Imaging in gynaecological oncology follow-up

Howard BR, **Soeters RP**
Department of Obstetrics and Gynaecology, Gynaecology Oncology Unit, University of Cape Town/Groote Schuur and Vincent Pallotti Hospitals
Correspondence to: Dr Bruce Howard, e-mail: bhoward@mweb.co.za
Keywords: X-rays; ultrasound; computed tomography; magnetic resonance imaging; positron emission tomography; combined PET/CT

Abstract
The early detection of a gynaecological cancer recurrence is important in order to institute early treatment. Numerous imaging techniques have been used to follow up patients after treatment of gynaecological malignancies. These include plain X-rays, ultrasound, CT scan, MRI scan and PET or PET/CT scans. This review article will attempt to analyse the clinical value of these different modalities taking into account sensitivity, specificity, availability and cost factors.

South Afr J Gynaecol Oncol 2010;2(2):43-48

Introduction

Gynaecological cancers are a leading cause of morbidity and mortality in women. The American Cancer Society estimated that, in the last year, there were 78 490 new gynaecological malignancies, with 28 490 deaths.[1] Cervical cancer is still the second most common cancer of women worldwide and the commonest cancer amongst black African women in South Africa.[2] Endometrial cancer is the commonest gynaecological cancer in developed countries and ovarian cancer is the leading cause of death worldwide from gynaecological malignancies.

The follow-up of patients with gynaecological cancers post-therapy is important for the early detection of recurrences to institute early treatment. This follow-up is provided by a variety of different medical personnel, depending on the patient's socioeconomic status, location and access to medical services. The follow-up may be provided by multidisciplinary units, individual gynaecological oncologists, gynaecologists, oncologists, general practitioners or nursing personnel.

All these medical personnel use numerous modalities to detect a recurrence. These include the patient's history, clinical examination, cytology (cervical/vault smears), histology (biopsies/curettage), blood biochemistry (CA125) and numerous imaging techniques.

The imaging techniques used in follow-up may be part of routine screening, e.g. pelvic ultrasound (U/S), or may be directed towards a specific symptom, e.g. chest X-ray (CXR) for a productive cough or a computed tomography (CT) scan for persistent pelvic pain. The imaging techniques vary according to their sensitivity and specificity in detecting certain pathologies, and therefore the imaging technique used may depend on the cancer with which the patient was initially diagnosed.

Imaging may assist the clinician in assessing which mode of treatment would be best in the individual patient with the recurrence. These treatment modalities may include 1) palliation only, 2) chemotherapy, 3) radiotherapy, 4) surgery, or a combination of the above. The decision on which therapy to institute may have an impact on the disease-free and overall survival of the patient, but often more important in these patients is the issue of quality of life (QOL).

The costs of the different techniques also vary dramatically and may depend on the socioeconomic status of the patient. In South Africa, there is a huge disparity in what is both available and affordable in the public and private sectors.

This article will attempt to give an overview of the various imaging techniques and their roles in the detection of gynaecological cancer recurrences.

X-rays

X-rays are normally used to detect distant metastases of gynaecologic cancers. X-rays are not very useful in detecting local recurrence.

A CXR is the commonest modality used and may be performed routinely at regular intervals, or directed at specific symptoms. A CXR is useful in detecting lung or bony metastases and pleural effusions (Figure 1).

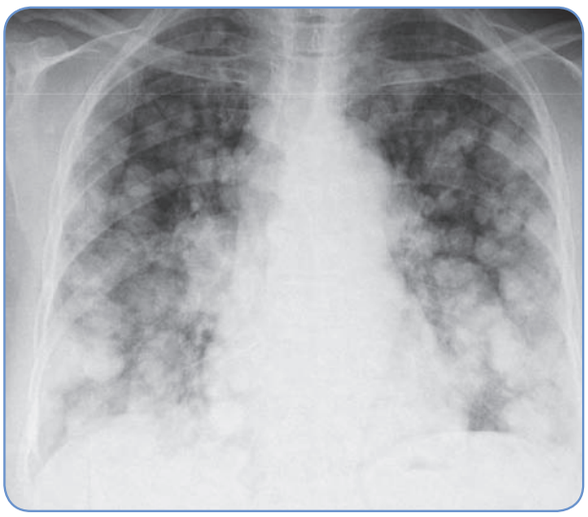

Figure 1: A CXR of a 42-year-old woman with "cannonball" chest metastases from cervical cancer

An analysis of the follow-up of 2 866 patients with endometrial cancer showed 9.9% of all recurrences were detected on CXR, but this had little impact on outcome due to the poor prognosis of patients with pulmonary metastases.[3] The role of routine CXR in the follow-up of gynaecological cancers is not evidenced in the literature, but should be reserved for patients with aggressive metastatic cancers e.g. sarcomas.

Other plain x-ray used in gynaecological cancers are the abdominal x-ray (AXR) in patients with suspected bowel obstruction or perforation (Figure 2), skeletal X-rays for bony metastases, intravenous pyelogram (IVP) for suspected ureteric obstruction and contrast-enhanced X-rays for suspected fistulas.

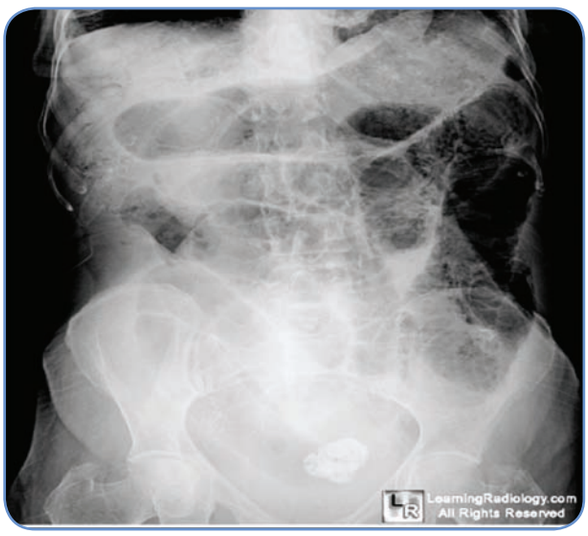

Figure 2: An AXR of bowel obstruction secondary to a pelvic ovarian recurrence

Ultrasound

The majority of gynaecologists and gynaecological oncologists have easy access to U/S. The relatively low cost and wide availability has made it the modality of choice to evaluate a suspected or palpable pelvic mass or pelvic recurrence.[4]

Both transvaginal (TVS) and transabdominal (TAS) ultrasonography are used in combination for the evaluation of pelvic masses and ascites. The use of the two in combination is due to the fact that TAS may be limited because of overlying intestinal gas or increased adipose tissue, and TVS has a limited field and thus may miss an intra-abdominal mass.[4] TAS may also be useful in detecting liver metastases and hydronephrosis.

U/S use in follow-up depends on which specific malignancy the patient was diagnosed with. U/S is relatively good at detecting cystic and solid masses and ascites, but has a limited role in detecting lymph nodes. U/S is, thus, more likely to be used routinely in the follow-up of ovarian cancer as opposed to cervix, endometrium, vulva, vagina or gestational trophoblastic neoplasia (GTN).

The majority of evidence in the gynaecological literature is based on the use of U/S in the assessment of adnexal and pelvic masses, at the initial diagnosis of ovarian cancer. This evidence can, however, be helpful in assessing recurrences by characterising pelvic masses, e.g. ovaries in a patient after radical hysterectomy for cervical cancer versus a lymphocyst. U/S has a sensitivity of 89% and a specificity of 73% of detecting malignancy when using a morphology index.[5]

The different methods used to differentiate between benign and malignant masses can also be used in recurrent pelvic masses. These include:

1. **Morphological scoring systems,** e.g. risk of malignancy index (RMI) (Table I). The RMI is normally used to triage patients with adnexal masses to decide who should manage or operate on a patient. Using a cut-off point of 250, a sensitivity of 70% and a specificity of 90% can be achieved.[6]
2. **Subjective assessment** of the B-mode grey-scale U/S – "pattern recognition" (Figures 3, 4, 5).
3. **Blood flow/Doppler studies** (Figure 6). A recent systematic review showed that the sensitivity of Doppler for detecting malignant ovarian lesions was 87% and the specificity was 90%.[7]
4. **Complex diagnostic models**: Logistic regression and artificial neural networks.

Table 1: RMI and incidence of cancer[6,8,9]

Risk	RMI	Women (%)	Risk of cancer (%)
Low	< 25	40	< 3
Moderate	25–250	30	20
High	> 250	30	75

RMI = U x M x CA125; where U = ultrasound score; M = menopausal status; CA125 in u/ml

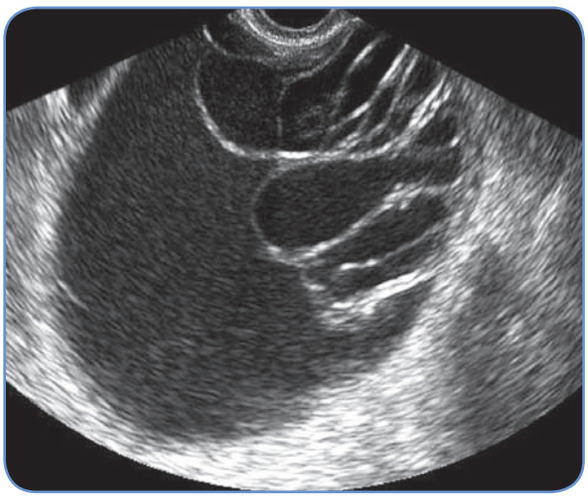

Figure 3: Benign mucinous cystadenoma

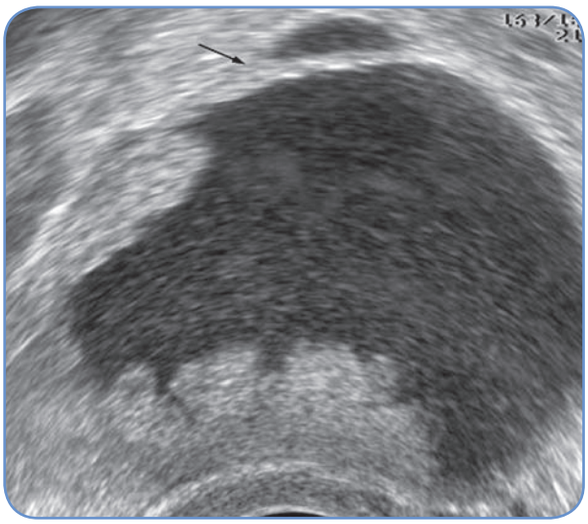

Figure 4: Borderline serous cystadenocarcinoma

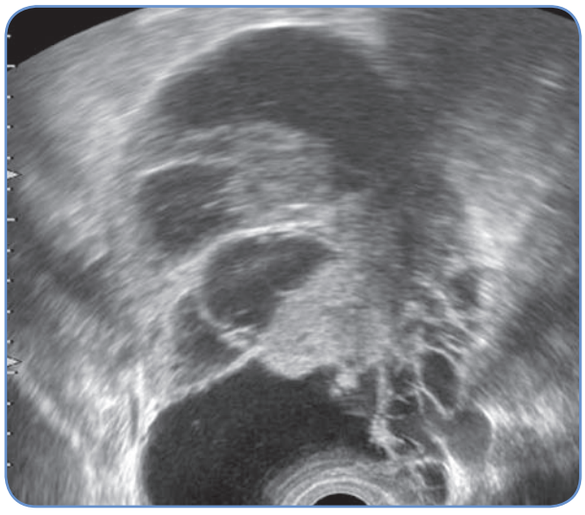

Figure 5: Malignant ovarian tumour

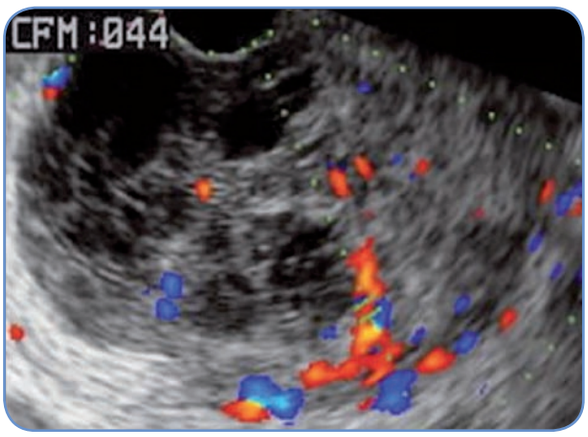

Figure 6: Increased Doppler flow in a malignant ovarian tumour

U/S thus is an important cost-effective modality used in gynaecological oncology follow-up, assisting in the detection and diagnosis of pelvic masses, pelvic recurrences, ascites, liver metastases and hydronephrosis.

Computed tomography

CT has, in the past, been commonly used in patients with suspected recurrent pelvic and abdominal gynaecological cancers. The suspicion of recurrence may be detected via history, clinical examination, U/S or biochemistry.

Traditional CT was not very useful in characterising whether a mass was malignant or benign because of its poor tissue contrast. Recent advances in CT technology and the availability of multidetector CT (MDCT), allows better detection and improved characterisation of pelvi/abdominal masses.[4] This is largely due to the ability to acquire thin (< 1 mm) sections and the ability to reformat images in any plane with spatial resolution similar to the original scanning plane.[4] Using this technology, studies have shown that MDCT has a sensitivity of 90% and specificity of 88.76% in diagnosing malignancy in pelvic masses in diagnosis and suspected recurrences[10] (Figure 7).

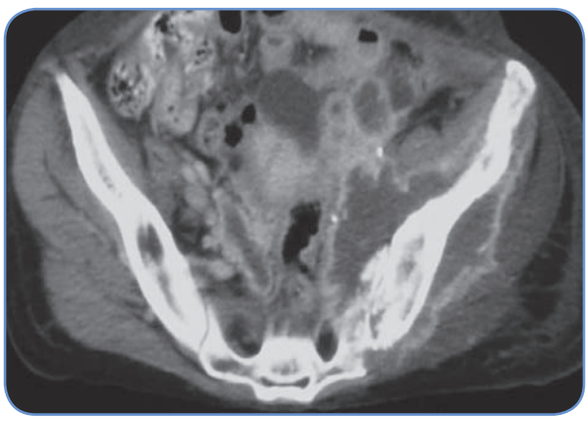

Figure 7: CT scan showing a pelvic side wall cervical cancer recurrence

The main uses of CT in the follow-up of gynaecological cancers are to detect bulky anatomical disease, ascites, liver/bony metastases or complications such as lymphocysts or fistulae (Figure 8). The limitations of CT are in the detection of smaller lesions < 1 cm in diameter and small lymph nodes.

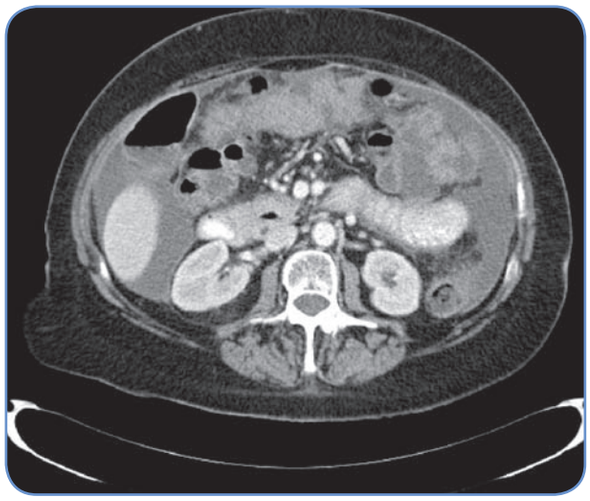

Figure 8: CT scan showing an omental cake and ascites in an ovarian cancer recurrence

Metastases from ovarian cancer are particularly difficult to detect with CT. The metastases are primarily peritoneal rather than parenchymal in location and usually occur on the surfaces of viscera.[11] Numerous studies have been done using CT in ovarian cancer surveillance, with a reported sensitivity of only 40–93% for detecting recurrent disease.[12–14] The advent of positron emission tomography (PET)/CT scans has improved the sensitivity and specificity and will be discussed later.

Although CT scans may be able to detect tumour recurrences > 1 cm, they are not very accurate in predicting resectability of recurrences. This may be more accurately determined by MRI which can differentiate better between radiation induced fibrosis and active tumour, as well as offering more information on tissue planes.

The wide availability and relative low cost of CT, in comparison to other imaging modalities, currently still makes it the imaging modality of choice in suspected recurrent gynaecological cancers.

Magnetic resonance imaging

MRI is well suited for the detection of gynaecological recurrences because of its excellent soft tissue contrast and multiplanar imaging ability and thus differentiates very well between normal and pathological tissues.[15]

The different properties of tissues can be evaluated depending on the times after each radiofrequency pulse. By varying these times, images can be "weighted" to change the contrast between different tissues resulting in T1- and T2-weighted sequences.[13] This has led to a marked improvement in image quality and thus information provided to clinicians.

MRI has been used with increasing frequency in the diagnosis, staging, planning and monitoring of treatment in gynaecological cancers, specifically cervical and endometrial cancer.

In endometrial cancer, MRI is being widely used to assess myometrial invasion, cervical stromal involvement, extra-uterine spread and enlarged lymph nodes. The overall accuracy of MRI for staging in endometrial cancer ranges from 82–92% and may be recommended for cases where there is a clinical suspicion of advanced disease, high grade lesions, or select histological subtypes such as papillary serous carcinoma.[15,16] In cervical cancer the overall accuracy of staging by MRI has been found to be 86% compared to clinical examination which was only 47%.[17] MRI is, however, largely unaffordable in developing countries where most cases of cervical cancer occur, and thus cannot be part of the FIGO (International Federation of Gynecology and Obstetrics) staging work up.

The development of new MRI techniques has provided further uses in gynaecological oncology. These include dynamic contrast-enhanced MRI (DCE-MRI), diffusion-weighted MRI (DW-MRI) and magnetic resonance spectroscopy (MRS). These techniques have the ability to evaluate tumour biology and function and thus may be used to evaluate response to therapies. This would enable the clinician to adjust a treatment regimen to meet the expected response, thereby reducing morbidity.[18]

The role of MRI in the follow-up of gynaecological malignancies is limited to patients with suspected recurrences, especially in the pelvis. MRI may assist in the decision on the appropriate therapy, especially if surgery is being considered. On T2-weighted MRI, recurrent tumour usually demonstrates heterogenous high signal intensity. After contrast is given, the tumour shows varying degrees of enhancement and can be used to differentiate between tumour and radiation-induced fibrosis[15] (Figure 9).

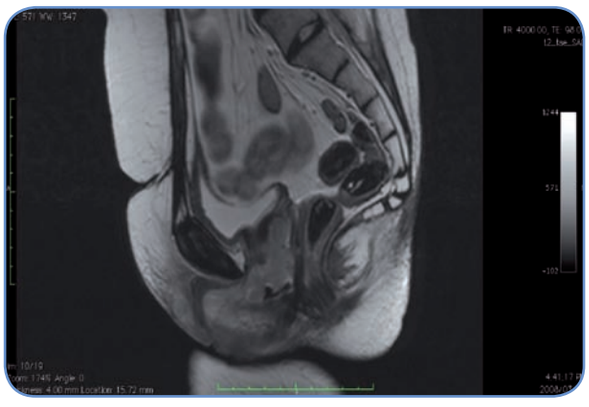

Figure 9: T2-MRI showing pelvic and perineal recurrence of a cervical cancer

Neither CT nor MRI perform well in predicting the presence of malignancy in enlarged lymph nodes, and neither is reliable in detecting small lymph nodes. The sensitivity in predicting lymph node involvement has, however, been reported as being marginally better for MRI at 60%, compared with 43% for CT.[19]

Positron emission tomography and PET/CT

PET is a relatively new imaging technique used in gynaecological oncology. PET functions by detecting the differential in metabolic activity between benign and malignant tissue. The radiopharmaceutical 2-(18F)fluoro-2-deoxy-D-glucose (FDG) is taken up preferentially by the high glycolytic rate in malignant tissue, compared to benign and normal tissue.[12]

The superiority of PET over other modalities is that it appears to be far more accurate in predicting malignancy in smaller lesions and lymph nodes and, thus, may have value, especially where surgery is being considered in recurrent disease. The limitation of this modality over others is the relatively high cost.

The limitation of PET on its own is that it lacks accurate anatomical resolution. This makes interpretation difficult, especially in the abdomen and pelvis where FDG is taken up normally by bladder, ureters and bowel. In order to improve the sensitivity and specificity, combined PET/CT scanners have been developed, combining the metabolic ability of the PET with the anatomical ability of the CT.[20]

PET/CT may be used to identify recurrences in all gynaecological malignancies but, because of the relatively high cost versus other modalities, the use should be restricted to cases where it will significantly affect the management of the patient. The main role at present seems to be in detecting ovarian cancer relapse, especially when secondary surgery versus chemoradiation is being considered.[21] PET/CT may be helpful in detecting peritoneal, lymphatic and other smaller metastases, where other modalities have failed (Figure 10).

Bristow et al performed PET/CT on 22 women with a raised CA125 and negative or equivocal CT, and found the overall accuracy of PET/CT in detecting recurrent disease > 1cm was 81.8%, with a sensitivity of 83.3% and PPV of 93.8%.[12] Fulham et al recently published a prospective trial on 90 patients and showed that PET/CT significantly affected treatment decisions in 60% of cases.[22]

PET/CT may thus be useful in detecting ovarian cancer recurrences, and may also assist in excluding other sites of metastases when surgery is being planned to remove an isolated recurrent tumour.

Conclusion

The choice of which imaging modality to use in gynaecological oncology follow-up depends upon a number of variables, including the individual patient, the specific cancer, what treatment is planned and the cost of the individual modalities.

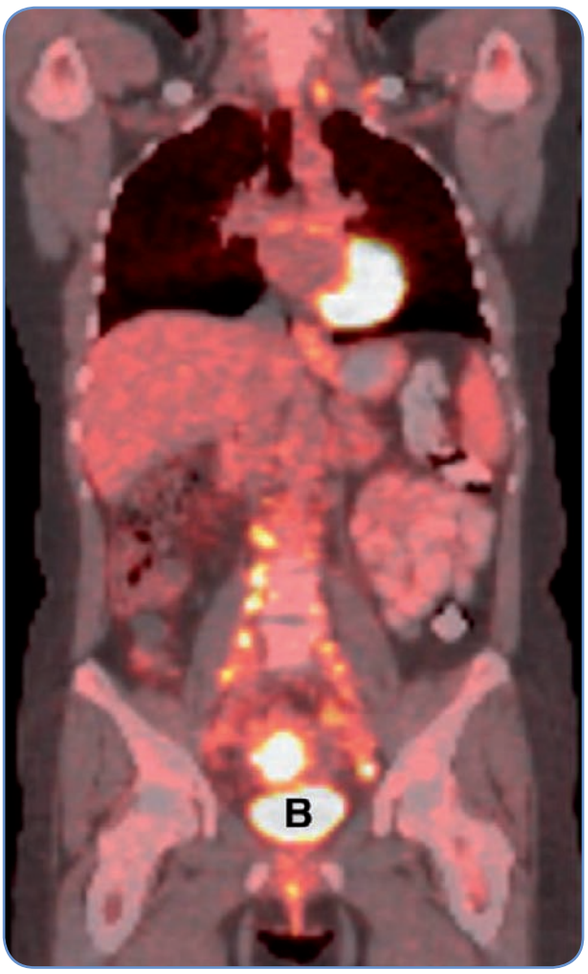

Figure 10: PET/CT showing pelvic recurrence with positive para-aortic lymph nodes

The role of plain X-rays in follow-up is mainly in the detection of metastases and not local recurrences. U/S is readily available and cost effective and plays an important role in the detection and diagnosis of pelvic recurrences, ascites, liver metastases and hydronephrosis.

Recent advances in CT technology allow better detection and improved characterisation of pelviabdominal masses. Its availability and relative low cost compared to MRI and PET/CT, make it the imaging modality of choice for bulky disease, liver or bony metastases or complications such as lymphocysts or fistulae. The limitations of CT are in the detection of lesions less than 1 cm, lymph nodes and peritoneal metastases.

MRI is useful, especially in pelvic recurrences, because of its ability to differentiate between malignant tumour and radiation-induced fibrosis. It may be especially useful when surgery is planned to assess resectability. It also has limitations

in distinguishing malignant from benign lymph nodes and in detecting smaller nodes. The overall accuracy of MRI may be improved by the development of newer techniques, such as DCE-MRI, DW-MRI and MRS.

PET/CT may be helpful in detecting smaller peritoneal, lymphatic, and other metastases where other modalities have failed. Its role is important in recurrent ovarian cancer, especially when surgery is planned.

Imaging in gynaecological oncology follow-up should not be performed just because it is available or we can afford it. Patients often attempt to pressurise medical personnel into performing imaging because of their anxiety, and often doctors agree in order to satisfy the patient and avoid litigation. The cost of medical services worldwide is escalating and everyone needs to attempt to keep costs down. Therefore, as with any investigation, any imaging modality used should be justified by how it will alter your management in that individual patient.

Acknowledgments
Dr Anthony Levy of Morton and Partners Radiologists and Dr Douglas Dumbrill for the images and valuable comments.

References

1. Maffione AM, Piva M, Tsamita CS, et al. Positive – emission tomography in gynaecologic malignancies. Arch Gynecol Obstet 2009;280:521–8.
2. Denny L. Prevention of cervical cancer. Reprod Health Matters 2008;16:18–31.
3. Tjalma WAA, Van Dam PA, Makar AP, Cruikshank DJ. The clinical value and the cost effectiveness of follow-up in endometrial cancer patients. Int J Gynecol Cancer 2004;14:931–937.
4. Shaaban A, Rezvani M. Ovarian Cancer: Detection and Radiologic Staging. Clin Obstet Gynecol 2009;52:73–93.
5. DePriest PD, Varner E, Powell J, et al. The efficacy of a sonographic morphology index in identifying ovarian cancer: a multi-institutional investigation. Gynecol Oncol 1994;55:174–8.
6. Rufford BD, Jacobs IJ. Ovarian Cysts in postmenopausal women. RCOG Green-top Guideline No.34. 2003.
7. Medeiros LR, Rosa DD, Rosa MI, Bozzetti MC. Accuracy of Ultrasonography with Color Doppler in Ovarian Tumor. Int J Gynecol Cancer 2009;19: 1214–1220.
8. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol 1990;97:922–9.
9. Davies AP, Jacobs I, Woolas R, Fish A, Oram D. The adnexal mass: benign or malignant? Evaluation of a risk of malignancy index. Br J Obstet Gynaecol 1993; 100:927–31.
10. Tsili AC, Tsampoulas C, Charisiadi A, et al. Adnexal masses: accuracy of detection and differentiation with multidetector computed tomography. Gynecol Oncol 2008;110:22–31.
11. Pannu HK, Bristow RE, Cohade C, Fishman EK, Wahl RL. PET-CT in Recurrent Ovarian Cancer: Initial Observations. Radiographics 2004; 24: 209–223.
12. Bristow RE, del Carmen MG, Pannu HK, et al. Clinically occult recurrent ovarian cancer: patient selection for secondary cytoreductive surgery using combined PET/CT. Gynecol Oncol 2003;90:519–528.
13. Buist MR, Golding RP, Burger CW, et al. Comparative evaluation of diagnostic methods in ovarian carcinoma with emphasis on CT and MRI. Gynecol Oncol 1994;52:191–8.
14. Topuz E, Aydiner A, Saip P, et al. Correlation of serum CA125 level and CT imaging with laparotomic findings following intraperitoneal chemotherapy in patients with ovarian cancer. Eur J Gynaecol Oncol 2000;21:599–602.
15. Harry VN, Deans H, Ramage E, Parkin DE, Gilbert FJ. Magnetic Resonance Imaging in Gynecological Oncology. Int J Gynecol Cancer 2009;19:186–193.
16. Hricak H, Rubinstein LV,Gherman GM, Karstaed N. MR imaging evaluation of endometrial carcinoma: results of an NCI cooperative study. Radiographics 1992;12:243–256.
17. Ozsarlak O, Tjalma W, Schepens E, et al. The correlation of preoperative CT, MRI, and clinical staging (FIGO) with histopathological findings in primary cervical carcinoma. Eur Radiology 2003;13:2338–2345.
18. Harry VN. Novel imaging techniques as response biomarkers in cervical cancer. Gynecol Oncol 2010;116:253–261.
19. Bipat S, Glas AS, van der Velden J, Zwinderman AH, Bossuyt PM, Stoker J. Computed Tomography and magnetic resonance imaging in staging of uterine cervical carcinoma: a systematic review.Gynecol Oncol 2003;91:59–66.
20. Blodgett T, Townsend D. Combined PET/CT in Gynecological Malignancies. Imaging Ergonomics 2003; www.imagingergonomics.com/issues/articles/ 2003–07.
21. Musto A, Rampin L, Nanni C, Marzola MC, Fanti S, Rubello D. Present and future of PET and PET/CT in gynaecologic malignancies. Eur J Radiol 2010,doi:10.1016/j.ejrad.2009.12.035.
22. Fulham MJ, Carter J, Baldey A, Hicks RJ, Ramshaw JE, Gibson M. The impact of PET/CT in suspected recurrent ovarian cancer: a prospective multi-centre study as part of the Australian PET Data Collection Project. Gynecol Oncol 2009;112:462–8.