

## EDITORIAL

# MR staging of endometrial cancer: needed or wanted?

John A Spencer, Christina Messiou<sup>1</sup> and Sarah E Swift

*Department of Clinical Radiology, St James's University Hospital, Leeds, LS9 7TF, UK*

*Corresponding address: John A. Spencer, MD FRCP FRCR, Department of Clinical Radiology,  
St James's University Hospital, Leeds, LS9 7TF, UK.*

*Email: johnaspencer50@hotmail.com*

Date accepted for publication 3 December 2007

**Keywords:** *Magnetic resonance imaging; endometrial cancer.*

Over the last Christmas and New Year period one of our 'urogenital' magnetic resonance (MR) lists which happened to fall on a public holiday in two consecutive weeks was lost. Just prior to the holiday one of our senior colleagues came to the department seeking an urgent MR examination of a young women for whom ovarian cancer was suspected on the basis of an 'indeterminate' ultrasound examination. He thought she probably had complex benign disease and that MR imaging would confirm his suspicions and allow a simple resection rather than cancer surgery. We looked at our packed diary and pointed to a handful of pending request cards. He made a wry comment that he could probably do without most of the endometrial cancer staging requests as they had far less impact on how he, as a Cancer Centre surgeon, managed his patients than did other gynaecological MR examinations. A lively discussion ensued.

MR imaging is recommended as a pre-surgical staging examination for women with newly diagnosed endometrial cancer based on meta-analysis and cost analysis<sup>[1,2]</sup>. Its management is primarily surgical. Its cardinal symptom of post-menopausal bleeding (PMB) brings patients to medical attention at an early stage and surgery is usually curative. The prior probability of information from MR imaging altering how an experienced surgeon manages the disease is low.

By comparison MR imaging has a major impact on treatment selection for women with cervical cancer.

When MR imaging shows parametrial tumour extension (FIGO stage IIB) surgery is abandoned in favour of radical radiotherapy ± chemotherapy. When it shows more advanced disease, e.g. invasion of the ureters, bladder, rectum or pelvic sidewall, an examination under anaesthesia (EUA), so long the mainstay of staging, is unnecessary. If unequivocal evidence of lymph node metastasis is shown by MR imaging (an assessment which, for historical reasons, forms no part of the FIGO staging scheme for cervical cancer) again surgery is contraindicated and radiotherapy may be planned or modified to encompass this site of disease. It is no surprise that MR imaging better predicts outcome of patients with cervical cancer than clinical staging<sup>[3]</sup>. The highly accurate tumour volume estimation provided by MR imaging also influences radiation treatment planning<sup>[4]</sup>.

Unlike cervical and endometrial cancer where a histological diagnosis precedes MR staging, most women with ovarian cancer actually undergo definitive surgical treatment without such a diagnosis. Historically, a significant minority of women who proceed for this 'cytoreductive' surgery have been found to have benign disease<sup>[5]</sup>. MR imaging has had a major impact by determining which ultrasound (US) 'indeterminate' adnexal masses represent complex benign pathologies<sup>[6]</sup>. This impacts not only on what surgery is performed but also where the surgery can or should take place. Benign surgery can be performed in the Cancer Unit ensuring appropriate and effective bed use in the Centre.

<sup>1</sup>Current address: Fellow in Radiology, Royal Marsden Hospital, Downs Road, Sutton, SM2 5PT, UK.

**Table 1** FIGO Staging: carcinoma of the corpus uteri

Stage <sup>a</sup>	Pathological staging FIGO nomenclature (Rio de Janeiro 1994)
Ia	Tumour limited to the endometrium
Ib	Invasion to less than half of the myometrium
Ic	Invasion equal to or more than half the myometrium
IIa	Endocervical glandular involvement only
IIb	Cervical stromal invasion
IIIa	Tumour invades the serosa of the corpus uteri and/or adnexae and/or positive peritoneal cytological findings
IIIb	Vaginal metastases
IIIc	Metastases to pelvic and/or paraaortic lymph nodes
Iva	Tumour invasion of bladder and/or bowel mucosa
Ivb	Distant metastases, including intra-abdominal metastasis and/or inguinal lymph nodes

<sup>a</sup>Either G1, G2 or G3.

So how might MR imaging impact upon management of newly diagnosed endometrial cancer? In the United Kingdom for the great majority of women, surgery comprises a simple hysterectomy and bilateral salpingo-oophorectomy with or without lymphadenectomy depending upon the grade and stage, with some geographic variation in practice. Women with high grade tumours (G3 endometrioid and clear cell adenocarcinoma) or those with tumours invading deeply into or through the myometrium (FIGO stage IC or IIIA, Table 1) should undergo lymphadenectomy as the likelihood of lymph node metastasis rises sharply in these circumstances<sup>[7-9]</sup>.

Clinical practice also varies for FIGO stage II (cervical invasion). If women with stage II disease can be identified preoperatively by MR imaging they may be spared adjuvant radiotherapy if they undergo a Wertheim type procedure. Conversely some clinical oncologists do not feel happy to omit vault therapy even if appropriate surgery has occurred, negating the impact of MR imaging. The decision to perform a Wertheim procedure for endometrial cancer historically relied upon clinical assessment of the cervix. And so if clinically detected, involvement probably reflected more advanced disease. We simply do not know if the small degrees of cervical invasion that can be shown by MR imaging warrant the more extensive hysterectomy procedure.

So for women with newly diagnosed endometrial cancer, the scope of MR imaging is to modify rather than contraindicate surgery. By confirming disease stages IA and IB for low grade (G1 and G2) tumours, MR imaging would prevent lymphadenectomy and its attendant morbidity. The Yorkshire Cancer Network covers a population of 4 million with inward referral to our hospital (the Cancer Centre in Leeds) from numerous Cancer Units. MR imaging of all newly diagnosed G1 and G2 endometrial cancers in these Units determines which women need more extensive surgery in the Centre. These MR examinations are performed in the Units using an identical protocol to that in the

Centre and reviewed in the weekly Multidisciplinary Team Meeting (MDTM). With a move towards minimally invasive (laparoscopically assisted) surgery, MR imaging can also help in case selection by excluding advanced or particularly bulky disease.

Lymphadenectomy practice varies within the United Kingdom (UK) in its extent and its intent. When lymphadenectomy is viewed as a sampling procedure, one potential advantage of MR staging is to identify sites of 'unequivocal' lymph node metastasis (Stage IIIC) which can focus surgical sampling and limit the morbidity of a more extensive sampling lymphadenectomy. This may be particularly relevant when the procedure is laparoscopic as lymphadenectomy requires additional skills. However, recent data suggest that more extensive lymphadenectomy with high grade tumours may actually confer a survival advantage<sup>[10]</sup>. The full results of the ASTEC trial, when published, are likely to impact on lymphadenectomy practice in the UK and the role of MR imaging in planning treatment of endometrial cancer will need to be revised accordingly.

By identifying even more advanced stage disease (bulky IIIC and IV), other forms of palliation might be planned. These women, however, are the exception and indeed often present down other pathways with the effects of distant metastases including peritoneal carcinomatosis and lymphadenopathy with general malaise, non-specific abdominal symptoms or weight loss. Radiotherapy achieves palliation of symptoms in women with advanced disease and may be offered as primary therapy in women whose comorbidity prevents primary surgery. Here MR imaging is valuable in accurately defining the target volume and disease extent and thus the options for brachytherapy (uterine confined) versus external beam therapy.

The alternative for staging endometrial cancer is computed tomography (CT) and this has a role for certain patients, notably the minority who present with systemic features. We also tend to use CT as a staging tool for women with papillary serous endometrial cancer as this disease may be multifocal and behave more like ovarian cancer, and for staging the lungs and liver in patients with endometrial sarcomas and malignant mixed Mullerian tumours.

Notwithstanding the above debate, the current perceived wisdom is that for newly diagnosed endometrial cancer MR imaging is an appropriate intervention<sup>[1,2]</sup>, a highly accurate staging test using basic T2-weighted (T2W) imaging and improved further by using dynamic contrast enhanced gradient echo imaging (DCEMR)<sup>[11-14]</sup>. Accuracy in local staging is in the order of 90% but data are more limited in respect of cervical involvement than for myometrial invasion.

Our own audit (CM) has produced some interesting results. First, MR imaging is not as accurate in our hands as others report for cervical assessment. This discrepancy may reflect the diligence of the pathologist.

Microscopic and non-contiguous involvement of endocervical glands (FIGO stage IIA), by 'drop' metastases, which escape our detection, is found by our expert pathologists. We cannot see these metastases even when we are directed back to look. This feels, therefore, like an inherent problem with MR imaging rather than operator error. It is not clear whether similar scrutiny of the cervical tissues occurred in reported studies. Whilst we do not know whether our patients with such tiny microscopic IIA disease are prejudiced by not having a Wertheim hysterectomy, we offer vault brachytherapy to these women.

We also compared two cohorts of patients staged by MR imaging, before and after the introduction of DCEMR. Our accuracy for myometrial invasion, which was already within the range of reported studies, did not improve after introducing DCEMR. Whilst some recent reports support older data that DCEMR improves staging with high accuracies maintained for assessment of cervical involvement<sup>[15]</sup> others gratifyingly confirm our concerns<sup>[16]</sup>. A group from another large UK Cancer Network found no improvement in staging by DCEMR over T2W<sup>[16]</sup>. Indeed for cervical involvement, DCEMR did worse<sup>[16]</sup> as might be anticipated with the lower contrast enhancement of the post-menopausal cervix than of the uterine corpus. We concur.

How can we reconcile these facts? Some of the early studies on which meta-analysis and cost analysis are based amount to small experiences. The studies so widely quoted in the literature comprised only 45, 40, 20 and 37 patients, respectively, with endometrial cancer<sup>[11–14]</sup>. One possibility is that the improved quality of T2W images from newer high field MR machines, using pelvic phased array imaging with small field of view, high resolution sequences focussed and correctly oriented for the endometrial cavity and cervical canal, negate the advantages of DCEMR found in earlier studies. When a high volume of feedback from surgical pathology is available, e.g. from a reported experience of over 100 cases, it may be possible to perform as well with T2W imaging as with DCEMR<sup>[16]</sup>. In other areas of cancer imaging adjunct MR techniques, such as DCEMR, help experts less than those further down the 'learning curve'<sup>[17]</sup>. Whilst it may be argued that meta-analyses evaluate large combined groups of patients<sup>[2]</sup>, they may also combine experience with the same inherent bias or weakness.

In cancer imaging audits of larger experiences often throw up discrepancies from early reports, most often a failure for the test in question to live up to its early promise. This usually reflects a changing case mix. Early in the 'proving and testing' phase, cases are referred across the whole spectrum of disease (including a lot of 'black' and 'white' cases). Yet in the 'maturation' phase, when clinical colleagues have become more sophisticated in their use of the technique, there is a higher proportion of 'grey' or problem cases. Some early studies have an

inappropriate case mix. One only has to think about endorectal MR imaging of prostate cancer; a landmark study included cases of far more advanced disease than are currently referred for MR staging<sup>[18]</sup>. It is of no surprise that working radiologists fail to achieve similar accuracies when examining cases diagnosed from what is more and more like a screening population.

Do we recommend abandoning DCEMR for endometrial cancer. No, but we suggest selective use for cases without adequate junctional zone (JZ) delineation on T2W images<sup>[19]</sup> (Fig. 1) or in the presence of coincident pathology such as fibroid disease (Fig. 2) or adenomyosis<sup>[20]</sup>. Our impression from reviewing examinations from a large number of referring hospitals within our 4 million catchment population is that DCEMR helps experienced radiologists in a position to plan the examination by scrutiny of the initial sagittal T2W images less than those with low examination volumes, those beginning in their practice or those unable to supervise the study. One cannot underestimate the value of feedback from surgical pathology and we encourage those keen to develop an interest in this area to attend a high volume MDTM.

Occasionally DCEMR may show brightly enhancing areas within bulky heterogeneous tumours and this has been reported as a feature of 'sarcomatous' elements within malignant mixed Mullerian tumours<sup>[21]</sup>. Sampling error with these usually bulky tumours means that the initial biopsy may fail to reflect these higher grade elements. We are not aware of any data to suggest that MR imaging can overcome the well recognised issue of misrepresentative grading of the final tumour histology by initial sampling biopsy.

There are thus some unresolved questions in the practice of MR imaging for newly diagnosed endometrial cancer. Some are issues of indication for the technique, and some of how to perform the examination including the need for patient fasting and the use of smooth muscle relaxant which differs widely between European experts (J.A.S., personal communication), reflecting the absence of an evidence base! But there are also uncertainties as to how information from MR imaging can and should alter management and consequently whether the technique will impact upon future patient outcomes.

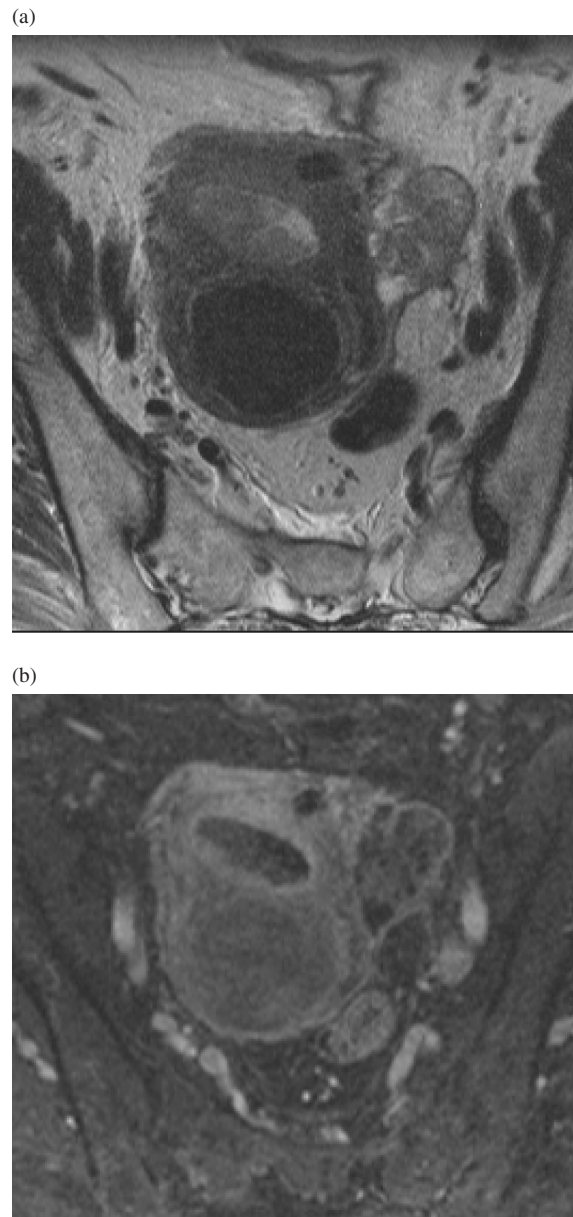
There are strong arguments for more published audits and research in selective use of MR staging of newly diagnosed endometrial cancer. The null hypothesis must be that for women with well and moderately differentiated cancer, of small bulk, or women with high grade endometrial cancer when lymphadenectomy is inevitable, MR staging has little to offer. It would seem reasonable to focus imaging resources on women believed to have bulky low grade tumour where the likelihood of deep myometrial invasion, invasion of the cervix, or of spread outside the uterus is greatest.

One simple audit would be to determine if the diagnostic methods routinely performed, transvaginal



**Figure 1** Corresponding MR staging images of a post-menopausal woman with newly diagnosed G2 endometrial cancer: (a) sagittal T2W showing an ill-defined junctional zone but expansion of the anterior wall; (b) sagittal DCEMR showing the depth of tumour invasion. Surgical pathology confirmed stage IC disease with invasion to within 3.8 mm of the serosa as predicted by MR imaging (to within 4 mm). Note that the signal characteristics of the cervix are similar to tumour on the DCEMR image.

US (TVUS) and/or hysteroscopy (HYS), can reliably identify those women for whom MR imaging will add nothing to the treatment plan. We have begun an audit to determine if there is a TVUS measurement of endometrial thickness below which outer half myometrial invasion (stage IC) can be excluded for lower grade (G1 and G2) differentiated tumours. We see over 200



**Figure 2** Axial images of post-menopausal woman with a distended endometrial cavity, indistinct junctional zone, large posterior wall fibroid and bulky left ovary: (a) T2W; (b) DCEMR showing no significant muscle invasion but an enlarged enhancing left ovary which was involved by endometrial cancer at surgical pathology.

new cases of endometrial cancer per year in our MDTM. TVUS is the primary examination of women with PMB and those with endometrial thickness (ET) less than 4 mm avoid endometrial sampling by HYS as the risk of cancer is so low<sup>[22]</sup>. But TVUS may have a valuable role in staging. Our audit will assess if a TVUS measurement of ET can be found which reliably confirms stage IA and IB disease in women with lower grade disease.

If we achieve our goal it would significantly reduce MR workload for staging. It would speed patients along the pathway to endometrial cancer surgery.



It would allow MR resources to be focussed on gynaecological conditions where it has a greater management impact. Currently our commonest indication for gynaecological MR imaging is for the 'indeterminate' adnexal masses with as many 'incidentalomas' thrown up in assessment of urological and gastrointestinal symptoms using US, CT urography, CT colonography and CT 'stone studies' as masses found in symptomatic women.

We would welcome collaboration with colleagues in this TVUS ET audit to increase the power of its findings.

## Acknowledgements

We are grateful to Mr Sam Saidi and Dr Rachel Cooper for constructive criticism and expert advice.

## References

- [1] Kinkel K, Kaji Y, Yu KK, *et al.* Radiologic staging in patients with endometrial cancer: a metaanalysis. *Radiology* 1999; 212: 711–18.
- [2] Hardesty LA, Sumkin JH, Nath ME, *et al.* Use of preoperative MR imaging in the management of endometrial carcinoma: cost analysis. *Radiology* 2000; 215: 45–49.
- [3] Hawnaur JM, Johnson RJ, Carrington BM, Hunter RD. Predictive value of clinical examination, transrectal ultrasound and magnetic resonance imaging prior to radiotherapy in carcinoma of the cervix. *Br J Radiol* 1998; 71: 819–27.
- [4] Hawnaur JM, Johnson RJ, Buckley CH, Tindall V, Isherwood I. Staging, volume estimation and assessment of nodal status in carcinoma of the cervix: comparison of magnetic resonance imaging with surgical findings. *Clin Radiol* 1994; 49: 443–52.
- [5] Kurtz AB, Tsimikas JV, Tempany CMC, *et al.* Diagnosis and staging of ovarian cancer: comparative values of Doppler and conventional US, CT, and MR imaging correlated with surgery and histopathologic analysis – report of the Radiology Diagnostic Oncology Group. *Radiology* 1999; 212: 19–27.
- [6] Sohaib SA, Mills TD, Sahdev A, *et al.* The role of magnetic resonance imaging and ultrasound in women with adnexal masses. *Clin Radiol* 2005; 60: 340–8.
- [7] Boronow RC, Morrow CP, Creasman WT, *et al.* Surgical staging in endometrial cancer: clinical-pathological findings of a prospective study. *Obstet Gynecol* 1984; 63: 825–32.
- [8] Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathological spread patterns of endometrial cancer: a gynaecologic oncology group study. *Cancer* 1987; 60: 2035–41.
- [9] Larson DM, Connor GP, Broste SK, Krawisz BR, Johnson KK. Prognostic significance of gross myometrial invasion with endometrial cancer. *Obstet Gynecol* 1996; 88: 394–8.
- [10] Cragun JM, Havrilesky LJ, Calingaert B, *et al.* Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. *J Clin Oncol* 2005; 23: 3668–375.
- [11] Hricak H, Stern JL, Fisher MR, Shapeero LG, Winkler ML, Lacey CG. Endometrial carcinoma staging by MR imaging. *Radiology* 1987; 162: 297–305.
- [12] Seki H, Kimura M, Sakai K. Myometrial invasion of endometrial carcinoma: assessment with dynamic MR and contrast-enhanced T1W images. *Clin Radiol* 1997; 52: 18–23.
- [13] Savci G, Ozyaman T, Tutar M, Bilgin T, Erol O, Tuncel E. Assessment of depth of myometrial invasion by endometrial carcinoma: comparison of T2W SE and contrast-enhanced dynamic GRE MR imaging. *Eur Radiol* 1998; 8: 218–23.
- [14] Manfredi R, Mirk P, Maresca G, *et al.* Local-regional staging of endometrial carcinoma: role of MR imaging in surgical planning. *Radiology* 2004; 231: 372–8.
- [15] Vasconcelos C, Felix A, Cunha TM. Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: comparison of magnetic resonance imaging and histopathologic evaluation. *J Obstet Gynaecol* 2007; 27: 65–70.
- [16] Rockall AG, Meroni R, Sohaib SA, *et al.* Evaluation of endometrial carcinoma on magnetic resonance imaging. *Int J Gynecol Cancer* 2007; 17: 188–96.
- [17] Futterer JJ, Engelbrecht MR, Huisman HJ, *et al.* Staging prostate cancer with dynamic contrast-enhanced endorectal MR imaging prior to radical prostatectomy: experienced versus less experienced readers. *Radiology* 2005; 237: 541–49.
- [18] Schnall MD, Imai Y, Tomaszewski J, Pollack HM, Lenkinski RE, Kressel HY. Prostate cancer: local staging with endorectal surface coil MR imaging. *Radiology* 1991; 178: 797–802.
- [19] Messiou C, Spencer JA, Swift S. MR staging of endometrial carcinoma. *Clin Radiol* 2006; 61: 822–32.
- [20] Utsunomiya D, Notsute S, Hayashida Y, *et al.* Endometrial carcinoma in adenomyosis: assessment of myometrial invasion on T2W SE and gadolinium enhanced T1W images. *AJR* 2004; 182: 399–404.
- [21] Park BK, Kim B, Park JM, *et al.* Differentiation of the various lesions causing an abnormality of the endometrial cavity using MR imaging: emphasis on enhancement patterns on dynamic studies and late contrast-enhanced T1-weighted images. *Eur Radiol* 2006; 16: 1591–8.
- [22] Gull B, Karlsson B, Milsom I, Granberg S. Can ultrasound replace dilation and curettage? A longitudinal evaluation of postmenopausal bleeding and transvaginal sonographic measurement of the endometrium as predictors of endometrial cancer. *Am J Obstet Gynecol* 2003; 188: 401–8.