EJGO European Journal of Gynaecological Oncology

Is intraoperative frozen examination sufficiently reliable for ovarian tumors: 11 years experience at a single center

N.B. Tepe[1], Z. Bozdağ[2], Ö. Balat[1], M.G. Uğur[1], H.Ç. Özcan[1], S. Sucu[1], Ö.K. Karuserci[1], Ö.F. Dizibüyük[2]

[1]Department of Obstetrics and Gynecology, [2]Department of Pathology, University of Gaziantep, Gaziantep (Turkey)

Summary

Objectives: To demonstrate the safety of intraoperative frozen section (IFS) examination in epithelial, borderline, sex-cord stromal (SCST), and germ-cell (GCT) ovarian tumors and to report causes of misdiagnosis in IFS. *Materials and Methods:* Six hundred forty-nine patients with ovarian masses who underwent IFS examination between January 2006 and December 2016 were evaluated retrospectively. The cases were grouped as benign, malignant, borderline, and deferred according to the IFS outcome. Cases that were deferred to permanent section were excluded from the study. According to the permanent paraffin section (PPS) results, epithelial ovarian tumor (EOT), borderline ovarian tumor (BOT), SCST, and GCT subgroups were formed in addition to benign, malignant, and borderline groupings. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the IFS were calculated for each group. Univariate and multivariate analyses were performed to identify the causes of misdiagnosis in IFS. *Results:* The IFS results were malignant, benign, and borderline in 130, 429, and 58 cases; respectively. According to PPS outcome, 143 patients were diagnosed as malignant, 423 were benign, and 51 were borderline. Four-hundred and nine (75.74%) cases were epithelial, 70 (12.96%) cases were GCT, and 61 (11.29%) cases were in the SCST subgroup. Sensitivity, specificity, PPV, and NPV of IFS were 97.89%, 99.60%, 98.94%, and 99.20% in EOT, 66.67%, 95.38%, 40.0%, and 98.41% in GCT, 78.57%, 100%, 100%, and 94.0% in SCST, 78.43%, 96.82%, 68.97%, and 98.03% in borderline tumors, respectively. The most important factors causing misdiagnosis in IFS were mucinous and borderline histology ($p = 0.016$,OR=2.54; $p = 0.001$, OR = 5.74) and tumor size larger than 10 cm ($p = 0.017$, OR = 2.45). *Conclusions:* IFS examination is an effective and reliable method for intraoperative management of ovarian tumors despite some limitations in large tumors (> 10 cm), particularly in tumors of mucinous, teratoma, and borderline histology when evaluated by non-gynecopathologists.

Key words: Frozen section; Ovarian tumor; Epithelial tumor; Germ-cell tumor; Sex-cord stromal tumor.

Introduction

Ovarian cancer is the second most common cancer in women and has the highest mortality rate among gynecological cancers [1]. Epithelial ovarian cancers are commonly diagnosed in advanced stages and require aggressive surgical procedures. However, in certain cases, conservative management can be performed in early stage epithelial ovarian tumors (EOT), sex-cord stromal tumors (SCST), and borderline ovarian tumors (BOT). This is especially true for germ- cell ovarian tumors (GCT), which are seen in the reproductive age and are mostly chemo-sensitive [2]. Intraoperative frozen section (IFS) examination is an intraoperative diagnostic procedure that allows classification of tumors as benign, borderline, and malignant, thus dictating the extent of surgical procedure, especially in patients desiring fertility [3].

The authors' aim is to demonstrate the safety of IFS in all subgroups of ovarian neoplasms compared with permanent paraffin sections (PPS) and to report causes of misdiagnosis in IFS. To the best of their knowledge, this is the first study to show the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) in all subgroups of ovarian tumors in English literature.

Materials and Methods

This retrospective study included 649 patients who underwent explorative laparotomy due to ovarian mass and required IFS examination between January 2006 and December 2016 at Gaziantep University Faculty of Medicine, in the Department of Obstetrics and Gynecology. IFS and PPS results were obtained from the archives of the Department of Pathology at the Gaziantep University Faculty of Medicine. Ethical committee approval was obtained from Gaziantep University Faculty of Medicine (Approval No: 2017/129). The informed consent was not needed because the study was retrospective and did not include personal information of the patients.

Age of the patients, mass characteristics (size, localization, solid-cystic patterns, and presence of ascites), IFS and PPS results, and names of pathologist that evaluated the specimen were recorded.

Oophorectomy or hysterectomy material including the mass was immediately delivered to the laboratory in a fresh state with clinical information. The specimens were examined macroscopically and sections were taken from the most representative areas by the pathologist. The limited number of tissue blocks ranged

Revised manuscript accepted for publication June 4, 2018

from 1 to 3, processed for frozen section according to the size and the macroscopic feature of the mass (including capsular integrity, presence of solid, cystic, haemorrhagic, and necrotic areas). A cryostat was used to cut 5-6 μm thick sections and these were stained by routine Hematoxylin and Eosin (H&E). After examining all the sections by the consultant pathologist, the frozen section report was conveyed to surgeons on telephone. The specimens were then allowed to fix in formalin overnight for routine histopathology process. The detailed gross examination and increased number of sampling were processed for permanent sections. The results of frozen section diagnosis were compared with the permanent section diagnosis.

There were two gynecopathologists and four non-gynecopathologists in the Department of Pathology that randomly reported IFS and PPS results. The cases that could not comment on the malignancy status in the IFS examination were accepted as 'deferred' and excluded from analysis. Results of IFS were classified as benign, malign, borderline, and deferred. PPS diagnoses were divided into three main groups as benign, malign, and borderline tumors and subdivided into EOT, SCST, GCT, non-neoplastic lesions, mesenchymal, hematological, and metastatic tumors.

Deferred cases were excluded from the study while sensitivity, specificity, PPV, and NPV was calculated. Sensitivity, specificity, NPV and PPV of IFS were investigated for EOT, SCST, GCT, and BOT groups. Univariate and multivariate analyzes were performed to identify the factors that led to misdiagnosis in IFS. Sensitivity, specificity, and 95% confidence intervals were calculated using Medcalc version 15.11. Sensitivity and specificity was considered as statistically significant when confidence intervals did not include '1'. Univariate and multivariate binary logistic regression analysis were performed to estimate ORs and 95% CIs.

Results

IFS examination was performed in 649 patients. The mean age was 52.19 (range from 14 to 86) years and the mean size of the tumors was 11.5 (ranged from 2 to 35) cm. In 71 cases, the lesions were bilateral. The distribution of cases according to IFS and PPS results is summarized in Table 1.

Histological distribution of ovarian masses according to PPS results revealed that 418 (64.4%) were epithelial (including 58 borderline tumors), 74 (11.4%) were SCST, 75 (11.6%) were GCT, 59 (9.1%) were non-neoplastic lesions, 19 (2.9%) were metastatic, two (0.3%) were mesenchymal, and two (0.3%) were hematologic neoplasia. The deferred group of patients consisted of nine (28.1%) epithelial, five (15.6%) GCT, 13 (40.6%) SCST, two (6.25%) non-neoplastic lesions, and three (9.37%) metastatic tumors.

There was discordance between IFS and PPS results in 39 cases (6.3%); 5/130 (3.8%) patients in the malignant group, 16/429 (3.7%) in the benign group, and 18/58 (31%) in the borderline group (Table 1). Among these discordant IFS results, 32 (82.1%) were reported by a non-gynecopathologist, while seven (17.9%) were reported by a gynecopathologist. Also, deferred IFS results were reported by a non-gynecopathologist in 30 (93.75%) cases and two (6.25%) were reported by a gynecopathologist.

When the univariate analysis of the cases was performed, tumor size larger than 10 cm ($p = 0.01$, OR = 2.45), borderline, and mucinous histology ($p = 0.001$; OR = 5.74, $p = 0.016$, OR = 2.54) were observed as major causes of the misdiagnosis in IFS results. In multivariate analysis, it was shown that the error rate increased especially in the cases with larger than 10 cm tumors and borderline tumors ($p = 0.05$; OR = 2.1, $p = 0.001$; OR = 5.06) (Tables 2 and 3). The rates of concordance and discordance of IFS and PPS in EOT, SCST, and GCT groups are shown in Table 4.

Table 1. — *The distribution of cases with IFS and PPS results.*

		PPS			Total
		Malign	Benign	Borderline	
IFS	Malign	125	4	1	130
	Benign	6	413	10	429
	Borderline	12	6	40	58
	Deferred	**13**	**15**	**4**	**32**
Total		156	438	55	649

IFS: intraoperative frozen section; PPS: permanent paraffin section.

Overall sensitivity, specificity, PPV, and NPV of IFS results in all ovarian tumors was 95.42%, 99.04%, 96.90%, and 98.57 %, respectively. The highest sensitivity and PPV were observed in the EOT group with 97.89% and 98.94%, the lowest sensitivity and NPV in the GCT group with 66.67% and 40%. Sensitivity, specificity, PPV, and NPV values of EOT, BOT, SCST, and GCT groups are shown in Table 5

Discussion

Management of ovarian neoplasms varies according to histological subtypes. Therefore, it is important for the surgeon to identify the neoplasm in the preoperative period. While ultrasonographic imaging and biochemical evaluation are used preoperatively for neoplasm identification, they are still inadequate especially in early stage cases. For this reason, IFS examination is needed to perform appropriate surgical procedure during an operation. However, the over-diagnosis of IFS examination leads to unnecessary surgical procedures and thus increases morbidity. Conversely, under-diagnosis in the IFS examination leads to the spread of tumor and necessitates another major surgical procedure later [4].

Frozen examination is a distressing process in terms of fertility for the pathologist, especially in young and middle-aged patients. Clinical, laboratory, and imaging method data sent to the pathologist, as well as the experience and technical skill of pathologist are very important in reaching an accurate diagnosis [3].

Most frequent cases of IFS examination are benign masses in the literature. Similarly benign masses were observed to be the most frequent cases of IFS examination in this study [5-7]. Although most of the cases were reported

Table 2. — *Univariate analysis of clinicopathological factors for misdiagnostic cases.*

Variables		Results					
		Accurate (n=578)		Misdiagnosis (n=39)			
		n	%	n	%	Univariate OR [95% CI]	*p*
Age (years)	< 60	381	65.9	29	74.4	1 (reference)	0.283
	≥ 60	197	34.1	10	25.6	0.67 [0.32-1.39]	
Size (cm)	< 10	265	45.8	10	25.6	2.45 [1.18-5.13]	0.017*
	≥ 10	313	54.2	29	74.4	1 (reference)	
Localization	BO	66	11.4	3	7.7	1 (reference)	
	LO	233	40.3	16	41.0	1.51 [0.43-5.34]	0.522
	RO	279	48.3	20	51.3	1.58 [0.46-5.46]	0.472
Tumor histology 1	Borderline	37	6.4	11	28.2	5.74 [2.65-12.42]	0.001*
	Others	541	93.6	28	71.8	1 (reference)	
Tumor histology 2	Mucinous	69	11.9	10	25.6	2.54 [1.19-5.45]	0.016*
	Non-mucinous	509	88.1	29	74.4	1 (reference)	

*OR: odds ratio; CI: confidence Interval; BO: bilateral ovary; LO: left ovary; RO: right ovary. *Significant at 0.05 level.*

Table 3. — *Multivariate analysis of clinicopathological factors for misdiagnostic cases.*

		p	OR	95% CI for OR	
				Lower	Upper
Tumor Histology	Mucinous vs. non-mucinous	0.056	2.131	.980	4.634
Size (cm)	≥ 10 *vs.* < 10	0.040	2.198	1.038	4.657

		p	OR	95% CI for OR	
				Lower	**Upper**
Tumor size (cm)	≥ 10 *vs*. < 10	.051	2.111	.996	4.477
Tumor histology	Borderline *vs.* others	.000	5.063	2.312	11.085

*OR: odds ratio; CI: confidence interval. *Significant at 0.05 level.*

Table 4. — *Concordance and discordance between the results of IFS and PPS.*

		PPS			
		Concordance	Discordance	Total	Total discordance (%)
IFS /EOT	Malign	93	2	95	7.09%
	Benign	247	12	259	
	Borderline	40	15	55	
IFS/GCT	Malign	2	3	5	8.5%
	Benign	62	1	63	
	Borderline	0	2	2	
IFS/SCST	Malign	11	0	11	4.9%
	Benign	47	3	50	

IFS: intraoperative frozen section; PPS: permanent paraffin section; EOT: epithelial ovarian tumor; GCT: germ-cell tumor; SCST: sex-cord stromal tumor

Table 5. — *Sensitivity, Specificity, PPV, and NPV of EOT, BOT, SCST, and GCT.*

	EOT	BOT	SCST	GCT
Sensitivity	97.89%	78.43%	78.57%	66.67%
Specificity	99.60%	96.82%	100.00%	95.38%
PPV	98.94%	68.97%	100.00%	40.00%
NPV	99.20%	98.03%	94.00%	98.41%

PPV: positive predictive value; NPV: negative predictive value; EOT: epithelial ovarian tumor; BOT: borderline ovarian tumor; SCST: sex-cord stromal tumor; GCT: germ-cell tumor.

as benign, the size of mass, high levels of tumor markers, and a gross image resembling malignancy were factors that necessitated an IFS examination.

The highest concordance was found in benign and malignant group when IFS results were compared with the PPS results of the cases. The main reason for this is that malignancy criteria (such as invasion pattern, pleomorphism, and nuclear atypia) were easily recognizable in benign and malignant differentiation. The lowest concordance was detected in the BOT group. These findings of this study correlated with similar studies in the literature [2, 7].

The effectiveness of the IFS has been reported to be quite high with some studies. The accuracy rates of the IFS have increased considerably in the last decade [8-10]. The results of this study indicate that IFS screening has a high sensitivity in intraoperative management of ovarian masses (sensitivity: 95.42%). In most studies, this value has been reported to be between 90% and 97% [11-14]. In the authors' view, sensitivity varies depending on the experience and technical skill of pathologist. Consequently, they re-examined IFS and PPS results according to pathologists that evaluated the specimen. Further analysis of 39 cases with discordance between IFS and PPS results in this study revealed that 32 (82.1%) were reported by a non-gynecopathologists, while seven (17.9%) were reported by a gynecopathologist. In the study conducted by Başaran *et al.* [15], there was no difference in the accuracy of the frozen examination among the cases examined by the gyneco-

pathologist and non-gynecopathologists (98.1% and 96.6%, respectively, $p = 0.56$). Brun *et al.* [16] analyzed the IFS results of 414 patients with epithelial tumors and indicated that IFS diagnosis of BOTs depended mostly on the pathologist's experience. Bige *et al.* [17] compared the results of IFS diagnoses according to the experience of pathologists in gynecologic pathologies. The sensitivity and specificity of the gynecopathologists were higher in all types of tumors.

In this study, the authors observed that the highest sensitivity value of IFS (sensitivity: 97.89%, PPV: 98.4%) was in the EOT subgroup followed with SCST, BOT, and GCT subgroups. The main factor here is that EOT are the most common type in all groups and they have distinctive features, therefore they are more easily recognizable by pathologists. Also, the malignancy criteria are more definable in the EOT group that makes the diagnosis more accurate.

The largest discordance between IFS and PPS results was observed in the GCT group (sensitivity: 66.67%, PPV: 40%), especially mature / immature teratomas at PPS results. The main factor in this misconception is that mucinous epithelium seen in teratomic cases is perceived as a primary epithelial tumors and the stratification observed in the epithelium is attributed to a borderline lesion. The main reason for this discordance in mature teratomas is considered as the areas belonging to the other components are overlooked or not sampled adequately. GCT and SCST may mimic superficial epithelial tumors in IFS examination that makes the diagnosis more difficult [7].

BOT constitute 10-20% of EOT and are histologically characterized by atypical epithelial proliferation without stromal invasion [18]. Differentiation of these tumors from invasive cancers especially in young patients is critically important because BOT do not only have a better prognosis but also requires a more conservative surgical procedure [19]. Studies indicate that the sensitivity of IFS in BOT varies between 48% and 79% [16, 17, 19-21) and the IFS sensitivity in BOT (78.43%, PPV: 68.97%) was similar in our study. Histological type, tumor size, and experience of pathologist were the factors effecting interpretation of IFS examination in BOT that may erroneously lead to misdiagnosis [16, 17, 22-24]. In the present study, the authors believe that the discordance between IFS and PPS probably resulted from misinterpretation of GCT such as mature teratomas, the fact that the epithelial stratification seen in borderline lesions during the sampling was not clearly assessed during IFS, and failure to detect invasive component due to inadequate sampling during IFS.

In the present study, analysis of 32 deferred cases revealed that the majority were SCST (13 SCST, nine EOT, five GCT, three metastases, and two non-neoplastic lesions). Also the experience and technical skill of pathologist counts in deferred cases. In this study, 30 (93.75%) frozen specimens were performed by non-gynecopathologist and two (6.25%) frozen specimens were performed by gynecopathologist in deferred cases. The present authors propose that various histological patterns of SCSTs and also their rare occurrence in routine practice may have resulted in overlooked diagnoses, especially by non- gynecopathologist.

IFS examination in this study had acceptable values in terms of sensitivity, specificity, PPV, and NPV. The diagnosis of only five patients that were reported with malignancy on IFS examination changed on PPS examination (four benign, one borderline in PPS) and tumor size was over 10 cm in all cases. Discordance was detected in 16 (six malignant, ten BOT in PPS) of the benign tumors reported in 429 patients on IFS examination. The tumor sizes were over 10 cm in 13 of these patients and the histologic diagnosis consisted mostly of mucinous histology.

Analysis of cases initially diagnosed with BOT in IFS, 18 had discordance (12 malignant, six benign in PPS). The sensitivity of 78.43% detected in the BOT group is consistent with the sensitivity rate of previous studies [12, 14]. Atypical and invasive characteristics in a large BOT may be common or limited in a single focus. For this reason, a large number of sections should be taken for the final report. Obviously there are difficulties in distinguishing borderline mucinous tumors from borderline serous tumors due to their larger size [14, 25]. The main reasons for the discordance between IFS and PPS in BOT are that they are large in size and they may have benign, borderline, or malignant components in the same tumor [26]. Samples should be taken from the thick and solid regions of the cystic neoplasm. In the present study, the limited number of tissue samples were most probably the main cause for the results that were previously diagnosed as benign in IFS but BOT in PPS or BOT in IFS but malignant in PPS. Examination of IFS and PPS in this hospital randomly by a non-gynecopathologists or a gynecopathologist may also be another factor resulting in discordance.

Misdiagnosis in the IFS examination of BOT was attributed to some clinical factors in previous studies. Houck *et al.* [27] have shown that there may be more misdiagnosis in cases confined to the ovary that have non-serous histology and over 20 cm in size. Brun et al. [16] underlined the importance of experience of the pathologist. In a large study of 354 cases, Song *et al.* [28] emphasized the factors that may cause an error in the IFS examination of BOT are mucinous histology, unilaterality, and a tumor size larger than 15 cm. Similarly misdiagnosis of BOTs was more common with larger tumors and mucinous histology in our study.

The IFS examination actually gives the pathologist an advantage because the specimen is sent in total. The pathologist would have seen the entirety of the sample in gross form, before the specimen is sliced in sections. The IFS technique or the tumor type may of course be misleading due to its own properties. The pathologist's responsibility is to be aware of these misconceptions, reduce the false pos-

itive and false negative rates, and inform the surgeon. Examination of the gross appearance, size, color, presence of solid-cystic-papillary components, and content of the mass, presence of necrosis, haemorrhage, and capsule invasion provides a reduction in the number of tumors to be considered in differential diagnosis. However there may be some obstacles on microscopic evaluation such as frozen artefacts that may camouflage underlying cytological features [29, 30].

To the best of the present authors' knowledge, this study is the first to show the sensitivity, specificity, PPV, and NPV values of all subgroups of ovarian tumors. In previous studies, the susceptibility of frozen specimens in benign, malignant, and borderline lesions were studied without respect to subgroup analysis. Also, the authors analyzed the factors which could potentially influence the accuracy of IFS and found that the most important factors of misdiagnosis in univariate and multivariate analyses were tumor size larger than 10 cm, borderline, and mucinous histology.

Conclusions

IFS examination is an effective and reliable method for intraoperative management of ovarian tumors despite some limitations in large tumors, particularly in tumors of mucinous and teratoma histology when evaluated by non-gynecopathologists. Since there may be sampling errors in the IFS examination, more cross-sections should be performed in order to minimize these errors and find the most concordant diagnosis with PPS results. The reliability of the frozen specimen could be further improved by increasing the number of frozen samplings in large tumors, obtaining samples from the most suspicious areas in masses that are likely to be non-epithelial tumors, and interpreting the samples by an experienced gynecopathologist. Careful consultation of the cases between the surgeon and the pathologist is important, especially in tumors with borderline or non-epithelial histology.

Acknowledgement

This study was presented in part at the 25th European Congress of Obstetrics and Gynecology, 15th Congress of Turkish Society of Obstetrics and Gynecology, Antalya, Turkey, May 17-21, 2017 (Oral presentation No.S-131).

References

[1] Morton R., Anderson L., Carter J., Pather S., Saidi S.A.: "Intraoperative frozen section of ovarian tumors: A 6- year review of performance and potential pitfalls in an Australian tertiary referral center". *Int. J. Gynecol. Cancer*, 2017, *27*, 17.

[2] Subbian A., Devi U.K., Bafna U.D.: "Accuracy rate of frozen section studies in ovarian cancers: A regional cancer institute experience". *Ind. J. Cancer*, 2013, *50*, 302.

[3] Acıkalın A., Torun G., Bagır E., Bayram F., Zeren H., Gulec U., et al.: "İntraopertaive frozen section in ovarian neoplasms; a tertiary center experience". *Turk. Patoloji. Derg*., 2014, *30*, 184.

[4] Tempfer C.B., Polterauer S., Bentz E.K., Reinthaller A., Hefler L.A.: "Accuracy of intraoperative frozen section analysis in borderline tumors of the ovary: a retrospective analysis of 96 cases and review of the literature". *Gynecol. Oncol*., 2007, *107*, 248.

[5] Tangjıtgamol S., Jesadapatrakul S., Manusurivithaya S., Sheanakul C.: "Accuracy of frozen section in diagnosis of ovarian mass". *Int. J. Gynecol. Cancer*, 2004, *14*, 212.

[6] Malipatil R., Crasta J.: "How accurate is intraoperative frozen section in the diagnosis of ovarian tumors?". *J. Obstet. Gynaecol. Res*., 2013, *39*, 710.

[7] Hashmi A.A., Naz S., Edhi M.M., Faridi N., Hussain S.D., Mumtaz S., *et al.*: "Accuracy of intraoperative frozen section for the evaluation of ovarian neoplasms: an institutional experience". *World J. Surg. Oncol.*, 2016, *14*, 91.

[8] Slavutin L., Rotterdam H.: "Frozen section diagnosis of serous epithelial tumors of the ovary". *Am. J. Diag. Gynecol Obstet*., 1979, *1*, 89.

[9] Hamed F., Badia J., Chuagui D., Wild R., Barrena N., Oyarzun E., *et al.*: "Role of frozen section biopsy in the diagnosis of adnexal neoplasms". *Rev. Chil. Obstet. Ginecol.,* 1993, *58*, 361.

[10] Cuello M., Galleguillos G., Zarate C., Cordova M., Branes J., Chuaquri R., et al.: "Frozen section biopsy in ovarian neoplasm diagnosis. Diagnostic correlation according to diameter and weight in tumors of epithelial origin". *Rev. Med. Chil*., 1999, *127*, 1199.

[11] Jacobs I., Menon U.: "The sine qua non of discovering novel biomarkers for early detection of ovarian cancer: carefully selected preclinical samples". *Cancer Prev. Res*., 2011, *4*, 299.

[12] Kokka F., Singh N., Reynolds K., Oram D., Jeyerajah A., Hassan L., *et al.*: "The accuracy of frozen section diagnosis in apparent early ovarian cancer-results from a UK centre". *Histopathology*, 2009, *55*, 756.

[13] Pinto PB, Andrade LA, Derchain S.F.: "Accuracy of intraoperative frozen section diagnosis of ovarian tumors". *Gynecol.Oncol*., 2001, 81, 230.

[14] Puls L., Heidtman E., Hunter J.E., Crane M., Stafford J.: "The accuracy of frozen section by tumor weight for ovarian epithelial neoplasms". *Gynecol. Oncol*., 1997, *67*, 16.

[15] Basaran D., Salman C.M., Boyraz G., Selcuk I., Usubutun A., Ozgul N., et al.: "Accuracy of Intraoperative Frozen Section in the Evaluation of Patients with Adnexal Mass: Retrospective Analysis of 748 Cases with Multivariate Analysis". *Pathol. Oncol. Res*., 2015, *21*, 113.

[16] Brun J.L., Cortez A., Rouzier R., Callard P., Bazot M., Uzan S., et al.: "Factors influencing the use and accuracy of frozen section diagnosis of epithelial ovarian tumors". *Am. J. Obstet. Gynecol*., 2008, *199*, 244e1.

[17] Bige O., Demir A., Saygili U., Gode F., Uslu T., Koyuncuoglu M.: "Frozen section diagnosis of 578 ovarian tumors made by pathologists with and without expertise on gynecologic pathology". *Gynecol. Oncol*., 2011, *123*, 43.

[18] Trillsch F., Mahner S., Ruetzel J., Harter P., Ewald-Riegler N., Jaenicke F., *et al.*: "Clinical management of borderline ovarian tumors". *Expert Rev. Anticancer Ther.,* 2010, *10*, 1115.

[19] Boran N., Cil A.P., Tulunay G., Ozturkoglu E., Koc S., Bulbul D., *et al.*: "Fertility and recurrence results of conservative surgery for borderline ovarian tumors". *Gynecol. Oncol*., 2005, *97*, 845.

[20] Anastasiadis P.G., Romanidis K.N., Polichronidis A., Koutlaki N.G., Tamiolakis D., Simoopoulos K.: "The contribution of rapid intraoperative cytology to the improvement of ovarian cancer staging". *Gynecol. Oncol*., 2002, *86*, 244.

[21] Baker P., Oliva E.: "A practical approach to intraoperative consultation in gynecological pathology". *Int. J. Gynecol. Pathol*., 2008, *27*, 353.

[22] Desfeux P., Camette S., Chatellier G., Blanch B., Querleu D., Lecuru F.: "Impact of surgical approach on the management of macroscopic early ovarian borderline tumors". *Gynecol. Oncol*., 2005, *98*, 390.

[23] Geomini P., Bremer G., Kruitwagen R., Mol B.W.: "Diagnostic accuracy of frozen section diagnosis of the adnexal mass: a meta-analysis". *Gynecol. Oncol*., 2005, *96*, 1.
[24] Heatley M.K.: "A systemic review of papers examining the use of intraoperative frozen section in predicting the final diagnosis of ovarian lesions". *Int. J. Gynecol. Pathol*., 2012, *31*, 111.
[25] Ilvan S., Ramazanoglu R., UlkerAkyıldiz E., Calay Z., Bese T., Oruc N.: "The accuracy of frozen section (intraoperative consultation) in the diagnosis of ovarian masses". *Gynecol. Oncol.,* 2005, *97*, 395.
[26] Akrivos N., Thomakos N., Sotiropoulou M., Rodolakis A., Antsaklis A.: "Intraoperative consultation in ovarian pathology". *Gynecol. Obstet. Invest*., 2010, *70*, 193.
[27] Houck K., Nikrui N., Duska L., Chang Y., Fuller A.F., Bell D.: "Borderline tumors of the ovary: correlation of frozen and permanent histopathologic diagnosis". *Obstet. Gynecol*., 2000, *95*, 839.
[28] Song T., Choi C.H., Kim H.J., Kim M.K., Kim T.J., Lee J.W., *et al.*: "Accuracy of frozen section diagnosis of borderline ovarian tumors". *Gynecol. Oncol*., 2011, *122*, 127.
[29] Usubutun A., Altinok G., Kucukali T.: "The value of intraoperative consultation (frozen section) in the diagnosis of ovarian neoplasms". *Acta Obstet. Gynecol. Scand*., 1998, *77*, 1013.
[30] Youngh R.H.: "From Krukenberg to today: The ever present problems posed by metastatic tumors in the ovary: part I. Historical perspective, general principles, mucinous tumors including the krukenberg tumor". *Adv. Anat. Pathol*., 2006, *13*, 205.

Corresponding Author:
N. BAYRAMOGLU TEPE, M.D.
Department of Obstetrics and Gynecology
University of Gaziantep, School of Medicine
27310 Gaziantep (Turkey)
e-mail: drneslihantepe@gmail.com