

# TV sonographic assessment in postmenopausal asymptomatic women

**P. Tsikouras**, *Assist. Prof.*; **G. Galazios**, *Assoc. Prof.*; **V. Liberis**, *Assoc. Prof.*; **A. Bouzaki**, *Assoc. Prof.*;  
**X. Grapsas**, *M.D.*; **G. Maroulis**, *M.D.*

*Department of Obstetrics and Gynecology, Democritus University of Thrace, General Hospital of Alexandroupolis, Alexandroupolis (Greece)*

## Summary

The aim of this study was to evaluate retrospectively the usefulness of transvaginal sonography for the detection of endometrial disease in postmenopausal women without symptoms. The study involved 750 postmenopausal women aged 52-65 (mean 58.5). None of them were on hormone replacement therapy and all had had amenorrhea for more than two years. Transvaginal sonography was performed in 750 women. An endometrium of < 5 mm and non-measurable (627 women) was not investigated further. The 627 cases of this group were reassessed one year later. In the remaining 123 postmenopausal women with suspicious endometrium > 5 mm, 19 endometrial polyps (7.13%), one cervical polyp with extension in the cavity (0.8%), 90 endometrial atrophies (73.17%), ten atrophic endometritis (8.13%), two simple hyperplasias (1.62%), and one hyperplasia with atypia (0.8%) were found. Transvaginal sonography is an efficient and acceptable noninvasive method for the early detection of endometrial pathology in postmenopausal asymptomatic women.

*Key Words:* Transvaginal ultrasound; Endometrial thickness; Postmenopausal asymptomatic women.

## Introduction

Endometrial cancer is the fourth most frequent malignancy in most developed countries [1-4]. The incidence of endometrial cancer in Germany was reported to be approximately 10,000 new cases in 1997, most of which occurred in postmenopausal women [5]. About 3,700 new cases of endometrial cancer are reported in the UK each year and in the US this figure approaches 33,000 per year [6]. The cumulative incidences of endometrial cancer in Sweden and Japan are 1.58% and 0.27%, respectively [7]. Screening by pap smear is not effective in the early tracing of endometrial cancer. Sampling of the endometrial cavity for a pap test brings about quite satisfactory results but has not been established at a routine procedure [8, 9]. The observed continued increase in endometrial cancer during the past few years has attracted the interest of many researchers in finding methods of early diagnosis of endometrial malignancies. The thickness of the endometrium seems to be factor that can under certain circumstances be related to endometrial hyperplasia or endometrial cancer.

Transvaginal sonography is a reliable, non-invasive method for the estimation of the thickness and morphology of the endometrium in postmenopausal women with or without symptoms in whom endometrial cancer is suspected [10, 11]. The objective of this study was to determine early findings of endometrial pathology in postmenopausal women without clinical symptoms utilizing ultrasonography.

## Material and Methods

This is a retrospective study of 750 postmenopausal women in the time period 1/1/99-31/12/06 who were examined at the Department of Obstetrics and Gynecology of Democritus University. Women who had vaginal bleeding or endometrial pathology in the past were excluded. The age of the women ranged between 52 and 65 years, and the period of the established menopause was between three and eight years. None of the women were receiving HRT. A 6.5 MHz scanner transducer was used and ultrasound evaluation of the uterus was both in the transverse and longitudinal axis. Endometrial thickness was measured in the usual manner [12] at the point of maximal thickness. If there was fluid in the endometrial cavity the thickness was calculated by adding the two layers [13, 14]. Endometrial thickness was considered to be normal if it was less than 5 mm. When the endometrial thickness was more than 5 mm, diagnostic curettage in combination with hysteroscopy was performed.

## Results

The method was well tolerated by all women. Transvaginal sonography (TVS) in the above women revealed the following results: 627 (83.6%) had an endometrial thickness of < 5 mm (Group A), 92 (12.26%) had between 5-7 mm (Group B), and 31 (4.13%) had a thickness  $\geq$  8mm (Group C). The thickest endometrium found was 18 mm. Women in Group A were advised to have annual TVS follow-up. Every woman in Group B and C underwent diagnostic curettage under hysteroscopic control. The histological results were as follows: 19 endometrial polyps (7.13%), one cervical polyp with extension to the cavity (0.8%), 90 endometrial atrophies (73.17%), ten atrophic endometritis cases (8.13%), two simple hyperplasias (1.62%), and one hyperplasia with

Revised manuscript accepted for publication April 5, 2007

atypia (0.8%) (Table 1). In the cases of hyperplasia with atypia the endometrial thickness was 9 mm, and in simple hyperplasia it was between 12 and 15 mm. The magnitude of endometrial thickness in atrophies was between 5 and 8 mm and in endometrial polyps it was between 11 and 18 mm. In every case (123) in which hysteroscopy was performed no pathology was revealed and there were no complications (Tables 2 and 3).

TVS was performed a year later in the women of Group A. There were no pathological changes in their sonography. Also, none of them had pathological clinical symptoms.

## Discussion

TVS examination for endometrial pathology includes the measurement of endometrial thickness [15]. In spite of the established association between a thickened endometrial stripe and endometrial carcinoma in postmenopausal women with irregular bleeding, there is a lack of consensus regarding the clinical significance of a thickened endometrial stripe in asymptomatic postmenopausal women. The few larger studies of asymptomatic women have indicated a wide normal range of endometrial thickness in healthy postmenopausal women

Table 1. — Correlation between histologic findings and endometrial thickness by transvaginal scan.

| Thickness of endometrium | 5-7 mm      | > 8 mm     |
|--------------------------|-------------|------------|
| Atypical hyperplasia     | 0           | 1 (0.8%)   |
| Simple hyperplasia       | 0           | 2 (1.62%)  |
| Atrophic endometrium     | 90 (73.17%) | 0          |
| Atrophic endometritis    | 2 (1.62%)   | 8 (6.51%)  |
| Cervical polyps          | 0           | 19 (7.31%) |
| Endometrial polyps       | 0           | 1 (0.8%)   |

Table 2. — Endometrial thickness and histological results.

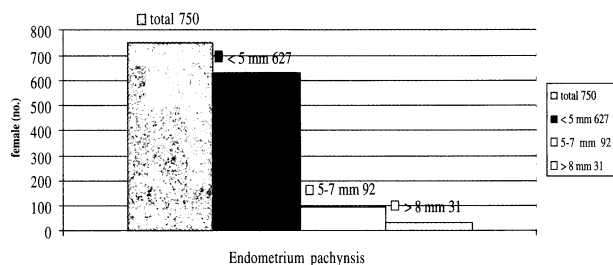
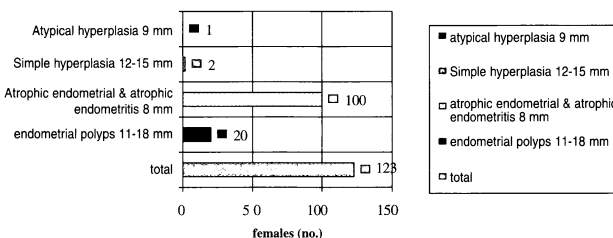


Table 3. — Endometrial thickness of different pathologies.



[14]. It is generally thought that screening for endometrial cancer is not necessary in asymptomatic postmenopausal women [7]; however, there are reports of the presence of endometrial cancer in asymptomatic patients [11, 16, 17]. Koss *et al.* stated that asymptomatic endometrial cancer often develops in an essentially atrophic or focally hyperplastic endometrium [16]. In untreated postmenopausal women without symptoms the prevalence of endometrial abnormality is < 1% [11]. The incidence of asymptomatic endometrial cancer has been reported to be between 1.3 and 1.7 per 1,000 screened postmenopausal women [18]. In postmenopausal women, the maximum thickness of the endometrium is one of the main criteria used in the assessment of sonographic endometrial features. Several studies (despite including both asymptomatic and symptomatic postmenopausal women) using this criterion for the detection of endometrial intracavity pathology are listed in Tables 4 and 5 [11, 19-21, 33]. The application of TVS in gynecology has been very instrumental in the early diagnosis of uterine abnormalities. Endometrial thickness is currently the most reliable sonographic criterion for the early detection of the endometrial neoplasms. The accuracy of sonographic measurement is high [22]. Fleischer *et al.* [23] have related abnormal US findings to endometrial pathology. They found that the sonographically determined endometrial thickness corresponds by  $\pm 1$  mm to the histological measurement. Forrest *et al.* reported that there was a correlation between an endometrial thickness of greater than 5 mm and the presence of simple hyperplasias and hyperplasias with atypia [24]. Auslender *et al.* reported, that endometrium of less than 3 mm is always associated with atrophy, which suggests that in these situations with postmenopausal bleeding, endometrial sampling can be omitted [25]. Bakos *et al.* reported that when the endometrium in women with bleeding was less than 6 mm, no endometrial cancer was found [26]. The determination of endometrial pathology based on TVS control renders the objective use of some measurable parameters necessary. A large multicentric study by Karlsson *et al.* in 1995 [27] revealed that all of the 114 women in whom endometrial cancer was found and 95% of 112 women with hyperplasia had endometrial thickness measured with TVS over 5 mm. All of the above women were postmenopausal and asymptomatic. The researchers of this team came to the conclusion that the risk of finding abnormal endometrium in curettage material when the endometrial thickness measured by TVS was  $\leq 4$  mm is about 5.5%. They also found a woman with endometrial cancer in whom endometrial thickness could not be established. However the same researchers emphasized that 50% of endometrial biopsies could be avoided in this population of women since less than 5 mm of endometrial thickness is considered relatively safe to exclude malignancies but may include other benign endometrial thickness pathology. In the same multicentric Scandinavian study, 2.7% of the women had different kinds of pathology besides cancer (hyperplasias and polyps) [27]. This percentage is comparable to the false-negative results of

Table 4. — Correlation between histologic findings and thickness of endometrium by TVS.

| Authors   | Histological findings of endometrial thickness < 3 mm    | Histological findings of endometrial thickness 3-6 mm     | Histological findings of endometrial thickness > 6 mm      |
|---|--|---|--|
| Fleischer A.C. <i>et al.</i> 2001 (No PMB) <sup>3</sup> | EC <sup>(1)</sup> : 1<br>AH <sup>(2)</sup> : 0           | EC <sup>(1)</sup> : 0<br>AH <sup>(2)</sup> : 4            | EC <sup>(1)</sup> : 1<br>AH <sup>(2)</sup> : 0             |
| Tsuda H. <i>et al.</i> 1995 (No PMB) <sup>3</sup>       | EC <sup>(1)</sup> : 1<br>AH <sup>(2)</sup> : 0           | EC <sup>(1)</sup> : 2<br>AH <sup>(2)</sup> : 2            | EC <sup>(1)</sup> : 3<br>AH <sup>(2)</sup> : 2             |
| Tsuda H. <i>et al.</i> 1997 (No PMB) <sup>3</sup>       | EC <sup>(1)</sup> : 0<br>AH <sup>(2)</sup> : 0           | EC <sup>(1)</sup> : 1<br>AH <sup>(2)</sup> : 5            | EC <sup>(1)</sup> : 0<br>AH <sup>(2)</sup> : 5             |
| Ferrazzi <i>et al.</i> 1996 (PMB) <sup>4</sup>          | EC <sup>(1)</sup> : 2<br>AH <sup>(2)</sup> : 0           | EC <sup>(1)</sup> : 4<br>AH <sup>(2)</sup> : 0            | EC <sup>(1)</sup> : 101<br>AH <sup>(2)</sup> : 7           |
| Randelzhofer <i>et al.</i> 2002 (PMB) <sup>4</sup>      | < 5 mm<br>EC <sup>(1)</sup> : 3<br>AH <sup>(2)</sup> : 0 | 6-10 mm<br>EC <sup>(1)</sup> : 9<br>AH <sup>(2)</sup> : 0 | > 10 mm<br>EC <sup>(1)</sup> : 83<br>AH <sup>(2)</sup> : 0 |

EC<sup>(1)</sup>: Endometrial cancer; (No. PMB)<sup>3</sup>: No postmenopausal bleeding; AH<sup>(2)</sup>: Atypical hyperplasia; (PMB)<sup>4</sup>: Postmenopausal bleeding.

Table 5. — The contribution of measurements of endometrial thickness by TVS to detect endometrial pathology.

| Authors                           | Histological biopsy findings of endometrial thickness ≤ 6 mm | Histological biopsy findings of endometrial thickness > 6 mm | Histological biopsy findings Total                          |
|-----------------------------------|--|--|---|
| Fleischer A.C. <i>et al.</i> 2001 | P. RES <sup>(1)</sup> 5<br>N. P. RES <sup>(2)</sup> 1,745    | P. RES <sup>(1)</sup> 1<br>N. P. RES <sup>(2)</sup> 41       | P. RES <sup>(1)</sup> 6<br>N. P. RES <sup>(2)</sup> 1,786   |
| Tsuda H. <i>et al.</i> 1995       | P. RES <sup>(1)</sup> 5<br>N. P. RES <sup>(2)</sup> 127      | P. RES <sup>(1)</sup> 5<br>N. P. RES <sup>(2)</sup> 13       | P. RES <sup>(1)</sup> 10<br>N. P. RES <sup>(2)</sup> 140    |
| Tsuda H. <i>et al.</i> 1997       | P. RES <sup>(1)</sup> 6<br>N. P. RES <sup>(2)</sup> 339      | P. RES <sup>(1)</sup> 5<br>N. P. RES <sup>(2)</sup> 25       | P. RES <sup>(1)</sup> 11<br>N. P. RES <sup>(2)</sup> 364    |
| Ferrazzi <i>et al.</i> 1996       | P. RES <sup>(1)</sup> 6<br>N. P. RES <sup>(2)</sup> 561      | P. RES <sup>(1)</sup> 108<br>N. P. RES <sup>(2)</sup> 620    | P. RES <sup>(1)</sup> 114<br>N. P. RES <sup>(2)</sup> 1,181 |
| Randelzhofer <i>et al.</i> 2002   | P. RES <sup>(1)</sup> 3<br>N. P. RES <sup>(2)</sup> 98       | P. RES <sup>(1)</sup> 92<br>N. P. RES <sup>(2)</sup> 128     | P. RES <sup>(1)</sup> 95<br>N. P. RES <sup>(2)</sup> 226    |

P. RES<sup>(1)</sup>: Pathologic results; N.P. RES<sup>(2)</sup>: Non pathologic results.

curettage which reach 10% [28, 29]. The percentage of polyps and hyperplasias confirmed histologically in women with an endometrial thickness < 5 mm varied from 0-14% in different studies [30-32].

Statistical analysis of the results of Ferrazzi *et al.*'s study [33] showed that the risk of missing endometrial pathology in thickness < 5 mm was 5.5%, and < 6 mm 8.5%, respectively. According to Mackenzie *et al.* the 5 mm limit is considered relatively safe to exclude pathology and the measured risk of 5.5% is comparable with the false-negative results of the curettage which reach 4-6%. TVS is an efficient and acceptable non-invasive method for early detection of endometrial pathology in postmenopausal women. Thickened endometrium during menopause is the most significant ultrasonographic crite-

ria implicating its pathology [34]. Transvaginal sonography has a very important role in the investigation of postmenopausal woman [35]. The diagnostic success of this method for the correct management depends of course on the experience and training of the examiner. There is a 70% decrease in the cost of future treatment of postmenopausal women, when the results of TVS are under consideration, because more than 70% of the curettages reveal benign histological results [36]. In cases of asymptomatic postmenopausal women with an endometrial thickness > 5 mm, we suggest histological checking of the endometrium with biopsy under hysteroscopic control to exclude the possibility of endometrial pathology which is < 1% in this group of women [37, 38]. Vaginal sonographic, measurement of a thickness of 5 mm and less, gives a relatively safe prediction of endometrial atrophy, whereas thickness above 5 mm requires explorative curettage and histopathologic examination of the endometrium, even if the woman has no uterine bleeding.

## References

- [1] Gambacciani M., Monteleone P., Ciapponi M., Sacco A., Genazzani A.R.: "Clinical usefulness of endometrial screening by ultrasound in asymptomatic postmenopausal women". *Maturitas*, 2004, 48, 421
- [2] Parker S.L., Tong T., Bolden S., Wingo P.A.: "Cancer statistics". *C.A. Cancer J. Clin.*, 1996, 46, 5.
- [3] Endometrial Cancer Mortality Rate "Climbs Sharply", Statistics Show Daily Reproductive Health Report, Reproductive Health Services; 24 September 2001.
- [4] Platz C.E., Benda J.A.: "Female genital tract cancer". *Cancer*, 1995, 75 (suppl.), 270.
- [5] Gerber B., Krause A., Müller H., Reimer T., Külz T., Kundt G., Friese K.: "Ultrasonographic detection of asymptomatic endometrial cancer in postmenopausal patients offers no prognostic advantage over symptomatic disease discovered by uterine bleeding". 2001, 37, 64.
- [6] Bourne T., Hamberger L., Hahlin M., Granberg S.: "Ultrasound in gynecology: endometrium". *Int. J. Gynecol. Obstet.*, 1997, 56, 115.
- [7] Tsuda H., Nakamura H., Takeshi I., Kawamura N., Adachi K., Bandera C.: "Transvaginal ultrasonography of the endometrium in postmenopausal Japanese women". *Gynecol. Obstet. Invest.*, 2005, 60, 218.
- [8] An-Foraker S.H., Kawada C.Y., Mc Kinney D.: "Endometrial aspiration studies on Isaacs cell sampler with cytohistologic correlation". *Acta Cytol.*, 1979, 23, 303.
- [9] Koss L.G., Schreiber K., Oberlander S.G., Moukhtar M., Levine H.S., Mousouri H.S.: "Screening of asymptomatic women for endometrial cancer". *Cancer J. Clin.*, 1981, 31, 300.
- [10] Fleischer A.C., Kalimeris G.C., Machin J.E. *et al.*: "Sonographic depiction of normal and abnormal endometrium with histopathologic correlation". *J. Ultrasound Med.*, 1986, 5, 445.
- [11] Fleischer A.C., Wheeler J.E., Lindsay I., Hendrix S.L., Grabill S., Kravitz B., MacDonald Brian: "An assessment of the value of ultrasonographic screening for endometrial disease in postmenopausal women without symptoms". *Am. J. Obstet. Gynecol.*, 2001, 184, 70.
- [12] Granberg S., Karlsson B., Wikland M., Gull B.: "Transvaginal sonography of uterine and endometrial disorders". In Fleischer A.C., Manning F.A., Jeanry P., Romero R. (eds.): "Sonography in Obstetrics and Gynecology: Principles & Practice", 5<sup>th</sup> edition, Stamford, CT, Appleton & Lange, 1996, 851.
- [13] Fleischer A., Applebaum M., Parsons A.: "Transvaginal sonography of the normal endometrium". In Fleischer A., Kurjak A., Granberg S. (eds.): "Ultrasound and the Endometrium", Progress in Obstetric and Gynecological Sonography Series, New York, Parthenon, 1997, 1.

- [14] Warming L., Ravn P., Skouby S., Christiansen C.: "Measurement precision and normal range of endometrial thickness in a postmenopausal population by transvaginal ultrasound". *Ultrasound Obstet. Gynecol.*, 2002, 20, 492.
- [15] Sit A.S.Y., Modugno F., Hill M.L., Martin J., Weissfeld J.L.: "Transvaginal ultrasound measurement of endometrial thickness as a biomarker for estrogen exposure". *Cancer Epidemiol. Biomarkers Prev.*, 2004, 13, 1459.
- [16] Koss L.G., Schreiber K., Oberland S.G., Mousouris H.F., Lesser M.: "Detection of endometrial carcinoma and hyperplasia in asymptomatic women". *Obstet. Gynecol.*, 1984, 164, 1.
- [17] J.E., Laippala P.J., Gronroo M., Salmi T.A.: "Screening for endometrial cancer in asymptomatic postmenopausal women with conventional and colour Doppler sonography". *Br. J. Obstet. Gynaecol.*, 1999, 106, 14.
- [18] Gull B., Karlson B., Milson I., Wikland M., Granberg S.: "Transvaginal sonography of the endometrium in a representative sample of postmenopausal women". *Ultrasound Obstet. Gynecol.*, 1996, 7, 322.
- [19] Tsuda H., Kawabata M., Kawabata K., Yamamoto K., Hidaka A., Umesaki N., Sachio Ogita: "Differences between Occidental and Oriental postmenopausal women in cutoff level of endometrial thickness for endometrial cancer screening by vaginal scan". *Am. J. Obstet. Gynecol.*, 1995, 172, 1494.
- [20] Tsuda H., Kawabata M., Yamamoto K., Inoue T., Umesaki N.: "Prospective study to compare endometrial cytology and transvaginal ultrasonography for identification of endometrial malignancies". *Gynecol. Oncol.*, 1997, 65, 383.
- [21] Randelzhofer B., Prömpeler H.J., Sauerbrei W., Madjar H., G. Emons: "Value of sonomorphological criteria of the endometrium in women with postmenopausal bleeding: a multivariate analysis". *Ultrasound Obstet. Gynecol.*, 2002, 19, 62.
- [22] Osmers R.G.W., Osmers M., Kuhn W.: "Prognostic value of transvaginal sonography in asymptomatic endometrial cancers". *Ultrasound Obstet. Gynecol.*, 1995, 6, 103.
- [23] Fleischer A.C., Arthur B., Stephens D., Stephen S., Entman D. et al.: "Myometrial invasion by endometrial carcinoma, sonographic assessment". *Rad.*, 1987, 162, 307.
- [24] Forrest T.S., Eiyaderani M.K., Muilenburg M.I., Bewtra C., Kable W.T., Sullivan P.: "Cyclic endometrial changes: Ultrasound assessment with histologic correlation". *Radiology*, 1988, 167, 233.
- [25] Auslender R., Bornstein J., Dirnfeld M., Kogan O., Atad J., Abramovici H.: "Vaginal ultrasonography in patients with postmenopausal bleeding". *Ultrasound Obstet. Gynecol.*, 1993, 3426.
- [26] Bakos O., Smith P., Heimer G.: "Transvaginal ultrasonography for indentifying endometrial pathology in postmenopausal women". *Maturitas*, 1994, 20, 181.
- [27] Karlsson B., Granberg S., Wikland M., Ylostalo P., Torvid K., Marsal K., Valentin L.: "Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding a Nordic multicenter study". *Am. J. Obstet. Gynecol.*, 1995, 172, 1488.
- [28] Grimes D.A.: "Diagnostic dilation and curettage: a reappraisal". *Am. J. Obstet. Gynecol.*, 1982, 142, 1.
- [29] Mac Kenzie L.Z., Bibby J.H.: "Critical assessment of dilatation and curettage in 1029 women". *Lancet*, 1978, 2, 566.
- [30] Osmers R.G., Kuhn W.: "Endometrial cancer screening". *Curr. Opin. Obstet. Gynecol.*, 1994, 6, 75.
- [31] Nasri M.N., Shepherd J.H., Setchell M.E., D.G. Lowe, T. Chard et al.: "The role of vaginal scan in measurement of endometrial thickness in postmenopausal women". *Br. J. Obstet. Gynecol.*, 1991, 98, 470.
- [32] Fleischer A.C., Gordon A.N., Entman S.S., Kepple D.M.: "Transvaginal scanning of the endometrium". *Clin. Ultrasound*, 1990, 18, 337.
- [33] Ferrazzi E., Torri V., Trio D., Zannoni E., Filiberto S., Dordoni D.: "Sonographic endometrial thickness: a useful test to predict atrophy in patients with postmenopausal bleeding. An Italian multicenter study". *Ultrasound Obstet. Gynecol.*, 2003, 7, 315.
- [34] Prömpeler H.J., Madjar H., Wilhelm C., Pfeleiderer A.: "Vaginal sonographie am endometriums in der postmenopause". *Arch. Gynecol. Obstet.*, 1993, 245, 746.
- [35] Prömpeler H.J., Madjar H., Du Bois A., Lattermann U., Wilhelm C., Kommos F., Pfeleiderer A. *Acta Obstet. Gynecol. Scand.*, 1994, 73, 343.
- [36] Granberg S., Wikland M., Karlsson B. et al.: "Endometrial thickness as measured by endovaginal ultrasonography for indentifying endometrial abnormality". *Am. J. Obstet. Gynecol.*, 1991, 164, 47.
- [37] Archer D.F., Mcintyre-Seltman K., Wilborn W.W. Jr., Dowling E.A., Cone F., Creasy G.W., Kafriksen M.E.: "Endometrial morphology in asymptomatic postmenopausal women". *Am. J. Obstet. Gynecol.*, 1991, 165, 317.
- [38] Zacchi V., Zini R., Canino A.: "Transvaginal sonography as a screening method for the identification of patients at risk of postmenopausal endometrial pathology". *Minerva Ginecol.*, 1993, 45, 339.

Address reprint requests to:  
 P. TSIKOURAS, M.D.  
 Department of Obstetrics and Gynecology  
 Democritus University of Thrace  
 General Hospital of Alexandroupolis  
 Lysimachou Petrina  
 68100 Alexandroupolis (Greece)