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Proximal suspensory desmopathy in hindlimbs: magnetic resonance imaging, gross post mortem and histological study

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Running head: Proximal suspensory desmopathy

Summary

Background: There have been no previous studies correlating high-field magnetic resonance imaging (MRI) findings with gross and histological post mortem examination in horses with hindlimb proximal suspensory desmopathy (PSD).

Objectives: To determine if adhesions between the suspensory ligament (SL) and adjacent tissues could be detected using high-field MRI and if collagen, adipose tissue and muscle pathology could be differentiated.

Study design: Retrospective study.

Methods: Nineteen horses with hindlimb PSD were humanely destroyed; 12 limbs of 11 horses with PSD underwent high-field MRI. All lame limbs were examined grossly and all SLs were examined histologically. The MR and histological images were graded blindly. Statistical analysis used a numerical Bayesian approach to simultaneously determine a pathology rating and the contribution of each MRI, gross post mortem and histological observation to this measure.

Results: Signal intensity (SI) in the collagenous tissue was abnormal in 2/12 limbs. Abnormalities of SI in the adipose tissue and muscle were identified in 6 and 11 limbs, respectively. Adhesions between the SL and adjacent tissues were suspected in 8 limbs, but only confirmed in 6. Histopathologic observations of abnormal muscle tissue were associated most closely with the measure of disease used in the study and were abnormal in every limb. Gross adhesions were also a sensitive indicator, along with changes to nerves which were observed in 10 limbs. Assessments of adipose tissue signal intensity and muscle tissue signal homogeneity in both lobes of the suspensory ligament were the MRI indicators most closely associated with the measure of disease.

Main limitations: Small sample size. Model assumption that all abnormalities reflected degrees of a single disease.

Conclusions: Adhesion formation between the SL and adjacent structures was detected by high-field MRI with reasonable accuracy. Muscle and adipose tissue pathology was identified either alone or in association with collagenous tissue pathology.

Introduction

Normal collagen, adipose tissue and muscle architecture in the equine suspensory ligament (SL) has been well described [1,2] and compared with magnetic resonance (MR) images [3,4,5]. Brief reference was made to reduction in signal intensity in the SL on high-field MR images of hindlimbs in horses with proximal suspensory desmopathy (PSD) [6,7]. One horse with unilateral hindlimb lameness had mild increased signal intensity of the collagenous tissue of the SL of the lame limb, but enlargement of, and diffuse reduction in signal intensity in, the adipose tissue and muscle in T1 and T2* weighted (W) gradient echo images [7]. Loss of muscle and adipose tissue, in association with extensive histological abnormalities of collagenous tissue, including areas of haemosiderin deposition, necrosis, hyalinisation of collagen, chondroid and cartilage metaplasia, neovascularisation and fibrosis, in horses with chronic proximal suspensory desmopathy (PSD) have been described [8,9]. In a recent study investigating the association between ultrasonographic abnormalities consistent with PSD and histological abnormalities, muscle pathology was common, being present with or without alterations in collagen architecture [10].

It has been suggested that magnetic resonance imaging (MRI) is superior to ultrasonography for diagnosis of PSD in hindlimbs [11]. MRI may be superior for detection of osseous pathology and adhesion formation compared with ultrasonography [6,7,11,12]. However, a recent study showed a good association between ultrasonography and histological abnormalities of the proximal aspect of the SL in horses with PSD [10], although the ability to detect adhesions between the SL and adjacent structures was limited. There have been no studies which have systematically assessed the muscular and adipose tissue in MR images, nor compared the MR findings with gross and histological post mortem findings.

The purposes of the current study were to correlate high-field post mortem MR examination with gross dissection findings and histopathology in horses with a clinical diagnosis of hindlimb PSD. It was hypothesised that detection of adhesions would be accurately assessed using MRI.

Materials and Methods

Horses (n = 19) were selected for inclusion in the original study [10] based on a premortem diagnosis of hindlimb PSD based on: 1. exclusion of the distal aspect of the limb as the principle source of pain by failure to improve lameness substantially by plantar (at the junction of the proximal ¾ and distal ¼ of the metatarsus) and plantar metatarsal nerve blocks ('low-4-point-block'); 2. substantial improvement in lameness following perineural analgesia of the deep branch of the lateral plantar nerve; 3. a negative response to intra-articular analgesia of the tarsometatarsal joint; 4. no radiological abnormalities of the proximal aspect of the metatarsal bones or the tarsus which could alone explain the lameness; 5. ultrasonographic abnormalities consistent with PSD. These comprised alteration in shape or size, poor demarcation of margins, focal or diffuse areas of reduced echogenicity, and loss of linear long parallel echos in longitudinal images. All horses had additional problems contributing to hindlimb lameness and/or forelimb lameness and were humanely destroyed for reasons unrelated to the study. The details of the clinical assessment and ultrasonography have been previously described [10].

Post mortem MRI was performed in 12 randomly-selected limbs of 11 horses using a 1.5T GE Signa Echospeed MRI system[1], and sequences routinely used for clinical assessment (Supplementary Item 1). Each limb was wrapped in a thin sheet of Play-doh[2] to improve signal from superficial structures. Images were acquired from the level of the tarsometatarsal joint to up to 7 cm distally. Images were interpreted blindly by an independent experienced analyst (an Associate of the European College of Veterinary Diagnostic Imaging) (R.M.),

who was not aware of whether the limbs were from clinically normal horses or horses with PSD. The images were graded according to Table 1.

All limbs were dissected within eight hours of death by an experienced clinician (Royal College of Veterinary Surgeons Specialist in Equine Orthopaedics, S.D.) and the gross observations were recorded and photographed. Histological examination was performed on the SLs of all limbs which had undergone MRI. The proximal one-third of each SL was fixed in 10% neutral buffered formalin and softened in 4% phenol in 70% alcohol for 1-5 days, depending on the hardness of the tissue. Tissues were embedded in paraffin wax and sectioned transversely and longitudinally at predetermined sites, using a heavy duty rotary sledge microtome. The proximal third of the SL was divided into two; transverse sections were acquired from the proximal aspect of the proximal and distal halves; longitudinal sections were acquired from the proximal and distal halves, distal to the respective transverse sections. Sections were stained with Harris's haematoxylin and eosin (H&E). The SLs were graded histologically by an experienced histopathologist (DVM, MVetMed; Member of the Royal College of Pathologists) (M.J.P.) according to predetermined criteria (Supplementary Item 2) at each sampling site in both transverse and longitudinal sections, without knowledge of the clinical, imaging and gross dissection findings. The overall grade assigned for each tissue was the highest grade assigned to either the transverse or longitudinal sections of the ligament.

Data analysis

Data analysis of the MRI and pathology observations was performed by one author (N.B.) with no knowledge of the clinical severity of lameness. Data were analysed according to the following model (Supplementary Item 3). A single latent 'pathology rating' for each limb was postulated, unobservable itself but representing the degree of abnormality from 0 (normal) to 1 (severe). Each gross post mortem, histopathology or MRI observation was

linearly converted from the appropriate subjective scale (normal/moderate/severe or normal/mild/moderate/severe) to a corresponding numerical value in the range 0-1 (0.167, 0.5, 0.833 or 0.125, 0.375, 0.625, 0.875 respectively). The degree to which each observed measure contributed to the overall pathology rating was assigned a value in the range 0-1, a measure of its sensitivity in determining pathology. The model recognised that the histological and MRI findings as graded are subject to random error, and allowed a degree of leeway in relating specific observations to each other and the overall state of disease.

Numerical Bayesian methods were used to estimate both the pathology rating for each limb, and the sensitivity for each finding, simultaneously from the complete set of observations. Uniform, non-informative priors over the range 0-1 were used for all estimates. Bayesian calculations used the Python library PyMC (https://pymc-devs.github.io/pymc/). Ten thousand iterations were made of which the first six thousand were an initial, discarded burn-in period. Calculation time was approximately 4 hours (MacBook Pro 2.4GHz Intel Core i5). The full method is described in Supplementary Item 3.

Results

The signalment, lameness duration and lameness characteristics, gross post mortem findings and the results of the comparison between ultrasonography and gross and histopathological post mortem findings in all 19 horses have been described [10]. The results presented focus on the 12 limbs which underwent post mortem MRI.

Magnetic resonance imaging

In eight of the 12 limbs both the medial and lateral lobes of the SL were of normal size; three limbs had mild enlargement and one limb had severe enlargement of both lobes. The margins of both lobes were well-defined in five limbs; the lateral lobe was well-defined in a further horse, although the medial lobe had poorly-defined margins. The margins of both lobes were poorly-defined in the remaining six limbs. This pattern was present at the origin as well as in the proximal 5-7 cm of the ligament.

The signal intensity of the collagenous tissue was normal for 10 limbs (with one having a relatively thin collagenous layer for the ligament size); there was mild increase in signal intensity of the collagenous tissue in two limbs (Fig 1). Separation between the collagenous and adipose tissue/muscle layers was well-defined in both lobes of seven limbs, poorly-defined in both lobes of four limbs (Fig 1) and in the lateral lobe of one further limb in which there was very poor definition of the tissue types in the medial lobe (Fig 2).

Adipose tissue was identified by the suppression of MR signal on short tau inversion recovery (STIR) images. Adipose tissue signal intensity in unsuppressed images varied between low, intermediate and high (Fig 4). High signal intensity was present in six limbs in both lobes, intermediate signal intensity in two medial lobes and three lateral lobes (Fig 1), and low signal intensity in four medial and three lateral lobes (Figs 2,3). Adipose tissue signal homogeneity was graded as homogeneous in both lobes of four limbs and intermediate in eight limbs biaxially. No adipose tissue was graded as heterogeneous signal intensity.

Muscle tissue signal intensity varied between low intermediate to high signal intensity, and was not suppressed on STIR images. High signal intensity was present in both lobes of one limb, intermediate signal intensity in three medial lobes and two lateral lobes, and low signal intensity in eight medial lobes and nine lateral lobes (Fig 3). Muscle signal homogeneity was

graded as homogeneous in both lobes of two limbs and in the medial lobe of a further limb, and intermediate in nine medial lobes and 10 lateral lobes. No muscle tissue was graded as heterogeneous signal intensity.

The SL had well-defined adhesions in one limb; both medial and lateral lobes could not be separated from the accessory ligament of the deep digital flexor tendon (Fig 3). The medial lobe was closely apposed to adjacent tissues in five limbs and the lateral lobe closely apposed in seven limbs. Tissue could be seen as intermediate signal intensity on T2W fast spin echo (FSE) images of varying structural definition, located between the SL and metatarsal bones and/or accessory ligament of the deep digital flexor tendon and digital flexor tendons. Overall adhesions between the SL and the accessory ligament of the deep digital flexor tendon were suspected on MR images in eight limbs and confirmed at post mortem examination in six limbs; in addition adhesions between the SL and the plantar cortex of the third metatarsal bone were suspected and confirmed in one limb.

The plantar cortex of the third metatarsal bone was thickened in one limb, with low signal intensity on all images sequences. Irregularity of the periosteal and/or endosteal margin was present in four limbs. Trabecular bone abnormalities were not detected in any limb.

Associations between MRI and gross dissection findings (adhesions)

Six limbs with adhesions detected on gross dissection findings had suspected adhesions on MR images, with poor separation of the SL from adjacent tissues, although only one of these had a clearly defined adhesion described. Two limbs had suspected adhesions on MR images, but did not have adhesions detected on gross dissection findings, giving MRI 100% sensitivity and 83% specificity for adhesion detection.

Associations among MRI, gross dissection and histopathology

Observation sensitivity for gross post mortem and histopathological observations

Histopathologic observations of abnormal muscle tissue were most closely associated with premortem diagnosis of PSD (Supplementary Item 4); neural abnormalities and gross adhesions were also sensitive indicators. Vascular and adipose tissue changes were the least sensitive measures.

There was a significant positive correlation between the calculated pathology rating (Supplementary Item 3) and total histological score (R^2 = 0.74, $p<0.001$). There was a significant positive correlation between the calculated pathology rating and the sum of histology scores weighted by the modelled observation sensitivity (Supplementary Item 3) (R^2 = 0.77, $p<0.001$).

Observation sensitivity for MRI observations

Adipose tissue signal intensity and muscle tissue signal homogeneity, in both lobes of the SL, were the indicators most closely associated with both the numerically determined pathology rating for each limb and the premortem diagnosis of PSD (Table 3). The apparent homogeneity of muscle tissue could be influenced by closely associated adipose tissue, so these may be alternative measures of the same underlying change. Signal intensity of collagenous tissue, and the thickness of the plantar cortex of the third metatarsal bone, were the indicators least associated with premortem diagnosis of PSD. There was no evident correlation between the calculated pathology rating and the total MRI score. There was a significant positive correlation between the calculated pathology rating and the sum of MRI scores weighted by the modelled observation sensitivity (R^2 = 0.90, $p<0.001$). There was a significant positive correlation between the weighted total MRI score and the weighted total histology score (R^2 = 0.56, $p<0.001$).

Discussion

In accordance with our hypothesis detection of adhesions was reasonably accurately assessed using MRI, however there was a small proportion of false positive results. Nonetheless the results were superior to ultrasonography [10]. Use of normal MR data aids identification of alterations in size and proximity to adjacent structures [4,5] and differentiation between normal fibres attaching to the fourth metatarsal bone and adhesions [5]. It has previously been suggested that MRI is superior to ultrasonography for detection adhesions of the body of the suspensory ligament to the second or fourth metacarpal or metatarsal bones [12,13]. Detection of adhesions between the SL and osseous or soft tissue structures in association with PSD may be important, because pre-existing adhesions may adversely influence the results of surgical management by neurectomy of the deep branch of the lateral plantar nerve and plantar fasciotomy [10,14].

It was possible to differentiate between pathological abnormalities of the collagen and muscle and adipose tissue using MRI. There were no detailed descriptions of the distribution of the lesions identified on MR images in the study of Labens *et al*. [11]. However, it was implied that abnormalities included diffuse enlargement of the SL and focal or diffuse increased signal intensity in the collagenous parts (n = 19 limbs), or normal signal intensity in the SL with periligamentous fibrosis and adhesion formation (n = 2 limbs). There was no mention of changes in signal intensity in the adipose tissue or muscle. However in a study of 13 horses with hindlimb PSD examined using high-field MRI, reduced signal intensity in the SL was described in two horses, although there was no specific mention of the muscle and adipose tissue [6]. Based on the current study, high-field MRI may be able to differentiate muscle/ adipose tissue pathology from collagen injury. It cannot be assumed that low-field MRI could give similar information, although with good image quality this may be possible.

In a previous study, which included the 12 limbs in the current study, the high frequency of occurrence of histological evidence of muscle ± adipose tissue pathology, either alone or in conjunction with collagen pathology, was demonstrated [10]. This highlights the importance of evaluating each of these tissues using MRI. Further information based on a larger number of horses is required to determine whether differentiation between muscle pathology and adipose tissue pathology can be achieved by using different image sequences. Alterations in signal intensity in different tissues may also be influenced by chronicity of injury, a feature that could not be assessed in the current study. This would require a larger number of horses with a known duration of injury of varying lengths.

The results of the current study are not necessarily representative of the entire equine population with hindlimb PSD. It is conceivable that the types of injury in horses with unilateral or bilateral hindlimb lameness attributable to PSD alone is different from the current group of horses in which other factors also contributed to pain or poor performance. There is a spectrum of injuries involving the proximal aspect of the SL not only a variety of tissues within the SL, but also the enthesis on the proximal aspect of the third metatarsal bone [6,7,10,11,14-17]. Whether this reflects a continuum of the same disease process, or a variety of conditions is unknown. Better understanding of the tissues involved may influence management strategy and success of treatment. It is conceivable that the types of injury in horses with unilateral or bilateral hindlimb lameness attributable to PSD alone is different from the current group of horses in which other factors also contributed to pain or poor performance.

The MR image interpreter was blinded to the origin of the images, and had been informed that the study included both normal and abnormal horses. This could potentially bias interpretation, leading to under interpretation of later images, but this seems unlikely based on the grading of the latter.

The statistical model assumed a single pathology rating, i.e. that all observations are related to a single condition or closely related set of conditions. This may not be the case, in particular there may be two different conditions, one involving collagenous tissue and only observed in two cases in this small sample, in contrast to two previous studies [6,11], and one related to adipose and muscle abnormalities. Subjective observations (e.g. Normal/Moderate/Severe) were converted to a numerical scale for analysis, assuming a uniform linear relationship. This may also not be the case. For example, if an observation was sufficiently insensitive then a Moderate rating may reflect a disease condition further removed from Normal than from Severe.

Nevertheless and despite these reservations, our Bayesian modelling method produced a single measure of pathology that correlated reasonably well with observed gross post mortem and histology findings. It also provided a finding sensitivity for each observation, indicating which contributed most to this pathology measure. When weighted by these finding sensitivities there was a clear and significant linear correlation between each of the pathology measure, the weighted histology score and the weighted MRI score. We believe this offers useful guidance as to which observations will be of most value diagnostically using MRI and other modalities.

In conclusion high-field MRI enables detection of adhesion formation between the SL and adjacent structures with reasonable accuracy. Muscle and adipose tissue pathology can be detected using MRI and can occur either alone or in association with collagenous tissue pathology.

Authors' declaration of interests.

The authors have no competing interests.

Ethical animal research

The study was approved by the Ethical Review Committee of the Animal Health Trust and had informed consent of the owners.

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Authorship

S. Dyson and R. Murray planned the study; S. Dyson performed all clinical and ultrasonographic assessments and the gross post mortem examinations. R. Murray read the MR images. M.J. Pinilla performed the histological examinations. N. Bolas performed the statistical analyses. S. Dyson, R. Murray and N. Bolas contributed to the manuscript, which was approved by all authors.

Manufacturers' addresses

1. GE Healthcare, Milwaukee, Wisconsin, USA.

2. Play-doh, China.

Figure legends

Fig 1: Transverse spoiled gradient echo (A) and T2* weighted gradient echo (B) images of hock 14; medial is to the right; dorsal is to the top. The suspensory ligament is of normal size. There is increased signal intensity within the dorsal collagenous tissue of the suspensory ligament (particularly affecting the lateral lobe) which was however graded as normal histologically, poor definition of the interface between the collagenous and adipose tissue/muscle tissue, and low intermediate signal intensity with mild heterogeneity in the adipose tissue/muscle tissue. On histological examination, there were moderate abnormalities within the muscle and mild abnormalities within the neural tissue. The limb is surrounded by a thin layer of hyperintense playdoh.

Fig 2: Transverse spoiled gradient echo (SPGR) (A), T2* weighted (W) gradient echo (GRE) (B) T2W fast spin echo (FSE) (C) images of hock 19; medial is to the right; dorsal is to the top. The adipose tissue/muscle tissue in the medial lobe of the suspensory ligament has low signal intensity with mild heterogeneity and very poor definition of the interface between the collagenous and adipose tissue/muscle tissue compared with the lateral lobe. These signal intensity changes are more obvious in the SPGR and T2*W GRE images than the T2W FSE images. The ligament margins are mildly irregular. Histological examination revealed severe abnormalities in the muscle and moderate abnormalities within the adipose tissue. The limb is surrounded by a thin layer of hyperintense playdoh. (D) is an enlargement of (A).

Fig 3: Transverse spoiled gradient echo (SPGR) (A), T2* weighted (W) gradient echo (GRE) (B) and T2W fast spin echo (FSE) (C) images of hock 18; medial is to the left and dorsal is to the top. The adipose tissue/muscle tissue in both lobes of the suspensory ligament (SL) has low signal intensity with intermediate homogeneity, the collagenous tissue is thinned (especially in the medial lobe) and heterogeneous in signal intensity and there is poor definition of the interface between the collagenous and adipose tissue /muscle tissue. These signal intensity changes are more obvious in the SPGR and T2*W GRE images than the T2W FSE images. There is poor separation of the SL from the accessory ligament of the deep digital flexor tendon (ALDDFT) with indication of tissue between the structures. On macroscopic examination there were adhesions between the SL and the ALDDFT. On histological examination there were moderate abnormalities in the muscle and neural tissue,

with poor fibroblast viability within the collagenous tissue. The limb is surrounded by a thin layer of hyperintense playdoh.

Fig 4: Transverse T2 weighted (W) fast spin echo (FSE) (A) and short tau inversion recovery (STIR) (B) images of hock 16; medial is to the left; dorsal is to the top. The muscle tissue has higher signal intensity than the collagenous tissue in both sequences. Comparison of the 2 images allows identification of the location of the adipose tissue, which has high signal intensity only in the T2W FSE image.

Tables

Table 1: Grading criteria for magnetic resonance images of the proximal metatarsal region from 12 limbs of 11 horses; the most proximal aspect before separation into 2 lobes, and the medial and lateral lobes were assessed independently.

Size: normal, mild enlargement, or severe enlargement

Signal intensity of collagenous tissue: normal, mildly increased, or markedly increased

Margins of suspensory ligament: well-defined, poorly-defined, or very poorly-defined

Separation between tissues within the ligament: well-defined, poorly-defined, or very poorly-defined.

Adipose tissue signal intensity: low intermediate, high intermediate, or high

Adipose tissue signal homogeneity: homogeneous, intermediate (slightly non-uniform), or heterogeneous

Muscle tissue signal intensity: low, intermediate, high

Muscle tissue signal homogeneity: homogeneous, intermediate (slightly non-uniform), or heterogeneous

Apposition of suspensory ligament to adjacent structures: well-separated, close to, or inseparable from

Plantar cortex of the third metatarsal bone: normal thickness, mild increase thickness, severe increased thickness, or thinned

Trabecular bone architecture of plantar aspect of third metatarsal bone: normal, mild abnormality, severe abnormality

Table 2: Modelled pathology compared with histology (Histo) and magnetic resonance imaging (MRI) observations (sum of gradings [normal, moderate, severe] converted to numbers [0,1,2]) in 12 limbs with a premortem diagnosis of proximal suspensory desmopathy. The weighted MRI score is the MRI score weighted by the observation sensitivities from the Bayesian model.

Limb number	Modelled pathology rating	Histology score	MRI score^{+}	Histology + MRI total	Weighted MRI score	Rank from weighted MRI score
19	0.91	10	20	30	16.7	1
17	0.84	9	13	22	14.8	3
13	0.77	6	20	26	15.3	2
21	0.74	9	7	16	11.6	5
20	0.70	7	7	14	10.5	8
18*	0.70	0	7	7	10.6	7
22	0.69	4	7	11	10.7	6
12	0.68	8	8	16	11.9	4
6	0.62	7	8	15	10.2	9
15	0.54	5	8	13	8.5	10
14	0.53	3	12	15	8.0	11
11	0.52	6	5	11	7.0	12

s.d. = standard deviation; *The only horse in which, at the predetermined anatomical sites from which sections were obtained, no histological abnormality was seen. There were tough adhesions between the suspensory ligament and the adjacent soft tissues at gross examination.

Table 3: Observation sensitivity for post mortem high-field magnetic resonance imaging observations of the suspensory ligaments of 12 hindlimbs with a premortem diagnosis of proximal suspensory desmopathy based on clinical findings and ultrasonography.

Observation	Mean	± s.d.	Credible interval
SI* of adipose tissue lateral lobe	0.91	0.06	0.79 - 1.00
SI of adipose tissue medial lobe	0.87	0.07	0.79 - 1.00
Muscle tissue signal homogeneity lateral lobe	0.63	0.08	0.48 - 0.79
Muscle tissue signal homogeneity medial lobe	0.58	0.07	0.42 - 0.70
Apposition to adjacent tissues lateral lobe	0.50	0.08	0.36 - 0.65
Adipose tissue signal homogeneity medial lobe	0.51	0.08	0.35 - 0.65
Adipose tissue signal homogeneity lateral lobe	0.49	0.07	0.37 - 0.64
Separation of tissues within medial lobe	0.46	0.07	0.31 - 0.59
Margin definition of medial lobe	0.44	0.07	0.30 - 0.57
SI of muscle tissue medial lobe	0.43	0.07	0.29 - 0.57
Margin definition of lateral lobe	0.41	0.07	0.28 - 0.55
Separation of tissues within lateral lobe	0.40	0.07	0.27 - 0.55
Size of medial lobe	0.38	0.07	0.26 - 0.53
Size of lateral lobe	0.38	0.08	0.23 - 0.51
SI of muscle tissue lateral lobe	0.38	0.07	0.24 - 0.52
Apposition to adjacent tissues medial lobe	0.37	0.08	0.24 - 0.51
MT3 cortex margins	0.37	0.08	0.23 - 0.52
Margin definition at proximal origin	0.36	0.07	0.24 - 0.51
SI of collagenous tissue medial lobe	0.32	0.07	0.18 - 0.45
SI of collagenous tissue proximal origin	0.32	0.07	0.19 - 0.46
SI of collagenous tissue lateral lobe	0.32	0.07	0.15 - 0.44
Size of proximal origin	0.29	0.07	0.16 - 0.44
MT3 cortex thickness	0.28	0.07	0.16 - 0.42

*SI = signal intensity; s.d. = standard deviation; Credible interval = 95% highest posterior density interval

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Supplementary Information

Supplementary Item 1: MRI Imaging parameters.

Supplementary Item 2: Histological grading criteria.

Supplementary Item 3: Statistical approach

Supplementary Item 4: Observation sensitivity for pathology features