

REVIEW

Artificial Intelligence & Precision Oncology

Advances of Artificial Intelligence Application in Medical Imaging of Ovarian Cancers

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Abstract Ovarian cancer is one of the three most common gynecological cancers in the world, and is regarded as a priority in terms of women's cancer. In the past few years, many researchers have attempted to develop and apply artificial intelligence (AI) techniques to multiple clinical scenarios of ovarian cancer, especially in the field of medical imaging. AI-assisted imaging studies have involved computer tomography (CT), ultrasonography (US), and magnetic resonance imaging (MRI). In this review, we perform a literature search on the published studies that using AI techniques in the medical care of ovarian cancer, and bring up the advances in terms of four clinical aspects, including medical diagnosis, pathological classification, targeted biopsy guidance, and prognosis prediction. Meanwhile, current status and existing issues of the researches on AI application in ovarian cancer are discussed.

INTRODUCTION

OVARIAN cancer is the one of the three most common gynecological cancers in the world, but is the most lethal cancer in women. Data from GLOBOCAN 2020 show that there were 313,959 cases of newly diagnosed ovarian cancer patients and about 207,252 deaths in 2020 globally, which have been increasing continuously.^[1] From the SEER (Surveillance, Epidemiology, and End Results) database, the authoritative source for cancer statistics in United States, the overall five-year relative survival rate for all types and stages of ovarian cancer is 48.6%.^[2] This awkward situation could be at-

tributed to the fact that early symptoms of ovarian cancer often go unnoticed and there is no reliable or recommended screening method for ovarian cancer. Early diagnosis, stratification, and treatment are the keys to reducing mortality and prolonging survival time.

The term of artificial intelligence (AI) was initially emerged in the 1950s, referring to the intelligence programming developed by modern computerized machine. It is usually used to mimic human intelligence, such as cognitive and learning abilities, and to solve practical problems in reality. As the most important subset of AI, machine learning is usually defined as a computerized algorithms that can independently improve itself during constant practice. Depending on the form of supervision information, machine learning has 3 major types, including supervised, unsupervised, and reinforcement learning. With the introduction and obvious success of convolutional neural network, deep learning has been recognized as a competent AI technique throughout

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the world. The most typical instance of AI application is the Google's product, AlphaGo, beating the best human chess player in 2016.^[3] Deep learning, an important branch of AI algorithm, can conduct imaging identification, language processing, etc., by using multi-layered artificial neural network analysis model, which mimics the neural network of a human brain.^[4]

In recent years, with the penetration and development of AI technology in medicine, many innovation have been made in imaging diagnosis, histological classification/grading, and prognostic prediction for malignancies. For the high efficiency in work force and excellent ability in autonomic learning, the machine learning algorithm and radiomics have expanded the applications to multiple imaging modalities in the diagnosis and treatment of ovarian cancer,^[5] and have obtained many achievements.

AI-ASSOCIATED CLINICAL INVESTIGATIONS ON OVARIAN CANCER

According to literature searches for clinical investigation from PubMed and Web of Sciences based on terms of ["artificial intelligence" OR "machine learning" OR "deep learning" OR "radiomics"] AND ["imaging" OR "medical imaging" OR "CT" OR "MR" OR "ultrasound" OR "ultrasonography"] AND ["ovarian cancer" OR "ovarian carcinoma"] in the field of full-text, we have identified totally 18 clinical investigations published by June 2021 (**Table 1**). The clinical scenarios involved in these studies include imaging diagnosis ($n=7$), metastasis ($n=2$), target biopsy guidance ($n=1$), and prognostic prediction ($n=9$). Only 2 of these studies were prospective, and the rest were retrospective. In terms of effectiveness validation of machine learning models or algorithms, 10 studies performed only internal validation, while only 2 performed both internal and external validations.

The greatest potentials for AI in clinical oncology lie in the integration of intelligent approaches with clinical workflows, e.g., cancer identification, diagnosis, treatment, and follow-up, to improve the management of cancers. The development of big data analysis and intelligent algorithms have provided solid foundations for the application of AI in the field of medicine, and have strengthened the capabilities of medical professionals. However, more prospective researches are needed to fully explore the potential of AI in practical clinical scenarios.^[6]

At present, researches on AI in the field of medical

imaging related to ovarian cancer mainly focus on imaging diagnosis, pathological classification, targeted biopsy guidance, and prognosis prediction. The sample size of these studies varies. Patient number in the studies on predicting tumor progression-free survival ranges from 88 to 364, while the sample sizes in AI-assisted imaging studies for differential diagnosis of ovarian tumors ranges from 32 to 451. Besides, the AI models and tool platforms used by researchers among studies are also different. Furthermore, most of these studies were in lack of external verification, the evaluation and verification of the established models were not sufficient. Therefore, effectiveness of these models in clinical practice need to be carefully determined by well-designed studies and high level evidences. These issues might be the main reasons that hinder the transformation of computer intelligent technologies into clinical practice.^[7]

Imaging diagnosis

Radiologists in oncological imaging usually detect and evaluate tumor and its growth patterns based on anatomical and morphological features, such as tumor location, size, shape, relationship with adjacent structures, as well as hemodynamic parameters in intravenous contrast enhanced imaging. Compared with subjective assessment by radiologists, machine learning algorithms and models could automatically extract large amount of objective quantitative information, such as histogram and texture features in tumor from conventional medical images. Several articles have shown that AI is capable to perform similarly or better than human intelligence in tumor recognition, characterization, and follow-up monitoring.^[8-12]

As ultrasound is the most convenient and available imaging method, machine learning assisted ultrasonography on ovarian cancer has been initially investigated. It was reported that a deep learning model based on ultrasound images achieved accuracy higher than 85% in differentiation of benign and malignant tumors.^[13] Zhang *et al.* used a deep learning model to predict definitive diagnosis of ovarian tumors and achieved an accuracy of 0.99.^[14] Aramedia-Vidaurreta reported that a machine learning algorithm based on ultrasound images in combination with clinical data reached a diagnostic accuracy of 0.98.^[15] However, due to the high sensitivity and low specificity of US, machine learning assisted US is mainly used in tumor detection instead of tumor classification and grading.

MRI is featured by multi-parameter, multi-plane

Table 1. Basic information of publications of AI associated medical imaging studies on ovarian cancers

Reference	Year	Country	Study type	Imaging modality	Patients No. (n)	Mean/Median age (y/d)	Clinical orientation	Radiomics model	AI model	Validations	Radiomics extraction tools	AI tools
Song XL, <i>et al.</i> [38]	2021	China	P	MRI	89	52	M	Radiomics nomogram	LASSO regression	Yes (internal)	ITK-SNAP	ND
Wang X, <i>et al.</i> [5]	2021	China	R	PET/CT	261	57	PFS	Cox regression	ND	Yes (internal)	SliverRadiomics	ND
Beer L, <i>et al.</i> [31]	2021	UK	P	CT/US	6	65	TB	Radiomic habitats	GMM	No	CERR	MATLAB
Ai Y, <i>et al.</i> [39]	2021	China	R	CT	101	52	M	Radiomics features	Mann-Whitney U tests, LASSO, and Ridge regression	Yes (internal)	LIFEX package	"Gimnet" package
Qian L, <i>et al.</i> [25]	2020	China	R	MRI	61	52	DD	Traditional/Combined/Mixed radiomics	LASSO regression	Yes (internal)	3D Slicer, PyRadiomics	ND
Wang R, <i>et al.</i> [8]	2020	USA	R	MRI	451	48	DD	BAG, MRMR, TPOT	CNN (EfficientNet, ResNet)	Yes (internal)	"Radiomics-develop" package	Sklearn package in python
Akazawa M, <i>et al.</i> [22]	2020	Japan	R	MRI	202	51	DD	ND	SVM, Random forest, Naive bayes, Logistic regression and XGBoost	No	ITK-SNAP	Keras and Scikit-learn package in python
Lu H, <i>et al.</i> [44]	2019	UK	R	CT	364	62	OS, PFS	RPV	ND	Yes (internal and external)	ITK-SNAP	MATLAB
Meier A, <i>et al.</i> [45]	2019	USA	R	CT	88	75	OS, PFS	ND	ND	No	ITK-SNAP	MATLAB
Wang S, <i>et al.</i> [50]	2019	China	R	CT	245	56	RFS	Cox-PH	CNN	Yes (internal)	Lifelines package in Python	Keras package in Python
Zhang H, <i>et al.</i> [23]	2019	China	R	MRI	280	53	DD, PP	MRI-radiomics	SVM	Yes (internal)	ITK-SNAP	MATLAB
Martinez-Mas J, <i>et al.</i> [13]	2019	Spain	R	US	ND	ND	DD	ND	KNN, LD, SVM, ELM	Yes (internal)	Fourier descriptors	MATLAB
Zargari A, <i>et al.</i> [46]	2018	USA	R	CT	120	67	PFS	ND	PSO	Yes (internal)	ND	ND
Rizzo S, <i>et al.</i> [47]	2018	Italy	R	CT	101	53	PFS	ND	ND	No	IBEX	ND
Wei W, <i>et al.</i> [48]	2018	China	R	CT	142	50	PFS	ND	Logistic regression	Yes (internal and external)	ITK-SNAP	MATLAB
Vargas HA, <i>et al.</i> [49]	2017	USA	R	CT	38	ND	OS	ND	ND	No	3D Slicer	ND
Mimura R, <i>et al.</i> [19]	2016	Japan	R	MRI	32	45	DD	ADC histogram	ND	No	SPM8, MRICron	ND
Aramendia-V V, <i>et al.</i> [15]	2016	Spain	R	US	145	43	DD	ND	MLPs	Yes (internal)	ND	MATLAB

R, retrospective; P, prospective; M, metastasis; OS, overall survival; PFS, progression-free survival; TB, targeted biopsy; RFS, recurrence-free survival; DD, differential diagnosis; PP, prognosis prediction; BAG, bagging classifier; MRMR, minimum redundancy maximum relevance; TPOT, tree-based pipeline optimization tool; RPV, radiomics prognostic vector; MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient; GMM, gaussian mixture modelling; LASSO, least absolute shrinkage selection operator; CNN, convolutional neural network; KNN, K-nearest neighbors; LD, linear discriminant; SVM, support vector machine; ELM, extreme learning machine; PSO, particle swarm optimization; MLPs, multilayer perceptron networks; CERR, computational environment for radiological research; IBEX, imaging biomarker explorer software; SPM, statistical parametric mapping; ND, not declared.

imaging and good soft tissue resolution. It is the most important imaging method for gynecological tumors. For suspicious adnexal lesions found by US, MRI can further provide a variety of anatomical and morphological information to help diagnosis. However, in some particular instance, it is still difficult to distinguish benign lesion, such as ovarian cystadenoma, from malignant ovarian tumors.^[16, 17] The performance of apparent diffusion coefficients (ADC) by region of interest (ROI) of ovarian lesions on MR diffusion weighted imaging in distinguishing ovarian borderline tumor from malignancy has shown sensitivity and specificity of 61.9% and 93.8%, respectively by semi-automatic delineated ROI, and of 100% and 80%, respectively by manual delineated ROI.^[18, 19] Comparably, Wang R *et al.* developed a deep learning model with neural network technique for diagnosis of ovarian tumors using routine MR imaging in combination with clinical variable, and compared its performance with that of radiologists. The results showed that the AI diagnostic model using neural network had higher specificity (0.92 vs. 0.64, $P < 0.001$), comparable sensitivity (0.75 vs. 0.63, $P = 0.407$), and higher accuracy (0.87 vs. 0.64, $P < 0.001$). With assistance of AI model, junior radiologists improved their diagnostic accuracy (0.77 vs. 0.64, $P < 0.001$) and specificity (0.81 vs. 0.64, $P < 0.001$); meanwhile, compared with senior radiologist, junior radiologists assisted with AI model showed higher specificity (0.81 vs. 0.70, $P = 0.005$), lower sensitivity (0.69 vs. 0.83, $P = 0.097$), with comparable accuracy (0.77 vs. 0.74, $P = 0.409$).^[8] These results indicate that AI is promising in improving differential diagnosis of ovarian tumors.

Pathological classification

Ovarian cancer usually presented as a heterogeneous mass that is composed of different histologic subtypes, such as high-grade serous, low-grade serous, endometrioid, clear cell, and mucinous type. Each histological type is associated with unique clinical etiology, response to a therapy, and molecular signatures, *e.g.*, diverse transcriptional regulatory programs.^[20, 21]

Several studies investigated AI technique in preoperative pathological classification of ovarian cancers. MRI and clinical parameters are usually used for histological prediction of ovarian cancer. Akazawa M *et al.* used 5 machine learning algorithms, including support vector machine, random forest, naive bayes, logistic regression, and XGBoost, to predict pathological classification

with 16 numerical values from preoperative examinations, including MRI. The machine learning algorithm of XGBoost demonstrated the highest accuracy of 0.80.^[22] Other studies have also taken the advantages of machine learning techniques to extract quantitative information from multiple sequences of MR imaging to diagnose, classify, and predict treatment effect on ovarian cancer.^[23, 24] Qian L *et al.* compared a traditional model which includes age, CA125, lesion texture, ascites, and ADC value, a combined radiomics model which contains 4 DWI and 1 DCE-MRI characters, and a mixed model (the traditional plus the combined radiomics parameters) in predicting the type of epithelial ovarian cancer (EOC). They found that the traditional model achieved the best diagnostic performance, while the combined radiomics model showed better performance in distinguishing pathological subtypes of EOC in early FIGO stage disease. However, the difference was not statistically significant,^[25] which is probably due to its small sample size. Prospective cohort studies with larger sample size and external validation are needed in the future to explore the value of AI techniques in predicting pathology.

Targeted biopsy guidance

AI-guided biopsy has been investigated on ovarian cancer. Precise US-guide biopsy *in vivo* is the key to improve stratification in patients with high-grade serous ovarian cancer (HGSOC), for heterogeneity in tumor microenvironment of HGSOC has been shown widespread among the patients.^[26-29] Machine learning-assisted radiomics models can capture the spatial heterogeneity of tumors by extracting quantitative information from conventional medical images.^[30] Beer L *et al.*^[31] tried to register CT radiomic tumor habitats atlas to the synchronous US images to develop a precise tissue sampling technique for US-targeted biopsy. Accurate spatial matching between CT and US images was achieved for larger tumors and failed in the registration for smaller lesions. The high degree of misregistration for small omental lesions in anterior-posterior axis was mainly caused by the variability of the anterior abdominal wall and omentum due to the local pressure of ultrasound probe. It is expected that patient tracker system is able to correct the local abdominal wall movement of patients and overcome this issue, thus improve the success rate of targeted biopsy.

Staging of ovarian cancer

Early detection of metastasis is important to the treatment,

prognosis and survival of patients.^[32] Although MRI has high accuracy in identifying local and distant metastases, traditional MRI technique is generally not sensitive enough to detect small metastases.^[33-35] Peritoneal metastases (PMs) usually induce surface invasion of organs and secondary lymph node metastasis through peritoneal blood and lymph circulation,^[36] which frequently result in even poor prognosis.^[37] Song XL *et al.* developed a radiomics model based on preoperative MRI to individually predict PM in ovarian cancer patients and achieved good performances in both the training group and the validation group.^[38] Recently, another study by Ai Y *et al.*^[39] use machine learning technologies to extract radiomics features from preoperative CT images of 101 patients with ovarian cancer and build an AI predictive model in combination with clinical models (including age and CA125 level), which has shown potentials in overcoming low sensitivity of CT in detecting small lymphatic metastasis. AI-assisted imaging diagnostic approaches have shown feasibility and accuracy in evaluating metastatic status, and is promising to facilitate the clinical decision-making processes in the treatment of patients with ovarian cancer.

Prognosis prediction

It is reported that over 75% patients with ovarian cancer are diagnosed at advanced stage due to obscure symptoms at early stage of the disease, with a 5-year survival rates only 15%–25%.^[40] Despite the high responsiveness to platinum-based chemotherapy, recurrences occur in up to 80% patients with advanced ovarian cancer, with a median progression-free survival (PFS) of 12–18 months.^[41] It is generally accepted that high genomic heterogeneity is related to the reduced PFS.^[26-28, 41-43]

Given the circumstances of the poor prognosis and high heterogeneity of ovarian cancers, many studies have attempted to predict prognosis through characterizing ovarian cancer. Our literature searching found that the investigations published are mainly about the associations of overall survival (OS), PFS, or relapse-free survival (RFS) with characteristics on CT images of ovarian cancer. Some studies demonstrated a significant association of radiomics features extracted from CT images with OS and PFS.^[5, 44-49] Different AI algorithms have been employed to extract CT image features and construct AI models to predict disease prognosis. Investigators integrated clinical parameters and the extracted image features together in selected combinations into AI models, some of which outper-

formed the clinical model for the predictive tasks.

Lu H *et al.* proposed a prognostic scoring system including 4 features by means of deep learning algorithm and named it as the radiomic prognostic vector (RPV), which was found to be four times more accurate in predicting ovarian cancer deaths than doctors' estimation using the standard method. They also found that RPV could identify 5% patients who has an OS less than 2 years, which improves the established prognostic prediction methods. In addition, high RPV score was also associated with chemotherapy resistance and poor surgical outcome, suggesting that RPV can be used as a potential biomarker to predict patient response to treatment.^[44] Meier A *et al.* reported that smaller value of similarity entropy of a machine learning model was significantly associated with longer OS, while inter-site textural heterogeneity metrics were significantly associated with longer PFS.^[45] Rizzo S *et al.* presented that the radiomic features drawn from CT images were significantly associated with disease progression at 12 months and disease residual after surgery; additionally, the authors demonstrated that the clinical-radiomic model outperformed the clinical model.^[47] Wei W *et al.* built a radiomic model for prediction of PFS with four radiomic features, which was shown to have a discriminative accuracy of 88.9% for predicting 3-year recurrence, significantly better than that of clinical prognostic model, *i.e.*, 73.7%.^[48] Wang S *et al.* developed a deep learning model to predict individual recurrence risk and 3-year recurrence probability in HG-SOC patients, which achieved a good performance.^[50]

Since histological sampling from different sites of ovarian cancer is not practically feasible, CT based radiomics model using machine learning techniques could be an optimal tool to capture the inter-site heterogeneity of the ovarian cancer. In 2017, Vargas *et al.* reported a study with 12 inter-site texture metrics to capture heterogeneity across metastatic lesions on preoperative CT images in 38 HGSOC patients, and found that metrics representing differences in texture similarities across sites were associated with shorter OS and incomplete surgical resection.^[49] Later, this research team further assessed the associations of inter-site texture heterogeneity parameters (inter-site cluster prominence, inter-site cluster variance, inter-site cluster entropy) with survival and BRCA status in 88 HGSOC patients, and demonstrated that high inter-site cluster variance was associated with low PFS and OS, and high values of all the three

metrics were significantly associated with lower complete surgical resection in BRCA-negative patients.^[45]

In a recent study, PET/CT imaging has been involved in prognostic prediction for non-small cell lung cancer,^[16] which indicated radiomic features extracted from PET/CT images by machine learning algorithm can be used to quantitatively assess intratumoral metabolic heterogeneity. Wang X *et al.* extracted radiomic signatures in PET and CT components from PET/CT images of advanced HGSOc patients for the purpose to predict PFS in combination with clinical factors. Comparing to the predictive model that simply including clinical factors, the predictive AI model that integrate clinical features and radiomic signatures of PET images showed significantly improved performance in both training set and validation set.^[5] However, the robustness of this study need to be further confirmed by external validation.

Although radiomics models based on modalities of CT and PET/CT have been shown promising in predicting outcomes and survival of patients with ovarian cancer, it has to be noted that in most of the studies, patient samples are relatively small and validations by larger clinical dataset are needed, especially for external validation. Therefore, clinical studies that conducted with multi-centric patients as validation cohorts are necessary before translation of AI predictive models into real world clinical practice.

SUMMARY

Medical imaging facilitated with AI has the ability to efficiently explore the heterogeneities of ovarian cancer and determine the probable inherent connections between original images and characters of the tumor essence. Utilization of image based AI algorithm has shown excellent performance in diagnosis, classification, staging, and prognosis prediction of ovarian cancers. However, most investigations of machine learning on medical imaging of ovarian cancers are retrospective approach with small sample size and lack external verification. High level clinical evidence is important to ensure that a novel technology benefits patients' outcome. Therefore, there is still a long journey to fully identify the clinical application values of AI techniques in particular scenarios of patient's care. It is expected that, with the development in intelligent algorithm technology and enhanced cooperation between medical professionals and AI scientists, more well-designed clinical trials in high evidence level will be coming up, based on which

medical imaging in the field of precise diagnosis and treatment for ovarian cancers will be developed greatly.

Conflict of interests

None.

REFERENCES

1. Reid F. World Ovarian Cancer Coalition. World Ovarian Cancer Coalition Atlas 2020. Global trends in incidence, mortality, and survival. Available from https://worldovariancancercoalition.org/wp-content/uploads/2020/10/2020-World-Ovarian-Cancer-Atlas_FINAL.pdf. Accessed June 2, 2021.
2. National Cancer Institute. Surveillance, Epidemiology, and End Result program. SEER Cancer Statistics Review, 1975-2017. Available from https://seer.cancer.gov/archive/csr/1975_2017/results_merged/sect_21_ovary.pdf. Released April 15, 2020. Accessed September 14, 2021.
3. Granter SR, Beck AH, Papke DJ. AlphaGo, deep learning, and the future of the human microscopist. *Arch Pathol Lab Med* 2017; 141(5):619-21. doi: 10.5858/arpa.2016-0471-ED.
4. Sone K, Toyohara Y, Taguchi A, et al. Application of artificial intelligence in gynecologic malignancies: a review. *J Obstet Gynaecol Res* 2021; 47(8):2577-85. doi: 10.1111/jog.14818.
5. Wang X, Lu Z. Radiomics analysis of PET and CT components of (18) F-FDG PET/CT imaging for prediction of progression-free survival in advanced high-grade serous ovarian cancer. *Front Oncol* 2021; 11:638124. doi: 10.3389/fonc.2021.638124.
6. Foronda M. The AI revolution in cancer. *Nature portfolio: milestone*. Released December 10, 2020; accessed June 10, 2021. Available from <https://www.nature.com/articles/d42859-020-00082-9>.
7. Panagiotou OA, Hogg LH, Hricak H, et al. Clinical application of computational methods in precision oncology: a review. *JAMA Oncol* 2020; 6(8):1282-6. doi: 10.1001/jamaoncol.2020.1247.
8. Wang R, Cai Y, Lee IK, et al. Evaluation of a convolutional neural network for ovarian tumor differentiation based on magnetic resonance imaging. *Eur Radiol* 2021; 31(7):4960-71. doi: 10.1007/s00330-020-07266-x.
9. Chang K, Beers AL, Bai HX, et al. Automatic assessment of glioma burden: a deep learning algorithm for fully automated volumetric and bidimensional

- measurement. *Neuro Oncol* 2019; 21(11):1412-2. doi: 10.1093/neuonc/noz106.
10. Papp L, Potsch N, Grahovac M, et al. Glioma survival prediction with combined analysis of in vivo (11)C-MET PET features, ex vivo features, and patient features by supervised machine learning. *J Nucl Med* 2018; 59(6):892-9. doi: 10.2967/jnumed.117.202267.
 11. Chang K, Bai HX, Zhou H, et al. Residual convolutional neural network for the determination of IDH status in low- and high-grade gliomas from MR imaging. *Clin Cancer Res* 2018; 24(5):1073-81. doi:10.1158/1078-0432.CCR-17-2236.
 12. Zhang X, Yan LF, Hu YC, et al. Optimizing a machine learning based glioma grading system using multi-parametric MRI histogram and texture features. *Oncotarget* 2017; 8(29):47816-30. doi: 10.18632/oncotarget.18001.
 13. Martinez-Mas J, Bueno-Crespo A, Khazendar S, et al. Evaluation of machine learning methods with fourier transform features for classifying ovarian tumors based on ultrasound images. *PLoS One* 2019; 14(7):e219388. doi: 10.1371/journal.pone.0219388.
 14. Zhang L, Huang J, Liu L. Improved deep learning network based in combination with cost-sensitive learning for early detection of ovarian cancer in color ultrasound detecting system. *J Med Syst* 2019; 43(8):251. doi: 10.1007/s10916-019-1356-8.
 15. Aramendia-Vidaurreta V, Cabeza R, Villanueva A, et al. Ultrasound image discrimination between benign and malignant adnexal masses based on a neural network approach. *Ultrasound Med Biol* 2016; 42(3):742-52. doi: 10.1016/j.ultrasmedbio.2015.11.014.
 16. Yang B, Zhong J, Zhong J, et al. Development and validation of a radiomics nomogram based on (18) F-fluorodeoxyglucose positron emission tomography/computed tomography and clinicopathological factors to predict the survival outcomes of patients with non-small cell lung cancer. *Front Oncol* 2020; 10:1042. doi: 10.3389/fonc.2020.01042.
 17. Pi S, Cao R, Qiang JW, et al. Utility of DWI with quantitative ADC values in ovarian tumors: a meta-analysis of diagnostic test performance. *Acta Radiol* 2018; 59(11):1386-94. doi: 10.1177/0284185118759708.
 18. Matondang S, Ekawati A, Andrijono, et al. Minimal apparent diffusion coefficient value of the solid component to differentiate borderline and malignant ovarian epithelial tumours: a preliminary report. *Pol J Radiol* 2020; 85:e250-e253. doi: 10.5114/pjr.2020.95921.
 19. Mimura R, Kato F, Tha KK, et al. Comparison between borderline ovarian tumors and carcinomas using semi-automated histogram analysis of diffusion-weighted imaging: focusing on solid components. *Jpn J Radiol* 2016; 34(3):229-37. doi: 10.1007/s11604-016-0518-6.
 20. Lee JM, Minasian L, Kohn EC. New strategies in ovarian cancer treatment. *Cancer* 2019; 125 Suppl 24: 4623-9. doi: 10.1002/cncr.32544.
 21. Tothill RW, Tinker AV, George J, et al. Novel molecular subtypes of serous and endometrioid ovarian cancer linked to clinical outcome. *Clin Cancer Res* 2008; 14(16):5198-208. doi: 10.1158/1078-0432.CCR-08-0196.
 22. Akazawa M, Hashimoto K. Artificial intelligence in ovarian cancer diagnosis. *Anticancer Res* 2020; 40(8):4795-800. doi: 10.21873/anticancer.14482.
 23. Zhang H, Mao Y, Chen X, et al. Magnetic resonance imaging radiomics in categorizing ovarian masses and predicting clinical outcome: a preliminary study. *Eur Radiol* 2019; 29(7):3358-71. doi: 10.1007/s00330-019-06124-9.
 24. Anastasi E, Gigli S, Ballesio L, et al. The Complementary role of imaging and tumor biomarkers in gynecological cancers: an update of the literature. *Asian Pac J Cancer Prev* 2018; 19(2):309-17. doi: 10.22034/APJCP.2018.19.2.309.
 25. Qian L, Ren J, Liu A, et al. MR imaging of epithelial ovarian cancer: a combined model to predict histologic subtypes. *Eur Radiol* 2020; 30(11):5815-25. doi: 10.1007/s00330-020-06993-5.
 26. Takaya H, Nakai H, Sakai K, et al. Intratumor heterogeneity and homologous recombination deficiency of high-grade serous ovarian cancer are associated with prognosis and molecular subtype and change in treatment course. *Gynecol Oncol* 2020; 156(2):415-22. doi: 10.1016/j.ygyno.2019.11.013.
 27. Bodelon C, Killian JK, Sampson JN, et al. Molecular classification of epithelial ovarian cancer based on methylation profiling: evidence for survival heterogeneity. *Clin Cancer Res* 2019; 25(19):5937-46. doi: 10.1158/1078-0432.CCR-18-3720.
 28. Macintyre G, Goranova TE, De Silva D, et al. Copy number signatures and mutational processes in ovarian carcinoma. *Nat Genet* 2018; 50(9):1262-70. doi: 10.1038/s41588-018-0179-8.
 29. Jimenez-Sanchez A, Memon D, Pourpe S, et al. Heterogeneous tumor-immune microenvironments among differentially growing metastases in an ovarian cancer patient. *Cell* 2017; 170(5):927-38. doi: 10.1016/

- j.cell.2017.07.025.
30. Gillies RJ, Kinahan PE, Hricak H. Radiomics: images are more than pictures, they are data. *Radiology* 2016; 278(2):563-77. doi: 10.1148/radiol.2015151169.
 31. Beer L, Martin-Gonzalez P, Delgado-Ortet M, et al. Ultrasound-guided targeted biopsies of CT-based radiomic tumour habitats: technical development and initial experience in metastatic ovarian cancer. *Eur Radiol* 2021; 31(6):3765-72. doi: 10.1007/s00330-020-07560-8.
 32. Forstner R, Sala E, Kinkel K, et al. ESUR guidelines: ovarian cancer staging and follow-up. *Eur Radiol* 2010; 20(12):2773-80. doi: 10.1007/s00330-010-1886-4.
 33. Javadi S, Ganeshan DM, Qayyum A, et al. Ovarian cancer, the revised FIGO staging system, and the role of imaging. *AJR Am J Roentgenol* 2016; 206(6):1351-60. doi: 10.2214/AJR.15.15199.
 34. Michielsen K, Vergote I, Op DBK, et al. Whole-body MRI with diffusion-weighted sequence for staging of patients with suspected ovarian cancer: a clinical feasibility study in comparison to CT and FDG-PET/CT. *Eur Radiol* 2014; 24(4):889-901. doi: 10.1007/s00330-013-3083-8.
 35. Nougaret S, Addley HC, Colombo PE, et al. Ovarian carcinomatosis: how the radiologist can help plan the surgical approach. *Radiographics* 2012; 32(6):1775-800, 1800-03. doi: 10.1148/rg.326125511.
 36. Solass W, Horvath P, Struller F, et al. Functional vascular anatomy of the peritoneum in health and disease. *Pleura Peritoneum* 2016; 1(3):145-58. doi: 10.1515/pp-2016-0015.
 37. Sehouli J, Grabowski JP. Surgery in recurrent ovarian cancer. *Cancer* 2019; 125 Suppl 24:4598-601. doi: 10.1002/cncr.32511.
 38. Song XL, Ren JL, Yao TY, et al. Radiomics based on multisequence magnetic resonance imaging for the preoperative prediction of peritoneal metastasis in ovarian cancer. *Eur Radiol* 2021; E-pub: May 4, 2021. doi: 10.1007/s00330-021-08004-7.
 39. Ai Y, Zhang J, Jin J, et al. Preoperative prediction of metastasis for ovarian cancer based on computed tomography radiomics features and clinical factors. *Front Oncol* 2021; 11:610742. doi: 10.3389/fonc.2021.610742.
 40. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021. *CA Cancer J Clin* 2021; 71(1):7-33. doi: 10.3322/caac.21654.
 41. Rambau PF, Vierkant RA, Intermaggio MP, et al. Association of p16 expression with prognosis varies across ovarian carcinoma histotypes: an ovarian tumor tissue analysis consortium study. *J Pathol Clin Res* 2018; 4(4):250-61. doi: 10.1002/cjp2.109.
 42. Parkinson CA, Gale D, Piskorz AM, et al. Exploratory analysis of TP53 mutations in circulating tumour DNA as biomarkers of treatment response for patients with relapsed high-grade serous ovarian carcinoma: a retrospective study. *PLoS Med* 2016; 13(12):e1002198. doi: 10.1371/journal.pmed.1002198.
 43. Schwarz RF, Ng CK, Cooke SL, et al. Spatial and temporal heterogeneity in high-grade serous ovarian cancer: a phylogenetic analysis. *PLoS Med* 2015; 12(2):e1001789. doi: 10.1371/journal.pmed.1001789.
 44. Lu H, Arshad M, Thornton A, et al. A mathematical-descriptor of tumor-mesoscopic-structure from computed-tomography images annotates prognostic and molecular-phenotypes of epithelial ovarian cancer. *Nat Commun* 2019; 10(1):764. doi: 10.1038/s41467-019-08718-9.
 45. Meier A, Veeraraghavan H, Nougaret S, et al. Association between CT-texture-derived tumor heterogeneity, outcomes, and BRCA mutation status in patients with high-grade serous ovarian cancer. *Abdom Radiol (NY)* 2019; 44(6):2040-7. doi: 10.1007/s00261-018-1840-5.
 46. Zargari A, Du Y, Heidari M, et al. Prediction of chemotherapy response in ovarian cancer patients using a new clustered quantitative image marker. *Phys Med Biol* 2018; 63(15):155020. doi:10.1088/1361-6560/aad3ab.
 47. Rizzo S, Botta F, Raimondi S, et al. Radiomics of high-grade serous ovarian cancer: association between quantitative CT features, residual tumour and disease progression within 12 months. *Eur Radiol* 2018; 28(11):4849-59. doi: 10.1007/s00330-018-5389-z.
 48. Wei W, Rong Y, Liu Z, et al. Radiomics: a novel CT-based method of predicting postoperative recurrence in ovarian cancer. *Annu Int Conf IEEE Eng Med Biol Soc* 2018; 2018:4130-33. doi: 10.1109/EMBC.2018.8513351.
 49. Vargas HA, Veeraraghavan H, Micco M, et al. A novel representation of inter-site tumour heterogeneity from pre-treatment computed tomography textures classifies ovarian cancers by clinical outcome. *Eur Radiol* 2017; 27(9):3991-4001. doi: 10.1007/s00330-017-4779-y.
 50. Wang S, Liu Z, Rong Y, et al. Deep learning provides a new computed tomography-based prognostic biomarker for recurrence prediction in high-grade serous ovarian cancer. *Radiother Oncol* 2019; 132:171-7. doi: 10.1016/j.radonc.2018.10.019.