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SHORT COMMUNICATION

T₂ relaxometry mapping in demonstrating layered uterine architecture: parameter optimization and utility in endometrial carcinoma and adenomyosis: a feasibility study

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Objective: We evaluate the feasibility of T₂ relaxometry mapping of the uterus and demonstrate its diagnostic utility in endometrial carcinoma and adenomyosis and discuss the optimum imaging parameters as used in our institute.

Methods: Institute review board approval was obtained and multispin echo (MSE) imaging of the pelvis was done with variable time to echo in three patients, two with endometrial carcinoma and one with adenomyosis. T₂ parametric maps and curves were plotted and the T₂ times of the diseased endometrium, superficial and deep myometrium were established.

Results: T₂ mapping of the uterus is feasible and demonstrated the four-layered uterine architecture with T₂ times of the diseased endometrium, inner myometrium and the outer myometrium being determined. The fourth myometrial layer was demonstrated in all the three cases on the parametric maps. The two cases with endometrial carcinoma had thinning and irregularity of the myometrial fourth layer which helped in predicting superficial myometrium invasion. Thickening of the fourth myometrial layer was demonstrated in the case with adenomyosis, which we believe might be a new imaging finding of adenomyosis.

Conclusion: Thinning and irregularity of the myometrial fourth layer in cases of endometrial malignancy might

help in identification of superficial myoinvasion—this might be a new imaging armamentarium in nulliparous females where uterine preservation might be a consideration. The T₂ relaxation times of the myometrium and endometrium described here will help optimize the time to echo for the acquisition of MSE for relaxometry of the female pelvis.

Advances in knowledge: Thinning and irregularity of the fourth myometrial layer helps in the identification of superficial myometrial invasion with a greater confidence and helps triage patients for uterine preservation when necessary. T₂ relaxometry might be undertaken in those nulliparous women with endometrial carcinoma in whom demonstration of no myometrial invasion will make them candidates for uterine preservation. Thickening of the fourth myometrial layer in adenomyosis requires further evaluation in a larger cohort of patients as an additional imaging finding. T₂ relaxation times of endometrial carcinoma is different from the normal endometrium in the three cases imaged, thus, further studies evaluating the T₂ values in a larger cohort might help in differentiating diseased from the healthy endometrium. T₂ time of the pelvic tissue described in the study will help select the time to echoes for MSE imaging of the female pelvis in further studies.

INTRODUCTION

The zonal anatomy of the uterus on T₂ weighted images has been described extensively in the literature and shows the innermost hyperintense endometrium, hypointense junctional zone and the outermost myometrium, which is moderately hypointense.

Imaoka et al have demonstrated that T₂* mapping of the uterine layers is feasible *in vivo* and have defined a three-layered myometrial structure where in addition to the endometrium they have described the deep myometrium, junctional zone and a thin fourth zone just superficial to the endometrium.¹

T_2 relaxometry mapping has found varied applications in cardiac and neurological imaging with T_2 parametric maps being sensitive to oedema occurring in the myocardium, which helps in the diagnosis of acute myocardial infarction, sarcoidosis, myocarditis, cardiac allograft rejection and stress cardiomyopathy.² T_2 relaxation times has also been used in the characterization of intracranial tumours.³

We evaluate the feasibility of T_2 mapping of the uterus and demonstrate its diagnostic utility in endometrial carcinoma and adenomyosis and discuss the optimum imaging parameters as used in our institute.

METHODS AND MATERIALS

Appropriate institutional review board clearance was obtained and informed consent was obtained from all patients.

A total of three patients were scanned, two cases of endometrial carcinoma who had undergone prior fractional curettage to establish the histological diagnosis before being taken for imaging and one case with adenomyosis. The patients were scanned on a Siemens 1.5-Tesla scanner, with a system type: Aera. In addition to the routine T_2 weighted, T_1 weighted, dynamic contrast enhanced imaging, post-contrast T_1W sequences and DWI sequences performed for the diagnosis of the pelvic disease, the patients underwent a multispin echo (MSE) sequence with a long relaxation time and multiple echo time (TE) for T_2 relaxometry mapping of the uterus. A 16 phased array pelvic coil was used for imaging. The field of view phase was 100%, with an acquisition time of 5:16 min, the resolution matrix was 256×192 , with a total of 15 slices acquired, the field of view read was 250 mm, a slice thickness of 4 mm was acquired with a slice gap of 20% the repetition time was 2000 ms and echo times of 11, 22, 33, 44, 55, 66, 77, 88, 99, 110, 121 and 132 milliseconds were used. The flip angle used was 180 degrees; however, no flow suppression, fat suppression or subtraction was used. No anti spasmodic was used in the imaging of the patients as per departmental protocol. The bladder was not over distended to avoid discomfort due to the over distended bladder and subsequent motion.

Multiple oval/round ROIs were placed on the superficial, deep myometrium, normal endometrium in the patient with adenomyosis and diseased endometrium in the patients with endometrial carcinoma. Both radiologists working separately evaluated the myometrial layers and drew the ROIs. In two cases where the junctional zone was visible in the base images, the ROIs were drawn on the junctional zone and the deep myometrium separately; when the junctional zone was not separately visualized, eye estimation was used to draw the ROIs on the inner and outer 50% of the myometrium. The base images obtained were post-processed using open source software on Mac Book Pro, OS X El Captain version 10.11.3 on OsiriX Lite v 8.0.1. T_2 relaxometry parametric voxel wise mapping was possible in all three patients with adequate image quality, signal to noise ratio and adequate delineation of the anatomy with comparable maps being produced by both radiologists with 2 and 10 years experience in pelvic imaging. The maps produced by the senior radiologists were further evaluated.

Statistical analysis

A mono-exponential decay curve fitting was done for the T_2 signal against the various echo times of the acquisition and the T_2 relaxation times were determined of the various ROIs drawn on the superficial, deep myometrium, endometrium and the endometrial mass using the non-linear curve fitting programme of GraphPad Prism version 6.00 for Windows, GraphPad Software, La Jolla California, www.graphpad.com.

RESULTS

Case 1

Mrs X, a 45-year-old multigravida patient presented with post-menopausal bleeding and was found to have a bulky uterus on examination, and on pelvic ultrasound was provisionally diagnosed as adenomyosis. T_2W sagittal image showed thickening of the junctional zone (Figure 1a) with the presence of multiple T_2 hyperintense foci seen in the deep myometrium (Figure 1a), consistent with the clinical diagnosis of adenomyosis. The post-processed parametric T_2 relaxation map of the uterus in the sagittal and parasagittal plane showed

Figure 1. (a) A 45-year-old multigravida patient presented with post-menopausal bleeding and was found to have bulky uterus on vaginal examination, and on pelvic ultrasound was provisionally diagnosed as adenomyosis. T_2W sagittal image shows the thickening of the junctional zone (arrow) with presence of multiple T_2 hyperintense foci seen in the deep myometrium (arrow head), consistent with the clinical diagnosis of adenomyosis. (b, c) Parametric T_2 relaxation map of the uterus in the sagittal and parasagittal plane shows thickening of the moderately hypointense junctional zone (annotated 2) and darker fourth myometrial layer (annotated 3). Hyperintense foci are seen in the deep myometrium (annotated 1).

Figure 2. (a) A 30-year-old nulliparous female on pelvic ultrasound was found to have a thickened endometrium. On fractional curettage the histological diagnosis was of Grade 1 endometrioid adenocarcinoma of the uterus. T_2 relaxation map shows the moderately hypointense junctional zone (annotated 2), isointense deep myometrium (annotated 1) and the dark fourth myometrial (annotated 3) layer and the hypointense mass in the endometrial cavity (annotated 5). Posterolaterally, the thinning and irregularity of the junctional zone and the fourth layer is well demonstrated (annotated 4). (b) T_2 W axial image shows the hypointense tumour mass invading the myometrium posterolaterally with ill-defined junctional zone posteriorly with tongue-like projection of the tumour into the myometrium seen (white arrow).

thickening of the moderately hypointense junctional zone (annotated 2 in Figure 1b,c) and more hypointense fourth myometrial layer (annotated 3 in Figure 1b,c). Hyperintense foci were seen in the deep myometrium (annotated 1 in Figure 1b,c). No evidence of endometrial growth was seen.

Case 2

Mrs Y, a 30-year-old nulligravida patient was being treated for infertility and had a previous diagnosis of polycystic ovarian disease, during workup for infertility transabdominal pelvic ultrasound revealed a thickened endometrium. Fractional curettage provided the histological diagnosis of a Grade 1 endometrioid adenocarcinoma. Routine dynamic contrast enhanced magnetic resonance imaging of the pelvis showed a mass lesion arising from the posterior endometrial wall with the invasion of the myometrium along the posterolateral aspect (Figure 2b). The parametric T_2 relaxation map (Figure 2a) showed the moderately hypointense junctional zone (annotated 2), isointense deep myometrium (annotated 1) and the dark fourth myometrial (annotated 3) layer and a hypointense mass in the endometrial cavity (annotated 5). Posterolaterally, the thinning and

irregularity of the junctional zone and the fourth layer was also well demonstrated (annotated 4).

Case 3

Mrs Z, a 65-year-old multigravida patient presented with excessive vaginal spotting, and on further workup, she was diagnosed to have endometrial carcinoma Grade I. She underwent a staging magnetic resonance imaging of the pelvis. On the T_2 weighted imaging, the junctional zone was not well delineated (Figure 3a); however, on the post-contrast images there was a suggestion of superficial myometrial invasion along the posterior myometrium. The parametric T_2 relaxometry maps did not show the junctional zone either (Figure 3b); however, the hypointense fourth layer was seen (white arrow) with a discontinuity at the tumour- myometrial- interface. There is also discontinuity of the fourth layer at the supero-anterior aspect noted; however, as there was no myometrial-tumour interface seen at this aspect we believe that the fourth layer might be deficient because of the post-menopausal status. Subsequent resection and histopathology showed myometrial invasion at the suspected site (Figure 3c).

Figure 3. (a) A 65-year-old multigravida patient shows an endometrial polypoidal growth on the T_2 weighted images, the junctional zone is not well delineated. (b) The parametric T_2 relaxometry maps did not show the junctional zone either; however, the hypointense fourth layer (white arrow) with discontinuity at the myometrial-tumour interface was seen. The fourth layer is discontinuous supero-anteriorly also; however, there was no myometrial-tumour interface seen at this aspect and we believe that the fourth layer might be deficient here because of the post-menopausal status. (c) Subsequent resection of the gross specimen and histopathology showed myometrial invasion at the suspected site (arrow).

Figure 4. Graph showing the T_2 relaxation curves of the superficial myometrium, deep myometrium, normal and diseased endometrium.

The T_2 relaxation times as calculated from the mono-exponential decay curves were 52.30 to 58.51, 57.53 to 61.23, 74.36 to 81.53 and 90.93 to 105.6 ms for superficial, deep myometrium endometrial carcinoma and normal endometrium, respectively (Figure 4). These T_2 times were found to be significantly different across the various uterine zones and in between the diseased and normal endometrium ($p < 0.0001$) using the extra sum-of-squares F test.

DISCUSSION

As described by Bloch in his paper on nuclear induction way back in 1946, a net magnetization vector (V) induced by a radio-frequency pulse has a transverse and a longitudinal component, each of which is a function of time. T_2 relaxation is due to the relaxation of nuclei to the basal state after being excited by an RF pulse with the loss of energy to the surrounding protons (spin-spin interaction). Bloch presumed this to be a mono-exponential decay function.⁴ The vectors V_x , V_y constitute the transverse magnetization, and T_2 relaxation is the process by which this component of the induced magnetization decays back to zero. The T_2 time of a material is the time constant of this exponential decay of the transverse magnetization after the pulse. This is unique for various different tissues and depends on the dipole interactions and spin-spin flip-flop.

The signal intensity on the T_2 weighted images acquired with different TEs when plotted as a mono-exponential function will give the *in vivo* T_2 relaxation time of the tissue being imaged. A parametric map of T_2 relaxation time can be generated from at least two spin echo image sequences acquired with different TE or alternatively an MSE sequence with a range of different TEs centred around the expected T_2 time of the tissue can be used to generate the maps.

The optimal choice of TE is essential; if the first TE is much lower than the T_2 time of the tissue in MSE sequence, repeated radio-frequency pulse deposition will result in radio-frequency induced tissue heating thus alerting tissue spin-spin relaxation behaviour, while if the first TE is long, sufficient echoes cannot be obtained to accurately calculate the T_2 time. Similarly, a TE

much longer than the actual T_2 will result in a fallacious curve being fitted to the relaxed part of the decay curve. Besides time to echo; the model, *i.e.* a mono-exponential or a bi-exponential curve fitting, the offset used, as well as the relaxation time affects the T_2 time obtained from the parametric maps. Moreover, increasing the number of TEs increases the signal to noise ratio, and thus, if an MSE sequence is used then multiple TEs should be selected in a range centred around the expected T_2 value of the tissue being imaged.⁵

T_2 relaxometry has been used extensively in neuroradiology to detect mesial temporal sclerosis,⁶ evaluation of brain tumours³ and in the characterization of knee cartilage in patients with osteoarthritis.⁷ Myocardial oedema is picked up by T_2 maps that helps in the diagnosis of acute myocardial infarction, sarcoidosis and other conditions with myocardial inflammation and oedema.²

The relaxation time of the myometrium has not been previously described in the literature and we used the T_2 relaxometry values of the myocardium and T_2^* values described by Imaoka et al as a guideline to perform the relaxometry of the myometrium.¹ Precise knowledge of the T_2 relaxation times of the uterus obtained from our preliminary study would help in time to echo selection for T_2 relaxometry imaging and mapping of the female pelvis in general and the uterus in specific.

The reason behind layer-wise difference in the myometrial architecture is debated with the difference in the signal intensity and relaxation times of the junctional zone and the outer myometrium being attributed to compact packing of the myometrial cells in the junctional zone with difference in blood supply leading to difference in the T_2^* relaxation curve.¹

Endometrial carcinoma is the most common gynaecological malignancy in the western world. Post-menopausal bleeding is the commonest presentation.⁸ Although FIGO staging is predominantly surgical,⁹ pelvic MR imaging with dynamic post-contrast imaging and diffusion weighted imaging has been used for the pre-operative staging of endometrial cancer.¹⁰

Based on the pre-operative staging and histology, extended lymph node resection is restricted to endometrial carcinomas with deep myometrial invasion or those with Type 2 endometrial carcinoma.¹¹ Based on our experience in these cases we believe that the lower TE values of 11 and 22 ms and the higher TE values of 121 ms onwards can be omitted because the largest T_2 relaxation time in the uterus was of normal endometrium being 90.93–105.6 ms, and thus the extraneous TE would avoid radio-frequency induced tissue heating as well as optimize the imaging acquisition times. Further, we assume the four-layered uterine architecture which is demonstrated would help in differentiating no myometrial invasion from superficial and deep myometrial invasion.

We expect that T_2 mapping of the myometrium would help in the better diagnosis of myometrial invasion and add to the imaging armamentarium and would add to the reporting confidence.¹ We know that uterus preserving surgery is a consideration for patients with endometrial carcinoma with an incomplete family provided no myometrial invasion is demonstrated on imaging.¹²

If we are able to demonstrate an intact fourth myometrial layer in these patients, the reporting confidence of the radiologist might be greatly increased and this would add to better management of such patients.

LIMITATIONS

Our series was small and our preliminary aim was to demonstrate the feasibility of T_2 mapping of the uterine architecture and demonstration of myoinvasion on T_2 parametric maps in endometrial carcinoma.

CONCLUSION

T_2 mapping of the myometrium would add to the pre-operative staging of endometrial cancers and would help in the intraoperative management of the patient.

Further relaxometry values of the diseased endometrium might be used to further characterize the biological behaviour of endometrial tumours and possibly differentiate benign and malignant endometrial pathologies.

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