

# Gynecological Tumours

## Other Gynecological Tumours

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### DNA-LOIDY (DI) AND S-PHASE FRACTION (SPF) AS PROGNOSTIC AND PREDICTIVE FACTORS IN ENDOMETRIAL CANCER

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In 161 patients (pts) with endometrial cancer DI and Spf were measured in a prospective study to evaluate their prognostic and predictive value. Snap frozen tissue gained by hysterectomy and bilateral oophorectomy was prepared for flow cytometric analysis. Stage I or II pts were included in a randomized adjuvant trial comparing tamoxifen (tam) 30 mg p.o. or medroxyprogesterone acetate (mpa) 500 mg p.o. for 2 years with no therapy (tx). Diploid ( $DI \leq 1.1$ ) tumors could be found in 25%, 7 of 38 aneuploid tumors were tetraploid ( $DI: 1.8 - 2.2$ ), and 15 showed a polyploid DNA histogram. Spf was elevated ( $> 5\%$ ) in 46 (30%) of the patients. Significant correlations of DI and Spf were found with classical parameters (stage, grade, histological type) and biochemical factors (estrogen and progesterone receptor status). No correlation was seen with myometrial infiltration or lymph node involvement. In Pts with FIGO stage I ( $n = 105$  pts) aneuploid tumors showed significantly shorter disease-free (DFS) ( $p = 0.0005$ ) and overall (OAS) ( $p = 0.00001$ ) survival. Recurrences ( $p = 0.016$ ) and deaths ( $p = 0.0009$ ) occurred more often in tumors with raised Spf. In these early stages clinical outcome was worst if both factors were unfavourable ( $p = 0.000001$ ). Pts who were treated with adjuvant hormonotx ( $n = 73$  pts) were found to have a better prognosis than pts with no tx ( $n = 88$  pts) ( $p = 0.005$  for DFS and  $p = 0.03$  for OAS). Pts with elevated Spfs  $> 5\%$  had more benefit from endocrine tx than pts with low Spfs ( $p = 0.004$  for DFS and  $p = 0.03$  for OAS). Pts with diploid and aneuploid tumors had prolonged DFS ( $p = 0.005$ ) and OAS ( $p = 0.05$ ), if they had received adjuvant hormonotx. In endometrial cancer, DI and Spf are objective parameters to characterize pts with poor prognosis. Elevated Spf is predictive for a positive response to adjuvant endocrine tx.

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### SIGNIFICANCE OF VULVAR NON-NEOPLASTIC EPITHELIAL DISORDERS IN ETIOLOGY OF VULVAR CANCER. Friedman M., Gynecologic Oncology, Ob/Gyn "B", Rambam Medical Center, The Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel.

The etiology of Vulvar Squamous Cell Carcinoma (VSCC) has not been fully explored. One of the most strongly linked (and most poorly understood) associations with VSCC is vulvar dystrophy, better known to gynecologists as "leucoplakia". Its contemporary classification unites under the name "vulvar non-neoplastic epithelial disorders" (NNED), Lichen Sclerosus (LS) and Squamous Cell Hyperplasia (SCH). The aim of this lecture is to evaluate the data of our 9-year prospective study, when 126 patients were treated. The cardinal point of the study was to assess the malignant ability of NNED among medically treated patients. LS was diagnosed in 68 (54%) cases, SCH in 47 (37%), and in 11 (9%) both lesions coexisted. In all, 10 (8%) of 126 cases developed VSCC. From 68 patients of LS, 5 (7.4%) progressed to malignancy; 3 (6.4%) out of 37 with SCH and 2 (18%) out of 11 from the last group. All these patients failed to complete the treatment advised. None of the treated women developed VSCC.

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### HYPERFRACTIONATED INTRACAVITARY ACCELERATED RADIOTHERAPY (HicART) FOR CARCINOMA OF THE CERVIX Kelly SA, Harrington KJ, Harrison M, Dunn P, Kam K, and Lambert HE Hammersmith Hospital, Du Cane Road, London, W12 0HS, England.

In October 1990 a high dose rate microelectron was installed in our department. Previously, patients with ca cervix undergoing intracavitary radiotherapy (icRT) following external beam treatment received either 20 or 25Gy to point A over 36 to 50 hours using low dose rate  $^{137}\text{Cs}$ . With high dose rate icRT, patients were treated twice daily for 4 or 5 fractions using a 6 hour gap. Applicators were left *in situ* for 48 to 72 hours. To compensate for the increased dose rate, initially a 40% dose reduction was made. 17 patients received 3Gy per fraction to point A. As the morbidity was minimal the dose per fraction was increased to 3.50Gy. 38 patients have now been treated, with a maximum follow up of 30 months.

Stage	Number of patients	Failed to achieve CR	Local recurrence	Metastatic disease
Ib	16	0	0	3
IIa	6	1	2	0
IIb	12	1	1	0
IIIB	4	0	1	0

In 2 patients, the ic applicators became displaced between treatments. 2 patients have died, both of metastatic disease. 1 patient who had pelvic inflammatory disease prior to XRT developed intractable diarrhoea and urinary symptoms and has required a colostomy and an indwelling catheter. 2 patients have persistent cervical ulceration, and 1 patient has a frozen pelvis. None of these has any evidence of local recurrence. These preliminary results show that HicART can be given safely, and this treatment does not appear to compromise local control.

### PROGESTERONE HORMONE AND SEX STEROID RECEPTORS IN RELATION TO S-PHASE FRACTION AND PLOIDY LEVEL IN ENDOMETRIAL CARCINOMA.

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The prognosis for endometrial cancer is correlated to receptor presence and the proliferative activity. Progesterone has an antiproliferative effect on the normal endometrium.

S-phase fraction (SPF) in tumor tissue and plasma levels of progesterone, androstenedione, testosterone were measured in 78 postmenopausal women with the diagnosis of endometrial adenocarcinoma.

There were no linear correlations between the hormone concentrations and S-phase fraction when all the patients were analysed.

The material was divided into subgroups according to grade and ploidy level. A stepwise analysis based on progesterone concentration showed that in well and moderately differentiated tumors the S-phase fraction fell when the progesterone reached a serum level above 0.8 nmol/l. This was also seen if all tumors were included, but more weakly.

Sixty of the tumor tissues were also examined for estrogen and progesterone receptors, by immunohistochemistry. The estrogen-receptor positive tumors were all diploid, while progesterone receptors were also found in aneuploid tumors. ER-positive tumors had a low S-phase fraction compared to the receptor negative ones.

The antiproliferative effect of the progesterone remained even in more malignant tumors. This indicates an importance for the prognosis. The stimulative effect of endogenous estradiol seems to be of limited importance for the proliferative activity.

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### BRACHYTHERAPY IN THE TREATMENT OF CLEAR CELL ADENOCARCINOMA OF VAGINA OR CERVIX. INSTITUT GUSTAVE-ROUSSY EXPERIENCE ON 30 PATIENTS

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Tailored LDR brachytherapy (BT) was used in a conservative approach in young patients (pts) presenting a clear cell adenocarcinoma (CCA) vagina or cervix. From 1974 to 1992, 30 pts were treated at Villejuif. Distilbene (DES) exposure was found in 20 cases (60 %), other drugs exposure or impossible to assess in 7 cases, no exposure in 3 cases. 40 % of pts presented an associated vaginal malformation. The FIGO stage distribution was : 6 I, 9 II (limited 5, extended 3), 9 III, 6 IV B. A nodal histologically proven invasion was observed in 40 % of cases. The treatment began by a surgical laparotomy with external iliac lymphadenectomy and ovarian transposition. The second step was radiation : external beam + BT in case of extended or bulky disease and in case of nodal invasion ; BT alone in one or several sessions in other cases. BT was based on Gustave-Roussy's method : moulded applicator, miniaturized sources, remote afterloading system (Curietron), computerized dosimetry. BT delivered 60 Gy to the primary tumoral site. The results are expressed on 28 pts with a minimal follow-up of 1 year : crude survival 71 %, DFS 68 %, local control by stage IB-IIIB 10/11, ext. II-III 8/11, IVB 1/6 ; complications : digestive (3 Gr. I, 1 Gr. II), urinary (2 Gr. II, 1 Gr. III, vascular (1 Gr. II), gynecological (10 Gr. I, 3 Gr. II). The gynecological organs (ovaries, uterus and vagina) could be preserved in 75 % of cases. One patient delivered a normal child 5 years after conservative treatment based on BT.

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### CLINICAL EXPERIENCES WITH 140 CASES OF UTERINE SARCOMAS Birgit Goetze, Ebert A, Weitzel H

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140 documented cases of uterine sarcoma were treated between 1969 and 1992. First symptoms were bleeding alone, pain in the lower abdominal region or a combination of fluor, bleeding and pain. Histologically, we found 73 leiomyosarcoma (52%), 8 mixed mesodermal sarcomas (6%), 12 carcinosarcomas (8.5%), 35 endometrial stromal sarcomas (25%), 1 reticulosarcoma (0.7%) and 11 no classifiable sarcomas (7.8%). Treatment consisted different surgery techniques alone in 49 patients, in 88 cases patients received no treatment. The tumors were staged utilizing the FIGO classification for carcinoma of the corpus uteri. The median survival (all stages, all treatments) was 44 month, the 3-year survival was 41%, the 5-year survival was only 26%, the 10-year survival was 7.7%. The value of postoperative radiation therapy and other aspects (histology, stage, age, diagnostic and disease free intervals, parity etc.) of these rare gynecologic tumors with poor prognosis will be discussed.