The high negative predictive value to pre-operative MRI in Grade I endometrial cancer in the clinical setting.

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PURPOSE
Currently, endometrial cancer is surgically staged, which includes a pelvic and paraortic lymphadenectomy. There are varying opinions regarding the need for lymphadenectomy in women with grade 1 endometrial cancer [1,2]. Both myometrial invasion (MI) and cervical invasion (CI) increase the risk of lymph node metastasis. In some of the larger studies to date, the prevalence of lymph node metastasis increases from less than 2-3% with superficial myometrial invasion to 11-25% with deep myometrial invasion [3,4]. MRI may be used pre-operatively to evaluate for these key prognostic indicators for lymph node metastasis, hence may be helpful in determining the need for lymphadenectomy in women with endometrial cancer. MRI has been shown to predict MI and CI accurately with sensitivities and specificities ranging from 70-95% [2,5,6]. At our institution, MRI was proposed as part of a clinical decision making protocol in women with Grade I endometrial cancer. If there was greater than 50% myometrial invasion or evidence of cervical stromal invasion, the surgeon would highly consider doing a pelvic and paraortic lymph node dissection, since both of these parameters increase the women’s risk of lymph node metastasis.

The goal of our study was to determine the sensitivity, specificity, PPV, and NPV of MRI in determining MI and CI in women with grade 1 endometrial cancer on preoperative MRI interpreted by abdominal radiologists in the clinical practice setting. Surgical pathology was the gold standard.

METHODS
IRB approval was obtained for this retrospective review of clinical MRI reports in 104 women with grade 1 endometrial cancer. All women were imaged on a 1.5T or 3.0T MR scanner (GE Healthcare, Waukesha, WI, USA) with an 8-channel cardiac or 32-channel torso coil. Sequences obtained included sagittal and axial T2-weighted images with fat saturation, 90sec sagittal and 180 sec axial T1 pre and post contrast-enhanced images, and sagittal and axial diffusion weighted images (DWI). Apparent diffusion coefficient maps were calculated from the DWI images. Myometrial invasion (MI) and cervical invasion (CI) as reported in the radiology report were compared to final surgical pathology to determine the number of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN). Eleven abdominal radiologists were involved in reading the clinical MRIs. Three of the 11 abdominal radiologists specialized in women’s imaging, and the remaining abdominal radiologists specialize in renal or hepatobiliary imaging. The sensitivity, specificity, NPV and PPV were calculated. The FP and FN were determined to analyze if there was a systematic error.

RESULTS
Of the 104 women with grade 1 endometrial cancer, three were excluded because the tumor was not easily detected on MRI, so CI and MI could not be assessed. Body mass index (BMI) of the women assessed ranged from 21.5 to 59.8, and age ranged from 28 to 84 years. In the 101 women, true positives, true negatives, false positives and false negatives where calculated (Figure 1). When comparing MRI detected MI and CI with pathology proven MI and CI, sensitivity was 88%; specificity was 89%; PPV was 73%; and NPV was 96%. Of the false negatives, 2/3 of the cases had tumor that was not apparent on the T2-weighted images or the post-contrast T1-weighted images, and the extent of myometrial invasion was only seen on DWI (Figure 1), on retrospective evaluation of the MR examination. Of the false positives, 2/8 cases were overcalled due to concurrent adenomyosis, 2/8 cases were overcalled in women >75 y/o and the junctional zone and myometrium were dark on T2-weighted images and DWI making it difficult to see the edge of the tumor; 3/8 cases were very large expansive tumors; and 1/8 cases there was cervical invasion detected; however, on pathology the tumor was 1mm from the cervical stroma.

DISCUSSION
In grade 1 endometrial cancer there is considerable debate whether or not a lymphadenectomy is necessary. Part of this debate includes assessing for prognostic indicators of women at an increased risk for lymph node metastasis, including but not limited to myometrial and cervical stromal invasion. There is strong evidence that suggests women with no myometrial invasion or cervical invasion have a decreased risk of lymph node metastasis (<2-3%); avoiding lymphadenectomy in women with very low risk of lymph node metastasis would be ideal.

Our study demonstrates MRI to be sensitive and specific for detecting MI and CI compared with surgical pathology in the clinical setting. More importantly the negative predictive value of MRI in detecting MI and CI is 96% when interpreted by clinical abdominal radiologists.

CONCLUSIONS
The high NPV of MRI to exclude MI and CI preoperatively gives the gynecologic oncologist confidence to potentially avoid lymphadenectomy in women with grade 1 endometrial cancer in those deemed MRI negative for these two parameters.

RESOURCES

Table 1: Calculated true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN), comparing MRI detected myometrial invasion (MI) and cervical invasion (CI) to the final pathology report in 101 women with Grade I endometrial cancer.

<table>
<thead>
<tr>
<th>MI or CI</th>
<th>TP=22</th>
<th>FN=3</th>
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<tbody>
<tr>
<td>+ MRI</td>
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<tr>
<td>- MRI</td>
<td>FP=8</td>
<td>TN=66</td>
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Figure 1: Example of a false negative. Note the path proven tumor is best seen on DWI (B=0, B=500, ADC map), and there is greater than 50% myometrial invasion. This invasion is not seen on the T2-wt or 90 second post-contrast T1-wt images.