Uitgangsvraag 5
Welk pre-operatief onderzoek geeft bij patiënten met endometriumcarcinoom de meest accurate informatie over endocervicale ingroei, myometrium invasie en/of metastasen op afstand?

Study (trial) ID	Study type	Source of funding/Conflicts of interest	Setting	Country	Hypotheses	Eligibility criteria	Sample size/ Lost to follow up
(1) Selman et al., 2008	Systematic review **Biopsy, CT, MRI and US**	No competing interests MRC/RCOG Clinical Research Training Fellowship held by Miss Tara Selman financed cost incurred in obtaining original manuscripts	All studies are in a hospital	United Kingdom	To review the evidence for the accuracy of minimally invasive and non invasive tests to determine the lymph node status in women with primary endometrial cancer	*Search terms* All text words and word variants were used for the population (endometrial cancer lymph nodes) and the interventions (sentinel node biopsy, magnetic resonance imaging, positron emission tomography, computer tomography and ultrasound). During the search there were made no restriction on study design due to the limited number of citations and no language restrictions were made. *Inclusion* Medline: 1966/2006 Embase: 1980-2006 Medion, the Cochrane library and hand searches. - Reported accuracy of the index tests - Compared to histological examination of the lymph nodes (reference standard) in women with a primary presentation of endometrial cancer of any histological type or stage - Allowed data extraction to create two by two tables	- 693 women (18 relevant primary studies)
(2) Kinkel et al., 1999	Meta-analyse **CT, MRI and US**	NR	All studies are in a hospital	USA	To compare the diagnostic performance of MRI, CT and US in assessing myometrial invasion and cervical extension and to define evidence based imaging guidelines for staging endometrial cancer	*Search terms* Uterine neoplasm, endometrial carcinoma with CT, MR imaging or US *Inclusion* Medline: For US and CT January 1980 – September 1997, for MRI January 1985 to September 1997 - Articles must present raw data - Published articles - The standard of reference was surgical staging with histopathologic results - Presented data were obtained by observers who were blinded to the pathologic result - Presented data allowed calculation of true-positive, true-negative, false-positive, and	- 84 articles were found, 37 articles were excluded (47 left, articles were included if they contained results for only one staging element (such as myometrial invasion) or if only a subgroup of patients fulfilled the inclusion criteria). Studies of myometrial invasion: 203 patients for CT, 611 patients for US, and 742 for MRI. Studies of cervical involvement: 56 patients for CT, 162 for US, and

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						false-negative results for imaging tests - Data of subset of date were not published more than once	318 for MRI
(3) Bijen et al., 2008	Comparative study (diagnostic accuracy) **ECC**	No conflicts of interest	Department of Gynecological Oncology of the University Medical Centre Groningen, the Netherlands	The Netherlands	To investigate the value of endocervical curettage (ECC) as a diagnostic procedure in the preoperative staging of patients with adenocarcinoma of the endometrium prior to primary surgery.	*Inclusion* - All consecutive endometrial cancer patients (n=771) treated between January 1978 and January 2006 *Exclusion* - Patients with a non-epithelial endometrial cancer (n=166) - Patients with macroscopically cervical involvement (i.e. clinical stage IIB) (n=47) - Patients with extended disease who did not undergo surgical treatment and patients who received preoperative radiotherapy (n=21). - No retrieval of histopathological reports (n=74). - Small sample size of preoperative assessment of cervical involvement by endocervical biopsy (ECB) (n=8)	- 290 patients with preoperative assessment - 165 patients without preoperative assessment
(4) Cicinelli et al., 2008	Comparative study (diagnostic accuracy) **diagnostic fluid hysteroscopy**	No conflicts of interest	Department of Obestrics and Gynecology, University Medical School of Bari, Bari, Italy	Italy	To assess the reliability of simple diagnostic fluid hysteroscopy to evaluate the cervical involvement in the case of endometrial carcinoma.	*Inclusion* - Consecutive postmenopausal women with histological diagnosis of endometrial carcinoma - Presence of endometrial adenocarcinoma histologically documented by means of endometrial biopsy and surgical candidates for staging with lymph node sampling based on clinical results *Exclusion* - Exclusion of 3 patients because the definitive histologic diagnosis was different than adenocarcinoma: 2 patients with carcinosarcoma and 1 patient with leiomyosarcoma.	- 100 postmenopausal patients with histological diagnosis of endometrial carcinoma
(5) Ortashi et al., 2008	Comparative study (diagnostic accuracy) **MRI**	NR	Dorset Cancer Centre, Poole General Hospital, Poole, UK	United Kingdom	The aim of this study was to assess the accuracy of preoperative MRI in staging endometrial cancer and to assess the sensitivity, specificity, PPV and NPV for each histological stage according to the FIGO classification	*Inclusion* - Patients diagnosed with endometrial cancer on histology either in the form of pipelle biopsy of hysteroscopic biopsy	- 100 consecutive patients
(6) Savelli et al., 2008	Comparative study (diagnostic	NR	Gynecologic Oncology Unit of the University of Sacred Heart in	Italy	The aim of the study was to evaluate and compare the accuracy of high-frequency TVS and contrast-enhanced	*Inclusion* - Patients with histological diagnosis of endometrial carcinoma	- 88 enrolled consecutive - 74 in analyses

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	accuracy) **TVS, MRI**		Rome, and the Department of Obstetrics and Gynecology, University of Bologna, Italy		MRI in preoperative staging of endometrial carcinoma. It seems reasonable to suppose that the diagnostic accuracy of ultrasound imaging will improve along with the quality and definition of the sonographic images produced by newer machines.	*Exclusion*: - Exclusions due to inconclusive sonographic results, unclear findings at MRI, uncertainty in the histological diagnosis	
(7) Vasconcelos -et al., 2007	Clinical trial (diagnostic accuracy) **MRI**	NR	Department of Gynaecology of the Portuguese Institute of Oncology, Portugal	Portugal	To evaluate the accuracy of MRI in the detection of endometrial carcinoma (invasion of the deep myometrium and of the uterine cervix), compared with surgicopathological findings	*Inclusion* - Women with endometrial carcinoma treated in the Department of Gynaecology of the Portuguese Institute of Oncology - Presence of endometrial carcinoma histologically documented by biopsy and confirmed on the surgical specimen - A preoperative pelvic MRI	- 108 consecutive patients, 7 patients lost to follow-up (1 because of surgery in another institution, 6 did not undergo surgery (4 referred to radiation therapy, 2 treated with hormonal therapy). - Study included therefore 101 patients
(8) Ávila et al., 2008	Comparative study (diagnostic accuracy) **continuous flow hysteroscopy and directed biopsy**	NR	Hospital Donostia de San Sebastián (Guipúzcoa, Spain)	Spain	To determine the diagnostic validity of using continuous flow hysteroscopy and directed biopsy to determine cervical involvement in endometrial carcinoma.	*Inclusion* - Patients diagnosed with endometrial carcinoma *Exclusion* - Patients who did not undergo surgical staging - Patients who underwent fractional curettage but did not undergo diagnostic hysteroscopy (3 of these patients were also in the group that did not undergo surgical staging) - Women with negative surgical specimens for endometrial carcinoma - Women who were diagnosed with another type of cancer	- 240 patients were finally included in the study
(9) Tsili et al., 2008	Comparative study (diagnostic accuracy) **CT**	NR	Department of Radiology of University Hospital of Ioannina, Greece	Greece	The purpose of this study was to evaluate the accuracy of multidetector CT (MDCT) on a 16-row CTscanner in local staging of endometrial carcinoma and more specificity in the assessment of the depth of myometrial invasion and the presence of cervical infiltration	*Inclusion*: - Women with newly diagnosed endometrial carcinoma by means of endometrial biopsy, who underwent CT examination and subsequently surgery *Exclusion*: - Treatment with also radiotherapy - Advanced-stage disease	- 29 consecutive women. - 21 underwent CT examination and surgery, and these patients constitute the study population
(10) Suzuki et al., 2007	Clinical trial (diagnostic accuracy)	NR	1 centre: Yokohama City University School of Medicine, Japan	Japan	To determine the efficacy of FDG-PET (positron emission tomography using fluoro-2-deoxyglucose) in the diagnosis	- Patients who underwent FDG-PET, whole-body CT, and pelvis MRI within 2 weeks before the surgery between April 2004 and	- 30 patients - 4 patients did not undergo lymph node dissection due

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	PET				of endometrial cancer, focus on the validity of FDG-PET as a pre-operative diagnostic tool comparing it with that of computer tomography (CT)/MRI and the postoperative evaluation of tumour spread in patients with endometrial cancer	August 2005 - Patients diagnosed as having primary endometrial cancer by biopsy-proven findings	to complications in two patients (one had severe liver dysfunction and the other had gross obesity) or peritoneal dissemination in the other two patients
(11) Nasi et al., 2005	Comparative study (diagnostic accuracy) **MRI**	NR	Department of diagnostic imaging and Department of Morphological Sciences and Forensic Medicine, University of Modena and region Emilia, Italy	Italy	The aim of this paper is to compare the results of FSE T2-w and Gadolinium-enhanced MFPSGR MR sequences in assessing the depth of myometrial invasion by endometrial cancer.	*Inclusion* - Women with histopathologically proven endometrial carcinoma	- 55 women, all patients underwent MRI and surgery
(12) Horowitz et al., 2004	Clinical trial (diagnostic accuracy) **PET**	NR	Division of Gynecologic Oncology, Departments of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, USA	USA	To evaluate the performance of FDG-PET for pre-operatively detecting metastases to pelvic and para-aortic lymph nodes in patients with newly diagnosed uterine corpus cancer	*Inclusion* - Patients with newly diagnosed FIGO grade 2 or 3, papillary serous, or clear cell carcinoma of the endometrium or uterine sarcoma, who were scheduled to undergo surgical staging, including a bilateral pelvic and para-aortic lymphadenectomy - Patients were initially evaluated with history and physical examination, endometrial biopsy, routine laboratory studies, and routine imaging studies, including chest radiography and CT of the abdomen and pelvis	- 20 patients, 1 patient was excluded because she had ovarian cancer instead of uterine corpus carcinoma. 1 patient did not undergo complete surgical staging. - The remaining 18 underwent complete surgical staging and pathologic evaluation
(13) Manfredi et al., 2004	Comparative study (diagnostic accuracy) **MRI**	NR	Department of Radiology, and Obstetrics and Gynecology, Gemilli University Hospital, Rome, Italy	Italy	The aim of the study was to prospectively assess MR imaging in depicting the depth of myometrial infiltration, cervical invasion, and presence of enlarged lymph nodes in patients with endometrial adenocarcinoma compared with surgicopathologic findings	*Inclusion*: - The presence of endometrial adenocarcinoma histologically documented by means of endometrial biopsy. - Surgical candidates for staging with lymph node sampling based on clinical results. *Exclusion*: - Surgery in different institution - Carcinosarcoma and leiomyosarcoma	- 46 consecutive women, - 37 patients fitted inclusion criteria
(14) Köse et al., 2003	Comparative study (diagnostic accuracy) **TVS**	NR	Department of Obestetrics and Gynecology, Haydarpasa Numune Education and Research Hospital, Istanbul, Turkey	Turkey	The aim of the study was to assess the depth of myometrial invasion and cervical involvement by endometrial cancer using preoperative 6.5-MHz, high-frequency transvaginal ultrasonography as compared with postoperative assessment using	*Inclusion* - Patients with confirmed endometrial carcinoma	- 47 patients. All patients underwent transvaginal sonography before surgery

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					histopathological examination		
(15) Fishman et al., 2000	Clinical trial (diagnostic accuracy) **TVS**	NR	Meir Hospital – Sapir Medical Center, Kfar Saba. Israel	Israel	To determine the accuracy of preoperative transvaginal sonography (TVS) in the detection of deep myometrial invasion in relation to the grade of disease, and to compare TVS and frozen section analysis in a sub-group of patients with grade I disease	*Inclusion* - Women with histologically confirmed endometrial carcinoma - Clinical stage I carcinoma and candidate for surgery - Patients with a histologic subtype of endometrioid carcinoma, in all grades	- 91 patients for TVS - Specimens of 41 out of 47 patients with grade I disease were assessed by frozen section analysis
(16) Saez et al., 2000	Clinical trial (diagnostic accuracy) **MRI**	NR	Hospital de Cruces, Spain	Spain	To determine the accuracy of MRI for evaluating the depth of myometrial invasion in endometrial carcinoma and to determine whether accuracy may be improved by the use of contrast enhancement	*Inclusion* - Women with a histologic diagnosis of endometrial carcinoma (obtained by fractional dilatation and curettage) underwent surgical treatment (hysterectomy and double anexectomy)	- 85 patients
(17) Seki et al., 2000	Comparative study (diagnostic accuracy) **MRI**	NR	department of Radiology, Niigata University School of Medicine, Japan	Japan	To evaluated enhancement patterns of the cervical epithelium, stroma, and tumour on dynamic MR imaging and correlated MR imaging with histologic findings. And to determine the value of dynamic MR imaging in evaluating endometrial carcinoma involvement of the cervix To evaluate endometrial carcinoma involvement of the cervix using	*Inclusion* - Patients with untreated endometrial carcinoma.	- 42 patients with endometrial carcinoma

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(1)	Medline 1966-2006, EMBASE, Cochrane Library issue II, 2006, MEDION 1980-2006	NA	- Studies were selected if they reported accuracy of the index tests, compared to histological examination of the lymph nodes (reference standard) in women with a primary presentation of endometrial cancer of any histological type or stage and allowed data extraction to create two by two tables.	- Positron emission tomography (PET), magnetic resonance imaging (MRI), computer tomography (CT), or ultrasound scanning	- Histological examination
(2)	Medline: For US and CT January 1980 – September 1997, for MRI January 1985 to September 1997	NA	- Articles were selected that included results in patients with proved endometrial cancer and imaging histopathologic correlation and that presented data that allowed calculation of contingency tables.	- A subgroup analysis was performed to compare contrast medium-enhanced MR imaging with non-enhanced MR imaging, US, and CT.	- The standard of reference was surgical staging with histopathologic results - The presented data were obtained by observers who where blinded to the pathologic results
(3)	January 1978 - January 2006	NA	- Women with endometrial cancer referred to the Department of Gynecological Oncology of the University Medical Centre Groningen - Mean age 63.4 years - 290 patients with clinical stage I disease - Differentiation grade (n=275): 139 had grade 1, 88 had grade 2, 46 had grade 3, and 2 had grade 4 - Histological subtype (n=290): 248 were adenocarcinoma, 11 were adenosquamous carcinoma, 14 were clear cell carcinoma 11 were papillary serous carcinoma, 3 were undifferentiated, and 3 were other - Depth of myometrial invasion (n=288): 31 involved endometrium only, 153 involved <1/2 in myometrium, and 104 involved ≥1/2 in myometrium - LVSI (n=271): 210 were negative, 61 were positive - Adjuvant radiotherapy (n=288): 56.3% received adjuvant radiotherapy	- Preoperative assessment of cervical involvement by endocervical curettage (ECC) - After preoperative clinical staging, patients underwent primary surgical therapy within 4-6 weeks according to protocol, which is total abdominal hysterectomy and bilateral salpingo oophorectomy in case of a clinical stage I disease and total abdominal hysterectomy and bilateral salpingo oophorectomy, pelvic and para aortic lymphadenectomy in case of a clinical stage IIA (positive ECC) disease. - Surgical pathological information was gathered from the pathology reports	- Preoperative histopathological results of ECC were compared with definitive histopathological results of cervical involvement obtained from the uterine specimen (gold standard) - An expert gynaecological pathologist judged the majority (~85%) of all slides. Misclassified slides and slides allocated to the separate group were revised, without prior knowledge of the definitive outcome. - Histopathological results of the ECC slides were divided into two different groups, namely endometrial cancer in the ECC (i.e. positive) and no endometrial cancer in the ECC (i.e. negative). The criterion for preoperative diagnosis of a positive ECC was as follows: endocervical tissue present and tumour in relation with cervical tissue. Criteria for preoperative diagnosis of a negative ECC were as follows: 1) endocervical tissue without cancer; 2) obtained tissue was insufficient to establish a diagnosis; 3) loose tumour fragments without relation with endocervical tissue.
(4)	January 2004 - January 2008	NA	- Postmenopausal women with histological diagnosis of endometrial carcinoma - Mean age 67.3 years, range 43-88 - Mean BMI: 28.2, range 23.2-35.5 - Histological subtype: 86 were endometrioid adenocarcinomas, 5 were papillary serous carcinomas, 3 were mucinous adenocarcinomas, 3 were adenocarcinoma with squamous differentiation, 2 were clear	- All patients underwent surgery. Before surgery (no more than 10 day before) the patients underwent fluid hysteroscopy, TVS and MRI. - Mini-hysteroscopy was performed using a lens-based 2.7 mm OD mini-telescope, 105° angle of visual field equipped with a 3.5 mm OD single-flow diagnostic sheath. - MR images were acquired with a high field intensity device (1.5 T) Achieva 1.5 (Philips Medical System, Best, Netherlands) equipped with 33 mT/m gradients using pelvic	- Histopathological analysis: Surgical specimens were sectioned along the longitudinal plane of the uterus. The cervical involvement was estimated grossly and then confirmed microscopically. - Pathologists were blinded to the results of TVS, MRI and hysteroscopy.

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			cells carcinomas and 1 was a small cell carcinoma. - Tumour grade: 20 patients had grade 1 tumours, 55 had grade 2 tumours, and 25 had grade 3 tumours (anaplastic carcinomas).	phased array coil. MR images were analyzed by one radiologist with experience in gynaecologic imaging and not aware of the other clinical findings. - Quantitative image analysis included signal-to-noise ratio in the tumour and myometrium during all phases of the dynamic study. All measurements were performed on a workstation with an electronic caliper by a radiologist who did not perform the qualitative analysis. - TVS was performed by using an Aloka 5500 SD until 2006 and then an Aloka Prosound α-10 ultrasound system (Aloka, Tokyo, Japan) equipped with a 5–8 MHz B-mode probe. Sonographies were performed by a single specialist.	
(5)	January 1999 – July 2003	NA	- Patients aged between 45-90 years, mean age 68.6 years ± 2 S.D - The average wait was 2 weeks, and 2 patients had their operation more than 8 weeks after MRI - Tumour differentiation: well differentiated: 44 moderately differentiated: 38 poorly differentiated: 18	- MR imaging with a Siemens Symphony 1.5T (72) cases and Siemens Symphony 1.0T (28) cases. In each examination axial T1-weighted and axial and sagittal T2-weighted images were acquired	- All the surgical specimens were subjected to histological analysis to assess
(6)	February 2000 – May 2004	NA	- Women, of mean ± SD age 63 ± 12, range 30-88. - 63 (85%) of the 74 were postmenopausal. - Surgical FIGO stages were: stage Ia: 20 stage Ib: 18 stage Ic: 22 stage IIa: 2 stage IIb: 12 - Histological subtypes: endometrioid adenocarcinomas: 70 serous papillary carcinomas: 3 mixed-type carcinomas: 1 - Differentiation: well differentiated: 24 moderately differentiated: 33 poorly differentiated: 17 - High frequency of miscellaneous myometrial diagnosis: 28 cases of myoma (38%), 12 cases of adenomyosis (16%) and 8 cases of both (11%)	- All patients 74 underwent MRI and TVS examinations - MR imaging studies were performed with a 1.5-T superconducting magnet (Echospeed; GE Medical System, Milwaukee, Wis). A pelvic phased-array coil was used in all patients. - Transvaginal scans were performed using the same commercially available ultrasound machine (Esaote Technos MP, Genova, Italy) equipped with a transvaginal wide-band 5.0 – 9.0-MHz transducer - The depth of myometrial invasion was evaluated subjectively and classified, for both TVS and MRI, into two groups <50% myometrial invasion >50%. Invasion of the cervix was diagnosed using B-mode sonography when the neoplastic tissue extended caudally merging with the endocervical mucosa.	- All patients underwent complete surgical staging (hysterectomy and bilateral oophorectomy, pelvic and lumboaortic lymphadenectomy when appropriate). Postoperative staging of the cancers was based on FIGO criteria. Specialized gynaecological histopathologists evaluated the specimens
(7)	July 1998 - April 2004	NA	- Women with endometrial carcinoma treated in the Department of Gynaecology of the Portuguese Institute of Oncology	- Preoperative MRI and surgery. The average time between MRI and hysterectomy was 45 days (range 0-90 days) - MRI images (T2-weighted and a dynamic study) were	- Surgicopathological findings

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			- Histological examination: 86 were endometrioid adenocarcinomas, 5 were papillary serous carcinomas, 3 were clear cell carcinomas, 3 were mucinous adenocarcinomas, 1 was mixed malignant Müllerian tumour, 1 was a glassy cell carcinoma and 2 were undifferentiated carcinomas - Tumour grade: 39 patients had grade 1, 34 had grade 2, and 28 had grade 3 - FIGO stages: 7 stage IA (7%), 40 stage IB (39%), 20 stage IC (20%), 19 stage II (18%), 11 stage III (10%) and 4 stage IV (4%) - Mean age 68.5, ranging from 48 to 89. - A total of 11 were premenopausal (11%) and 90 were postmenopausal (89%)	independently analysed prospectively by two radiologists prior to surgery	
(8)	1 January 2000 – 31 December 2005	NA	- Women diagnosed with endometrial carcinoma at Hospital Donostia de San Sebastián (Guipúzcoa, Spain) - Histological subtype: 198 endometrioid carcinomas, 17 papillary serous carcinomas, 7 clear-cell carcinomas, 8 nondifferentiated carcinomas, 9 carcinosarcomas, and 1 villoglandular carcinoma. - Tumour grade of the endometrioid carcinomas: 102 were grade 1, 80 were grade 2, and 16 were grade 3.	- Office hysteroscopy was performed using a 4-mm-diameter Olympus hysteroscope with a 30° viewing angle and a 5.5-mm continuous flow sheath.	- Histological analysis of the surgical specimens
(9)	February 2004 – May 2006	NA	- Women, range age: 45-78 years, mean age: 65 years. - 14 (66%) of the 21 neoplasms were endometrioid adenocarcinomas, 3 (14%) were papillary serous adenocarcinomas, 1 (5%) was clear-cell carcinoma, 1 (5%) mixed, endometrioid and papillary,6 serous adenocarcinoma and 1 (5%) mixed, transitional cell carcinoma and adenocarcinoma of clear cell and papillary serous type. In one patient, histologic diagnosis was of atypical endometrial hyperplasia. - Stage IA: 3 (14%) - Stage IB: 2 (10%) - Stage IC: 16 (76%)	- The CT examinations were performed on a 16-row CT scanner with 24 mm scanning span per rotation (Mx8000 IDT, Philips) - The CT protocol included scanning of the abdomen after the intravenous administration of 120 ml of non-ionic iodinated contract material (320 mg I/ml, flow rate 3 ml/s) using the following parameters: detector collimation 16*0.75 mm, pitch 1.2, section thickness 0.8 mm, rotation time 0.5 s and kV 120 - Scanning began 70 s (portal phase) after the administration of contrast material.	- CT images were interpreted by two radiologists in consensus, without the knowledge of the histopathologic results.
(10)	April 2004 - August 2005	NA	- Patients diagnosed as having primary endometrial cancer by biopsy-proven	- FDG-PET, whole-body CT, and pelvis MRI within 2 weeks before the surgery. PET scan was performed 40 min after	- Preoperative CT/MRI findings and postoperative evaluation of tumour spread in patients with

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			findings - 13 patients had FIGO clinical stage I (IA: 5, IB: 6, IC: 2), stage II in 5 patients (IIA: 2, IIB: 3), stage III in 10 patients (IIIA: 5, IIIC: 5), and stage IV in 2 patients - Histology consisted of endometrioid carcinoma in 29 cases and adenosquamous carcinoma in 1 case - Mean age 55.4 years, ranging from 27 to 73	injection of 200-370 MBq of FDG using multi-bed positron technique	endometrial cancer
(11)	January 2000 – October 2003	NA	- Women, aged 39 to 82 years - At surgical pathology the cancer was found to have intramucosal localisation in 11 cases,; 31 cases revealed myometrial invasion lees than 50%, 12 cases greater than 50% and 1 case had transmural invasion. There was cervical invasion in 8 cases	- All patients underwent MRI, with high field-strength magnet (Signa, 1.5 Tesla, General Electric, Milwaukee, USA) and all cases were imaged with a body coil. - Axial SE T1-weigted, axial, sagittal and para-coronal FSE T2-wiegted and para-coronal Gadolinium-enhanced FMPSGR sequences were performed using a high field strength magnet (1.5T) - Gadolinium-enhanced FMPSGR: 30, 60 and 120 seconds from the IV administration of Gadolinium-DOTA, injected via an automatic injector at a dose of 0.2 ml/kg of body weight and followed by 20 ml of saline	- Within 1 month of the MRI examination all patients underwent bilateral hysteroadnexectomy with histopathological examination of the surgical specimen - The pathologist received the entire specimen which was sectioned in the coronal plane, orthogonal to the long axis of the uterus. To obtain histological macro sections for Haematoxilin & Eosin staining that were easy to correlate with the para-coronal MR images. The grade of myometrial invasion was therefore defined and quantified according to the MRI parameters, as was invasion of the cervix
(12)	NR	NA	- Women with newly diagnosed FIGO grade 2 or 3, papillary serous, or clear cell carcinoma of the endometrium or uterine sarcoma - Median age was 66 years (range 54-90 years) - 16 were Caucasian, 2 were African American, and 1 Middle Eastern - FIGO stages: 12 patients had stage I (IA: 3, IB: 7, IC: 2), 3 had stage II, 2 had stage III, and 2 patients had stage IV - Number of lymph nodes removed: median 20, range 1-49 - Histology: 15 were endometrioid adenocarcinoma, 1 clear cell carcinoma, 1 MMMT, 1 mixed epithelial - Tumour grade: 3 patients had Grade 1 (pre-operative grade 2), 4 had grade 2, and 12 had grade 3 - Lymphvascular invasion: 10 patients had no invasion, 5 had focal, 3 had diffuse invasion, and in 1 patient it was not recorded - Tumour location: Fundus: 7, Lower uterine segment/cervix: 4, Complete uterine cavity: 5, and not recorded: 3	- FDG-PET was performed within 30 days of diagnosis, according to a standard protocol described previously (15). Surgery was performed within 30 days after completion of FDG-PET	- Pathologic findings during surgery: tumour size, depth of invasion, location within uterine cavity, and retroperitoneal disease - Two experienced nuclear medicine physicians, blinded to clinical information and the results of other imaging studies, independently interpreted the PET studies - - The treating surgeon was blinded to the results of the FDG-PET. However, the protocol stipulated that the surgeon would be informed of any PET abnormalities seen outside the normal surgical field

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(13)	June 1997 – February 2001	NA	- Women mean age 58.8 years, range 36-79 years. - 31 (84%) patients were postmenopausal - None of the patients underwent exogenous hormonal replacement therapy or tamoxifen treatment - 31 (84%) of the 37 tumours were endometrioid adenocarcinomas, 5 (13%) were papillary serous adenocarcinomas	- All patients underwent surgery and MRI examinations - MR imaging studies were performed with a 1.5-T superconducting magnet (Echospeed; GE Medical System, Milwaukee, Wis). A pelvic phased-array coil was used in all patients. - Transverse T1-weighted spin-echo and transverse T2-weighted rapid acquisition with relaxation enhancement (RARE) images were obtained	- Histopathologic findings - Surgical specimens were sectioned along the longitudinal plane of the uterus. The depth of myometrial invasion was estimated grossly, was confirmed microscopically without knowledge of MR findings. - Lymph node dissection was performed with anatomic labelling into common, internal and external iliac, internal obturatory, and lumboaortic node groups by surgeons n the operating room.
(14)	NR	NA	- Women, mean age 59.3 $\pm$ 6.4 years - Tumour confined to the endometrium: 11 (23.4%), tumour infiltrated the upper half of the myometrium: 17 (36.1%) invaded the deeper half: 19 (40.4%) - Cervical spread was found in 4 (8.5%) cases - The pathological diagnosis in all patients were adenocarcinoma. - Stage-I: 40 (85%) Stage-II:6 (13%) Stage-III: 1 (2%) - Lymph node metastases were detected in only 1 of the cases	- To assess the depth of myometrial invasion and the cervical involvement of endometrial cancer, a 6.5-MHz, high-frequency transvaginal ultrasonography was used preoperatively. All the measurements were performed by a single operator.	- Total abdominal hysterectomy and bilateral salpingo-oopherectomy followed by surgical staging were performed in all patients. Surgery was guided by the results of TVS. Furthermore the pathologist was blind to TVS results. - The preoperative sonographic findings of the uterus and cervix were compared to the final histopathology report of myoinvasion and cervical involvement.
(15)	NR		- 91 patients with histologically confirmed endometrial carcinoma, stage I disease - Mean age was 62 years (range 40-83 years) - 47 patients had grade I disease, 44 patients had grade 2-3 disease	- TVS was performed by a single examiner, using a 5-7.5 MHz transducer probe and within 3 days of surgical intervention - Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and systematic exploration of the abdominal cavity with sampling of peritoneal washing for cytology - Selective retroperitoneal lymph node sampling was carried out in all grade 2 and 3 tumours. In patients with grade 1 tumours, myometrial invasion was intraoperatively evaluated by frozen section; if deep invasion was determined, retroperitoneal lymph node sampling was performed	- Histologic results of the uterine specimens were the gold standard, to which the TVS findings for all cases and the frozen section analysis for the grade I cases were compared - The physician who performed the TVS scans was unaware of the endometrial cancer grade - Pathologist was unaware of the sonography findings
(16)	January 1992 - December 1996		- Eighty-five patients with a histologic diagnosis of endometrial carcinoma (obtained by fractional dilatation and curettage, all of them underwent surgical treatment (hysterectomy and double anexectomy) - The patients were between 49 and 84 years of age (mean 66 years)	- All patients were imaged with a 0.5-T system (Gyroscan T5-II, Philips Best, The Netherlands), in the 2 weeks prior to surgery - Hysterectomy and double anexectomy	- Histologic examination was considered the gold standard for the study - MR findings were retrospectively evaluated by two separate groups of radiologists (two radiologists in each group), who were blinded to pathologic results.
(17)	April 1996 - May 1999	NA	- Women age range 30-75 years, mean 57 years. - All patients were referred for MR imaging	- Of 42 patients, 39 patients underwent surgery 4-19 days (mean 9,5 days) after MR imaging. - MR imaging was performed with a 1.5-T superconducting	- The data was correlated with histologic findings. Surgical specimens were sectioned along the longitudinal plane of the uterus, and cervical

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			after histologic diagnosis of the disease made by endometrial curettage. - Staging: 5 stage IA, 14 stage IB, 7 stage IC, 4 stage IIB, 4 stage IIIA, 7 stage IIIC, and 1 stage IVA carcinomas. - The histologic type was endometrioid adenocarcinoma in 38 patients, adenosquamous carcinoma in two, and clear cell adenocarcinoma in two.	magnet (Vision; Siemens, Erlangen, Germany) - In all 42 patients T2-weighted MR imaging using acquisition with relaxation enhancement, dynamic MR imaging using gradient-echo sequences, and contrast-enhanced T1-weighed MR imaging using spin-echo sequences were performed before treatment.	involvement was evaluated grossly and confirmed microscopically.

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
(1)	- Sensitivity - Specificity - Positive likelihood ratio - Negative likelihood ratio	*Sentinel Node (SN)* - Mean sensitivity 0.79 (95% CI 0.58-0.91) - Mean specificity 0.96 (95% CI 0.89-0.99), - Positive likelihood ratio 18.88 (6.70-53.24) - Negative likelihood ratio 0.22 (0.10-0.48) *CT scan* - Mean sensitivity 0.45 (95% CI 0.28-0.64) - Mean specificity 0.88 (95% CI 0.78-0.94) - Positive likelihood ratio 3.81 (2.00-7.28) - Negative likelihood ratio 0.62 (0.45-0.86) *MRI* - Mean sensitivity 0.72 (95% CI 0.55-0.85) - Mean specificity 0.97 (95% CI 0.93-0.99) - Positive likelihood ratio 26.72 (10.56-67.64) - Negative likelihood ratio 0.92 (0.17-0.49) *Sensitivity* - p-value SN vs. CT = 0.018 - p-value SN vs. MRI = 0.546 - p-value CT vs. MRI = 0.039 *Specificity* - p-value SN vs. CT = 0.095 - p-value SN vs. MRI = 0.546 - p-value CT vs. MRI = 0.014 ➔ MRI is most accurate method	No studies reported the accuracy of PET Only one study (18) using ultrasound, poor sensitivity (0.33), positive likelihood ratio 50.3, negative likelihood ratio 0.67, failure rate to detect sentinel node ranged from 6.6% (1/16 patients) to 100%. It is difficult to draw conclusions concerning this technique	- The results must be interpreted with caution as the quality of studies available for review was variable, with many of poor methodological quality that may result in the introduction of bias. - Results of test are combined over a wide time scale - Comparison of tests is indirect and hence subject to bias	A1
(2)	Summary ROC curves, Q* values (where sensitivity and specificity are equal)	*Q* values for overall performance* - CT: 0.80 (95% CI: 0.62-0.98) - US: 0.86 (95% CI: 0.81-0.91) - MRI 0.87 (95% CI: 0.85-0.89) *Q values for myometrial invasion* - CT: 0.79 (95% CI: 0.61-0.96) - US: 0.85 (95% CI: 0.81-0.88) - MRI: 0.83 (95% CI: 0.79-0.879) - Contrast-enhanced MRI: 0.91 (95% CI: 0.89-0.92) ➔ No statistically significant difference in the performance of CT, US and MRI. ➔ Significantly better results for contrast-enhanced vs. non-enhanced MRI-imaging (p<0.001). Difference in Q* values reached statistical	The lack of reported data on the assessment of cervical invasion at CT and US may be related to diagnostic difficulties with these imaging modalities. MR imaging sensitivity ranged from 66% to 100% (mean 86%), from 92% to 100% (mean 97%) for specificity, and from 87% to 95% for the CI's of the Q* values	- Attempted to minimize the problem of combining poor results of different studies by using strict inclusion and exclusion criteria - Publication bias is not excluded, which tends to cause overestimation of diagnostic performance because of the greater likelihood of publication of positive results rather than negative results	A1

<table>
<tr><th>ID</th><th>Primary Outcome Measure(s)
Secondary outcome(s)</th><th>Effect size-Primary Outcome(s)
Effect size-Secondary outcome(s)</th><th>All other outcomes, endpoints</th><th>Critical appraisal of study quality</th><th>Level of evidence</th></tr>
<tr><td></td><td></td><td>significance between contrast-enhanced MRI and US (p=0.02)

Q* values for cervical involvement only
- MRI: 0.92 (95% CI: 0.87-0.95)</td><td></td><td></td><td></td></tr>
<tr><td>(3)</td><td>Sensitivity, specificity (not in paper, self calculated) positive (PPV) and negative predictive values (NPV), misclassification, relation between ECC and FIGO stage</td><td>ECC
Sensitivity 0.67 (self calculated)
Specificity 0.97 (self calculated)
PPV 86.7%
NPV 92.2%
Misclassification 8.6%
False-negative samples 6.6%
(>63 years independently related to presence of false negative samples (OR: 4.0; 95%-CI: 1.3–12.4))
False-positive samples 2.1%

Relation between ECC and FIGO stage
Multivariate analysis
Positive ECC result (OR: 41.0; 95%-CI: 11.4–146.8)
Poorly or undifferentiated tumour cells (OR: 3.2; 95%-CI: 1.4–7.4)
Depth of invasion≥1/2 of myometrium (OR: 7.3; 95%-CI: 1.6–33.4)
were independently associated with FIGO≥II stage disease.
After correlation of ECC with extra uterine spread (i.e. FIGO III, IV) the effect remained significant (OR: 2.77; 95%-CI: 1.2–6.3).

➔ The authors conclude that ECC is an acceptable diagnostic tool to predict the presence or absence of cervical involvement in early stage endometrial</td><td>Clinicopathological characteristics
Multivariate analysis
Depth of invasion ≥1/2 of the myometrium (OR: 7.0; 95%-CI: 1.6–31.3) was statistically significantly associated with presence of cervical involvement.

Due to curetting, endometrial tumour cells can be implanted in the endocervical glandular tissue called cervical implantation metastasis</td><td>- 2.1% of all cases were false positive. The reason for the amount of changed false-positive cases after reviewing by H.H. was due to a wrong interpretation by other pathologists (referral patients, not revised by H.H) of the ECC samples with free floating tumour fragments without cervical tissue (i.e. separate group). These samples were interpreted as being positive, but according to the study protocol considered as being negative. Several hypotheses are argued to explain the occurrence of false positive ECC results. In the study, in three cases the curetting might have had a therapeutic value by removing all tumour from the endocervix.</td><td>A2</td></tr>
<tr><td>(4)</td><td>Cervical infiltration either absent (stage I) or present (stage II). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios (LRs) for positive and negative results</td><td>Efficacy of fluid hysteroscopy (HYS), transvaginal sonography (TVS) and magnetic resonance (MRI) in detecting cervical invasion by endometrial carcinoma
<table><tr><th></th><th>HYS</th><th>TVS</th><th>MRI</th></tr><tr><td>Sensitivity (%)</td><td>0.93</td><td>0.53</td><td>0.67</td></tr><tr><td>Specificity (%)</td><td>0.88</td><td>0.82</td><td>0.95</td></tr><tr><td>PPV (%)</td><td>0.58</td><td>0.34</td><td>0.71</td></tr><tr><td>NPV (%)</td><td>0.98</td><td>0.91</td><td>0.94</td></tr><tr><td>Accuracy (%)</td><td>0.89</td><td>0.78</td><td>0.91</td></tr><tr><td>LR for positive test result</td><td>7.93</td><td>3.02</td><td>14.16</td></tr><tr><td>LR for negative test result</td><td>0.07</td><td>0.56</td><td>0.35</td></tr></table>PPV and NPV mean positive and negative predictive values, respectively. LR means likelihood ratio.

Test comparison</td><td>NR</td><td>- The likelihood ratios were calculated (LR) in order to indicate how much a hysteroscopic finding increases or decreases the probability of cervical involvement.</td><td>A2</td></tr>
</table>

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
		Sensitivity HYS vs. TVS P<0.000001 HYS vs. MRI P<0.000001 MRI vs. TVS P<0.001 *Specificity* MRI vs TVS P<0.001 MRI vs. HYS P<0.05 HYS vs. TVS P<0.05 *PPV* MRI vs. HYS P<0.000001 MRI vs. TVS P<0.000001 HYS vs. TVS P<0.0001 *NPV* HYS vs. MRI – no difference HYS vs. TVS P<0.05 *Diagnostic accuracy* HYS vs. TVS P<0.005 MRI vs. TVS P<0.001 *LR+* MRI vs. HYS P<0.000001 MRI vs. TVS P<0.000001 *LR-* HYS vs. MRI P<0.000001 HYS vs. TVS P<0.000001 ➔ Hysteroscopy is reliable in excluding cervical involvement ➔ MRI is helpful in the assessment of the extent of cervical invasion ➔ Poor performance of TVS in detecting cervical involvement			
(5)	sensitivity, specificity, PPV, NPV, accuracy	stage Ia/Ib: sensitivity 87%, specificity 90%, PPV 93%, NPV 81%, accuracy 88% stage Ic: sensitivity 56%, specificity 86%, PPV 43%, NPV 91%, accuracy 81% stage II: sensitivity 19%, specificity 96%, PPV 50%, NPV 86%, accuracy 84% stage III/IV: sensitivity 100%, specificity 99%, PPV 86%, NPV 100%, accuracy 98%	- The high values of the sensitivity and specificity of MRI for accurately staging early endometrial cancer can be used confidently in deciding which patients can be treated in local cancer units with TAH and BSO without the need for more extensive pelvic surgery - The presence of fibroids, adenomyosis and high grade tumour progression are artefacts known to affect MRI staging. The sensitivity of MRI in detecting cervical extension was low (19%). This is unsurprising as very small endocervical tumour foci can only be detected by meticulous	- No information on blinding of pathologists. Written that surgeons were not blinded for MR imaging results. - Of 2 patients in whom MRI underestimated the degree of invasion, there was a protracted delay between the timing of the MRI and the time of surgery (62 days and 75 days)	A2

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
			histopathological sampling of the cervix		
(6)	sensitivity, specificity, PPV, NPV, accuracy, Cohen's kappa, area under receiver ROC curves	myometrial invasion: TVS 84% / 83% / 79% / 88% / 84%; MRI 84% / 81% / 77% / 87% / 82% cervical involvement: TVS 93% / 92% / 72% / 98% / 92%; MRI 79% / 87% / 58% / 95% / 85% (sensitivity / specificity / PPV / NPV / accuracy) ➔ Differences in the performance of TVS and MRI were not statistically significant.	- Myometrial invasion, TVS Cohen's kappa: 0.672 p<0.0005, Area under curve: 0.854 p<0.0005. MRI Cohen's kappa: 0.646 p<0.0005, Area under curve: 0.837 p<0.0005 - Cervical involvement, TVS Cohen's kappa: 0.762 p<0.0005, Area under curve: 0.852 p<0.0005. MRI Cohen's kappa: 0.574 p<0.0005, Area under curve: 0.741 p<0.0005	- Possible bias due to exclusion of patients with a high level of uncertainty in the pathological staging.	A2
(7)	Diagnostic accuracy, sensitivity, specificity, positive a predictive value (PPV), negative predictive value (NPV)	*Deep myometrial invasion (≥ 50% of the thickness of myometrium)* - MRI correctly assessed 43 of 48 (90%) cases with deep myometrial invasion and underestimated 5 (10%) - MRI sensitivity for deep myometrial invasion was 90%, specificity 100%, diagnostic accuracy 95%, PPV 100% and NPV 91% *Cervical extension* - MRI found invasion in 19 of 31 cases (61%). In the 12 patients understaged by MRI, six cases had only endocervical epithelial extension (stage IIA) - MRI sensitivity for cervical invasion was 61%, specificity 100%, diagnostic accuracy 88%, PPV 100% and NPV 85%	Among the imaging modalities that have been proposed for the evaluation of myometrial invasion, contrast enhanced MRI has a substantially higher sensitivity and specificity than endovaginal US and CT (19). MRI studies allow tumour visualization, determine the degree of myometrial invasion, and also evaluate cervical extension, obtaining good accuracy in endometrial tumour evaluation The presence and depth of myometrial infiltration can be assessed on T2-weighted images as an interruption of the junctional zone, which appears with low signal intensity. However, in postmenopausal women, this could be more difficult to assess because uterine involution makes the junctional zone poorly visible and the myometrium thinner. To overcome this limitation, a dynamic study should be performed, because it can depict different enhancement times of the adenocarcinoma compared with those of the adjacent myometrium, improving the contrast resolution of the tumour and myometrium	- The presence of leiomyomas, high-grade tumour progression and the presence of small. isolated tumoural foci were factors that in the authors' opinion decreased the accuracy in their study as previously described - Results are in keeping with previous series	A2
(8)	Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)	Sensitivity 79.48% Specificity 88.05% PPV 56.36% NPV 95.67% ➔ The authors summarize that office hysteroscopy is a valid method to rule out cervical involvement, but not to detect tumour involvement.	43% of all positive hysteroscopy had undergone an excessive surgical treatment	- Unclear if this study was conducted prospectively or retrospectively - No description how initial diagnosis was made (pre-test diagnosis)	B
(9)	sensitivity, specificity,	*Myometrial invasion*	- The presence of leiomyomas or adenomyosis	- Small study population	B

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
	PPV, NPV, accuracy	Sensitivity: 100% Specificity: 80% PPV: 94% NPV: 100% Accuracy: 95% *Cervical involvement* Sensitivity: 78% Specificity: 83% PPV: 78% NPV: 83% Accuracy: 81% ➔ MDCT on a 16-row CT scanner proved accurate in local staging of endometrial carcinoma.	may be a factor interfering with the prediction of depth of myometrial invasion on imaging. Nevertheless, ,myometrial infiltration was correctly assessed by MDCT in six tumours associated with adenomyosis or fibroids in our series. - It was found that diagnostic performances of MDCT in assessing the presence of cervical infiltration in patients with endometrial carcinoma are similar to those of MR imaging and much improved compared with single-slice CT scanners.		
(10)	Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy Retroperitoneal lymph nodes beyond 1 cm in diameter were diagnosed as the significant swelling in CT and/or MR imaging	*Detecting primary lesion* Sensitivity FDG-PET in detecting primary lesion was 96.7% (29/30), in CT/MRI 83.3% (25/30), difference is not statistically significant. (The one false-negative case in FDG-PET was a microscopic grade 1 endometrioid carcinoma localized within the superficial endometrial layer) *Prediction of pelvic lymph node metastasis* FDG-PET CT/MRI Sensitivity 0% (0/5) 40% (2/5) Specificity 100% (21/21) 85.7% (18/21) Positive predictive value 0% 40% Negative predictive value 80.8% 85.7% Accuracy 80.8% 76.9% - The results of CT and MRI to identify pelvic lymph node metastasis were identical *Detecting para-aortic lymph node metastasis* FDG-PET CT/MRI Sensitivity 0% (0/1) 100% (1/1) Specificity 100%(18/18) 94.4% (17/18) Positive predictive value 0% (0/0) 50% (1/2) Negative predictive value 94.7% (18/19) 100% (17/17) Accuracy 94.7% 94.7% ➔ There was no significant difference between FDG-PET and CT	- FDG-PET was not able to detect microscopic metastasis in pelvic lymph nodes. (5 patients were positive for retroperitoneal lymph node metastasis, ranging from 0.1 to 0.6 cm in diameter, all were microscopic metastasis). There was no significant difference in the ability of evaluating retroperitoneal lymph node between FDG-PET and CT is this study - Macroscopic solid tumours were clearly detected by FDG-PET. One case was false negative, this endometrial lesion was a superficial microscopic lesion of 1 cm in diameter without myometrial invasion - Currently, any of FDG-PET, CT, MRI, or their combination cannot be used for the definitive diagnosis of lymph node metastasis	- Small sample size: 30 patients	B
(11)	sensitivity, specificity, PPV, NPV	**T2-w** sensitivity specificity PPV NPV intramucosal neoplasma 100% 95% 84% 100% myometrial invasion 92% 88% 79% 92%	- Gadolinium-enhanced dynamic sequence increase the accuracy of MR imaging in diagnosing the depth of myometrial invasion. In particular they improve the visualisation of the inner myometrium, the so called subendometrial enhancing zone, whose disruption or changes	- Not described if population is made of consecutive patients - Blinding of pathologists not reported	B

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)					All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
		<50% invasion >50% **Gadolinium-enhanced** intramucosal neoplasma invasion <50% invasion >50% **T2-w Gadolinium-enhanced** **sequences** **at 30 sec** **60 sec** **120 sec**	50% 100% 96% 76%	80% 97% 88% 95%	50% 91% 90% 83%	86% 100% 96% 93%	accuracy 78% 95% 87% 88% 79%	are essential for diagnosing myometrial invasion. The major diagnostic advantages of the enhanced sequences were found in postmenopausal women, where visualization of the junctional zone may be difficult in the T2w sequences. ➔ Gadolinium-enhanced MR imaging is more accurate than plain T2 weighted MR imaging.		
(12)	Sensitivity and specificity	- FDG-PET sensitivity on a lymph node group basis is 60% (3/5), specificity 98% (68/69) for predicting pelvic or para-aortic lymph node metastasis - FDG-PET sensitivity on patient-by-patient basis is 67% (2/3), specificity is 94% (15/16)						- The FDG-PET study was well tolerated by all patients - PET showed abnormally increased FDG uptake in 16 of the 19 primary tumours (84%). 2 of the remaining 3 patients had very small tumours (FIGO stage IB and IA), the 3rd was a grade 3 endometrioid adenocarcinoma, FIGO stage IB - Overall, FDG-PET had only moderate sensitivity for pre-operative detection of pelvic and para-aortic lymph nodes in women with endometrial carcinoma. However, it did have a high specificity, thus suggesting its potential to assist in the preoperative management of this malignancy	- Small sample size (19 patients/74 lymph nodes) - The study includes uterine corpus sarcoma. - Study fell short on accrual goals - An additional limitation of FDG-PET in the study was the high frequency of false-positive focal FDG uptake. Although there was only one false-positive lymph node in our study population, there were six incidental foci of increased FDG uptake. In this pilot study, the nuclear medicine physicians interpreting the PET studies were blinded to the results of other imaging studies. In the clinical setting, PET images are routinely interpreted in conjunction with other available imaging studies, and this might be	B

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
				expected to reduce the number of false-positive results	
(13)	MR imaging findings were compared with surgicopathologic findings, and sensitivity, specificity, positive and negative predictive values, diagnostic accuracy	Myometrial infiltration sensitivity: 87% specificity: 91% diagnostic accuracy: 89% PPV: 87% NPV: 91% Cervical invasion sensitivity: 80% specificity:96% diagnostic accuracy: 92% PPV: 89% NPV: 93% Lymph node metastases sensitivity: 50% specificity: 95% diagnostic accuracy: 90% PPV: 50% NPV: 95%	- At histopathologic examination, 338 lymph nodes were examined. When the site of the lymph nodes was taken into consideration, the patient with true-positive findings had a left internal iliac node, and the one with false-negative findings had seven positive lymph nodes (four left internal obturator and three left external iliac nodes). - Myometrial and cervical invasion and lymph node enlargement were correctly preoperatively assessed at MR imaging in 28 (76%) of 37 patients, were overstaged in four (11%) patients, and were downstaged in five (13%) patients.		B
(14)	Sensitivity, specificity, PPV	depth of myoinvasion TVS: sensitivity 91.6%, specificity 81.8%, PPV 94.7% degree of myoinvasion TVS: sensitivity 94.4%, specificity 93.3%, PPV 94.4% cervical involvement TVS: sensitivity 75.0%, specificity 100.0%, PPV 100.0%	- The accuracy of TVS in detecting cervical spread was superior to that achieved in myometrial assessment cases (97.8 vs. 85%; *p*=0.02) - When the TVS data are combined with results from other preoperative tests, the prognostic information obtained provides a useful basis for choosing the appropriate therapy. - Based on the data presented, the value of preoperative TVS results as the sole criterion in the decision to perform extensive surgical procedures or radiation therapy in endometrial cancer is questionable and warrants further evaluation.	- Not described if population is made of consecutive patients. - Little information about method - Study period is missing	B
(15)	Sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV)	*TVS in detecting deep invasion in grade 1-3 disease (n=91)* - Sensitivity 87.8% (29/33) - Specificity 82.7% (48/58) - PPV 74.3% (29/39) - NPV 92.3% (48/52) *TVS in subgroup of patients with grade I disease (n=47)* - Sensitivity 77.7% (7/9)	- Thus, accuracy of TVS in detection of deep invasion in grade 2-3 cases was superior to that achieved in grade 1 cases (91% (40/44) vs. 78.7% (37/47); p=0.002) - Frozen section was superior compared to TVS in specificity (p=0.008) and accuracy (97.5% (40/41) vs. 78.7% (37/47); p=0.005) in detecting	- It is not clear in which years the patients were diagnosed and underwent surgery - Incorporation of TVS into the standardized pre-operative work-up recommended for grade 1 tumours is premature	B

<table>
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Secondary outcome(s)</th><th>Effect size-Primary Outcome(s)
Effect size-Secondary outcome(s)</th><th>All other outcomes, endpoints</th><th>Critical appraisal of study quality</th><th>Level of evidence</th></tr>
<tr><td></td><td></td><td>- Specificity 79% (30/38)
- PPV 46.6% (7/15)
- NPV 93.7% (30/32)

TVS in cases with grade 2-3 disease (n=44)
- Sensitivity 90% (18/20)
- Specificity 91.6% (22/24)
- PPV 90% (18/20)
- NPV 91.6% (22/24)

Frozen section analysis grade 1 (n=41, was not performed in 6 out of the 47 patients)
- Sensitivity 85.7% (6/7)
- Specificity 100% (34/34)
- PPV 100% (6/6)
- NPV 97.1% (34/35)

➔ TVS is more accurate in grade 2-3 compared to grade 1</td><td>deep invasion in grade 1 disease. No statistically significant difference was found between the sensitivity of either technique

- Based on these data the value of preoperative TVS results as the sole criterion in the decision to perform extensive surgical procedures in grade 1 is questionable and warrants further evaluation</td><td>- Grade 1 cases commonly presented with superficial invasion in this study (38/47; 81%), hence, a plausible explanation for the diverse accuracy of TVS between low and high grades is that this method, in the face of superficial invasion presents poor tumour/myometrium contrast identification</td><td></td></tr>
<tr><td>(16)</td><td>Sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV), Accuracy of MRI in assessing the depth of myometrial tumour invasion, Cohen’s kappa statistic, degree of interobserver agreement between 2 groups of radiologists</td><td>Diagnostic Efficacy for Plain and Whole Study Series (95% CI)
<table><tr><th></th><th>Observer 1[a]</th><th>Observer 2[a]</th></tr><tr><td>Sensitivity</td><td>64.1 (47.2–78.3)</td><td>64.1 (47.2–78.3)</td></tr><tr><td></td><td>89.7 (74.8–96.7)</td><td>87.2 (71.8–95.2)</td></tr><tr><td>Specificity</td><td>93.5 (81.1–98.3)</td><td>100 (90.4–100)</td></tr><tr><td></td><td>87.0 (73.0–94.6)</td><td>95.7 (84.0–99.2)</td></tr><tr><td>PPV</td><td>89.7 (70.6–97.2)</td><td>100 (83.4–100)</td></tr><tr><td></td><td>85.7 (70.1–93.9)</td><td>94.6 (80.0–99.0)</td></tr><tr><td>NPV</td><td>75.4 (62.0–85.5)</td><td>76.7 (63.7–86.2)</td></tr><tr><td></td><td>90.0 (77.4–97.0)</td><td>89.8 (77.0–96.2)</td></tr></table>PPV = positive predictive value, NPV = negative predictive value.
[a]Values in parentheses are standard deviations. Values in plain characters are data for plain series, and values in bold characters are data for the whole study series.</td><td>- Interobserver variability showed good agreement for assessing depth of myometrial invasion in the plain series (k 5 0.644) and very good agreement when the whole study series (pre and contrast-enhanced; k 5 0.752) were evaluated

- In this study the accuracy for plain series was 80.2% and 83.7% for the two groups (group 1: FIGO stages Ia and Ib and group 2: FIGO stage Ic)</td><td></td><td>B</td></tr>
<tr><td>(17)</td><td>Accuracy, sensitivity, specificity, PPV, NPV</td><td>Accuracy
T2-weighted 85%
Dynamic 95%
CE T1-weighted spin echo 90%

Sensitivity
T2-weighted 80%
Dynamic 90%
CE T1-weighted spin echo 90%</td><td>- The authors believe that, in combination with T2-weighted MR imaging sequences, dynamic MR imaging is useful in assessing endometrial carcinoma involvement of the cervix</td><td>- Poor description of the study population</td><td>B</td></tr>
</table>

ID	Primary Outcome Measure(s) Secondary outcome(s)	Effect size-Primary Outcome(s) Effect size-Secondary outcome(s)	All other outcomes, endpoints	Critical appraisal of study quality	Level of evidence
		Specificity T2-weighted 86% Dynamic 97% CE T1-weighted spin echo 90% PPV T2-weighted 67% Dynamic 90% CE T1-weighted spin echo 75% ➔ Dynamic MR imaging performed better than T2-weighted MR imaging and CE T1-weighted spin-echo MR imaging, but was not statistically different			

NR= Not Reported; NA= Not Applicable; CI=Confidence Interval; ECC= Endocervical Curettage; ECB=Endocervical Biopsy; LVSI=Lymph Vascular Space Invasion; PPV=Positive Predictive Value; NPV= Negative Predictive Value; BMI=Body Mass Index; MRI=Magnetic Resonance Imaging; FIGO=International Federation of Gynecology and Obstetrics

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