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# Outcome and prognostic factors in primary uterine lelomyosarcoma: a rare cancer network study

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**Purpose:** This retrospective multicentric study aims to assess the outcome and prognostic factors in patients with primary uterine leiomyosarcoma, a rare cancer with a definite pathological identity among the different categories of uterine sarcomas.

Methods: Eighty women, treated between 1980 and 2000 in the member institutions of the Rare Cancer Network, were evaluated. Mean of age was 52 years. Fifty-six patients presented with FIGO stage I, 8 FIGO stage II, 8 FIGO stage III, 4 FIGO stage IV, and in 4 patients the stage could not be determined. Regarding grading, 15 patients had grade 1 or 2 disease, 22 patients grade 3, and in 43 patients grade was not assessed. All patients benefited from a TAH-BSO or from a Wertheim operation. Following surgery, 54 patients were treated with pelvic external beam radiation therapy (EBRT), 15 of them receiving also brachytherapy. Twelve patients received also adjuvant chemotherapy. Median follow-up was 32 months (6-240).

Results: The 5-year overall and disease-free survival were 51% and 37%, whereas the 5-year local and locoregional control were 80% and 72%, respectively. A total of 14 local recurrences, 16 locoregional recurrences, and 38 systemic metastases were observed. In univariate analyses (Log-Rank test) the factors influencing significantly the overall survival were age, FIGO stage, and histological grade. Multivariate analysis (Cox model) revealed that previous uterine surgery (curretage or myomectomy), FIGO stage > I, and grade 3 represented independent adverse prognostic factors. EBRT influenced neither overall survival nor local or locoregional control. Thirty-four patients presented with acute toxicity during EBRT, and 8 patients with late toxicity grade 3 or more. The only factor influencing the development of grade 3 or more late toxicity was the use of brachytherapy.

Conclusions: In our series, patients with stage I and grade 1 or 2 disease had a very good prognosis. Patients with previous uterine surgery had a poor prognosis. Adjuvant radiation therapy did not seem to improve either survival or local control. In addition, brachytherapy increased the treatment-related morbidity. Chemotherapy seemed to increase local and systemic control for advanced stages. The patterns of failure and prognostic factors found in this study could be considered in the overall management of this rare cancer.

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# Post-operative HDR bracytherapy and EBT of Invasive endometrial carcinoma; Our 25-year experience

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**Purpose:** At the beginning of 1974, we are started to use high-dose rate brachytherapy and external beam megavoltage teletherapy for uterine (cervix, corpus) carcinoma (Merkaš, Čikarić, Vujnić). From '74 to this time we treated on this way about 30 thousand cases. A retrospective analysis is reported on the results of post-operative irradiation of 526 invasive endometrial carcinoma: St. lb - 192, St. lc - 234, St. II a, b - 77 and IIIa, b, c - 23 patients (FIGO).

**Methods:** HDR brachytherapy (Co-60 or Ir-192): 2 vag. ovoids or vag. cylinder -  $4 \times 7.5$  Gy/0.5 cm, I fraction/w; EBT (x,  $\gamma$ ): midplane pelvic dose 30–40 Gy, 15–20 f, 2 parallel opposite pelvic fields without central Pb shield.

**Results:** Five-year relapse – free survival was: St. lb - 93.5%, St. lc - 80.4%, St. lla, b - 81.8%, At. Illa, b, c - 61.0% and all stages - 85.0%. Pelvic and vaginal relapses were 2.9%, distant metastases were 2.7% and late postirradiation sequelae were 10.6% (G1 - 6.5%, G2 - 3%, G3 + 4 - 1.1% - French-Italian Glossary).

Conclusion: Post-operative HDR brachytherapy and external beam megavoltage therapy of invasive endometrial carcinoma leads to excellent vaginal and pelvic control with few serious late sequelae. Belgrade results (5-year survival) are statistically significant better than average world results (FIGO annual reports - '88, '91, '94) (5-year survival of all stages: Belgrade vs. FIGO - 85% vs. 65.1%, 69.7% and 72.7%).

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### Results of radiation therapy in the management of vaginal carcinoma

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**Purpose:** The aim of this study was to evaluate the results of radiotherapy (RT) treatment for vaginal carcinoma at a single institution in the period of 1990-2000. Twenty three patients with a median age of 65 years (range 38-87) were diagnosed during this time with following stages: in situ-1, st I-2, st II-5, st III-5, st IV-10 patients. Twenty out of 23 had RT.

Treatment: The primary treatment was RT in 20 patients, surgery in 2 patients and no treatment in 1 patient. External RT alone in 6 cases, combined with brachytherapy (BT)(cylinder, remote afterloading Co-60 unit) in 8 cases, in 5 cases RT+BT was combined with surgery and one patient had BT alone. The mean external RT dose was 44 Gy (range 36-60 Gy) to the planning target volume and the mean BT dose was 26 Gy (range 10-46 Gy) prescribed to the depth of 2 cm from the middle of the applicator.

Results: One recto-vaginal fistula and one vesico-vaginal fistula in RT+BT+surgery group. Overall disease free survival (DFS) in alive patients is 46 month (11-84 month), overall survival in RT group was 24 month (1-54 month), in RT+BT group 25 month (6-64 month), in RT+BT+surgery group 31 month (11-84 month) and in BT alone group 1 month.

Conclusion: The clinical stage was the most significant prognostic factor, most of the patients were in advanced stages. Other significant factor was histological type (small cell, adeno-mesonephroid). These data showed that the prognosis for vaginal cancer is poor, especially for advanced stages, median survival for stages I-II was 40 month and for stages III-IV 21 month.

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#### Prognostic significance of microvessel density in endometrial cancer

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**Purpose:** Tumor angiogenesis is an important step in the progression of cancer and the developement of metastases. Microvessel density (MVD) as a marker of angiogenesis might be of prognostic significance in endometrial cancer.

Methods: Immunostaining was performed on paraffin embedded blocks from 71 endometrial cancer patients using CD31. MVD was calculated using magnification 200x and 400x and compared to other prognostic factors (e.g. tumor size, Grading). Average follow-up was 122 months. Kaplan-Meier analysis and Cox-Regression were used for statistical evaluation of recurrence free (RFS) and overall survival (OS).

**Results:** During follow-up, 27% of the patients died, 14% because of endometrial cancer. There was a n.s. tendency to longer survival influenced by tumor size, FIGO stage and Grading. No correlation was found when comparing size and FIGO stage to MVD. MVD correlates to Grading (p=0,07; n.s.), but had no influence on overall or disease free survival estimated by Cox regression.

**Conclusion:** Microvessel density as a marker for angiogenesis correlates to histopathological grading in endometrial cancer, but not to tumor size. Although no correlation to survival was found, angiogenesis may be useful as a target for new therapeutic agents or to optimize radiotherapy.

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# Primary squamous cell carcinoma of the vagina: Experience at the Gustave-Roussy Institute

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Purpose: To analyse the treatment of primary vaginal squamous cell carcinoma (PVSCC) at the Gustave-Roussy Institute between 190 and 1998.

**Patients and Methods:** 104 patients (pts) of median age 65 years (27–90) were treated for a PVSCC. Forty-three patients had a previous history of hysterectomy (2 pts had cervix carcinoma 22 and 30 years before PVSCC). Stages were (FIGO classification): I (n = 29). II (n = 31), III (n = 31)