TVS. 26 patients had at least one polyp (total 47, all benign). The sensitivity and specificity of TVS were 85 and 100%, respectively. The corresponding values for office hysteroscopy were 77 and 92%. The low sensitivity of office hysteroscopy was the result of 10 failed procedures because of the presence of cervical stenosis or intrauterine adhesions. SIS failed in 6 of these patients. Significantly more patients preferred TVS to office hysteroscopy ($P < 0.001$). This last finding is in agreement with a report comparing SIS and office hysteroscopy in patients presenting with abnormal uterine bleeding [10].

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III.3 Tamoxifen and Endometrium: Preliminary Results of a Follow-up Study

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SINCE 1992, we have studied the prospective effect of tamoxifen on the endometrium. We compared 2 groups: a group of 381 patients exposed to tamoxifen and a control group of 814 women without breast cancer, never exposed to tamoxifen and without hormone replacement therapy. The main duration of tamoxifen treatment was 14 months. The screening test used to evaluate the endometrium was an endovaginal ultrasonography (US). The endometrial thickness was considered abnormal if equal or superior to 8 mm. The patients with abnormal US were explored by diagnostic hysteroscopy and endometrial biopsy. Treatment by hysteroscopic endometrial ablation or classical surgery was performed if indicated. The compliance to assessment in the control group was worse than in the exposed group. Statistical results were corrected for compliance. Abnormal US was seen at first observation in 166 of the 381 treated patients (prevalence = 43.6%) and in 112 of the 814 controls (prevalence = 13.8%), with relative risk (RR) of 3.2 (2.6–3.9); $P < 0.001$. The mean thickness of the endometrium was 8 mm in the tamoxifen group versus 3 mm in the control group ($P < 0.001$). At first observation, the prevalence of endometrial pathology, confirmed by biopsy was 11.5% in the treated group and 4.1% in the control group. The RR is 2.8 [1.8–4.3] ($P < 0.001$). During the follow-up, within the tamoxifen group, 48 new cases of abnormal US have been observed. These results show an incidence rate (IR) of 22.9 for 100 person-year. Within the control group, 21 new cases of abnormal US occurred (IR = 4.8 for 100 person-year) with a RR of 4.8 (3.02–7.56) ($P < 0.001$) for the tamoxifen group. During the follow-up, 18 new cases of endometrial pathologies occurred in the exposed group. In the control group, 8 new cases were observed. The corrected RR to develop a pathology is 2.3 ($P < 0.05$) for treated versus control group. We observed that the cumulative risk increased regularly. Chi square for trend was significant ($P < 0.001$). No peak of annual incidence seemed to appear. The types of pathology observed by the group during the whole study, were respectively, in the treated group versus the control group: 6 cystic atrophia versus 5; 3 stromal hypertrophia versus none; 43 polyps versus 12; and 9 hyperplasia versus 5. Two well differentiated endometrial adenocarcinomas occurred in the treated group versus 1 in the control group. The 2 patients with endometrial carcinoma were treated with 40 mg of tamoxifen daily. Five seropapillary carcinomas of the ovaries and/or of the peritoneum

occurred in the treated group versus none in the control group. Poisson test for all cancers was highly significant $P < 0.001$). We did not observe a difference in endometrial cancers due to the small number of events in our study. The difference between groups for ovarian and peritoneal cancers can probably be explained by the well known association between breast and ovarian cancer rather than by tamoxifen intake. Our results confirmed that tamoxifen increased the endometrial thickness. In any case, the true endometrial pathologies under tamoxifen were more often benign (55/62).

These results support the hypothesis that tamoxifen, in association with breast cancer, seems to be a 'revealing agent' of benign endometrial abnormalities found in a normal population. The small number of true endometrial pathologies found supports our policy of using an endovaginal echography as the first screening test. Because of the lack of a peak of incidence of pathology under tamoxifen, we propose an annual endovaginal echography as follow-up of the patients treated by tamoxifen.

The design of our study does not allow us to attribute the observed effects to tamoxifen intake alone, but to the global exposition to breast cancer and tamoxifen. Perhaps our current prospective study of women, for which we have an ultrasonography before and during tamoxifen intake, will provide further arguments about the specific effects of tamoxifen on endometrial pathology.

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III.4 Tamoxifen and the Uterus: Potential Uterine Risks of Anti-oestrogens. The Approach of the European Institute of Oncology

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Tamoxifen has been widely used as adjunctive therapy for women with breast cancer because it acts as an excellent anti-oestrogen for breast tissue. However, tamoxifen has been found to be associated with various endometrial pathologies, such as endometrial hyperplasia, endometrial polyps and endometrial carcinoma [De Muylder and colleagues. *Int J Gynecol Pathol* 1991, 36, 127–129]. Transvaginal ultrasonography has been found to be an accurate diagnostic method in assessing endometrial thickness in correlation with various physiological and pathological endometrial conditions. Consistently, an endometrial thickness less than 4–5 mm has been associated with inactive endometrium on biopsy [Granberg S and colleagues. *Am J Obstet Gynecol* 1991, 164, 47–52]. However, transvaginal ultrasonography has limited use in the diagnosis of specific abnormalities because of many false positive monographic findings in patients receiving tamoxifen. Some patients taking tamoxifen show heterogeneous centrally located uterine changes when initially viewed with vaginal probe ultrasound. When such patients are viewed with a technique of fluid enhancement (sonohysterography), some changes thought to be in the endometrium were actually in the proximal myometrium, probably due to reactivation of adenomyosal foci in the form of microcysts [Goldstein SR. *Am J Obstet Gynecol* 1994, 170, 447–451]. The aim of this study is to assess the clinical value of sonohysterography in identifying endometrial diseases among asymptomatic, postmenopausal breast cancer patients treated with tamoxifen 20 mg/day, and to compare its accuracy with that of transvaginal ultrasonography, hysteroscopy and endometrial sampling. © **1998 Elsevier Science Ltd. All rights reserved.**

THE ENDOMETRIUM of 75 tamoxifen-treated patients was scanned by transvaginal ultrasound to evaluate thickness and morphology. Endometrial thickness was measured in the antero-posterior dimension and was considered normal when less than 8 mm. Those patients with endometrial thickness ≥ 8 mm were prospectively evaluated by sonohysterography and subsequently evaluated within 4 weeks by hysteroscopy

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