, respectively; $P < .0001$; and cellulitis: 4.5% v 21.3%, respectively; $P < .0001$. Long-term morbidity also was less frequently observed after removal of only the sentinel node compared with sentinel node removal and inguinofemoral lymphadenectomy recurrent erysipelas: 0.4% v 16.2%, respectively; $P < .0001$; and lymphedema of the legs: 1.9% v 25.2%, respectively; $P < .0001$. CONCLUSION: In early-stage vulvar cancer patients with a negative sentinel node, the groin recurrence rate is low, survival is excellent, and treatment-related morbidity is minimal. We suggest that sentinel node dissection, performed by a quality-controlled multidisciplinary team, should be part of the standard treatment in selected patients with early-stage vulvar cancer.

Vidal-Sicart, S., B. Domenech, et al. 2009. "[Sentinel node in gynaecological cancers. Our experience]." *Rev Esp Med Nucl* **285**: 221 -228.

Although sentinel lymph node (SLN) identification is widespread used in melanoma and breast cancer some concerns exist in other malignancies, such gynaecologic cancers, and this staging method has not been adopted in many centers due to lack of large validation studies. AIM: To evaluate the applicability and results of SLN technique in gynaecological malignancies referred to our institution. METHOD: We studied 155 patients with different malignancies 70 vulvar, 50 cervical and 35 endometrial cancers. The day before surgery a lymphoscintigraphy was performed by injecting 111 MBq of ^{99m}Tc -nanocolloid in several ways depending on the type of cancer studied. Intraoperative detection of the SLN was always performed by using a hand-held gammaprobe and, in 100 cases with the aid of blue dye injection 70 vulvar and 30 in cervical cancer few minutes before surgical intervention. Pathological study of SLN was performed in all cases. Lymphadenectomy was done in all cervix and endometrial cancer patients and in the first 35 vulvar cancer patients. RESULTS: Pre-surgical lymphoscintigraphy demonstrated one, at least, SLN in 97% of vulvar cancer patients, 92% in the cervical malignancy and 64% in the endometrial cancer patients. During surgery, SLN was harvested in 97%, 90% and 62% of patients, respectively. The pathological study showed metastases in 24.2%, 8.8 and 4.5% of patients with vulvar, cervical and endometrial cancer, respectively. The false negative percentage was 5.5% in vulvar cancer patients, with 2 cases in the endometrial cancer and without any case in the cervical cancer patients. CONCLUSION: Lymphoscintigraphy is a relatively simple and useful technique to identify the SLN in this kind of tumours. However, in endometrial cancer more effort has to be made to reach a suitable result. Sentinel lymph node biopsy seems to be a reliable technique in vulvar and cervical malignancies.

Vidal-Sicart, S., L. M. Puig-Tintore, et al. 2007. "Validation and application of the sentinel lymph node concept in malignant vulvar tumours." *Eur J Nucl Med Mol Imaging* **343**: 384 -391.

PURPOSE: Inguinal lymphadenectomy, unilateral or bilateral, is widely used in cases of vulvar squamous cell carcinoma and melanoma but has a high morbidity. Sentinel lymph node (SLN) biopsy may be used in the management of these patients. The aims of this study were firstly to determine the reliability of SLN biopsy in predicting regional lymph node status and secondly to apply this technique in the routine clinical setting. METHODS: We prospectively studied 70 women with vulvar malignancies. The first 50 cases were of squamous vulvar cancer and were used to validate the SLN technique in this clinical setting validation group. Once a satisfactory success rate had been achieved in the validation group, the SLN technique was applied to a further 20 patients with vulvar malignancies, i.e. squamous cell carcinoma $n=12$ and melanomas $n=8$ application group. Dynamic and static images were acquired after the injection of 74-148 MBq of a colloidal albumin, and continued until SLN identification. Fifteen minutes before surgery, blue dye injection was administered in a

similar manner to the radiocolloid. After incision, a hand-held gamma probe was used to find the SLN. In the validation group, dissection of the SLN was always followed by lymphadenectomy. In the application group, this procedure was only performed if the SLN was positive for metastases. For pathological staging, samples were evaluated using haematoxylin and eosin and immunohistochemistry. RESULTS: In the validation group, lymphoscintigraphy allowed SLN detection in 49/50 patients 98%. Blue dye detected the SLN in 40/50 patients 80%. In 16 patients 33%, the SLN showed metastases in the pathology study. All 33 patients with negative SLN had regional lymph nodes negative for metastases negative predictive value 100%. In the application group, lymphoscintigraphy showed drainage to an SLN in 19 out of 20 patients 95% and blue dye demonstrated a stained SLN in 17/20 patients 85%. Seven of the 19 SLN -identified nodes 37% were positive for metastases. CONCLUSION: SLN identification permits the accurate pathological study of regional nodes and could reduce the high morbidity of current surgical treatment in vulvar tumour patients if the technique were to be adopted on a routine clinical basis.

Vidal-Sicart, S., L. M. Puig-Tintore, et al. 2002. "Localization of sentinel lymph nodes in cancer of the vulva." *Ginecologica y Obstetricia Clinica* **3**: 67-71.

Volgger, B., C. Marth, et al. 1997. "Fulminant course of a microinvasive vulvar carcinoma in an immunosuppressed woman." *Gynecol Oncol* **65**: 177 -179.

Iatrogenic immune suppression following renal transplantation is frequently associated with certain neoplasms, including vulvar carcinoma. We describe a patient with a vulvar carcinoma less than 1 mm depth of invasion and less than 3 mm superficial spread 12 years after renal transplantation. A simple vulvectomy was performed but 4 months later disease recurred in the inguinal nodes. The patient died 20 months later with progressive disease in the retroperitoneum and liver metastases.

Wagenaar, H. C., N. Colombo, et al. 2001. "Bleomycin, methotrexate, and CCNU in locally advanced or recurrent, inoperable, squamous-cell carcinoma of the vulva: an EORTC Gynaecological Cancer Cooperative Group Study. European Organization for Research and Treatment of Cancer." *Gynecol Oncol* **81**: 348 -354.

OBJECTIVE: To investigate tumor response rate and treatment toxicity of a modified combination chemotherapy consisting of bleomycin B, methotrexate M, and CCNU C for patients with locally advanced, squamous-cell carcinoma of the vulva not amenable to resection by standard radical vulvectomy or recurrent disease after incomplete resection. Tumor resectability was reassessed in patients who had responded to chemotherapy. METHODS: The regimen consisted of bleomycin 5 mg intramuscular im days 1 -5, CCNU 40 mg per os po days 5 -7, and methotrexate 15 mg po days 1 and 4 during the first week. During weeks 2-6 the patient was administered bleomycin 5 mg im days 1 and 4, and methotrexate 15 mg po on day 1 of the week. This 6-week cycle was repeated at 49-day intervals. RESULTS: Twenty-five eligible patients with a median age of 66 years range, 39 -82 years were entered in this phase II trial. Twelve patients had primary locally advanced disease, 13 patients had a locoregional recurrence, and all received up to three BMC cycles. Two complete and twelve partial responses were observed response rate, 56%; 95% confidence limits, 35-76%. The BMC regimen was associated with major hematological side effects and mild signs of bleomycin-related pulmonary toxicity. At a median follow-up of 8 months, 3 patients were alive, 18 had died due to malignant disease, 2 had died due to toxicity, and 2 had died due to intercurrent disease and unknown cause. The median progression-free survival was 4.8 months and the median survival was 7.8 months. The 1-year survival was 32% 95% confidence limits, 13 -51%. CONCLUSION: The present data confirm the therapeutic activity of the BMC regimen in locoregionally advanced or recurrent squamous-cell carcinoma of the vulva. Following neoadjuvant chemotherapy, the overall response rate was 56%. BMC is an outpatient treatment that may play a role in the palliative therapy of advanced or recurrent vulva cancer.

Wahlen, S. A., J. D. Slater, et al. 1995. "Concurrent radiation therapy and chemotherapy in the treatment of primary squamous cell carcinoma of the vulva." *Cancer* **75**: 2289 -2294.

BACKGROUND: Interest in combined modality treatment and in quality of life issues may affect the choice of radical vulvectomy as the treatment of choice in many vulvar carcinomas. To evaluate the potential role of combined radiation and chemotherapy with or without local excision as primary treatment for squamous cell carcinoma of the vulva, the outcomes of 19 patients with this disease treated with combination therapy were reviewed. **METHODS:** Nineteen patients were treated between September 1987 and October 1992. Fifteen patients had American Joint Committee on Cancer Stage III disease; 4 had Stage II. All had clinically negative inguinal lymph nodes with the exception of two patients who had positive ipsilateral inguinal nodes that were removed before treatment. The patients received 45-50 Gy to the pelvis and inguinal nodes with concurrent chemotherapy that consisted of 5-fluorouracil given as a 96-hour continuous infusion 1000 mg/m²/d during weeks 1 and 5 of radiation. A single dose of mitomycin-C 10 mg/m² during the first day of chemotherapy has been used since November 1991. Ten patients were boosted with implants or electrons and 6 others underwent local excision. **RESULTS:** The median follow-up was 34 months. Responses were determined clinically 1 month after completion of the radiation and chemotherapy. Clinically, complete responses were obtained in 10 patients 53%, partial responses in 7 37%, and no response in 1; 1 patient progressed during treatment. The combined modality therapy radiation/chemotherapy/ with or without wide local excision resulted in a local control rate of 74% 14/19. All five treatment failures occurred within 6 months of treatment. Four of these patients were rendered disease free by radical vulvectomy and/or exenteration, for an overall local control rate of 95% 18/19. **CONCLUSION:** Concurrent radiation therapy and chemotherapy with local excision performed as needed, appears to be a reasonable alternative to radical vulvectomy in patients with primary squamous cell carcinoma of the vulva. Radical surgery remains a viable option for patients in whom primary therapy has failed.

Whitaker, S. J., P. Kirkbride, et al. 1990. "A pilot study of chemo -radiotherapy in advanced carcinoma of the vulva." *Br J Obstet Gynaecol* **975**: 436 -442.

Advanced squamous cell carcinoma of the vulva (FIGO stages III and IV) has a poor cure rate even with exenterative surgery. We report a pilot study of combined pre-operative chemo-radiotherapy CHT/RT in all patients with advanced vulval carcinoma presenting to St Bartholomew's Hospital between July 1987 and March 1989. Twelve patients have been treated, of whom nine had primary lesions (four FIGO stage III and five stage IV) and three had recurrent disease after simple or radical vulvectomy. Seven patients were treated with an initial split course of CHT/RT: there was one treatment-related death and the others have all died following recurrence with a median disease-free survival of 5 months (range 3 -12) and a median survival of 7 months (range 3 -16). Five patients have received a continuous course of CHT/RT: one died before operation with pulmonary metastases, three patients are disease free at 6 to 9 months, and another patient has been treated with only palliative intent. Toxicity was acceptable in the continuous regimen and this treatment seems to have a promising role in the management of advanced carcinoma of the vulva. A review of the literature on combined therapy is presented.

Wilkinson, E. J., M. J. Rico, et al. 1982. "Microinvasive carcinoma of the vulva." *Int J Gynecol Pathol* **11**: 29-39.

Thirty cases of microinvasive squamous cell carcinoma of the vulva were seen from 1972 to 1978 inclusive. They comprised 37.7% of 77 cases of squamous carcinoma of the vulva seen during this period of time. The results of analysis of multiple factors, including tumor depth and pattern of invasion, nuclear and histologic grade, volume, inflammatory response, presence of vascular invasion, and depth of invasion as compared to the depth of adjacent skin appendages and rete ridges are presented. Two patients were found to have inguinal lymph node metastasis: in one of these patients the tumor was deeper than the adjacent deepest skin appendages while in the second patient skin appendages were not adjacent to the tumor. These tumors measured 2.25 and 1.8 mm in depth, respectively. In both patients the tumor was of high nuclear grade and had a diffuse pattern of infiltration. No nodal metastases were found in patients whose tumors did not invade deeper than 1.5 mm or deeper than the adjacent deepest skin appendage. Tumors measuring 1.5 mm in depth had tumor

volumes under 1,000 mm³. The only death from tumor that occurred in this series occurred in a woman who had a second primary tumor of the vulva following a local excision for her microinvasive carcinoma. The definition and measurements of microinvasive carcinoma of the vulva are discussed and an improved method of measurement is proposed.

Witteveen, P. O., J. van der Velden, et al. 2009. "Phase II study on paclitaxel in patients with recurrent, metastatic or locally advanced vulvar cancer not amenable to surgery or radiotherapy: a study of the EORTC-GCG European Organisation for Research and Treatment of Cancer --Gynaecological Cancer Group." *Ann Oncol* **20**: 1511 -1516.

BACKGROUND: No standard treatment options are available for patients with advanced, recurrent or metastatic vulvar carcinoma not amenable for locoregional treatment. **PATIENTS AND METHODS:** In this phase II study, patients with advanced vulvar cancer received paclitaxel (Taxol) every 3 weeks for up to 10 cycles. Primary objective was response rate. Secondary objectives were response duration and toxicity. Response evaluation was assessed by World Health Organisation criteria, toxicity according to Common Toxicity Criteria. **RESULTS:** Thirty-one women from 10 institutions were included, with a median age of 64 (range 47 -84), of which 29 were assessable for response. On study patients received a median of four cycles (range 1 -10). **SAFETY:** Grade 3 and 4 neutropenia was seen in eight patients (8/29 = 27.6%), which in one patient resulted in neutropenic fever and treatment-related death. Further treatment-related grade 3/4 toxicity includes fatigue in three patients (10.3%) and neuropathy in one patient (3.4%). **EFFICACY:** Overall response was 13.8% (n = 4; two complete responses + two partial responses). With a median follow-up of 24 months, median PFS was 2.6 months (95% confidence interval 2.04-4.21). **CONCLUSION:** Paclitaxel shows moderate activity for local control in advanced vulvar cancer.

Woelber, L., D. Grimm, et al. 2013. "Secondary sentinel node biopsy after previous excision of the primary tumor in squamous cell carcinoma of the vulva." *Ann Surg Oncol* **20**: 1701 -1706.

BACKGROUND: To reduce morbidity of radical groin dissection, the sentinel-node (SLN) procedure was implemented for the treatment of vulvar cancer. It has been proven to be a safe alternative in early-stage disease. Feasibility and safety of the procedure after previous vulvar surgery remain unclear. **METHODS:** A total of 106 patients with primary vulvar cancer undergoing the SLN procedure were analyzed. Seventy-four patients received the SLN procedure concomitant to vulvar surgery [primary-sentinel group (PSG)], whereas 32 patients had vulvar surgery before secondary SLN [secondary-sentinel group (SSG)]. **RESULTS:** SLN detection was possible in all patients. Three (9.4%) patients in the SSG and 30 (40.5%) in the PSG had metastatic spread to the SLN and underwent radical groin dissection. Median interval between vulvar surgery and secondary sentinel was 34 days (range, 7 -98). In the SSG tumor stages were earlier with smaller tumor size (median 19 mm in the PSG vs. 9 mm in the SSG) and lesser invasion depth (4 vs. 2 mm; p < 0.001). There were no groin recurrences in the SSG and 5.4% in the PSG. No significant difference regarding disease-free survival (DFS) could be detected (3-year DFS of 72.5% in the PSG compared with 92.5% in the SSG; median DFS not reached, p = 0.114). Adjusting for potential confounders tumor stage, nodal status, tumor size, invasion depth did not alter the results with regards to DFS. **CONCLUSIONS:** Our results suggest that a secondary SLN procedure after previous vulvar surgery is feasible and can accurately reflect the groin status of selected patients. Ideally, prospective trials should be conducted to verify accuracy and oncologic safety of the procedure.

Woolderink, J. M., G. H. de Bock, et al. 2006. "Patterns and frequency of recurrences of squamous cell carcinoma of the vulva." *Gynecol Oncol* **103**: 293 -299.

OBJECTIVE: To analyze patterns and frequency of recurrences of squamous cell carcinoma (SCC) of the vulva after wide local excision (WLE) and superficial inguinal lymphadenectomy with separate incisions and to identify prognostic factors for the development of recurrences. **METHODS:** Between January 1985 and December 1999, all 125 consecutive patients with primary SCC of the vulva, treated

with WLE and superficial inguinal lymphadenectomy, were retrospectively analyzed. Recurrences were registered by localization as: local, skin bridge, groin or distant. **RESULTS:** A local recurrence was diagnosed in 29 23% patients, 11 9% developed a groin and 4 3% a distant recurrence. No skin bridge recurrences were identified. The 5 years local relapse-free survival was 70%. After a first local recurrence, 72% of these patients developed a second local recurrence. Adjusted for other predictors, older age >74 years is an independent risk factor for local recurrences HR: 2.38; 95% -C.I.: 1.08-5.23 and stage III/IV cancer for developing groin/distant recurrences HR: 3.03; 95% -C.I.: 1.0-9.18. **CONCLUSION:** WLE and superficial inguinal lymphadenectomy with separate incisions result in a high groin recurrence rate in this study; superficial lymphadenectomy should be replaced by deep inguinofemoral lymphadenectomy. After a local recurrence, 72% of the patients developed a second local recurrence. These patients are at high risk and need a close follow-up.

Wydra, D., S. Sawicki, et al. 2005. "Evaluation of sentinel node detection in vulvar cancer." *Nucl Med Rev Cent East Eur* **82**: 128 -130.

BACKGROUND: In vulvar cancer, in a large portion of patients with early stages of the disease, the inguinal lymphadenectomy not only does not influence the overall survival and recurrence rate but may increase the incidence of complications. Sentinel lymph node (SN) detection is a promising technique for detecting groin lymph nodes, which may in future lead to less extensive use of surgical treatment. The aim of the study was to evaluate the feasibility of the sentinel node detection technique in patients with vulvar cancer. **MATERIAL AND METHODS:** Between the years 2003 and 2005, we performed intraoperative lymphatic mapping on 10 patients with planoepithelial vulvar cancer. In eight cases, vulvar lesion was localized centrally, around the clitoris. The extent of the surgery included radical vulvectomy with bilateral inguinal lymphadenectomy in nine cases and unilateral inguinal lymphadenectomy in one case. For the lymphatic mapping, we employed two detection methods: 99mTc -labelled radiocolloid activity 35 -70 MBq and blue dye 3 -5 ml). Both techniques were used in six cases 60%, blue dye only in three cases and radiocolloid only in one case. **RESULTS:** In each patient, we detected at least one sentinel lymph node. Sentinel nodes were localized in 14 of 19 operated groins 73.7%; a total of 25 SNs in all. The mean number of SNs for one groin was 1.78. Nodal metastases were found in four cases. In three cases, metastases were detected only in the SN. In one patient, two SNs with metastases were found in one groin and in the contralateral groin without any SN) there was one unchanged node, which transpired to be metastatic. This can be explained by a complete overgrowth of neoplasm in the lymph node resulting in lymph flow stasis and disabling tracer uptake. In five cases, an SN was found only in one groin of the first case is described above, in the second case the vulvar tumor was localized laterally, opposite to the groin without any SN. In the remaining three cases, we have used only one method of SN detection. **CONCLUSIONS:** Lymphatic mapping in vulvar cancer based on the combined detection technique is a highly accurate method after adequate training of the surgeons.

Zambo, K., E. Schmidt, et al. 2002. "Preliminary experiences with sentinel lymph node detection in cases of vulvar malignancy." *Eur J Nucl Med Mol Imaging* **299**: 1198 -1200.

Lymph node status is the most important prognostic factor in vulvar malignancy. The aim of this pilot study was to explore the clinical significance of radionuclide lymphoscintigraphy in the management of vulvar neoplasms. Eight patients with squamous cell carcinoma and two patients with malignant melanoma of the vulva were studied with 100 MBq technetium-99m nanocolloid Sentscint, OSSKI, Budapest) 1 day before surgery. The location of the sentinel lymph node was checked by a single-head gamma camera-computer system MB 9200, Mediso, Budapest). Vulvectomy with bilateral inguinofemoral lymphadenectomy was performed in each case. At lymphadenectomy, the sentinel lymph node was separately removed and histologically studied. Three of the ten patients had positive sentinel lymph nodes micrometastasis. Five months later one of them had local recurrence of the vulvar cancer, and another had inguinal recurrence of the tumour 6 months postoperatively; the third patient was operated on only recently. Our preliminary results are impressive and suggest that

lymphoscintigraphy is an easy and reliable method for detection of the sentinel lymph node in vulvar malignancy.

Zekan, J., A. Mutvar, et al. 2012. "Reliability of sentinel node assay in vulvar cancer: the first Croatian validation trial." *Gynecol Oncol* **126**: 99 -102.

OBJECTIVE: To evaluate the reliability of sentinel node assay in early stage vulvar cancer patients by using preoperative lymphoscintigraphy. **METHODS:** Technetium-99m colloid albumin was injected intradermally around the tumor for lymphoscintigraphic mapping and intraoperative hand-held gamma probe detection of sentinel nodes. For all patients, sentinel node biopsy was followed by inguinofemoral lymphadenectomy, regardless of the sentinel lymph node status. **RESULTS:** From December 2008 until May 2011, 25 consecutive patients with T1 or T2 stage of vulvar squamous cell cancer were enrolled. The median age of patients was 69 years range, 48 -79. The detection of sentinel lymph node was successful in all 25 patients. A total of 36 sentinel lymph nodes were harvested and metastatic carcinoma was identified in 12 sentinel nodes from 8 patients. There was 1 patient with metastatic non-sentinel lymph node despite the negative sentinel node. Two patients with negative sentinel nodes proven by routine histopathological examination were positive by immunohistochemical staining. The sensitivity, specificity and negative predictive value of sentinel node assay with immunohistochemistry included were 89%, 100%, and 94%, respectively. **CONCLUSIONS:** Lymphoscintigraphy and sentinel lymph node biopsy under gamma-detecting probe guidance proved to be an easy and reliable method for the detection of sentinel node in early vulvar cancer. Immunohistochemical analysis improves the sensitivity for the detection of regional micrometastases. The sentinel node assay is highly accurate in predicting the status of the remaining inguinofemoral lymph nodes. Our results indicate that patients best suited to SLN assay have had a simple punch biopsy to confirm the diagnosis rather than a previous tumor excision. This technique represents a true advance in the selection of patients for less radical surgery.

Zhang, S. H., A. K. Sood, et al. 2000. "Preservation of the saphenous vein during inguinal lymphadenectomy decreases morbidity in patients with carcinoma of the vulva." *Cancer* **89**: 1520 -1525.

BACKGROUND: Traditional inguinal lymphadenectomy includes the removal of a portion of the saphenous vein. The authors hypothesized that preserving the saphenous vein would decrease morbidity without affecting treatment outcome. **METHODS:** A retrospective review of 83 patients with carcinoma of the vulva who underwent inguinal lymphadenectomy between 1990-1998 was performed. Postoperative short term and long term complications were evaluated. **RESULTS:** A total of 139 inguinal dissections were performed in 83 patients. The saphenous vein was preserved in 62 patients and ligated in 77 patients. The clinical characteristics of the patients, the operating time, and the estimated blood loss were not significantly different between the two groups. The incidence rate of short term complications including fever, seroma, phlebitis, lymphocyst, and deep venous thrombosis also was similar. Cellulitis occurred in 39% of the patients who underwent vein ligation compared with 18% of the patients who underwent a vein-sparing procedure $P = 0.006$. Short term < 6 months lower extremity lymphedema occurred in 70% of the vein-ligated group compared with 32% of the vein-spared group $P < 0.001$. Chronic edema ≥ 2 years was present in only 3% of the patients who underwent saphenous vein preservation compared with 32% of those who underwent vein ligation $P = 0.003$. Chronic lymphedema in the vein -spared group was observed in only one patient who received postoperative radiation. Overall, individuals with preservation of the saphenous vein were less likely to develop complications 56% vs. 23%; $P < 0.001$. There was no difference in the rate of incidence of recurrent disease between the two groups. **CONCLUSIONS:** Preservation of the saphenous vein during inguinal lymphadenectomy reduces both the short term and long term postoperative complications without affecting treatment outcome. The saphenous vein should be preserved routinely in patients undergoing inguinal lymphadenectomy.

Zhang, X., X. Sheng, et al. 2007. "Sparing of saphenous vein during inguinal lymphadenectomy for vulval malignancies." *Gynecol Oncol* **105**: 722 -726.

OBJECTIVE: This work was set out to investigate the effect of saphenous vein preservation during inguinal lymphadenectomy for patients with vulval malignancies. **METHODS:** 64 patients with vulval malignancies were allocated into two groups depending on their clinical stages, with one of them 31 patients included being subjected to sparing of saphenous vein and the other to saphenous vein ligated surgery while treated with inguinal lymphadenectomy. The operative time, blood loss, 5-year survival rate, short- and long-term postoperative complications, 5-year survival rate and groin recurrence were selected as the monitored parameters, through which the above two groups were compared with each other using t test, chi2 and life table analysis. **RESULTS:** 1 The median operative time for bilateral inguinal lymphadenectomy was 155 min 130 -170 min in the sparing group, compared to 140 min 120 -170 min in the excision group $P>0.05$. The median intraoperative blood loss was 295 mL 100 - 450 mL in the sparing group, and 270 mL 150 -390 mL in the excision group $P>0.05$. 2 Short -term lower extremity lymphedema occurred with 27 patients 43.5% in the sparing group and 44 patients 66.7% in the excision group $P<0.01$. Still, short -term lower extremity phlebitis was observed with 7 patients 11.3% in the sparing group while 17 developed phlebitis 25.8% in the excision group $P<0.05$. However, there was no statistical difference in postoperative fever, acute cellulites, seroma, or lymphocyst formation. 3 Long -term complication occurrence rate decreased by about 50% in patients subjected to saphenous vein sparing surgery compared with those to ligated surgery, while there was no remarkable difference between two groups in the occurrence rates of phlebitis and deep venous thrombosis $P>0.05$. 4 The overall 5 -year survival rate was 67.3%, with 66.7% and 68.0% for the excision group and the sparing group, respectively $P>0.05$. **CONCLUSION:** The application of saphenous vein preservation technique during inguinal lymphadenectomy for patients with vulval malignancies could significantly decrease the occurrence rate of postoperative complications without compromising outcomes and should be widely put into clinical practice.