

Ultrasound in Gynecological Cancer: Is It Time for Re-evaluation of Its Uses?

Daniela Fischerova¹ · David Cibula¹

Published online: 17 May 2015
© Springer Science+Business Media New York 2015

Abstract Ultrasound is the primary imaging modality in gynecological oncology. Over the last decade, there has been a massive technology development which led to a dramatic improvement in the quality ultrasound imaging. If performed by an experienced sonographer, ultrasound has an invaluable role in the primary diagnosis of gynecological cancer, in the assessment of tumor extent in the pelvis and abdominal cavity, in the evaluation of the treatment response, and in follow-up. Ultrasound is also a valuable procedure for monitoring patients treated with fertility-sparing surgery. Furthermore, it is an ideal technique to guide tru-cut biopsy for the collection of material for histology. Taking into consideration that besides its accuracy, the ultrasound is a commonly available, non-invasive, and inexpensive imaging method that can be carried out without any risk or discomfort to the patient; it is time to reconsider its role in gynecologic oncology and to allocate resources for a specialized education of future experts in ultrasound imaging in gynecology.

Keywords Ultrasound · Cervical cancer · Endometrial cancer · Ovarian cancer · FIGO staging · IOTA

This article is part of the Topical Collection on *Gynecologic Cancers*

✉ Daniela Fischerova
daniela.fischerova@seznam.cz

¹ Gynecologic Oncology Centre, Department of Obstetrics and Gynecology, First Faculty of Medicine and General University Hospital, Charles University in Prague, Apolinarska 18, 120 00 Prague, Czech Republic

Introduction

In the last five years, our view on the use of imaging in gynecological malignancies, in particular of ultrasound diagnostics, has changed dramatically. The inclusion of ultrasound imaging alongside modern imaging methods in gynecological oncology was limited until recently. In the assessment of cervical cancer, for example, ultrasound was only recommended to detect renal pelvic dilatation. Ultrasound has, however, undergone significant technical development in the last ten years. In particular, the development of high-resolution endovaginal probes allows a detailed view of the pelvic anatomy comparable to magnetic resonance imaging (MRI) and has led to the routine use of ultrasound in gynecology. Transabdominal scans provide detailed information on the status of parenchymatous organs, lymph nodes, and peritoneum in the abdomen. Ultrasound has the additional advantages of being cheap, commonly available, and posing no risk or discomfort for the patient (Table 1).

Many recent prospective single-unit and multicenter studies that were carried out under strictly defined protocols for ultrasound, clinical, and histopathological examinations demonstrated high accuracy in regard to preoperative ultrasound diagnostics and staging of gynecological cancers. For interested readers, a very detailed set of reviews addressing all these studies was published last year [1•, 2•, 3•, 4•, 5•]. Furthermore, ultrasound is an optimal technique to guide tru-cut biopsy for the collection of material for histology from inoperable, metastatic, or recurrent tumors in order to start appropriate treatment without any delay [6, 7].

International unification of ultrasound terminology and methodology as well as compliance with uniform diagnostic algorithms should ensure maximum objectivity of examination and reproducibility of results, even in the hands of a less-experienced sonographer. A very good example is the

Table 1 Comparison of different imaging methods for application in ovarian cancer patients

	Ultrasound	MRI	CT	PET/CT
Costs (approximate)	1×	4×	2×	6×
Availability	Universal	Specialized centers	Most hospitals	Specialized centers, such as university hospitals
Examination duration (min)	15–20	30–45	1	30
Dynamic examination ^a	Yes	No	No	No
Preparation before imaging	None	Antiperistaltic agents	4 h fasting	4 h fasting and 1 h physical rest
Contrast agent	None	Gadolinium-based ^b	Iodine-based	FDG-radiotracer and iodine-based
Radiation exposure	None	None	10–20 mSv	20–30 mSv
Limitation for application	None	Claustrophobia, metal components, cochlear implants, cardiac pacemaker	Contraindication for iodine-based contrast agent: renal insufficiency, hyperthyroidism, iodine allergy	Contraindication for iodine-based contrast agent: renal insufficiency, hyperthyroidism, iodine allergy
Dependence of expertise	Yes	Yes	Yes	Yes

CT computed tomography, MRI magnetic resonance imaging, PET/CT positron emission tomography combined with CT, FDG ¹⁸F-fluoro-deoxyglucose

^a Ultrasound can provide information on site-specific tenderness and information on how pelvic structures move in relation to each other (sliding effect) [51]

^b In patients with renal insufficiency, gadolinium-based contrast media must be used with caution [52]

effective, objective, and reproducible work-up of preoperative differentiation between benign and malignant ovarian lesions presented by a working group, IOTA (the International Ovarian Tumor Analysis) [8–13].

In many leading gynecological oncology units, ultrasound is already accepted as an obligatory imaging method, significantly affecting the management of gynecological cancer treatment and the cost of implementation into routine care in these centers is considered to be a very good investment.

Cervical Cancer Imaging

Gynecological oncologists require for an adequate treatment planning an accurate information on tumor size and location (tumor topography within the cervix), the presence of infiltrated parametria, and lymph node status. In 2009, the International Federation of Gynecology and Obstetrics (FIGO) undertook a review of the clinical staging of cervical cancer, which recommends the use of modern imaging methods in determining these significant prognostic parameters [14].

Magnetic resonance imaging, due to the ability of high tissue resolution in the pelvis, is offered as a suitable technique for determining the local stage of cervical cancer [15]. On the other hand, it is not a broadly available technique and has known contraindications for the patient (Table 1). Its accuracy and usage depend on the presence of an experienced radiologist with knowledge of gynecologic oncology. Therefore, data reporting high accuracy of MRI in the staging of cervical cancer, which mostly came from single-unit studies, was not confirmed in a multicenter study organized by the American College of Radiology Imaging Network (ACRIN) and Gynecology Oncology Group (GOG) [16–19].

Conversely, an ultrasound scan can be carried out directly by gynecological oncologists with all the benefits that their knowledge of the disease brings. High-resolution endoluminal probe allows a detailed view of the pelvic structures comparable to MRI. The probe can be introduced transvaginally or transrectally. The transrectal approach is preferred for cervical cancer due to the risk of bleeding from the tumor while performing transvaginal scan. Additionally, the transrectal approach guarantees better acoustic conditions to show the distal portion of the cervix [20]. The combination of transvaginal and transabdominal ultrasound allows the complete assessment of the abdomen and pelvis for staging of cervical cancer (Fig. 1) [21]. In the case of para-aortic lymph node involvement, the assessment can also be supplemented with an examination of peripheral supraclavicular nodes using ultrasound linear array probe.

Local Staging in Patients With Early-Stage Disease

One of the largest prospective studies comparing the diagnostic accuracy of ultrasound and MRI in the local staging of

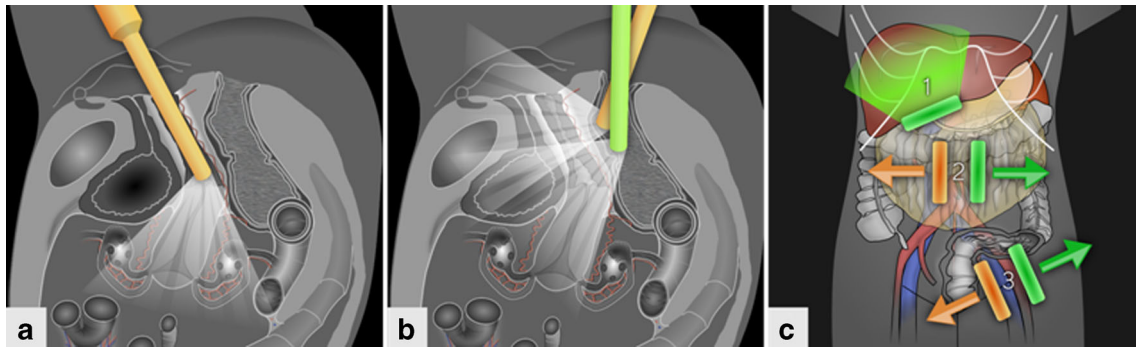


Fig. 1 Ultrasound for cervical cancer staging. Transvaginally inserted probe (a). Transrectally inserted probe (b). Transabdominal scanning (c), including steps of transabdominal scanning (1—evaluation of

parenchymatous organs; 2—assessment of peritoneal surfaces including omentum; and 3—detection of inguinal, retroperitoneal and visceral lymphadenopathy)

cervical cancer was published by Fischerova et al. in 2008 and included 95 patients with early-stage disease [22]. The study showed a significantly higher accuracy of ultrasound when compared with MRI in tumor identification and identification of residual tumor after previous biopsy (93.7 vs 83.2 %, $p \leq 0.006$) and in the measurement of tumors including small tumors $\leq 1 \text{ cm}^3$ (90.5 vs 81 %, $p \leq 0.049$). Achieving these results was made possible by a significant improvement in the technical quality of the ultrasound device, which included the ability to detect an enhanced perfusion within a tumor assessed by a sensitive color Doppler in the majority of cases (98 % of cases). The data confirmed the insignificantly higher accuracy of ultrasound in the evaluation of parametrial spread compared to MRI (99 vs 95 %, $p \leq 0.219$).

Promising data were validated a year later in a study of Testa et al. on 75 patients with early-stage disease [23]. Ultrasound detected the presence of a tumor, deep stromal tumor invasion, infiltrated parametria, and other monitored parameters with accuracy at least similar to or greater than MRI.

The verification of previous study results in a multicenter prospective study was crucial for the general acceptance of ultrasound in the staging of cervical cancer. A European multicenter trial initiated by Epstein et al. ran from 2007 to 2010 and consequently included 182 patients with histologically confirmed early-stage cancer [24]. Results of a study published in 2013 are presented in Table 2. The diagnostic agreement between ultrasound and pathology was significantly better at detecting residual tumor and parametrial invasion than MRI ($p < 0.001$). A surprising finding was the maintenance of diagnostic accuracy of ultrasound in the detection of residual tumor after cone biopsy, where it is difficult to distinguish postinflammatory and reparative changes after the procedure from the presence of residual tumor.

Parameters for Individualized Surgical Treatment

In addition to evaluation of the local extent of the disease, it was necessary to verify whether ultrasound is also able to reliably determine the parameters necessary for the

individualization of surgical treatment. In a prospective study of Fischerova et al. of 99 patients with early-stage cervical cancer, the accuracy of ultrasound in the measurement of the lateral tumor-free margin reached an accuracy of 87.5 %, sensitivity and specificity of 91.3 and 86.2 %, positive and negative predictive values of 70.0 and 96.6 % [25]. A lateral tumor-free margin were evaluated as a shortest distance between the tumor and pericervical fascia at the point where ventral, lateral, and dorsal parametria attached to the cervix. In this study, a cranial tumor-free margin was also measured (a shortest distance between the upper edge of the tumor and the internal cervical os) to assist in the planning of fertility-sparing therapy with a proven accuracy of 94.3 %, a sensitivity of 91.3 %, a specificity of 95.4 %, and positive and negative predictive values of 87.5 and 96.9 %, respectively [25].

Preoperative Assessment of Infiltrated (Metastatic) Lymph Nodes

In early-stage cervical cancer, the sensitivity of ultrasound in the detection of positive lymph nodes was low (38–43 %) [25, 26]. It is important to emphasize that in these two recent studies the positive (infiltrated) lymph nodes were of normal size in most cases (median maximum size of affected nodes 14.0 mm, the minimum and maximum range of 0.7 to 25.0 mm), and the metastases were detected mainly only microscopically (median size of intranodal metastasis 3.5 mm, minimum and maximum range from 0.3 to 20.0 mm) [25]. At the same time, ultrasound achieved high specificity (96 %) in the assessment of lymph nodes [25, 26].

Other modern imaging methods have similar limitations in the detection of affected nodes in early stages of cervical cancer. Magnetic resonance imaging evaluates the affected nodes based on their size ($>10 \text{ mm}$ in short-axis), changes in shape (rounded lymph node), the presence of irregular node edges, necroses, and signal intensities within the nodes similar to the primary tumor [15]. Positron emission tomography combined with computed tomography (PET/CT) also has its limitations when displaying lesions smaller than 5–

Table 2 Sensitivity, specificity, agreement, and kappa values of ultrasound (US) and magnetic resonance imaging (MRI) in the evaluation of residual tumor, tumor size, and extension of cervical cancer using histology as a reference standard (*n*=182)

US	Histology		Results	MRI	Histology		Results	Comparing US to MRI
	No	Yes			No	Yes		
Residual tumor detection								
No	27	5	Kappa = 0.84 (95% CI, 0.74-0.95)	No	20	16	Kappa = 0.52 (95% CI, 0.36-0.68)	-
Yes	3	147	Sens = 90%	Yes	10	136	Sens = 67%	p = 0.008
			Spec = 97%				Spec = 89%	p = 0.005
			Agreement = 96%				Agreement = 86%	p < 0.001
Tumor < 2 cm								
No	71	11	Kappa = 0.78 (95% CI, 0.69-0.87)	No	67	13	Kappa = 0.71 (95% CI, 0.61-0.81)	-
Yes	9	91	Sens = 89%	Yes	13	89	Sens = 84%	p = 0.29
			Spec = 89%				Spec = 87%	p = 0.56
			Agreement = 89%				Agreement = 86%	p = 0.24
Tumor > 4 cm								
No	148	7	Kappa = 0.82 (95% CI, 0.70-0.93)	No	143	6	Kappa = 0.76 (95% CI, 0.63-0.88)	-
Yes	2	25	Sens = 78%	Yes	7	26	Sens = 81%	p = 0.32
			Spec = 99%				Spec = 95%	p = 0.03
			Agreement = 95%				Agreement = 93%	p = 0.10
> 2/3 stromal invasion								
No	95	10	Kappa = 0.81 (95% CI, 0.73-0.90)	No	90	9	Kappa = 0.77 (95% CI, 0.67-0.86)	-
Yes	7	70	Sens = 88%	Yes	12	71	Sens = 89%	p = 0.74
			Spec = 93%				Spec = 88%	p = 0.17
			Agreement = 91%				Agreement = 88%	p = 0.39
Parametrial invasion								
No	166	3	Kappa = 0.75 (95% CI, 0.56-0.94)	No	155	4	Kappa = 0.45 (95% CI, 0.24-0.66)	-
Yes	3	10	Sens = 77%	Yes	14	9	Sens = 69%	p = 0.56
			Spec = 98%				Spec = 92%	p < 0.001
			Agreement = 97%				Agreement = 90%	p = 0.001

A table comprising results of Epstein et al. study [24]
Sens sensitivity, *Spec* specificity, *CI* confidence interval

10 mm. Therefore, the sensitivity of MRI and PET/CT for evaluation of infiltrated nodes was low (58 and 30 %) [27]. Similar results were obtained in a study that compared the

benefits of hybrid MRI/PET and PET/CT with proven sensitivity of 54.2 % for MRI/PET and 44.1 % for PET/CT [28]. The specificity of both imaging methods (MRI and PET/

CT) was high (92.6 %) [27] and comparable to ultrasound (96 %) [25, 26].

Endometrial Cancer

Preoperative stratification for surgery is based on the results of preoperative biopsy and an appropriate imaging technique that should reliably assess the depth of tumor invasion into the myometrium and into the cervical stroma [29]. If a stratification of patients for surgery were based solely on the preoperative biopsy, then 64 % of high-risk patients would be erroneously underestimated according a multicentre study of Holsbeke et al. [30].

Currently, there are two comparably accurate methods for determining the local extent of endometrial cancer, and those are MRI and ultrasound [31]. To date, three studies published by Savelli et al., Antonsen et al., and Ortoft et al. have evaluated the accuracy of both imaging methods in detecting myometrial and cervical invasion [32–34]. Using MRI and ultrasound, the accuracy of myometrial invasion assessment reached 66–82 % and 72–84 % and of cervical invasion 82–85 % and 78–92 % [32–34]. Comparable diagnostic inaccuracy reflects the same limitations of both methods. Both methods have a similar tendency to overestimate myometrial invasion and underestimate cervical stromal invasion [35, 36]. Because of imaging availability, ultrasound remains the preferred option, whereas MRI is used in cases of reduced acoustic visibility due to myomas, acoustic shadows, etc.

Combination of the preoperative biopsy with ultrasound achieved sensitivity 81.5 %, specificity 74.7 %, positive and negative predictive values of 75.6 and 80.8 %, respectively, and accuracy of 78.6 % in the preoperative differentiation of patients at high risk for metastasis [36] (unpublished data). Similar results were obtained by an Ortoft et al. study in which the combination of transvaginal sonography or MRI with hysteroscopic-directed biopsies reached 72–83 % accuracy in the diagnosis of high-risk endometrial cancer [34]. In both studies, low-risk cancers were defined as well or moderately differentiated endometrioid or mucinous cancers with only superficial myometrial and no cervical invasion, whereas all others belonged to high-risk cancers.

Ultrasound Prediction of Histological Type

According to the literature data, there is a notable lack of correlation between preoperative histological grading and definitive pathology [37]. The main reason may be a tumor heterogeneity or unrepresentative biopsy sampling. Therefore, an interesting scientific goal was to find the ultrasound parameters that could predict the adverse histotype and grading of the tumor in cases where the preoperative biopsy was underestimated. The multicenter prospective study organized by Epstein et al. analyzed data from 144 consecutive patients included in a study from 2007 to

2009 [38]. The results revealed sonomorphological and Doppler characteristics associated with the presence of low-risk and high-risk endometrial cancer. These results were externally validated by a subsequent prospective study [36]. Low-risk endometrial cancers were often hyperechoic, with no or minimal density of blood vessels within the tumor. Non-hyperechoic tumors with moderate or abundant tumor perfusion and multiple vessels multifocally entering at different locations in the tumor from the myometrium were more frequently found in poorly differentiated tumors or tumors with deep myometrial infiltration and/or cervical stromal invasion. As a consequence, if ultrasound tumor characteristics do not correlate with the findings of the preoperative biopsy, the intraoperative frozen section may be recommended to eliminate inadequate surgical procedure.

Factors Affecting the Preoperative Staging

Subjective evaluation of tumor spread into the myometrium and cervix, whether during ultrasound or MRI, remains imprecise in 15–25 % cases [36, 39]. The recent research effort was to identify significantly important factors that contribute to the ultrasound staging error. In a single unit study by Fischerova et al., 211 patients with histologically confirmed endometrial cancer were included from 2009 to 2011 [36]. Surprisingly, the expected correlation between ultrasound failure and obesity (BMI), position of the uterus, or the quality of ultrasound imaging was not confirmed. In this study, there was a trend to underestimate cervical stromal invasion (10 %) in the presence of small tumors with superficial myometrial invasion, minimal tumor perfusion, and favorable histological grading. Conversely, myometrial invasion was often overestimated (17 %) in the presence of bulky and less differentiated tumors with a thin rim of healthy myometrium and rich tumor perfusion. The study showed a tendency to underestimate local tumor stage in tumors with favorable sonomorphological and Doppler features and overestimate tumors with less favorable pattern.

Reproducibility of Results Between Investigators

In the recently published study by Ericsson et al., 15 sonographers with varying degrees of experience evaluated clips of ultrasound examinations obtained from 53 cases with histologically verified endometrial cancer [40]. In the study, a good agreement between investigators in determining myometrial invasion (expert vs non-expert, kappa value 0.52 vs 0.48, $p=0.11$) and cervical stromal invasion (expert vs non-expert, kappa value 0.58 vs 0.45, $p<0.001$) was shown. Experienced examiners were more accurate in cervical stromal invasion than less-experienced examiners.

The results of this study contributed to the implementation of ultrasound alongside obligatory staging examination in

patients with biopsy-proven endometrial cancer, with emphasis on the use of specialized ultrasound [29].

Ovarian Tumors

There is enough evidence to demonstrate a significant difference in the outcome of patients operated by surgeons without an adequate training and those referred for diagnosis and primary treatment to specialized gynecologic oncology units with multidisciplinary teams [41, 42]. One of the main reasons for an insufficient centralization of patients with ovarian cancer is the absence of an accurate preoperative diagnostic work-up in patients with pelvic masses. In the case of malignant tumor, the detailed assessment of tumor extension using modern imaging is crucial for individualization of further management. The role of ultrasound in these areas of interest has been evaluated in recent studies.

Preoperative Differentiation of Benign and Malignant Ovarian Tumor

Transvaginal ultrasonography is the first-line and best imaging technique for characterizing adnexal masses preoperatively. The optimal approach is the subjective assessment of ultrasound images by experts [43, 44]. An alternative evidence-based approach to the presurgical diagnosis of adnexal tumors is to use simple ultrasound rules or logistic regression models (LR1 and LR2) developed by the International Ovarian Tumor Analysis (IOTA) group [8, 10]. The condition for the functioning of predictive models is maintaining uniform ultrasound terminology of ovarian lesion defined by the IOTA group [13]. Performance of the predictive models developed by the IOTA group matches the subjective assessment by experienced examiners and should be adopted as the principal test to characterize masses as benign or malignant [11]. Measurements of serum CA 125 are not necessary for the characterization of ovarian pathology in premenopausal women and are unlikely to improve the performance of experienced ultrasound examiners even in the postmenopausal group [44–46]. However, in postmenopausal patients, the serum CA 125 may play a role as a second-stage test, especially in centers with less-experienced ultrasound examiners [47].

For clinical practice, it is important not only to distinguish benign and malignant tumors, but also to specify the type of malignant tumor. The IOTA group proposed a mathematical model, the so-called ADNEX model (the assessment of different neoplasias in the adnexa), which is able to distinguish benign ovarian tumor, borderline ovarian tumor, primary early ovarian cancer, primary advanced ovarian cancer, or metastatic (secondary) ovarian tumor [48]. The model developed by Van Calster et al. was tested using the data from 6000 women with ovarian lesions and contains nine variables: age of the patient, serum CA 125, the maximum size of the lesion, the proportion of solid components, more than 10 cyst locules, the number of

papillary prominences, the presence of acoustic shadows, ascites, and type of center (oncology centres vs other hospitals). The test reliably distinguished between benign and malignant lesions (area under the curve (AUC) 0.94), and the accuracy of the test, with different tumor types, ranged from AUC 0.71 to 0.99 [48].

Staging

It has been shown that ultrasound can assess pelvic and intra-abdominal spread with satisfactory concordance with laparotomic findings. The ability of ultrasound to evaluate the tumor spread and to predict the likelihood of suboptimal cytoreduction was analyzed in a study by Testa et al. [49]. In a study of 147 patients enrolled between 2005 and 2008, ultrasound revealed the best results in the assessment of pelvic and hepatic involvement, a very reliable result in the detection of abdominal peritoneal parietal involvement, but lower sensitivity in the assessment of mesenterial involvement, splenic hilum infiltration, and splenic metastases. In this study, a model for the prediction of suboptimal cytoreduction showed sensitivity of 31 % and specificity of 92 %.

Ultrasound scanning of the pelvis and abdomen for staging requires an experienced examiner. A detailed review on how to scan gynecological cancers for staging (methodology, terminology, clinical implementation) has been published [21]. The advantages and limitations of modern imaging methods in preoperative staging of ovarian cancer including the ultrasound technique are summarized in another recent review [2].

Ultrasound-Guided Tru-cut Biopsy

Ultrasound and CT enable reliable navigation of tru-cut (core-cut) biopsy in order to achieve a histological diagnosis using a minimally invasive approach. The method is used particularly for primary inoperable ovarian tumors, tumors suspected to be from extragenital origin (e.g., tumors of the stomach, pancreas, or breast cancer may mimic primary advanced ovarian carcinoma), and in the case of diagnostic uncertainty of tumor relapse. Also, patients with history of multiple oncological diseases benefit from biopsy, allowing us to reliably distinguish the type of recurrent cancer [6, 7]. CT guidance of tumor biopsy entails risks associated with CT scans and requires patient preparation (oral iodinated contrast agent, fasting) [50]. Therefore, CT guidance of biopsy is only used in poorly accessible metastatic sites.

Ultrasound-guided tru-cut biopsy can be performed transvaginally, transrectally, and/or transabdominally. The procedure can be done in one session after the completion of ultrasound staging, because it does not require any special preparation of the patient or fasting. It is only necessary to exclude a higher risk of bleeding (the level of platelets $>10 \times 10^9/l$, INR [International Normalized Ratio] <1.4). The biopsy is performed on an outpatient basis and without general anesthesia. The result in most cases is available within 48 h after

the procedure. Ultrasound guidance allows us to obtain samples which are 95 % adequate for histological processing. Histological examination of the biopsy is accurate in 98 % of cases. The risk of complications (bleeding from the lesion after biopsy which required surgical revisions) is less than 1 % [6, 7].

Conclusion

Ultrasound is a reliable imaging modality, which is commonly available, non-invasive, inexpensive, and free of risk for the patient. Results of numerous studies published within the last 5 years, including international multicenter trials, showed that the ultrasound is an accurate procedure in diagnostics and clinical staging of pelvic gynecological malignancies. Its role in gynecological oncology should be broadly reconsidered, and financial and logistic resources should be allocated for the training of future experts.

Acknowledgments This work was supported by the Internal Grant Agency of the Ministry of Health (grant no. 13070), by the research project RVO-VFN64165, and by Charles University in Prague (UNCE 204024 and PRVOUK-P27/LF1/1). The authors would like to thank Adam Preisler from the Faculty of Architecture, Czech Technical University in Prague, for providing the illustrations and tables.

Compliance with Ethics Guidelines

Conflict of Interest Daniela Fischerova and David Cibula declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

•• Of major importance

- 1.•• Kaijser J, Vandecaveye V, Deroose C, et al. Imaging techniques for the pre-surgical diagnosis of adnexal tumors. *Best Pract Res Clin Obstet Gynaecol.* 2014;in print. **A review article summarizing the results of recently published studies on the role of imaging in diagnostics of ovarian cancer.**
- 2.•• Fischerova D, Burgetova A. Imaging techniques for the evaluation of ovarian cancer. *Best Pract Res Clin Obstet Gynaecol.* 2014;28(5):697–720. **A review article summarizing the results of recently published studies on the role of imaging in ovarian cancer staging.**
- 3.•• Epstein E, Blomqvist L. Imaging in endometrial cancer. *Best Pract Res Clin Obstet Gynaecol.* 2014;28(5):721–39. **A review article summarizing the results of recently published studies on ultrasound in diagnostics and staging of endometrial cancer.**
- 4.•• Testa AC, Di Legge A, De Blasis I, et al. Imaging techniques for the evaluation of cervical cancer. *Best Pract Res Clin Obstet Gynaecol.*

- 2014;28(5):741–68. **A review article summarizing the results of recently published studies on ultrasound in diagnostics and staging of cervical cancer.**
- 5.•• Testa AC, Di Legge A, Virgilio B, et al. Which imaging technique should we use in the follow up of gynaecological cancer? *Best Pract Res Clin Obstet Gynaecol.* 2014;28(5):769–91. **A review article summarizing the results of recently published studies on ultrasound in the follow-up of gynecological cancer.**
6. Fischerova D, Cibula D, Dunder P, et al. Ultrasound-guided tru-cut biopsy in the management of advanced abdomino-pelvic tumors. *Int J Gynecol Cancer.* 2008;18(4):833–7.
7. Zikan M, Fischerova D, Pinkavova I, et al. Ultrasound-guided tru-cut biopsy of abdominal and pelvic tumors in gynecology. *Ultrasound Obstet Gynecol.* 2010;36(6):767–72.
8. Timmerman D, Van Calster B, Testa AC, et al. Ovarian cancer prediction in adnexal masses using ultrasound-based logistic regression models: a temporal and external validation study by the IOTA group. *Ultrasound Obstet Gynecol.* 2010;36(2):226–34.
9. Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol.* 2008;31(6):681–90.
10. Timmerman D, Ameye L, Fischerova D, et al. Simple ultrasound rules to distinguish between benign and malignant adnexal masses before surgery: prospective validation by IOTA group. *BMJ.* 2010;341:c6839.
11. Kaijser J, Bourne T, Valentin L, et al. Improving strategies for diagnosing ovarian cancer: a summary of the International Ovarian Tumor Analysis (IOTA) studies. *Ultrasound Obstet Gynecol.* 2013;41(1):9–20.
12. Sayasneh A, Kaijser J, Preisler J, et al. A multicenter prospective external validation of the diagnostic performance of IOTA simple descriptors and rules to characterize ovarian masses. *Gynecol Oncol.* 2013;130(1):140–6.
13. Timmerman D, Valentin L, Bourne TH, et al. Terms, definitions and measurements to describe the sonographic features of adnexal tumors: a consensus opinion from the International Ovarian Tumor Analysis (IOTA) group. *Ultrasound Obstet Gynecol.* 2000;16(5):500–5.
14. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet.* 2009;105(2):103–4.
15. Balleyguier C, Sala E, Da Cunha T, et al. Staging of uterine cervical cancer with MRI: guidelines of the European Society of Urogenital Radiology. *Eur Radiol.* 2011;21(5):1102–10.
16. Hricak H, Lacey CG, Sandles LG, et al. Invasive cervical carcinoma: comparison of MR imaging and surgical findings. *Radiology.* 1988;166(3):623–31.
17. Subak LL, Hricak H, Powell CB, et al. Cervical carcinoma: computed tomography and magnetic resonance imaging for preoperative staging. *Obstet Gynecol.* 1995;86(1):43–50.
18. Hricak H, Gatsonis C, Chi DS, et al. Role of imaging in pretreatment evaluation of early invasive cervical cancer: results of the intergroup study American College of Radiology Imaging Network 6651-Gynecologic Oncology Group 183. *J Clin Oncol.* 2005;23(36):9329–37.
19. Mitchell DG, Snyder B, Coakley F, et al. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 intergroup study. *J Clin Oncol.* 2006;24(36):5687–94.
20. Chiappa V, Di Legge A, Valentini AL, et al. Agreement of two-dimensional and three-dimensional transvaginal ultrasound with magnetic resonance imaging with regard to parametrial infiltration in cervical cancer. *Ultrasound Obstet Gynecol.* 2014.
21. Fischerova D. Ultrasound scanning of the pelvis and abdomen for staging of gynecological tumors: a review. *Ultrasound Obstet Gynecol.* 2011;38(3):246–66.

22. Fischerova D, Cibula D, Stenhova H, et al. Transrectal ultrasound and magnetic resonance imaging in staging of early cervical cancer. *Int J Gynecol Cancer*. 2008;18(4):766–72.
23. Testa AC, Ludovisi M, Manfredi R, et al. Transvaginal ultrasonography and magnetic resonance imaging for assessment of presence, size and extent of invasive cervical cancer. *Ultrasound Obstet Gynecol*. 2009;34(3):335–44.
24. Epstein E, Testa A, Gaurilcikas A, et al. Early-stage cervical cancer: tumor delineation by magnetic resonance imaging and ultrasound—a European multicenter trial. *Gynecol Oncol*. 2013;128(3):449–53.
25. Fischerova D, Zikan M, Pinkavova I, et al. The role of ultrasound in planning fertility sparing surgery and individual treatment in early stage cervical cancer. *Ultrasound Obstet Gynecol*. 2012;40 Suppl 1: 51.
26. Palsdottir K, Fischerova D, Franchi D, et al. Preoperative prediction of lymph node metastasis and deep stromal invasion in women with invasive cervical cancer—a prospective multicenter study on 2D and 3D ultrasound. *Ultrasound Obstet Gynecol*. 2014.
27. Choi HJ, Roh JW, Seo SS, et al. Comparison of the accuracy of magnetic resonance imaging and positron emission tomography/computed tomography in the presurgical detection of lymph node metastases in patients with uterine cervical carcinoma: a prospective study. *Cancer*. 2006;106(4):914–22.
28. Kim SK, Choi HJ, Park SY, et al. Additional value of MR/PET fusion compared with PET/CT in the detection of lymph node metastases in cervical cancer patients. *Eur J Cancer*. 2009;45(12): 2103–9.
29. Colombo N, Preti E, Landoni F, et al. Endometrial cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2013;24 Suppl 6:vi33–8.
30. Van Holsbeke C, Ameye L, Testa AC, et al. Development and external validation of new ultrasound-based mathematical models for preoperative prediction of high-risk endometrial cancer. *Ultrasound Obstet Gynecol*. 2014;43(5):586–95.
31. Valentin L. Ultrasound deserves to play a prominent role in the diagnosis and management of endometrial cancer. *Ultrasound Obstet Gynecol*. 2014;43(5):483–7.
32. Savelli L, Ceccarini M, Ludovisi M, et al. Preoperative local staging of endometrial cancer: transvaginal sonography vs. magnetic resonance imaging. *Ultrasound Obstet Gynecol*. 2008;31(5):560–6.
33. Antonsen SL, Jensen LN, Loft A, et al. MRI, PET/CT and ultrasound in the preoperative staging of endometrial cancer—a multicenter prospective comparative study. *Gynecol Oncol*. 2013;128(2):300–8.
34. Ortoft G, Dueholm M, Mathiesen O, et al. Preoperative staging of endometrial cancer using TVS, MRI, and hysteroscopy. *Acta Obstet Gynecol Scand*. 2013;92(5):536–45.
35. Shin KE, Park BK, Kim CK, et al. MR staging accuracy for endometrial cancer based on the new FIGO stage. *Acta Radiol*. 2011;52(7):818–24.
36. Fischerova D, Fruhauf F, Zikan M, et al. Factors affecting sonographic preoperative local staging of endometrial cancer. *Ultrasound Obstet Gynecol*. 2014;43(5):575–85.
37. Benedet JL, Bender H, Jones 3rd H, et al. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO committee on gynecologic oncology. *Int J Gynaecol Obstet*. 2000;70(2):209–62.
38. Epstein E, Van Holsbeke C, Mascilini F, et al. Gray-scale and color Doppler ultrasound characteristics of endometrial cancer in relation to stage, grade and tumor size. *Ultrasound Obstet Gynecol*. 2011;38(5):586–93.
39. Hricak H, Rubinstein LV, Gherman GM, et al. MR imaging evaluation of endometrial carcinoma: results of an NCI cooperative study. *Radiology*. 1991;179(3):829–32.
40. Eriksson LS, Lindqvist PG, Floter Radestad A, et al. Transvaginal ultrasound assessment of myometrial and cervical stroma invasion in women with endometrial cancer—interobserver reproducibility among ultrasound experts and gynaecologists. *Ultrasound Obstet Gynecol*. 2014.
41. Verleye L, Vergote I, van der Zee AG. Patterns of care in surgery for ovarian cancer in Europe. *Eur J Surg Oncol*. 2010;36 Suppl 1: S108–14.
42. Woo YL, Kyrgiou M, Bryant A, et al. Centralisation of services for gynaecological cancers—a Cochrane systematic review. *Gynecol Oncol*. 2012;126(2):286–90.
43. Valentin L, Hagen B, Tingulstad S, et al. Comparison of ‘pattern recognition’ and logistic regression models for discrimination between benign and malignant pelvic masses: a prospective cross validation. *Ultrasound Obstet Gynecol*. 2001;18(4):357–65.
44. Van Calster B, Timmerman D, Bourne T, et al. Discrimination between benign and malignant adnexal masses by specialist ultrasound examination versus serum CA-125. *J Natl Cancer Inst*. 2007;99(22):1706–14.
45. Van Gorp T, Veldman J, Van Calster B, et al. Subjective assessment by ultrasound is superior to the risk of malignancy index (RMI) or the risk of ovarian malignancy algorithm (ROMA) in discriminating benign from malignant adnexal masses. *Eur J Cancer*. 2012;48(11):1649–56.
46. Valentin L, Jurkovic D, Van Calster B, et al. Adding a single CA 125 measurement to ultrasound imaging performed by an experienced examiner does not improve preoperative discrimination between benign and malignant adnexal masses. *Ultrasound Obstet Gynecol*. 2009;34(3):345–54.
47. Ameye L, Timmerman D, Valentin L, et al. Clinically oriented three-step strategy for assessment of adnexal pathology. *Ultrasound Obstet Gynecol*. 2012;40(5):582–91.
48. Van Calster B, Van Hoorde K, Valentin L, et al. Evaluating the risk of ovarian cancer before surgery using the ADNEX model to differentiate between benign, borderline, early and advanced stage invasive, and secondary metastatic tumours: prospective multicentre diagnostic study. *BMJ*. 2014;349:g5920.
49. Testa AC, Ludovisi M, Mascilini F, et al. Ultrasound evaluation of intra-abdominal sites of disease to predict likelihood of suboptimal cytoreduction in advanced ovarian cancer: a prospective study. *Ultrasound Obstet Gynecol*. 2012;39(1):99–105.
50. Spencer JA, Anderson K, Weston M, et al. Image guided biopsy in the management of cancer of the ovary. *Cancer Imaging*. 2006;6: 144–7.
51. Testa AC, Van Holsbeke C, Mascilini F, et al. Dynamic and interactive gynecological ultrasound examination. *Ultrasound Obstet Gynecol*. 2009;34(2):225–9.
52. Abu-Alfa AK. Nephrogenic systemic fibrosis and gadolinium-based contrast agents. *Adv Chronic Kidney Dis*. 2011;18(3):188–98.