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SOLICITED REVIEW

Adnexal lesions: Imaging strategies for ultrasound and MR imaging

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Ovarian cancer

Abstract Adnexal lesions are routinely encountered in general practice. Ultrasound is the first line of investigation in determining the benign or malignant potential of an adnexal lesion. In the cases of classic simple cysts, hemorrhagic cysts, endometriomas, dermoids and obviously malignant lesions, ultrasound may be sufficient for management recommendations. In cases where there is an isolated adnexal lesion, without peritoneal disease or serum CA-125 elevation, and in lesions considered indeterminate on ultrasound, MR imaging with incorporation of the ADNEx MR score can increase the specificity for the diagnosis of benignity or malignancy. This article will review the imaging evaluation of adnexal lesions and how to incorporate the ADNEx MR score to help guide clinical management.

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Adnexal lesions are commonly encountered in daily radiology practice with an estimated prevalence of 4—18% in the general population [1—6]. The management of adnexal lesions varies based on the imaging appearance and clinical picture [7—15]. The importance of accurately characterizing adnexal lesions on imaging is to help avoid inappropriate surgery in benign lesions and triage suspected cancers to a gynecological oncologist. The treatment options for ovarian cancer have expanded given recent morphological and molecular studies which have led to the realization that ovarian cancer is a heterogeneous group of tumors and that treatments need to be tailored to the specific subtype for the best clinical outcomes [16—19]. For example, preoperative counseling may be needed in younger patients desiring fertility sparing surgery if the lesion is suspected to be a borderline tumor or possible benign ovarian neoplasm. The purpose of this review article is to address the evaluation and management of adnexal lesions seen on imaging.

Ultrasound: characterization of adnexal lesions and management consideration

Gray scale and Doppler ultrasonography is the first modality with which an adnexal lesion is evaluated due to the ability of ultrasound to characterize the majority of adnexal lesions [7—10,14,20—23]. Ultrasound is excellent at classifying classic simple cysts, hemorrhagic cysts, endometriomas and dermoids, as well as identifying lesions suspicious for malignancy (Fig. 1) [20,23—26]. Multiple large studies have shown that classic simple cysts are benign and do not represent ovarian carcinoma [2—5,11,12,27,28]. The majority of simple cysts resolve on subsequent imaging and those cysts, which do not resolve are benign lesions, such as follicular cysts or cystadenomas [2—5]. Classic hemorrhagic cysts, endometriomas and dermoids all have a very low risk of cancer on the order of 1—2% [29,30]. Therefore, when classic simple cysts, hemorrhagic cysts, endometriomas and dermoids are discovered on ultrasound, the patient can be assured of a benign process in the majority of cases [7,9,15]. On the other end of the spectrum, cystic adnexal lesions with vascular soft tissue and solid vascular adnexal lesions are considered suspicious for ovarian cancer, particularly when there is associated peritoneal disease on ultrasound or in the setting of a markedly elevated serum CA-125 [9—11,13,23,24,26,31—33]. In these patients, prompt referral to a gynecologic oncologist is the most advantageous [34]. Sometimes, in early stage cancers and certain subtypes of tumor, the serum CA-125 levels will not be elevated [16,35]. In these cases, MRI could be used to increase the specificity for the diagnosis of cancer and assist in triaging the patient to follow up versus surgical consultation [36].

In approximately 20% of patients, initial ultrasound exam is not able to characterize the adnexal lesion as benign or suspicious for malignancy and these lesions are considered intermediate on imaging [11,23,37—42]. There is no universally accepted definition of a sonographically ''indeterminate'' adnexal lesion; however, several descriptions exist in the literature. For the purposes of this monograph, an indeterminate adnexal lesion is a lesion in the pelvis that is of indeterminate anatomic origin or an adnexal lesion with avascular internal soft tissue components or irregular septations or a non-classic appearing endometrioma, dermoid and hemorrhagic cyst [9,11,14,37,40,42] (Fig. 2). Given the rate of ovarian cancer in a sonographically indeterminate adnexal lesion ranges between 5—40% [11,37,42], these lesions pose a dilemma for radiologists. If indeterminate lesions are referred for surgical evaluation, there is a risk of overtreatment. On the other hand, if imaging surveillance is suggested, there is a risk of losing the ''window'' for catching early stage disease. In these cases, further assessment by MR imaging can help the referring clinician decide if further assessment by a gynecologist or gynecologic oncologic surgeon should be performed, versus continued imaging follow up. MR imaging has been shown in multiple studies to have a high sensitivity and specificity for characterizing adnexal lesions as benign or potentially malignant, averaging greater than 95% [36,43—46].

MR imaging of sonographically indeterminate adnexal lesions: background and imaging requirements

MRI is capable of further assessing adnexal lesions. The benefit of MR imaging, particularly in an isolated adnexal lesion, is that MR imaging can potentially help avoid surgical referrals for benign lesions. A recent study assessing the ability of the SRU guidelines to risk stratify adnexal cysts demonstrated that the use of MR imaging would potentially have reduced the number of surgical evaluations for benign cysts by 89% [41]. This reduction in surgical referrals is not surprising given MR imaging's ability to distinguish between benign and malignant adnexal lesions. MR imaging has been shown to have a high NPV (100%) when there is no enhancing solid tissue associated with the adnexal lesion, which is highly reassuring for benignity [36]. Furthermore, time-intensity enhancement curves can be used to stratify lesions. If a lesion contains solid tissue that has an initial rise in signal post-contrast, which is steeper than the myometrium, the positive predictive value for malignancy is greater than 90% [36]. In these cases, prompt referral to a gynecologic oncologist is most advantageous [34].

MR imaging of an adnexal lesion can be performed on a 1.5 or 3T scanner. The MR imaging protocol for adnexal lesion characterization should include a pre-contrast axial T1-weighted, T2-weighted (preferably in two planes), post-contrast T1-weighted (dynamic sequence) and DW (with the higher b-value > 1000) images. There should be a fat saturated and non-fat saturated set of either T1-weighted or T2-weighted images in order to detect fat within the lesion. Papillary projections within ovarian neoplasms can be quite small (3 mm) and therefore a slice thickness of 3 mm or less for the T2-weighted and contrast enhanced T1-weighted images is ideal. Use of a dynamic contrast enhanced perfusion series enables evaluation of time-intensity curves and improves risk stratification. An attempt should be made to acquire the dynamic contrast series in a plane that includes both the suspected solid tissue associated within the ovarian lesion and the myometrium and should have a temporal resolution of less than or equal to 15 seconds per phase. From

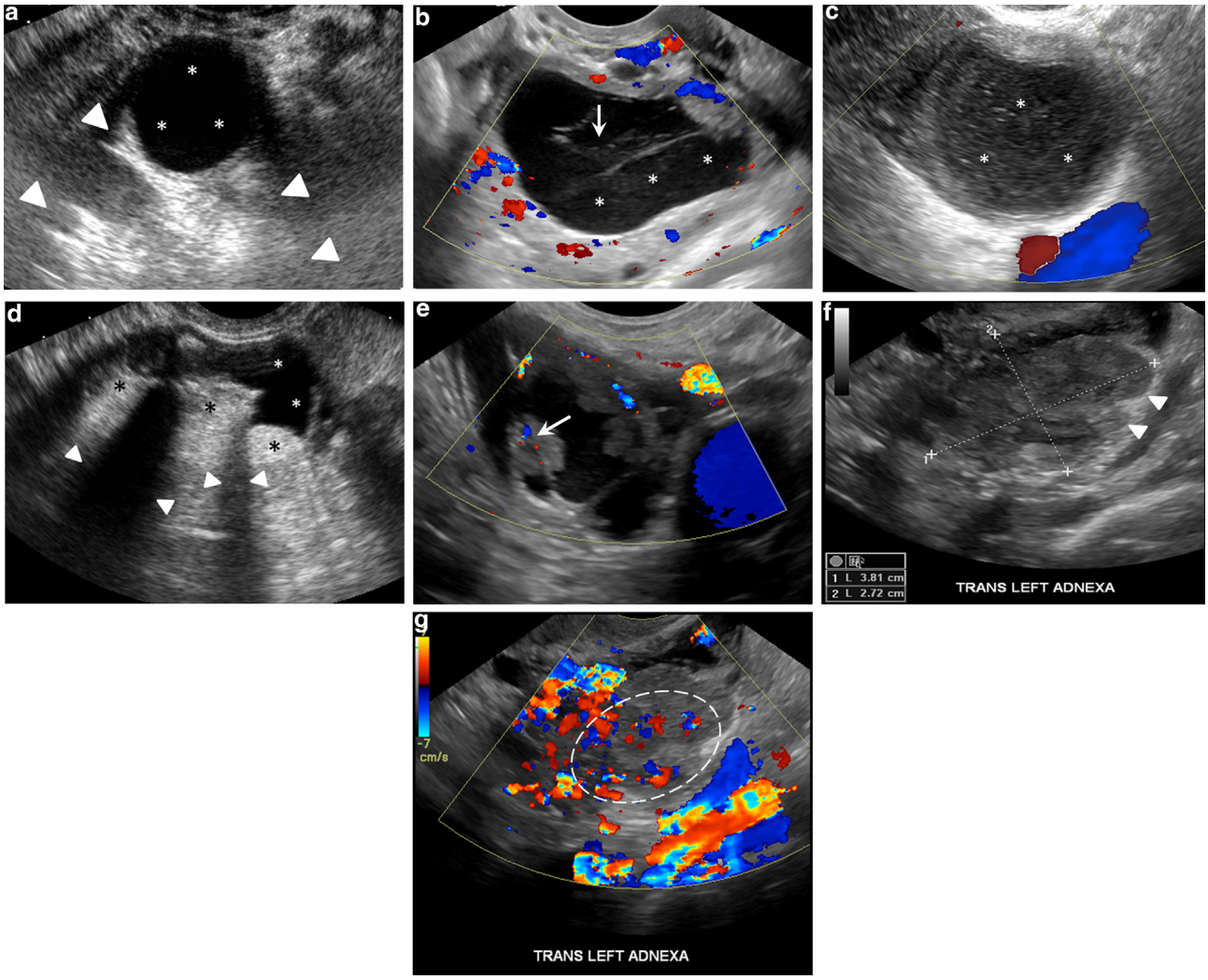


Figure 1. a: Gray scale and color Doppler ultrasound image of a classic simple cyst, with anechoic fluid (asterisks) and increased through transmission posteriorly (arrowheads); b: Gray scale and color Doppler ultrasound image of a classic hemorrhagic cyst, with internal debris (asterisks), retractile clot (arrow) and no internal color Doppler blood flow; c: Gray scale and color Doppler ultrasound image of a classic endometrioma, with ground glass or homogeneous low-level echoes throughout the lesion (asterisks); d: Gray scale and color Doppler ultrasound image of a classic dermoid, with simple fluid (white asterisks) and echogenic components (black asterisks) with associated acoustic shadowing (arrowheads); e: Gray scale and color Doppler ultrasound image of a partially cystic left adnexal lesion with internal nodules, one of which exhibits color Doppler flow (arrow). On pathologic evaluation, this was a borderline serous tumor; f: Gray scale and color Doppler ultrasound image of a solid left adnexal lesion with lobular borders (arrowheads); g: Gray scale and color Doppler ultrasound image of the same solid left adnexal lesion as pictured in (f), with significant internal color Doppler flow (dashed oval). On pathologic evaluation, this was a high grade serous tumor.

the perfusion series, time intensity curves for the lesion and the myometrium should be generated using commercially available perfusion analysis software (i.e. software packages used in breast or prostate MR). To optimize MR images, patient preparation may include: fasting for 4—6 hours prior to the MR exam, use of an anti-peristaltic agent, and instructing the patient to void within 30 minutes of imaging [47].

MR imaging analysis of adnexal lesions: ADNEx MR scoring system

The ADNEx MR scoring system can be used to assess and risk stratify adnexal lesions. The system combines both anatomical and functional MR images to assign a numeric score: the ADNEx MR score. This score communicates the malignancy risk to the referring clinician, with a higher score correlating with a higher risk of malignancy (Table 1). Within this scoring system, malignancy includes borderline, low grade and high-grade ovarian tumors; all other adnexal lesions are considered benign.

Prior to scoring, the radiologist needs to assess the internal composition of the lesion and whether the lesion contains solid tissue (Table 2). If any tissue is present, the T2 signal, high B-value DW signal and the perfusion curve characteristics of the solid tissue should be assessed. If a dynamic contrast enhanced MR series is not obtained, the ADNEx MR score can still be utilized, however, the specificity

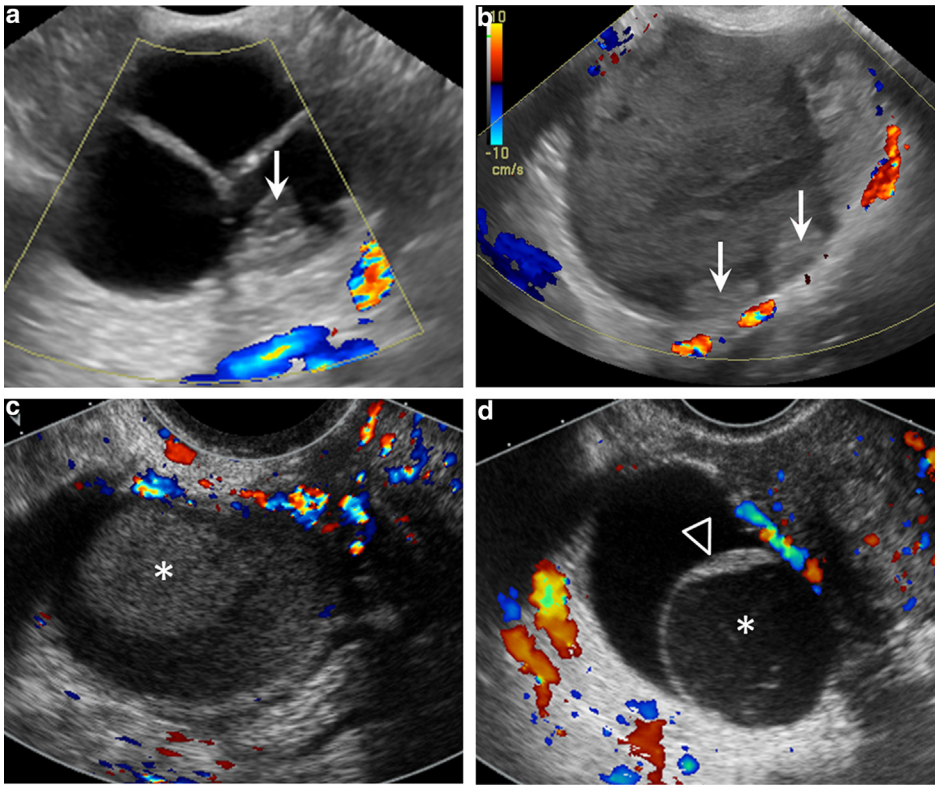


Figure 2. a: Gray scale and color Doppler ultrasound image of a partially cystic adnexal lesion with internal septations and a nodule, which does not have any internal color Doppler flow (arrow). The lack of color Doppler flow makes this lesion indeterminate on US; b: Gray scale and color Doppler ultrasound image of an adnexal lesion with internal heterogeneous echoes, and nodular areas along the posterior wall which lacks color Doppler flow (arrows). The presence of avascular solid nodules along the posterior wall makes this lesion indeterminate on ultrasound; c: Gray scale and color Doppler ultrasound image of a partially cystic adnexal lesion with internal homogeneous low level echoes and a spherical hyperechoic area (asterisk) with no posterior acoustic shadowing. This appearance is atypical of a dermoid because of the lack of posterior acoustic shadowing adjacent to the hyperechoic area; d: Gray scale and color Doppler ultrasound image of a partially cystic adnexal lesion, with simple fluid in a portion of the lesion and homogenous low level echoes in a portion (asterisk), separated by an irregularly thickened septations which lacks color Doppler flow (arrowhead). This appearance is atypical of a hemorrhagic cyst because of the avascular irregular thickened septation.

Table 1 The ADNEx MR score and positive predictive value for malignancy.

MRI finding	ADNEx MR score	PPV for malignancy (%)
No adnexal lesion	1	N/A
Adnexal cyst: no wall enhancement or solid tissue	2	0
Adnexal cyst: one locule, smooth enhancing wall and no solid tissue		< 1
Adnexal cyst: fat containing, no solid tissue (May have multiple locules)		< 1
Solid tissue[a]: very low homogenous signal on T2WI and the high b-value DW image		< 1
Adnexal cyst: one locule, irregular enhancing wall	3	< 5
Adnexal cyst: multilocular with simple, proteinaceous, hemorrhagic or endometriotic fluid		< 5
Solid tissue: Type 1 dynamic perfusion curve (*excludes solid tissue meeting score 2 criteria)		< 5
Solid tissue: Type 2 dynamic perfusion curve (*excludes solid tissue meeting score 2 criteria)	4	5—95
Solid tissue: Type 3 dynamic perfusion curve (*excludes solid tissue meeting score 2 criteria)	5	> 90
Definite peritoneal or omental thickening or nodules		> 95

[a] Excludes solid tissue meeting score 2 criteria.

Table 2 Imaging examples of solid tissue. Solid tissue is the enhancing component of an adnexal lesion, which exhibits one of the following morphologic features: irregular septations, papillary projections, nodules or solid portions. Enhancing smooth septations and non-enhancing debris are not considered solid tissue.

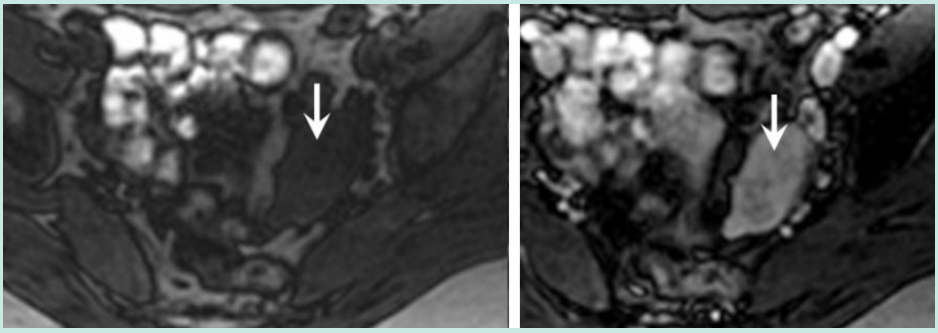
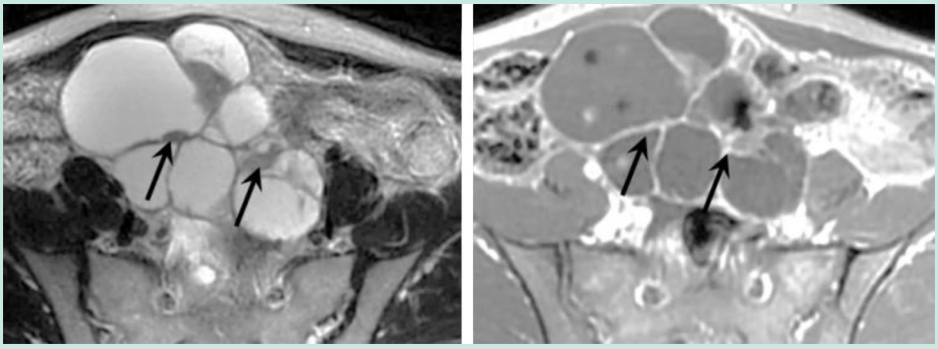
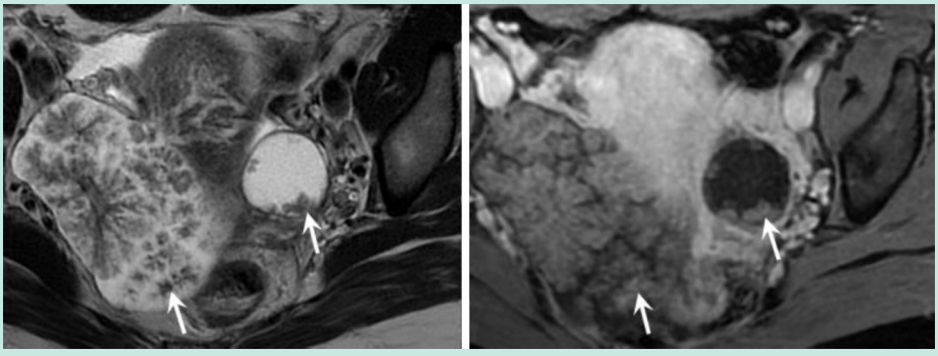
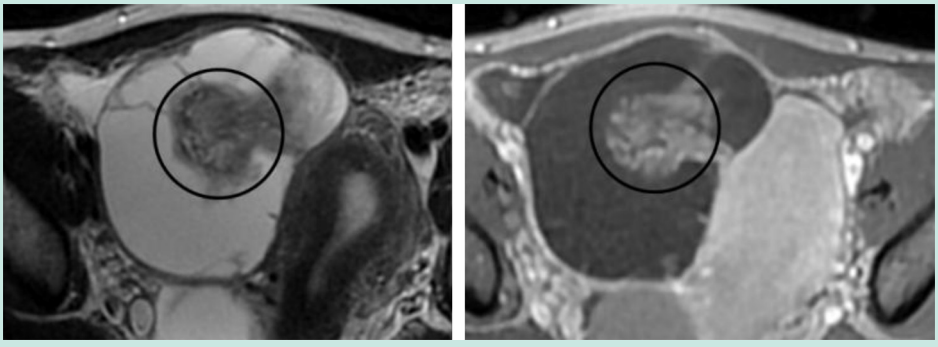
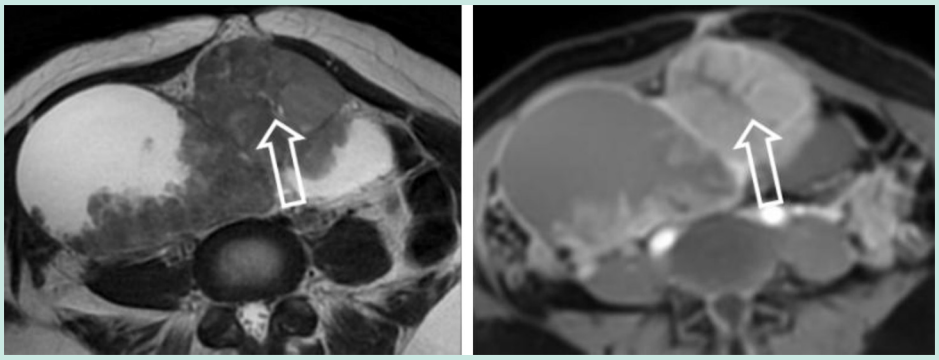
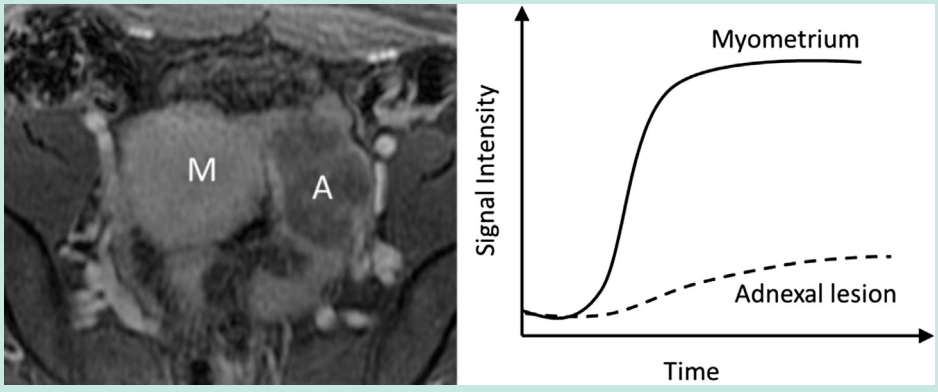
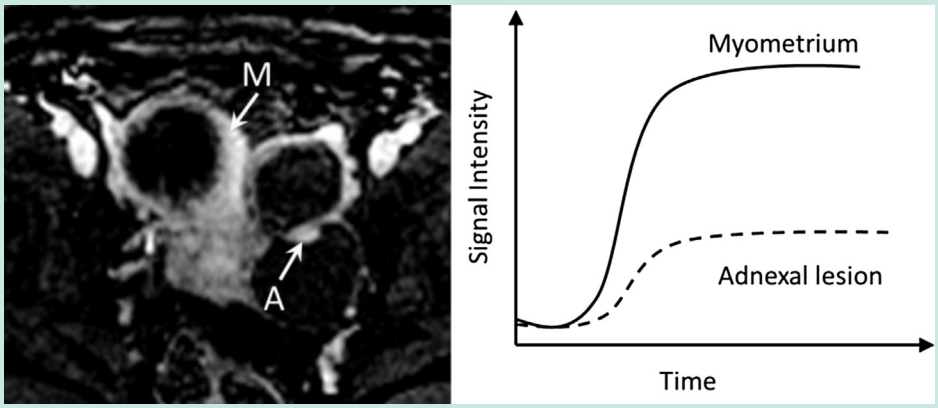
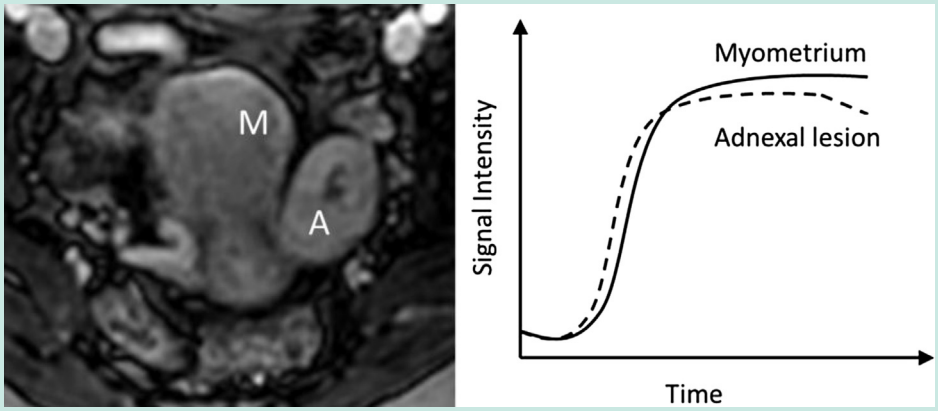
Solid tissue definitions	Images
Non-fluid component which enhances on post-contrast images (arrows)	
Morphologic features	
Irregular septations (black arrows)	
Papillary projections (white arrows)	
Nodules (black circles)	

Table 2 (*Continued*)

Solid tissue definitions	Images
Solid portions (open white arrows)	
Time intensity curves	
Type 1 time-intensity curve: Enhancement of the solid tissue with an initial slope less than the myometrium, minimal and gradual increase in signal over time with no plateau	
Type 2 time-intensity curve: Enhancement of the solid tissue with an initial slope less than the myometrium, moderate increase in signal intensity with a plateau	
Type 3 time-intensity curve: Enhancement of the solid tissue with an initial slope greater than the myometrium, marked increase in signal intensity with a plateau	

for malignancy will drop below 90% due to the lack of perfusion curve characteristics. Even without dynamic contrast series, the system remains highly accurate in the diagnosis of a benign lesion (score 2), with an accuracy of 96.4% [36]. Furthermore, the lack of enhancement of any part of the lesion yields a PPV equal to zero for malignancy and is extremely reassuring for benignity [36].

Two guiding principles are important to understand before applying this system to the characterization of adnexal lesions. First, the system was developed on an average risk population of women presenting to MR imaging for the assessment of a known adnexal lesion discovered on ultrasound imaging. Clinical history, including acute symptoms or increased risk of ovarian cancer (eg. BRCA gene mutation), should guide treatment of the patient in addition to the imaging features. Second, several basic definitions are important in the assessment of adnexal lesions, including:

- lesion: that portion of the adnexa or ovary which is not normal ovarian parenchyma, a follicle or corpus luteum;
- cyst: lesion which contains fluid; may have one locule or multiple locules; may contain solid tissue;
- solid tissue: non-fluid component of the lesion, which enhances on dynamic post-contrast images (includes irregular septations; papillary projections, nodules, solid portions). Enhancing smooth septations and non-enhancing debris are not solid tissue;
- Dynamic perfusion curves. In cases where the internal content of a cyst is hyperintense on T1, it is important to use subtraction images to assess for internal enhancing components.

Type 1 time-intensity curve: enhancement of the solid tissue with an initial slope less than the myometrium, minimal and gradual increase in signal over time with no plateau.

Type 2 time-intensity curve: enhancement of the solid tissue with an initial slope less than the myometrium, moderate increase in signal intensity with a plateau.

Type 3 time-intensity curve: enhancement of the solid tissue with an initial slope greater than the myometrium, marked increase in signal intensity with a plateau.

Table 1 outlines the ADNEx MR score findings, correlative scoring system and the associated PPV for malignancy. The method for assessing a lesion can begin with determining if there is any enhancement of the wall or any portion of the lesion. If there is none, then a score 2 can be assigned (Fig. 3). It is also helpful to determine if the lesion contains fat. Fat will be high in signal on T1-weighted images, high in signal on T2-weighted images and the foci of fat will saturate out, or become low in signal, on fat-saturated images (Fig. 3). Dermoids may also have wall enhancement, contain non-enhancing components such as hair, calcifications and debris, and may be unilocular or multilocular. Dermoids with these characteristics can be assigned a score 2. Dermoids may have a small component of enhancing tissue and remain benign. However, because of the minimal risk of malignant transformation in mature teratomas or small risk of an immature teratoma if the patient is young, the presence of enhancing tissue within a dermoid takes the lesion out of the ADNEx MR framework and clinical management is recommended.

If there is no fat present in the lesion and there is enhancement of the any portion, the next step would be to assess the wall, number of locules and determine if there is any solid tissue in the lesion. If the lesion is a unilocular cyst with an enhancing smooth wall and no solid tissue, then a score 2 can be assigned (Fig. 3). If the lesion is unilocular with an irregular wall or the lesion is multilocular with no solid tissue, then a score 3 can be assigned. If there is solid tissue, then assessing the signal of the solid tissue can help categorize the lesion. If the solid tissue is homogenously dark on T2-weighted and the high B-value DW images, then the lesion can be assigned a score 2 (Fig. 3). If the solid tissue is homogenously or heterogeneously isointense or hyperintense on T2-weighted images and hyperintense on the high B-value DW image, then the score would be based on the dynamic curve type: type 1 time-intensity curve would be a score 3, type 2 time-intensity curve would be a score 4 and type 3 time-intensity curve would be a score 5 (Figs. 4 and 5).

Management of adnexal lesions by ADNEx MR score: on-going studies

ADNEx MR score relays the radiologist's suspicion of ovarian cancer to the clinician with a high level of accuracy in prospective multicenter studies testing the ADNEx MR scoring system for the characterization of adnexal masses [36,48,49]. The ASCORDIA protocol (ClinicalTrials.gov Identifier: NCT02664597), which aims to standardize clinical practice for adnexal lesions by:

- limiting surgery on benign adnexal lesions in order to decrease morbidity and maintain fertility;
- to assure patients with ovarian cancer undergo the correct primary surgery to assure the best outcomes [34,50—52].

This is a currently ongoing prospective French multicenter randomized diagnostic study involving 7 centers. In the control group, the complex adnexal mass will be managed according to the standard strategy and treatment plan routinely used by the multidisciplinary team. In the intervention group, patients will undergo pelvic MR imaging (1.5 or 3T) to include routine anatomic imaging sequences: T2-weighted, T1-weighted with and without fat suppression and T1-weighted with fat suppression after dynamic gadolinium injection and functional imaging sequences (perfusion and diffusion-weighted sequences). Prospectively, a senior radiologist will independently analyzes any adnexal masses and classify them using the ADNEx MR scoring system. The patient will be managed according to the ADNEx MR score as follows:

- for masses less than 4 cm:
  - score ≤ 3: follow-up imaging/score = 4: diagnostic surgery/score 5 = oncologic cytoreduction surgery;
- for masses between 4 and 6 cm:
  - score ≤ 3: follow-up imaging, except for suspicion of dermoid cysts and endometriomas/score = 4: diagnostic surgery/score 5 = oncologic cytoreduction surgery;
- for masses greater than 6 cm:
  - score ≤ 2: no surgery except for dermoid cysts and endometriomas/score 3 and 4: diagnostic surgery/score 5: oncologic cytoreduction surgery.

The primary assessment criterion is the rate of inappropriate surgical intervention during the two first months

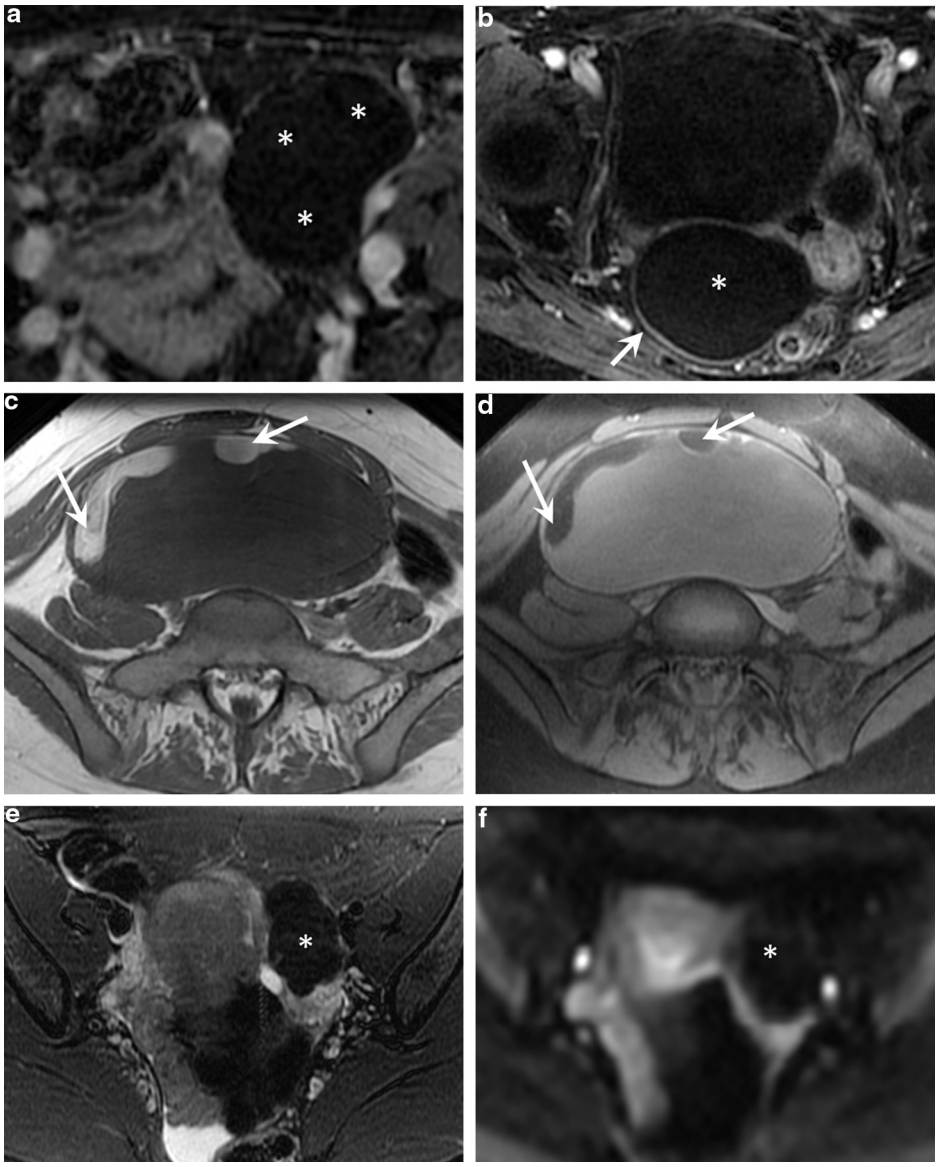


Figure 3. Examples ADNEx MR Score 2 lesions. a: axial fat-saturated post-contrast T1 image depicts a left adnexal cyst (asterisks) with no wall enhancement or solid tissue. Pathologic evaluation revealed a cystadenoma; b: axial fat-saturated post-contrast T1 image depicts a simple adnexal cyst (asterisk) involving the right ovary with wall enhancement (arrow) and no solid tissue. Pathologic evaluation revealed a benign serous cyst; c: axial T1 image shows a large midline adnexal cyst with hyperintense T1 signal in lobular solid components along the anterior aspect of the lesion (arrows); d: axial T1 fat-saturated image of the same lesion pictured in (c), with drop out of signal in the lobular solid components along the anterior aspect of the lesion (arrows). Pathologic evaluation revealed a mature teratoma (dermoid); e: axial fat-saturated T2 image shows a left adnexal lesion with homogenously hypointense signal (asterisk); f: axial DW B = 1200 image of the same lesion pictured in (e), with homogenously hypointense signal within the lesion (asterisk). Pathologic evaluation revealed an ovarian fibroma.

after MR imaging (i.e unnecessary diagnostic surgery for benign lesions and incomplete staging for borderline or invasive cancer). The standard reference diagnosis will be given either by oncologic cytoreduction with histology, diagnostic surgery with histology and follow-up during 24 months after the initial diagnostic imaging or only follow-up until 24 months after the initial diagnostic imaging depending on the strategy. This study began in December 2016 and has enrolled 255/640 patients.

A second multicenter trial in the UK (NIHR funded MROC (MR in Ovarian Cancer) study: ClinicalTrials.gov Identifier: ISRCTN51246892) is a prospective multicenter study evaluating the MR imaging assignment of correct tumor stage and avoidance of inappropriate surgery when compared to computed tomography (CT) in women with suspected or confirmed ovarian cancer. The study includes 645 women in whom imaging and/or tumor markers have raised the concern for ovarian cancer. The definition of inappropriate surgery includes over-extensive surgery for ovarian lesions that were benign or borderline at histology or attempted radical cytoreductive ovarian cancer surgery, which could not be achieved due to extensive disease. All patients will have standard of care CT. This will be reported by the local

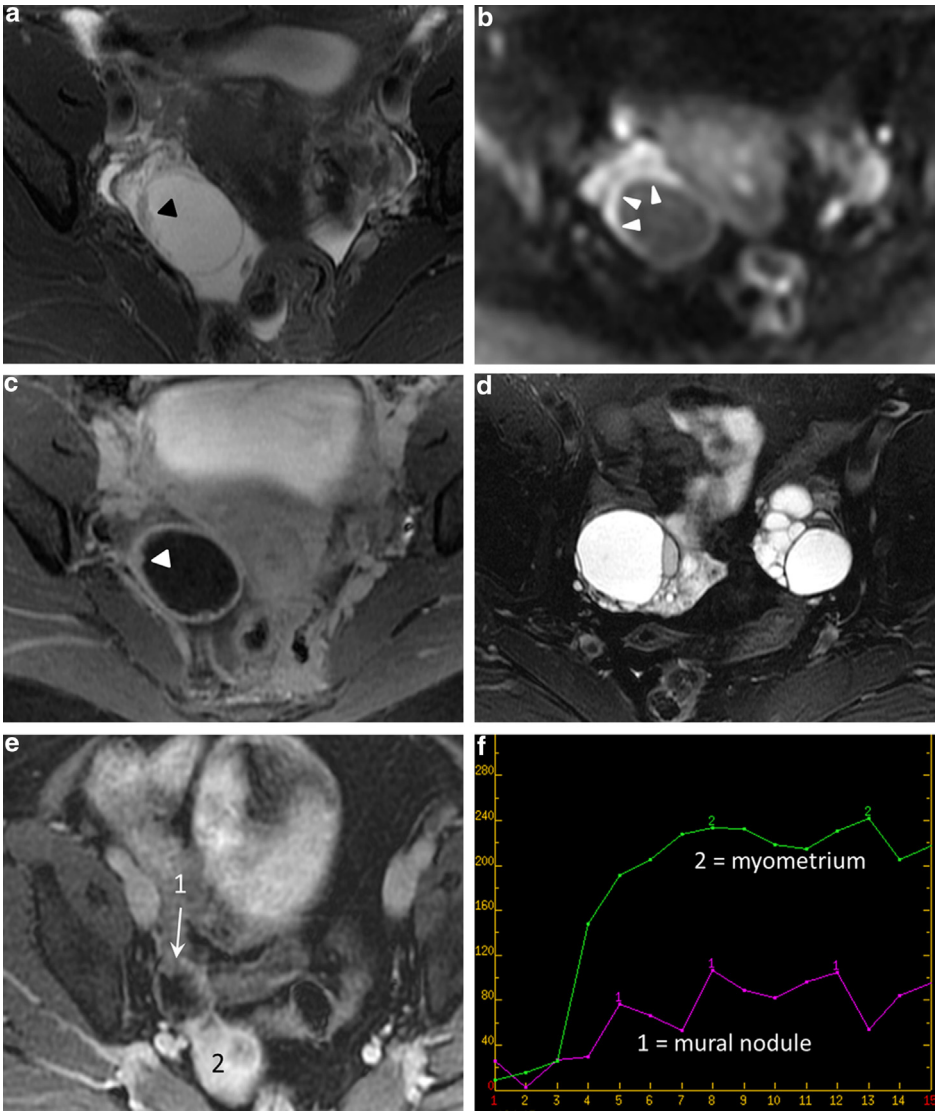


Figure 4. Examples of ADNEx MR score 3 lesions. a: axial fat-saturated T2 image shows a right adnexal lesion with an irregularly thickened wall (arrowhead); b: axial B = 1200 DW image depicts the same lesion as in (a) and the irregular portion of the wall exhibits high signal (arrowheads); c: axial fat-saturated post-contrast T1 image depicts the same lesion as in (a) and shows there is enhancement of the irregular wall (arrowhead). On pathologic evaluation, this was a borderline serous tumor; d: axial fat-saturated T2 image demonstrates bilateral multilocular adnexal lesions. Pathologic evaluation revealed bilateral mucinous cystadenomas; e: axial fat-saturated post-contrast T1 image depicts a right adnexal lesion with an enhancing mural nodule (1 and arrow); f: the mural nodule exhibits a type 1 time-intensity curve (1), with an initial slope less than the myometrium (2), minimal and gradual increase in signal over time with no plateau.

gynecologic oncology tumor board radiologist and a treatment plan will be recorded electronically by the clinical team. MR imaging will be then performed according to study protocol and reported by a different blinded radiologist. The MR imaging protocol will include adnexal mass characterization as well as evaluation of the mediastinum, diaphragm and entire peritoneal cavity on MR imaging, with DW and post-contrast T1-weighted imaging. The clinical team will then be provided with the ADNEx MR score of the mass, sites of peritoneal disease, suspicious lymph nodes and sites of metastases beyond the abdomen. If the MR imaging alters the treatment plan, the change in plan will be recorded. Treatment options, which will be captured, include:

- benign follow-up;
- fertility preserving surgery;
- cytoreductive surgery and commencement of chemotherapy.

The findings at surgery, histology and 9 months follow-up will be recorded. There are separate blinded evaluations by multiple clinical teams who provide theoretical treatment plans on each of the imaging paradigms (CT alone, MR imaging alone or CT and MR imaging combined). The reference standard for stage and appropriate treatment choice will be final expert panel review with all results from surgery, histology, complications and clinical outcome at 9 months following the first treatment. The study is due to complete recruitment in December 2019.

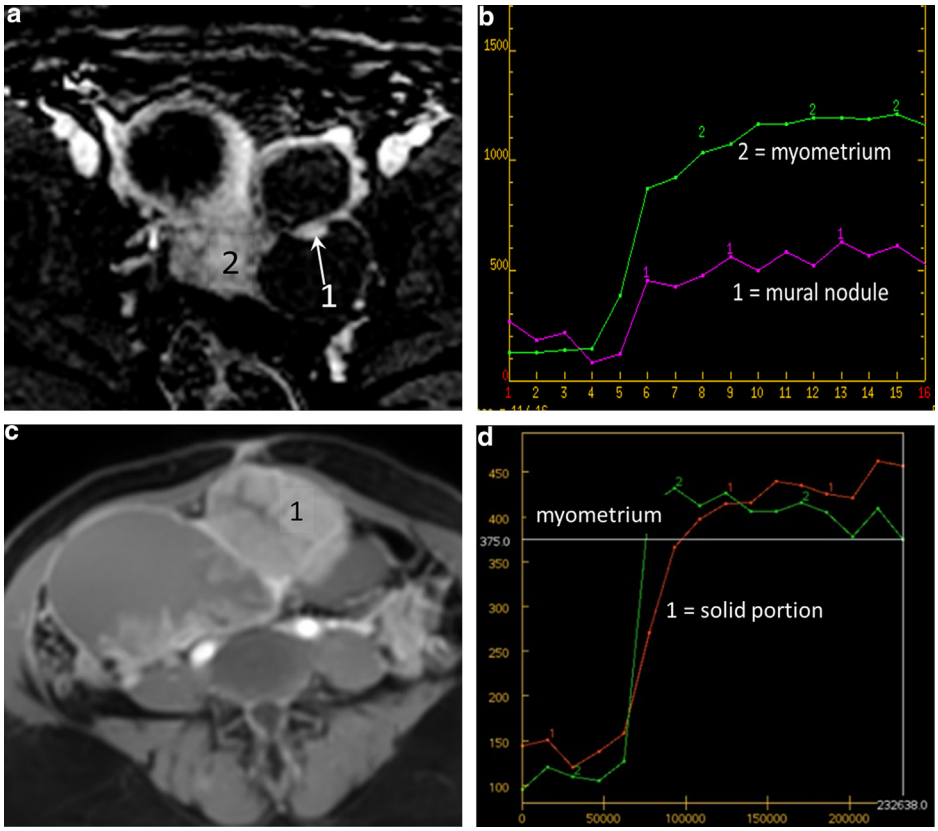


Figure 5. Examples of ADNEx MR Score 4 and 5 lesions. a: axial subtraction post-contrast T1 image depicts a right adnexal lesion with an enhancing mural nodule (1 and arrow); b: the mural nodule exhibits a type 2 time-intensity curve (1), with an initial slope less than the myometrium (2), moderate increase in signal intensity with a plateau, compatible with an ADNEx MR score 4 lesion; c: axial fat-saturated post-contrast T1 image depicts a right adnexal lesion with an enhancing solid portion (1); d: the solid portion exhibits a type 3 time-intensity curve (1), with an initial slope greater than the myometrium, moderate increase in signal intensity with a plateau, compatible with an ADNEx MR score 5 lesion.

Limitations of the MR ADNEx Score

There are limitations to using any image-based classification system for the characterization of adnexal lesions. The ADNEx MR score was developed on an average risk population of women presenting to MR imaging for the assessment of a known adnexal lesion discovered on ultrasound imaging [36]. The quoted PPV for malignancy in this monograph are for this specific population. The PPV in other populations may differ, such as women at higher risk for ovarian cancer (eg. *BRCA* gene mutation) or women with symptoms suggestive of infection, inflammation or endometriosis. The medical history and clinical scenario should be utilized to guide treatment of the patient. This is particularly true with ADNEx MR score 3 and 4 lesions because there is overlap between malignant lesions and benign entities such as hemorrhagic cysts, endometriomas, luteal cysts and inflammatory adnexal cysts. Correlation with history and physical examination is helpful in avoiding removal of a benign entity.

Another limitation of the ADNEx MR score is the evaluation of dermoids with enhancing soft tissue. A small number of dermoids have enhancing components and current research to assess the true risk of malignancy in these lesions is being performed. Up to 1–2% of benign teratomas will undergo malignant degeneration according to the pathology literature; however, this cannot be translated to a PPV for malignancy for dermoids evaluated with MR imaging. Given the lack of data regarding the PPV for malignancy of a dermoid with enhancing components, such dermoids should currently not be scored using the ADNEx MR framework and be managed clinically.

Conclusion

Ultrasound has a high specificity for the diagnosis of a benign lesion in cases of classic simple cysts, hemorrhagic cysts, endometriomas and dermoids. Likewise, ultrasound is fairly specific for the diagnosis of ovarian neoplasms when there is vascular solid tissue associated with the lesion, particularly when associated peritoneal disease is seen on ultrasound or in the setting of a marked elevated serum CA-125. However, ultrasound is less specific in the case of isolated adnexal lesions (without peritoneal disease or serum CA-125 elevation) and in lesions considered indeterminate on ultrasound. MR imaging with the ADNEx MR score can increase the specificity for the diagnosis of malignancy in isolated adnexal lesions and sonographically indeterminate adnexal lesions. Incorporating the ADNEx MR score into the evaluation of adnexal lesions can enhance diagnostic certainty and guide clinical management potentially avoiding inappropriate surgery in benign

lesions and expediting appropriate treatment in malignant lesions.

Disclosure of interest

The authors declare that they have no competing interest.

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