

Carcinoma of the Cervix: Role of MR Imaging

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Abstract

Staging is of paramount importance in cancer management. In cervical carcinoma, it is performed using the clinical International Federation of Gynaecology and Obstetrics (FIGO) staging system. However, besides some inherent inaccuracies, it does not include important prognostic factors such as tumour size, which may help determine treatment strategies. These shortcomings of the clinical FIGO staging system underline the importance of accurate imaging evaluation of cervical carcinoma. Although magnetic resonance (MR) imaging is not officially incorporated into current staging work-up assessment, it has been shown by a number of studies to be the most reliable imaging modality in the evaluation of cervical cancer and in treatment planning. It has the advantages of direct tumour visualisation, accurate assessment of the depth of stromal invasion and tumour volume, and lymph node evaluation. In this article, the utility of MR imaging in the evaluation of cervical carcinoma is reviewed.

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Introduction

In females with cancer, cervical carcinoma is second to breast cancer in both incidence and mortality worldwide. About 465,000 new cases are diagnosed each year in both developing and industrialised nations,¹ with a higher incidence in women of low socioeconomic status. In Singapore, cervical cancer is the fourth most common tumour among women, with approximately 1126 cases reported from 1993 to 1997.² Current screening with Papanicolaou (Pap) smear and pelvic examination allows for early cancer detection and has led to a decline in both incidence and mortality from cervical cancer. In fact, over the last decade, the incidence has dropped from 18.1 to 14.2 per 100,000 population. Despite this decline, the incidence rate in Singapore females, especially the Chinese, is still higher compared to that in developed countries.

The average age at diagnosis is approximately 50 years, with peaks at 38 and 62 years. The risk factors are early age at first sexual intercourse, high number of sexual partners, multiparity, cigarette smoking and history of sexually transmitted disease. There is strong evidence to suggest human papilloma virus as the main cause of cervical carcinoma, with increased incidence in women with high-risk male sexual partners who are promiscuous, have former sexual partners with cervical cancer, and have

history of penile condylomas.

Cervical intraepithelial neoplasm (CIN) is a precursor of cervical cancer and may be categorised into minor dysplasia (CIN 1), moderate dysplasia (CIN 2) and severe dysplasia or carcinoma *in situ* (CIN 3). If left untreated, 40% of CIN 3 lesions will progress to invasive carcinoma.

In younger females, tumours tend to arise from the squamocolumnar junction and have a large exophytic component with vaginal extension. In contrast, tumours in older women with atrophied cervixes commonly occur in the endocervical canal due to the endocervical location of the squamocolumnar junction. These tumours commonly involve the supravaginal portion of the cervix with frequent lateral extension through the cervical wall.

The commonest histological type of cervical carcinoma is squamous cell carcinoma, which accounts for 80% to 90% of cases seen. Adenocarcinoma is less common, but is associated with a poorer prognosis. Besides histological type, other important prognostic factors include histological grade of the tumour, its location within the cervix (exocervix versus endocervix), tumour volume, depth of tumour invasion, adjacent tissue involvement and lymph node involvement at the time of treatment.

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Role of Magnetic Resonance (MR) Imaging

Accurate staging is of utmost importance in the management of patients with cervical cancer. Currently, the clinical International Federation of Gynaecology and Obstetrics (FIGO) staging system (Table I) is widely used for treatment planning. This system is based on findings at clinical examination performed under anaesthesia, chest radiography, intravenous urography, barium enema studies, cystoscopy and proctoscopy. However, besides excluding important prognostic factors such as tumour volume and lymphadenopathy, clinical FIGO staging has significant inaccuracies with a 24% to 39% error rate in gynaecological examinations.^{3,4} When compared with intra-operative and pathological findings, clinical staging also shows error rates of 17% to 32% with stage IB disease and up to 67% with stages II to IV disease.^{5,6} In addition, up to 25% of patients have pelvic or para-aortic lymph node metastases that are not detected during the clinical examination. Tumour extension to the urinary bladder or adjacent bowel may also be difficult to determine clinically.

At present, MR imaging is not officially incorporated into the staging work-up system, but has been shown to be the most reliable imaging modality for the evaluation and

treatment planning of cervical cancer. Comparative studies have shown overall staging accuracy of 77% to 83% for MR imaging and 70% for clinical staging.^{7,8}

Performed at high field strengths, MR imaging is the most reliable imaging modality for the detection or exclusion of parametrial spread, overall tumour staging and lymph node metastasis, all of which are important prognostic factors. The best treatment modality can then be determined more accurately with MR imaging, and this has been shown to influence the treatment plan in one-half of the patients. It can also reduce the number of conventional radiological examinations, including intravenous urography and invasive procedures, such as cystoscopy and proctoscopy performed. Moreover, evaluation of the shape and direction of lesion growth in MR imaging enables brachytherapy and external beam therapy to be optimised.⁹

Comparison with Computed Tomography (CT) and Ultrasonography

Unlike MR imaging, CT with intravenous contrast gives poor differentiation between cancer and the surrounding normal cervical tissue, resulting in difficulty in the assessment of tumour size and stromal invasion. In general, the accuracy of CT in cervical cancer staging is limited at 65%, which is significantly lower than that of MR imaging at 90%.^{4,8} CT accuracy in identifying parametrial involvement is also low at 55% to 77%. Although several CT criteria have been used to assess parametrial invasion, such as eccentric parametrial soft tissue mass, irregular cervical margin and thick parametrial stranding, loss of the peri-ureteral fat plane is the only reliable finding.¹⁰ Accuracy in lymph node detection is, however, similar for both modalities.¹¹

Ultrasonography is considered as an adjunct to physical examination. Though it may be of value in the evaluation of urinary obstruction in advanced disease, it has many technical limitations caused by patient's habitus, operator dependence and low signal-to-noise ratio, and low contrast resolution. These result in poor differentiation of the tumour and surrounding normal tissues. The advantages of transvaginal and transrectal ultrasonography in the evaluation of tumour size are inconclusive. Hence, ultrasonography is not suitable for staging cervical cancer.

MR Imaging Technique

Fasting of 4 to 6 hours prior to imaging and administration of antiperistaltic agent is recommended to reduce bowel motion artefacts. A pelvic phased-array coil is preferred to body coil as it increases the signal-to-noise ratio by a factor of 2 to 3.5.¹² It improves resolution, detection of stromal invasion, and evaluation of tumour size. Phased-array coil also decreases duration of examination¹³ and reduces motion

TABLE I: FIGO STAGING SYSTEM FOR CERVICAL CARCINOMA

Stage	Definition
0	Carcinoma <i>in situ</i>
I	Carcinoma strictly confined to the cervix
IA	Invasive cancer detected only microscopically IA-1: Stromal invasion <3 mm deep and <7 mm wide IA-2: Stromal invasion >3 mm and <5 mm deep, <7.0 mm wide
IB	Invasive cancer visible clinically (>5 cm) IB-1: <4 cm in diameter IB-2: >4 cm in diameter
II	Carcinoma extends beyond the cervix with no involvement of the lower third of the vagina or pelvic wall
IIA	No parametrial involvement
IIB	Parametrial involvement
III	Carcinoma extends to the pelvic wall or lower third of the vagina with hydronephrosis
IIIA	Extension to lower third of the vagina, with no pelvic wall involvement
IIIB	Pelvic wall involvement with hydronephrosis
IV	Carcinoma extends beyond true pelvis or involvement of the urinary bladder or rectum
IVA	Urinary bladder or rectal involvement
IVB	Distant metastasis

FIGO: International Federation of Gynaecology and Obstetrics

artefacts. However, it may not be suitable for very obese patients or patients with a protuberant abdomen. Endorectal or endovaginal coils have been reported to give images with high signal-to-noise ratio, thus providing excellent anatomical details.¹⁴ However, they are not employed on a routine basis as there is limited experience with their use and a lack of conclusive evidence of their advantage over phased-array coils.

Scan coverage extends from the lower pole of the kidneys to the vulva to include the para-aortic region and pelvis. Anterior saturation bands are routinely used to minimise respiratory motion artefacts, while posterior saturation bands are not necessary. Imaging in the sagittal plane is useful to demonstrate the relationship of the tumour to the cervix, corpus, vagina and adjacent bladder and rectum. Axial images, on the other hand, are important for assessment of parametrial tumour extension.¹⁵

As lymph nodes can be easily differentiated from hypointense muscles and blood vessels in the T2-weighted (T2W) sequence, T2W sequence is the imaging of choice for the evaluation of lymph nodes. Turbo spin-echo (TSE) T2W non-fat-saturated high-resolution sequence delineates normal zonal anatomy and pathologic changes of the uterus and vagina, and is mandatory in the imaging of the uterus, tumour and surrounding structures. Short tau inversion recovery (STIR) sequences, by suppressing the signal intensity of normal fat, are thought to increase the ability to identify structures or lesions surrounded by fat, such as parametrium and lymph nodes. Nonetheless, STIR sequence has not been shown to be better than TSE T2W sequence in the detection of parametrial invasion.¹⁶

The role of contrast enhancement is controversial. It is primarily used to identify recurrent or residual disease in patients with previous radiation or surgery.¹⁷ It may also be useful for detection of invasion of the urinary bladder, rectum and pelvic sidewall, and fistulous tracts in advanced disease. However, it can also cause overestimation of tumour size, depth of stromal invasion and tumour extension,^{18–20} and is not routinely used in our practice. Intravaginal contrast administration has also been used to better visualise the vaginal wall, lumen and fornices. It may improve non-invasive staging of cervical cancer.²¹ However, there is limited experience with its use and it is not routinely employed.

Tumour Detection

Accuracy

Ninety-five per cent of invasive tumours appear as a hyperintense mass on T2W images with disruption of low signal intensity fibrous stroma. Preinvasive disease accounts for more than 70% of cervical cancer and cannot be identified on T2W images, but may be depicted as a

strongly enhancing area in the early arterial phase on dynamic MR imaging.^{22,23}

The accuracy in the evaluation of the depth of stromal invasion is about 80%,^{7,8} but can be further improved by dynamic MR imaging. Studies have shown accuracy of 76% for T2W, 98% for dynamic MR imaging and 63% for contrast-enhanced T1-weighted (T1W) images in differentiating deep invasion (lesions with >3 mm of stromal invasion) from superficial invasion (lesions with ≤3 mm of invasion²²).

Identification of Clinically Problematic Lesions

MR imaging helps to identify lesions that are entirely within the cervical canal or infiltrative endophytic lesions that develop beneath a relatively normal epithelium which cannot be detected by inspection and colposcopy. MR imaging is especially useful in the identification of lesions, where even the highly sensitive Pap smear can show negative results, such as adenoma malignum (minimal deviation adenocarcinoma) and well-differentiated adenocarcinoma of the mucin-producing type. On MR imaging, these lesions appear as hyperintense masses embedded with multiple cysts or a cluster of cysts.^{24,25}

Histologically, malignant lymphoma can be mistaken for poorly differentiated carcinoma and may require specific stains to make a definitive diagnosis. Though the lesion has variable MR appearances, occasionally MR imaging helps to detect simultaneous findings that give a clue to the diagnosis, such as extensive lymphadenopathy. Malignant lymphoma is more likely than cervical cancer if the uterus is involved extensively with a relatively preserved endometrium.

Staging

Parametrium Assessment

Parametrial invasion is an important prognostic factor that influences tumour staging and management. With parametrial invasion (stage IIB disease), surgery is contraindicated. Normal cervical stroma appears as a hypointense ring in T2W images. When preserved, this hypointense ring has a high negative predictive value for parametrial invasion. Full thickness stromal invasion (Fig. 1a) is indicated by segmental disruption of the hypointense stromal ring.^{7,8,26,27} When seen in isolation, evaluation of parametrium involvement is difficult, with a reported accuracy of about 60%.²⁷ However, if it occurs in association with nodular or irregular tumour signal intensity extending into the parametrium, parametrial invasion can be confidently diagnosed (Fig. 1b). Pericervical fat stranding may indicate parametrial invasion, but is non-specific as peritumoral inflammation can also give a similar appearance. Contrast-enhanced T1W MR imaging has not

been shown to be superior to T2W scan in the evaluation of parametrial invasion.^{28,29}

Pelvic Wall Invasion

The pelvic wall is involved if there is complete loss of the normal parametrial signal, presence of tumour stranding or extension to the pelvic musculature or iliac vessels. Ureteric obstruction at the level of the tumour also indicates pelvic wall invasion. However, presence of tumour extension to the internal obturator, piriform or levator ani muscles without ureteric dilatation does not exclude the possibility of pelvic wall invasion.

Invasion of Urinary Bladder and Rectum

Urinary bladder or rectal invasion indicates stage IVB disease. Bladder invasion may be difficult to determine by clinical examination alone. MR imaging, however, has been shown to be reliable in detecting urinary bladder invasion with a sensitivity of 83%, specificity of close to 100% and an accuracy of 99%.^{30,31} When the urinary bladder is involved, the normal hypointense bladder wall shows focal or diffuse area of increased signal intensity, regardless of whether there is a mass protruding into the lumen. Presence of the “bullous oedema sign” with hyperintensity in the internal surface of the posterior bladder wall, bladder wall nodularity or irregularity, and protruding mass into the lumen also indicate bladder wall invasion. The vesico-ureteric junction, on the other hand, cannot be well assessed due to poor visualisation of the ureters on MR imaging.

Direct invasion of the rectum is infrequent. More commonly, rectal invasion occurs by tumour spread along the uterosacral ligaments. Segmental thickening and/or disruption of normal hypointense signal of the anterior rectal wall^{26,27} and prominent strands between the tumour and the rectum are MR imaging features of rectal invasion. Some studies have shown dynamic contrast-enhanced T1W sequences to be helpful in the identification and confirmation of fistulous tracts.³⁰

Vaginal Invasion

MR imaging has a high sensitivity in the detection of vaginal invasion with a reported accuracy of 93%.²⁷ Signs of vaginal involvement include segmental disruption of the normal hypointense vaginal signal or a hyperintense thickening of the vagina in stage IIA disease (Figs. 2a & 2b). Caution must be practised in assessing a thin, stretched vaginal fornix as it may not be seen, even if intact.

Lymph Node Evaluation

As with CT, assessment for lymph node involvement on MR imaging is based only on size. There is no significant

advantage of MR imaging over CT in the detection of lymph node involvement, although both techniques are superior to lymphangiography.¹¹ Presently, signal intensity is not useful in differentiating benign from malignant lymph nodes, though preliminary work suggests that the use of ultrasmall superparamagnetic iron oxide (combidx) may be helpful.³²

The size criterion of metastatic node is still debatable, resulting in varying accuracy being reported. Diameter >1 cm is commonly used as the threshold for metastatic nodal involvement, with accuracy rates ranging from 75% to 88%.^{8,26} Minimal axial diameter (MIAD) >1 cm, as a sign of nodal metastasis, is reported by Kim et al³³ to give a sensitivity of 62%, a specificity of 98% and an accuracy of 93%. They also reported that the mean maximal axial diameter to MIAD ratio was 1.09 for true-positive and 1.76 for false-positive nodes. This ratio may help to improve the specificity of MR imaging if used in adjunct with the size criterion, but should not be used in isolation or as a replacement for the size criterion. False-positive results are commonly due to reactive or inflammatory adenopathy, which can only be confirmed on biopsy.

Accuracy

With the high overall reported staging accuracy of 77% to 83%,^{7,8,26} MR imaging is currently the most reliable method of staging. It has been shown to be superior to clinical and CT staging, especially in parametrial evaluation; comparative studies reported an accuracy rate of 92% for MR imaging compared to 78% for clinical staging and 70% for CT.^{7,22}

Residual Tumour after Irradiation or Chemotherapy

While Pap smear is usually highly reliable, it is less sensitive shortly after irradiation.³⁴ MR imaging is useful in such situations; it has a 97% negative predictive value in the presence of an apparently normal cervix and a 86% positive predictive value in the presence of a distinct hyperintense mass.^{19,35,36} Delayed responders show a hyperintense mass on MR imaging and a viable tumour on histology even after 6 months,³⁶ while the mass will later resolve. A preliminary study has shown usefulness of the magnetisation transfer ratio in assessing the efficacy of radiation therapy,³⁷ but further studies are required.

Recurrence Versus Fibrosis

MR imaging has shown promise in the early depiction and accurate assessment of extent of recurrence. This helps to select patients suitable for repeated surgery, which has been very difficult prior to the use of MR imaging. Late fibrosis (>1 year) shows distinct T2W signal hypointensity, whereas recurrent tumour appears hyperintense on T2W images (Figs. 3a & 3b). In cases that recur within 1 year,

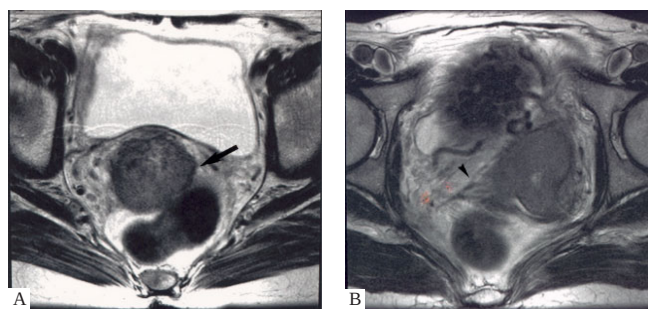
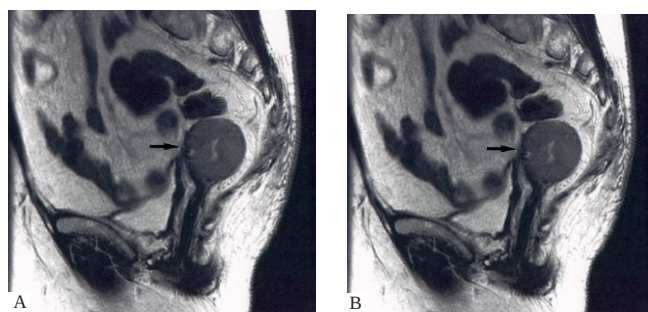


Fig. 1. (A) Axial T2-W MR image shows a bulky cervical tumour with full-thickness stromal involvement. There is only a thin rim of hypointense stroma on the left posterolateral aspect (arrow). (B) Axial T2-W MR image shows an eccentrically-placed cervix with parametrial stranding on the right (arrowhead) indicating parametrial invasion. This was confirmed at surgery.

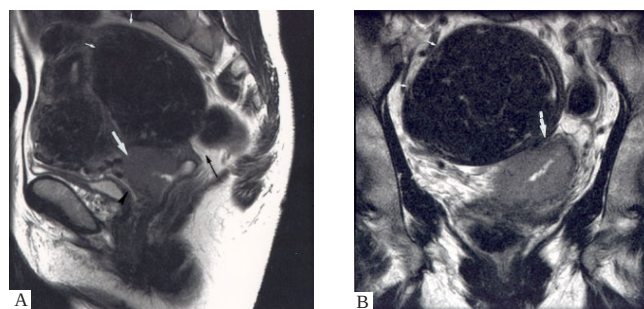


Figs. 3. (A) Sagittal and (B) axial T2-W MR images of a patient with total hysterectomy show local recurrence at vaginal vault seen as a hyperintense mass. Note the susceptibility artefacts due to the metallic surgical clips (arrow). The fat plane between the tumour and the rectum is obliterated in the posterior aspect of the tumour (arrowheads) in the axial image, a sign of rectal invasion, which was confirmed at surgery.

recurrent tumour appears hyperintense on T2W images. Distinction between tumour recurrence and fibrosis is, however, difficult within a year of treatment,³⁸ although dynamic MR imaging is reported to be useful.^{17,39,40} In these cases, hypointense T2W signal is reported to be a reliable sign of benign conditions,⁴⁰ whereas signal hyperintensity is not reliable for malignancy. Early enhancement on dynamic MR imaging is a more reliable sign for tumour recurrence. Using these criteria, dynamic MR imaging has an 82% accuracy rate in depicting recurrent tumour compared to the T2W sequence, which has a reported accuracy rate of 64%.¹⁷

Imaging Strategies for Detection, Diagnosis and Staging

The role of diagnostic MR imaging in cervical carcinoma is not to prove the presence of the tumour, but to define tumour size (Fig. 4) and extent and to help determine the appropriate course of treatment. In stage IA tumours with size <2 cm, if clinical examination is sufficient, no further



Figs. 2. (A) Sagittal and (B) axial T2-W MR images show an exophytic tumour invading the vagina anteriorly (white arrow). The fat planes between the tumour and rectum (black arrow) and urinary bladder (arrowhead) are clearly preserved, indicating no invasion of these organs. However, the axial image shows right parametrial involvement. Note the incidental fibroids (small white arrows) distorting the uterine cavity, which may pose a problem for probe insertion for brachytherapy.

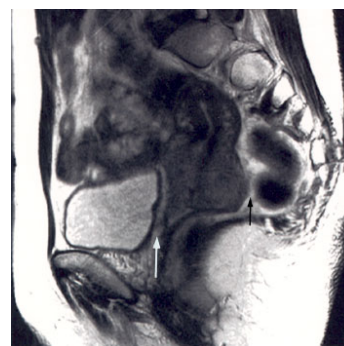


Fig. 4. Sagittal T2-W MR image shows a bulky cervical carcinoma infiltrating the uterine body and posterior vaginal fornix. The fat planes of the cervix with the urinary bladder (white arrow) and rectum (black arrow) are preserved.

imaging is usually necessary. If there is a need for imaging evaluation, MR imaging—which provides for more accurate staging than clinical examination or CT—is the modality of choice. For bulky FIGO stages I or II and above, MR imaging is generally recommended. By providing a “one-stop” solution for the diagnosis of parametrial involvement, invasion of pelvic sidewall, bladder and rectum, and ureteric obstruction and lymph node metastasis, MR imaging can obviate the need for additional imaging, such as intravenous urography or rectal enema.

Impact of Imaging on Treatment Decision and Planning

Factors that affect treatment are bulky tumour (>4 cm in diameter), parametrial invasion, invasion of bladder, rectum, pelvic sidewall and ureters, nodal involvement (particularly above the true pelvis) and distant metastasis. Surgery is usually the treatment of choice for FIGO stage I tumours <3 to 4 cm in size. There is no consensus on the treatment for patients with large stage I cancers and patients with early

FIGO stage IIB with early parametrial invasion. Some centres advocate chemotherapy and radiotherapy, while others prefer surgery. While there is no difference in survival rates between radiotherapy and surgery, there is increased morbidity when surgery is combined with radiotherapy.

As the clinical FIGO staging has significant inaccuracies, preoperative staging with MR imaging plays an important role in selecting patients who may benefit from surgery (stage I and minimal stage IIA). Use of MR imaging as the pre-treatment work-up leads to significantly fewer procedures and fewer invasive studies are performed. Additional studies to exclude invasion of urinary bladder and rectum, such as barium enema, proctoscopy and cystoscopy, are deemed unnecessary and this results in significant cost savings.⁴¹ Schwartz et al⁴² have shown that MR imaging may alter treatment, reduce the number of invasive surgical procedures and total healthcare expenditures.

Conclusion

Although MR imaging is not officially incorporated into the staging work-up system of cervical cancer, it is the most accurate imaging modality for tumour evaluation and plays a crucial role in directing treatment planning. It is reported to be superior to clinical staging and to reduce the number of conventional radiological investigations and invasive procedures, thus resulting in a reduction in total healthcare cost. Therefore, MR imaging is recommended as the first imaging modality for cervical cancer of stage IB and greater.

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QUESTIONS

1. Which of the following is true of clinical FIGO staging?
 - a) Its inaccuracy is too small to be significant.
 - b) It includes important prognostic factors that determine treatment planning.
 - c) It comprises clinical examination under anaesthesia and radiological imaging, such as MR imaging.
 - d) It plays a major role currently in staging of cervical cancer.
 - e) It is highly accurate in assessment of parametrial involvement.
2. Cervical carcinoma
 - a) mainly occurs in patients >60 years of age.
 - b) is increasing in incidence in Singapore.
 - c) of the squamous histological type is the most common.
 - d) of the adenocarcinoma histological type has a worse prognosis.
 - e) should be detected by MR imaging.
3. In MR imaging in the staging of cervical cancers,
 - a) post-contrast T1-weighted sequence should be used whenever possible.
 - b) hypointense T2 signal in the cervical stroma indicates presence of cervical cancer.
 - c) its accuracy in the detection of nodal metastasis is similar to CT.
 - d) recurrent tumour cannot be differentiated from fibrosis.
 - e) STIR sequence is not shown to be better than T2-weighted sequence in the detection of parametrial invasion.
4. In MR imaging of cervical cancers,
 - a) the overall accuracy is higher than 70%, which is higher than that of clinical staging, but lower than that of CT.
 - b) the accuracy in the detection of urinary bladder invasion is in the range of 60% to 80%.
 - c) the accuracy in the detection of vaginal invasion is over 90%.
 - d) the accuracy in the assessment of stromal depth is near 80%.
 - e) rectal invasion is identified in 50% of cases.
5. MR imaging of cervical cancers
 - a) commonly uses intravaginal contrast.
 - b) increases total healthcare costs as MR imaging is expensive.
 - c) is not widely accepted yet.
 - d) does not benefit patients who will be going for surgery anyway.
 - e) plays an important role in treatment planning.

For answers, log on to the Annals website at <http://www.annals.edu.sg/>