EXTENDED REPORT

Adipose tissue at entheses: the rheumatological implications of its distribution. A potential site of pain and stress dissipation?

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Objectives: To describe the distribution of adipose tissue within and adjacent to entheses in order to assess its functional significance at attachment sites.

Methods: Entheses were removed from 29 different sites in the limbs of formalin fixed, elderly, dissecting room cadavers and the samples prepared for paraffin and/or methylmethacrylate histology. Entheses from four young volunteers with no history of significant musculoskeletal injury were examined by magnetic resonance imaging using T_1 weighted sequences.

Results: Adipose tissue was present at several different sites at numerous entheses. Many tendons/ligaments lay on a bed of well vascularised, highly innervated, ''insertional angle fat''. Endotenon fat was striking between fascicles, where entheses flared out at their attachments. It was also characteristic of the epitenon, where it occurred in conjunction with lamellated and Pacinian corpuscles. Fat filled, meniscoid folds often protruded into joint cavities, immediately adjacent to attachment sites.

Conclusion: Adipose tissue is a common feature of normal entheses and should not be regarded as a sign of degeneration. It contributes to the increase in surface area of attachment sites, promotes movement between tendon/ligament and bone, and forms part of an enthesis organ that dissipates stress. The presence of numerous nerve endings in fat at attachment sites suggests that it has a mechanosensory role and this could account for the rich innervation of many entheses. Because damage to fat is known to lead to considerable joint pain, our findings may be important for understanding the site of pain in enthesopathies.

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The presence of adipose tissue within tendons and ligaments is well documented, but generally viewed as a sign of degeneration or regarded as age related changes.[1] The possibility that fat may be functionally significant at entheses in promoting stress dissipation or act as a ''mechanosensory organ'' by virtue of nerves within it, has not been properly considered. Yet, such roles for fat are well documented elsewhere. It is widely acknowledged that adipose tissue mixed with fibrous tissue can act as pressure tolerant material in the palms and soles, and that fat allows movement between adjacent structures—for example, the globe and the bony orbit.[2] By virtue of their rich sensory innervation, fat pads can be a significant source of anterior knee pain.[3] Moreover, damage to fat at other sites, including the heel pad, can be associated with protracted periarticular pain, suggesting that fat in, or adjacent to, joints might contribute significantly to joint pain. As a prelude to investigating the role of adipose tissue in entheseal related disease, we have performed a comprehensive histological survey of the distribution of fat at entheses in the upper and lower limbs. This has been complemented by selective magnetic resonance imaging (MRI) in younger subjects. We have used the data to suggest different functions that fat might serve at tendon and ligament attachment sites.

MATERIALS AND METHODS

Paraffin wax histology

Entheses were removed from the arms and legs of elderly (mean age 82 years; range 73–101) dissecting room cadavers of both sexes. Table 1 shows the precise location of the attachment sites. Twenty nine different entheses were examined from 1–10 cadavers at each location. The cadavers were selected according to the quality of preservation and the absence of gross abnormalities in the region concerned. Detailed medical histories were not available. The bodies had been previously fixed for student dissection with a formaldehyde based embalming fluid. In all cases, entheses were removed by cutting the tendon or ligament transversely, approximately 1–2 cm from the bone and making saw cuts into the latter that were parallel to the long axis of the tendon or ligament. The samples were then easily removed by a sharp tap with a bone chisel. Contact radiographs were taken at this stage and the tissue processed for routine histology, as described previously.[4]

Briefly, the samples were further postfixed in 10% neutral buffered formol saline, decalcified with 5% nitric acid, dehydrated with alcohols, cleared in xylene, and embedded in paraffin wax. Serial sections were cut at 4–8 µm throughout the entire block, and 12 sections were collected and mounted at 1 mm intervals. Most tendons/ligaments were cut longitudinally. To remove the risk of artefactual damage that might have resulted from the saw cuts, the peripheral sections were discarded. Slides were stained with alcian blue, haematoxylin and eosin, Masson's trichrome, and toluidine blue.

On the basis of a preliminary assessment of the results, two samples of the tibial enthesis of the anterior cruciate ligament (ACL) were obtained from younger cadavers (18 years male; 39 years female) in the Department of

Abbreviations: ACL, anterior cruciate ligament; MMA, methylmethacrylate; MRI, magnetic resonance imaging

Table 1 Distribution of fat at entheses as seen in histological sections

Enthesis	Epitenon fat	Endotenon fat	Insertional angle fat	Meniscoid fat
Upper limb				
Triceps insertion	*			
Coracoid attachment of coracoclavicular ligament	*	*		
Origin of short head of biceps/coracobrachialis			*	
Subscapularis insertion		*		
Extensor pollicis longus insertion			*	*
Flexor digitorum profundus insertion			*	
Flexor carpi ulnaris insertion			*	
Abductor pollicis brevis insertion	*			
Epicondylar attachment of the medial collateral ligament of the elbow/common flexor origin		*		
Extensor carpi ulnaris insertion		*		
Lower limb				
Anterior cruciate ligament (tibial attachment)	*	*		
Anterior cruciate ligament (femoral attachment)	*	*		
Posterior cruciate ligament (tibial attachment)	*			
Adductor longus origin		*	*	
Sartorius origin	*	*		
Extensor hallucis longus insertion			*	*
Flexor hallucis longus insertion		*	*	
Gluteus medius insertion	*	*		
Gluteus minimus insertion			*	
Pes anserinus insertion	*			
Biceps femoris insertion		*	*	
Iliopsoas insertion			*	
Fibularis brevis insertion	*	*	*	
Fibularis longus insertion	*	*	*	
Popliteus insertion	*	*		
Tibialis anterior insertion	*		*	*
Patellar tendon origin	*		*	
Patellar tendon insertion	*		*	
Quadriceps tendon insertion		*	*	

Forensic Medicine (Institut für Rechtsmedizin, Ludwig-Maximilians-Universität) in accordance with the ethical regulations of Munich University. The specimens were fixed in 10% neutral buffered formal saline and processed as described above.

Methylmethacrylate histology

Formalin fixed, non-decalcified samples of the entire antero-posterior extent of the tibial plateau were taken from two male and two female donors, aged 73–86 years, to determine whether fat at the ACL enthesis was sufficiently substantial to be visible in thick (100–200 µm) sections. The samples were embedded in methylmethacrylate (MMA) according to the method described by Milz and Putz.[5] Briefly, tissue was dehydrated in a graded series of alcohols, infiltrated with MMA, and polymerised at 26–28℃. After the resin had set, blocks were cut with a Leica saw microtome, the sections were stained with Azan or Masson's trichrome, and mounted in Eukitt on glass slides.

Magnetic resonance imaging

Four volunteers without a history of significant musculoskeletal injury and of mean age 33 years (range 27–39; one male, three female) were examined on a 1.5 T MR system (Siemens, Erlangen, Germany) using T_1 weighted pulse sequences (repetition time 473 ms, effective echo time 13 ms), 512×512 matrix size, field of view 9–18 cm in the coronal, transverse, or sagittal plane using circular or planar surface coils. The slice thickness was 3 mm. Table 2 lists the sites imaged.

Table 2 Distribution of fat at entheses as visualised by MRI

Enthesis	Epitenon fat	Endotenon fat	Insertional angle fat	Meniscoid fat
Triceps insertion	*	*		
Anterior cruciate ligament (tibial attachment)	*	*		
Anterior cruciate ligament (femoral attachment)	*	*		
Posterior cruciate ligament (tibial attachment)	*	*		
Fibularis longus insertion	*	*	*	
Fibularis brevis insertion	*	*	*	
Tibialis anterior insertion	*	*	*	
Patellar tendon origin	*	*		
Patellar tendon insertion	*	*	*	
Quadriceps tendon insertion	*	*	*	
Achilles tendon insertion	*	*		*

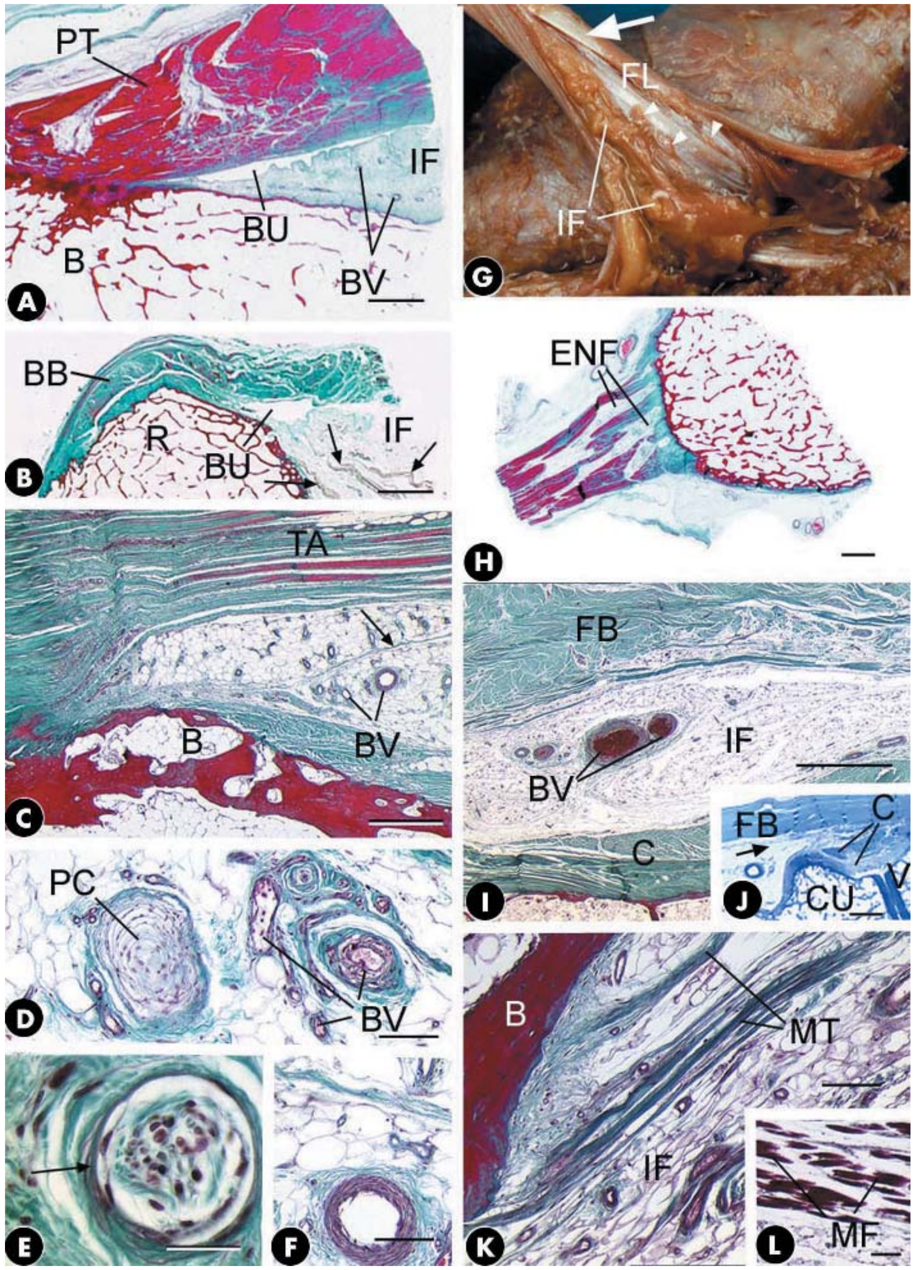

Figure 1 **(A)** The tibial enthesis of the patellar tendon (PT) showing the presence of ''insertional angle fat'' (IF) in the interval between the tendon and the bone (B) in association with the deep infrapatellar bursa (BU). BV, blood vessels. Masson's trichrome. Scale bar = 2 mm. **(B)** Insertional angle fat (IF) protruding into the bursa (BU) that lies deep to the tendon of biceps brachii (BB) at its attachment to the radial tuberosity (R). Note the occasional skeletal muscle fibres (arrows) running through the fat pad. Masson's trichrome. Scale bar = 4 mm. **(C)** Insertional angle fat filling the interval between the tendon of tibialis anterior (TA) and the bone (B) at its cuneiform attachment. Note the presence of numerous blood vessels (BV) and strands of fibrous tissue (arrow) in the fat. Masson's trichrome. Scale bar = 500 μm. **(D)** A small Pacinian corpuscle (PC) and numerous small blood vessels (BV) embedded in the insertional angle fat associated with the cuneiform attachment of the tendon of tibialis anterior. Masson's trichrome. Scale bar = 100 μm. **(E)** A lamellated corpuscle (arrow) surrounded by fibrous tissue in the insertional angle fat of biceps femoris at its fibular enthesis. Masson's trichrome. Scale bar = 30 μm. **(F)** A small muscular artery in the insertional angle fat at the cuneiform enthesis of tibialis anterior. Masson's trichrome. Scale bar = 100 μm. **(G)** Abundant insertional angle fat (IF) between the bone and the tendon of fibularis longus (FL) at its enthesis. The tendon has been cut and reflected so that its dorsal surface is visible. Note the spiralling of the tendon fascicles near its enthesis (arrow) and the increased surface area of the tendon near the bone. The insertional angle fat extends into the tendon as endotenon fat through gaps between the fascicles (arrowheads). **(H)** Conspicuous seams of endotenon fat (ENF) in the tendon of fibularis longus at its enthesis. Note how the tendon flares out as it approaches its bony interface. Masson's trichrome. Scale bar = 2 mm. **(I)** A transverse section of the tendon of fibularis brevis (FB) to show the layer of insertional angle fat (IF) that lies beneath the tendon and separates it from the capsule (C) of the 5th tarsometatarsal joint. Note the presence of blood vessels (BV) within this adipose tissue. Masson's trichrome. Scale bar = 1 mm. **(J)** A longitudinal section of the tendon of fibularis brevis (FB), near its metatarsal enthesis showing the presence of insertional angle fat (arrow). C, joint capsule; CU, cuboid; V, base of the 5th metatarsal. Toluidine blue. Scale bar = 2 mm. **(K)** Groups of collagen fibres that form microtendons (MT) running through the insertional angle fat (IF) and attaching to bone (B) at the enthesis of iliopsoas. Such microtendons are quite distinct from the macroscopic tendon (not shown) that attaches to the lesser trochanter. Masson's trichrome. Scale bar = 100 μm. **(L)** A short distance proximal to the microtendons featured in (K) are small numbers of skeletal muscle fibres (MF) that are attached to them. Masson's trichrome. Scale bar = 100 μm.

RESULTS

White adipose tissue was found at several distinct sites in many different entheses. The results of the histological survey are summarised in table 1 and illustrated in figs 1 and 2. The MRI data are summarised in table 2 and illustrated in fig 3.

Insertional angle fat

Adipose tissue was commonly found in the angle between tendon or ligament attachments to bone. In some cadavers and/or locations, this fat was covered by a synovial membrane and protruded into a subtendinous bursa (figs 1A, B and 2G). In others, it directly linked the tendon or ligament to the bone and no synovium was present at all (fig 1C). Most adipose tissue of both types was well supplied with blood vessels and lamellated corpuscles (figs 1A, C–F) and was not simply a collection of fat cells. Among the best examples of insertional angle fat were those associated with the entheses of fibularis longus and brevis. In many specimens of the former, the insertional angle fat was striking enough to be clearly visible in gross dissections (fig 1G). Strands of fibrous tissue ran through it, and where the tendon flared out, the fat extended through interfascicular gaps as endotenon fat (see below) into the tendon proper (fig 1H). Those gaps were mainly created by the twisting of fascicles proximal to the insertion site, and the marked flaring of the tendon attachment near the first tarsometatarsal joint (fig 1G). This allowed for protrusion of the insertional angle fat pad as a space filler between the fascicles. In fibularis brevis, the most flared part of the tendon lay on a bed of fat which largely separated the tendon from the capsule of the fifth tarsometatarsal joint, with which it ultimately fused distally (figs1I and J). The diverging bundles of longitudinally oriented collagen fibres were associated with transversely arranged, ''collagen ties'' that may have reduced the risk of longitudinal splitting. Intriguingly, at the tendinous attachment of iliopsoas, the insertional angle fat contained small bundles of skeletal muscle fibres and associated ''microtendons'' (figs 1K and L).

Endotenon fat

The endotenon is the connective tissue that separates adjacent tendon fascicles. We have used the term to embrace what should strictly be called ''endoligament''. Fat in the endotenon was a typical feature of some entheses (figs 2A, B, and 3) and when present was usually continuous with fat in the epitenon (see below) or with insertional angle fat (see above). However, at other entheses it was rarely found, because fascicular organisation was not always present at entheses (as it is in tendon or ligament mid-substance). At several attachment sites where endotenon fat was striking (notably the insertions of fibularis longus and brevis and the tibial attachment of the ACL), the tendon or ligament flared out markedly at its attachment site (figs 1G and H). This increased the surface area of bone to which load was transferred. The seams of endotenon fat were substantial in some cases and were thus visible both in the 100 μm thick, methacrylate embedded material (fig 2C) and paraffin embedded material, as well as on MR images (fig 3).

The ability to visualise fat with MRI, enabled us to confirm that the presence of fat was not restricted to elderly subjects but was also present in younger people. This was also evident in the two specimens of the tibial ACL enthesis obtained from the younger cadavers (18 and 39 years). Adipose tissue in the endotenon generally contained conspicuous blood vessels (fig 2D), although sensory nerve endings were less prominent than in the epitenon.

In some specimens the seams of adipose tissue extended to the bony interface and were even continuous with fatty marrow through local defects in the subchondral plate (fig 2A). Of particular note was the location of endotenon fat at the insertion of gluteus medius. This tendon flared out around the convex contour of its bony insertion site, and adipose tissue was conspicuous opposite the summit of the convexity (fig 2E). A similar pattern was seen in parts of the fibularis longus attachment (fig 1H).

Epitenon fat

The epitenon is a layer of surface connective tissue that is clearly demarcated from the tendon itself, which can be recognised histologically as well as with ultrasound and MRI. For the sake of simplicity, we have used the term to include the equivalent tissue on ligaments. Indeed, such a layer is a particularly prominent feature of the cruciate ligaments in association with the synovial membrane reflected onto their surfaces (fig 2F). The epitenon covering many entheses frequently contained adipose tissue, which in all cadavers was rich in blood vessels and sensory nerve endings (table 1). Numerous, lamellated corpuscles and occasional Pacinian corpuscles were evident in epitenon fat (figs 2H and I), with Pacinian corpuscles most typical of subcutaneous tendons—for example, the origin of the common extensor tendon and the insertion of abductor pollicis brevis (figs 2I and J).

Meniscoid fat

Where tendons were attached close to a synovial joint cavity, synovial folds containing adipose tissue protruded in meniscoid fashion from the undersurface of their entheses. This was typical of the extensor tendons of the digits and tibialis anterior (figs 2K and L). Most of the adipose tissue was well supplied with blood vessels and lamellated corpuscles. It may serve as a variable space filler.

DISCUSSION

The purpose of this study was to investigate the distribution of adipose tissue at entheses. Our extensive survey shows that it is common within, and adjacent to, attachment sites. The adipose tissue was not simply a collection of fat cells alone but also contained nerves and blood vessels—with the proportions varying according to site. Thus ''insertional angle fat'' was generally more richly innervated than endotenon fat and some regions of fat may be more susceptible to inflammation than others by virtue of their greater blood supply. We suggest that our demonstration of adipose tissue within and around entheses is of potential importance to rheumatologists, as the relatively high forces acting at insertion sites might damage well innervated fat and lead to joint pain—as described for fat at other sites, including the knee and heel.[6 7]

It is the consistent and distinctive distribution of adipose tissue in many different entheses, including those in relatively young and asymptomatic subjects, that suggests that most of the fat reported by us is likely to be of functional significance, rather than simply a sign of degeneration or aging. This is not to say that we think fat accumulation in tendons and ligaments never indicates structural degeneration, for any marked accumulation of fat in the mid-substance of tendons and ligaments clearly compromises their mechanical integrity.[1] Although neither we nor other authors have reported similar ''degenerate fat'' at entheses, we cannot exclude this possibility. Indeed, to some extent the distinction between fat which indicates degeneration and that which is a normal functional adaptation is subjective, for the structure of the tissue is essentially the same whatever its significance. Key issues, therefore, are whether the distribution of fat suggests a functional role and whether the strength of the tendon or ligament is likely to be compromised by its presence.

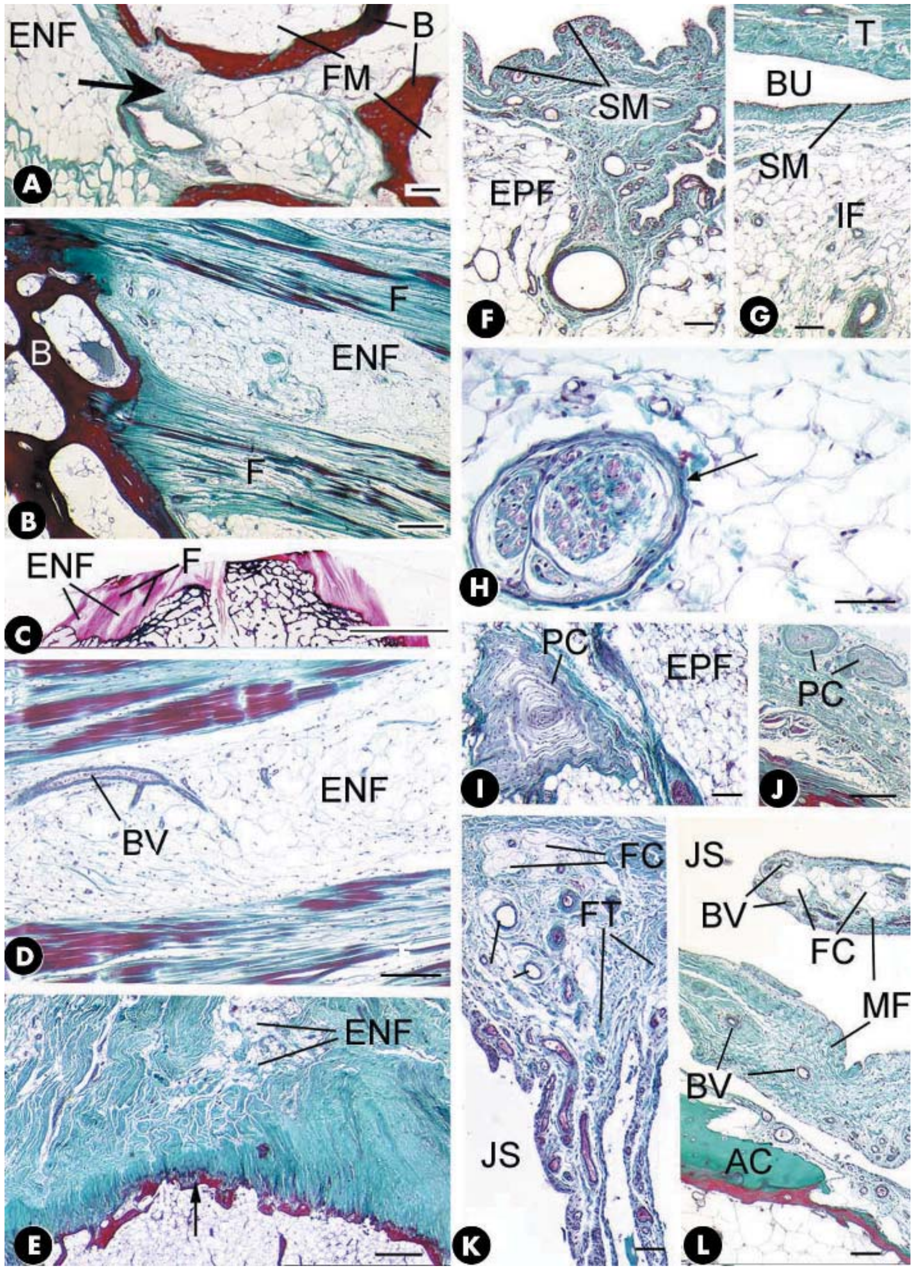

Figure 2 **(A)** Endotenon fat (ENF) at the attachment of fibularis longus that is continuous with fatty marrow (FM) through a small defect (arrow) in the subchondral bone (B) plate. Masson's trichrome. Scale bar = 100 μm. **(B)** Alternating seams of endotenon fat (ENF) and ligament fascicles (F) at the tibial enthesis of the anterior cruciate ligament. B, bone. Masson's trichrome. Scale bar = 300 μm. **(C)** A 100 μm thick methacrylate section of the tibial plateau showing seams of endotenon fat (ENF) between ligament fascicles (F) at the attachment of the anterior cruciate ligament. Azan. Scale bar = 1 cm. **(D)** A small blood vessel (BV) in the endotenon fat (ENF) at the tibial enthesis of the anterior cruciate ligament. Masson's trichrome. Scale bar = 200 μm. **(E)** The trochanteric enthesis of the tendon of gluteus medius. Note the presence of endotenon fat (ENF) opposite the point of maximum convexity of the bone surface (arrow); the tendon flares out to attach either side. Masson's trichrome. Scale bar = 500 μm. **(F)** Epitenon fat (EPF) on the surface of the anterior cruciate ligament lying beneath a synovial membrane (SM). Masson's trichrome. Scale bar = 100 μm. **(G)** Insertional angle fat (IF) covered in synovial membrane (SM) in the wall of the deep infrapatellar bursa (BU). T, tendon. Scale bar = 100 μm. **(H)** A lamellated corpuscle (arrow) in the epitenon fat on the surface of the posterior cruciate ligament at its tibial enthesis. Masson's trichrome. Scale bar = 50 μm. **(I)** A small Pacinian corpuscle (PC) embedded in epitenon fat (EPF) on the surface of the common extensor tendon at its lateral epicondylar enthesis. Masson's trichrome. Scale bar = 100 μm. **(J)** Two small Pacinian corpuscles (PC) in the fibroadipose tissue of the epitenon on the surface of the tendon of abductor pollicis brevis at its metacarpal enthesis. Masson's trichrome. Scale bar = 500 μm. **(K)** A meniscoid fold, covered with synovial membrane and containing a mixture of fat cells (FC), fibrous tissue (FT) and blood vessels, protruding into the joint space (JS) of the interphalangeal joint of the thumb at the insertion of the tendon of extensor pollicis longus. Masson's trichrome. Scale bar = 100 μm. **(L)** A meniscoid fold (MF) containing fat cells (FC) and blood vessels (BV) protruding into the tarsometatarsal joint space (JS) from the metatarsal enthesis of the tendon of tibialis anterior. AC, articular cartilage. Masson's trichrome. Scale bar = 100 μm.

Fat forms part of the "enthesis organ" that reduces wear and tear at attachment sites[8] and immediately adjacent structures. In the Achilles tendon, it probably acts as a "variable plunger" that moves in and out of the retrocalcaneal bursa according to foot position, thus minimising stress during locomotion.[9] There is a comparable "fat apron" associated with the deep infrapatellar bursa at the insertion of the patellar tendon.[10] It is an extension of the retropatellar

Figure 3 **(A)** A sagittal MR image of the knee joint of a 29 year old man. Regions of endotenon fat (arrows) are conspicuous at the attachments of the quadriceps tendon (QT) to the patella (P) and the anterior cruciate ligament (ACL) to the tibia (T). **(B)** An oblique coronal MR image through the knee joint of the same subject showing endotenon fat (arrow) at the tibial enthesis of the anterior cruciate ligament (ACL). F, femur; T, tibia. **(C)** A coronal MR image of the proximal enthesis of the patellar tendon of a 39 year old woman showing seams of fat (arrows) in the endotenon extending from the bony interface. P, patella. **(D)** A coronal MR image of the attachment of the quadriceps tendon (QT) to the patella (P) in the same subject showing seams of fat (arrow) in the endotenon near the bony interface. VM, vastus medialis.

fat pad and partly divides the bursa into anterior and posterior compartments. The reader should note that this fat apron is probably not evident in our illustration (fig 1A) simply because the tendon was cut too close to its tibial insertion. However, the fat we reported at this site does lie directly in the posterior wall of the bursa and may well be continuous with that of the fat apron.

Until now, little or no attention has been paid to the fat which fills insertional angles (such as that associated with the Achilles tendon), but is *not* covered by synovium. We suggest that such ''subtendinous fat'' could also facilitate movement between tendons/ligaments and bone—even in the absence of an associated bursa. The adipose tissue previously described between bundles of the superomedial part of the calcaneonavicular ligament at its enthesis, as well as between the ligament and the navicular attachment of the tibialis posterior tendon, might similarly dissipate stress.[11]

It is worth noting that lipid has previously been highlighted as a major component of tendon surfaces. According to Banes *et al*, it accounts for up to 43% of the epitenon matrix, whereas collagen only accounts for 23%.[12] These authors argue that lipid has a role in boundary lubrication and pulse dampening—functions equally applicable to the enthesis and the tendon/ligament mid-substance.

Our findings are relevant to the interpretation of MR images of tendon, ligaments, and entheses. With most MR images used routinely for clinical purposes, normal tendons and ligaments have a very low signal and appear dark. Abnormalities are frequently recognised because they produce an increase in this signal intensity and are manifest as light areas against the dark background of the normal tissue. An exception to this pattern is the high signal seen within normal tendons or ligaments close to their origins or insertions. Common sites where endotenon fat is seen with MRI include the triceps and quadriceps tendon insertions and the tibial attachment of the ACL.[13] We have confirmed the presence of fat with MRI at all these sites, and have also demonstrated it histologically. Hitherto, the imaging significance of our current findings stemmed mainly from the fact that the normal high signal from fat could be wrongly attributed to disease, but the wide distribution and specific location of fat within entheses strongly suggests that this tissue may also have a physiological significance.

Possibly, subtendinous fat pads have an unheralded mechanosensory function at entheses, by virtue of the lamellated corpuscles within them. Highly innervated fat may be important in giving proprioceptive feedback for the sensorimotor control of loading conditions. If naked nerve terminals containing substance P are present—as in the fat pads of the knee,[6 14] subtendinous fat might be a notable source of pain. Certainly, the abundance of neural elements within subtendinous (and epitenon) fat argues against the possibility that it is a sign of degeneration. Attachment sites elsewhere have previously been identified as regions rich in mechanoreceptors,[15 16] and lamellated corpuscles are a recognised feature of myotendinous junctions.[17] Like the enthesis, this is also a region of stress concentration.

Although endotenon fat occasionally contained nerves, these were not conspicuous. Restricting nerves to the periphery of attachment sites (that is, within the epitenon or insertional angle fat) may ensure an appropriate threshold for sensory stimulation in structures that are heavily mechanically loaded. We think that endotenon fat may have a particular role at flared-out entheses. This shape change promotes secure anchorage to bone and allows stress concentration to be dissipated. It is reasonable to assume that a packing material must be present between the bundles of collagen fibres in regions of flaring. This is particularly so if the surface area occupied by the tendon/ligament at its attachment site exceeds that of its mid-substance. Simple inspection of the tibial attachment of the ACL or the insertion of fibularis longus shows that this is the case. Fat has an important role as a packing tissue elsewhere in the body—notably, in synovial joints. Here, fat pads form flexible and deformable cushions that fill potential spaces in the joint cavity that appear and disappear as the joint moves.[18] Similar potential spaces may exist between fascicles or groups of fascicles, as some tendons/ligaments approach their entheses—particularly if the "insertional angle" (that is, the angle at which the tendon/ligament meets the bone) changes with joint movement. A reservoir of fat on the surface of tendons/ligaments (insertional angle fat or epitenon fat) could be squeezed in and out of the endotenon compartments according to joint movement. We suggest that one of the functions of the conspicuous endotenon fat at the tibial enthesis of the ACL may be to allow fascicles to slide over each other during flexion and extension of the knee. In extension, the length of the ACL is greater anteriorly than posteriorly because of the different orientation of its femoral and tibial entheses.[19] A shift in the axis of rotation of the knee joint occurs during flexion and extension (because the femur slides on the tibial plateau). As a result, the distance between two points at the attachment sites changes with the knee position. In a short ligament such as the ACL, this can only be accommodated by ensuring that the fascicles can move relative to each other. We suggest that seams of fat promote this movement. Future imaging studies in symptomatic subjects will determine whether abnormalities in endotenon fat are clinically relevant.

The development of the fat seen in the endotenon is unclear and the scope of the current project precludes detailed comment: our histology was entirely restricted to adult material. Nevertheless, it is important to appreciate the plasticity of endotenon, for fibrocartilage can also develop within it—notably, in regions where tendons press against bony pulleys to change the direction of muscle pull.[20] It is known that both chondrogenic and adipogenic cells separate from the same mesenchymal stem cell[21] and that certain tendon cell lines express genes related to both lineages.[22] Significantly, when the tendon cell line TT-E4 was cultured in adipogenic medium, the cells lost their fibroblastic morphology, rounded up, and formed lipid droplets in their cytoplasm. We thus support the contention of Salingcarnboriboon *et al* that tendons contain a population of mesenchymal stem cells, and suggest that the endotenon is the most likely location.[22]

Finally, any of the fatty regions associated with entheses may have endocrine or paracrine roles in line with emerging views on the broader significance of fat at other sites within the body.[23] It is particularly interesting that the infrapatellar fat pad releases growth factors and proinflammatory cytokines into the knee joint. These have previously been thought to be produced solely by synovium or articular cartilage.[24] Thus, fat at, or near, entheses may also be implicated in inflammatory responses.

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