

Magnetic Resonance Imaging Pre and 4 Months Post 6 Physiotherapy Treatments for OA Knee Pain - A Pilot Study

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Abstract

The source of osteoarthritic (OA) knee pain is perplexing. Bone marrow Lesions (BMLs) and the Infrapatellar Fat Pad (IPFP) are hypothesized to cause symptoms in this patient population. With escalating costs for OA treatment, physiotherapy could be an inexpensive option for managing OA knee pain. The aim of this study was to examine the Magnetic Resonance Imaging (MRI) of OA knee pain patients, pre and post, a specific physiotherapy program to determine if there were any changes in patellar position, IPFP volume and appearance as well as BMLs. The study included 12 patients with radiological evidence of tibio-femoral, patello-femoral or tri-compartmental OA. 1.5 T MRIs were obtained pre and 4 months post 6 physiotherapy sessions. MRI comparisons were made for changes in (a) IPFP oedema signal b) patellar alignment c) IPFP depth, area and perimeter and d) cyst presence or size in the subspinous tibial bone marrow and subchondral bone marrow. After treatment, both pain scores and IPFP signal reduced in all subjects. The patella was 1.7 mm higher ($p=0.004$), 1.2 mm more medial (patellar drift, $p=0.0001$) and 2° more varus (patellar roll, $p=0.001$). No consistent pattern was found in distribution, size or intensity in BMLs. IPFP oedema seems to be associated with increased pain in knee OA.

Keywords: Knee osteoarthritis; MRI; Physical therapy; Infra-patellar fat pad; Bone marrow lesions

Introduction

Worldwide, arthritis is a major cause of long-term disability, costing governments billions of dollars annually in both direct (health care) and indirect (loss of income and early retirement) costs [1-6]. Knee osteoarthritis (OA) is the most commonly diagnosed cause of knee pain in individuals over 50 years of age [7]. Pain is the major reason for an individual with OA to seek a knee joint replacement. The severity of pain can range from barely perceptible to immobilizing, but the cause of pain in OA is poorly understood, particularly as the reported pain intensity does not always correlate with the severity of change on X-ray [8-11].

As articular cartilage is completely aneural, it is unlikely to be the actual pain generator. Alternative explanations for OA-related knee pain have been suggested and include both primary effects on subchondral bone or synovium and secondary effects on structures such as menisci or ligaments [12-18]. However, a recent study by Guermazi et al. [19] involving 710 participants of more than 50 years age found that, although 89% had structural abnormalities on MRI consistent with OA, only 29% complained of pain. The most common abnormalities were osteophytes (74%) followed by bone marrow lesions (52%). These authors concluded that most middle aged and elderly people with "normal" knee X-rays have degenerative tibiofemoral joint lesions on MRI regardless of the presence or absence of pain. Nevertheless, Javaid et al. [13] found that the presence of bone marrow lesions (BMLs), particularly in the non-weight bearing, subspinous tibial region of asymptomatic, radiographically normal knees, predicted the development of pain 15 months later.

Interestingly, Felson et al. [12] found that BMLs could fluctuate in volume over 6-12 weeks, suggesting that BMLs were strongly related to focal overloading of the joint, usually from mal-alignment. They postulated that the rapid change in volume of these lesions could either reflect a fluctuating mechanical environment or some as yet undescribed temporary pathological change causing oedema and inflammation.

The deep infrapatellar fat pad (IPFP), a large intra-capsular but extra-synovial collection of adipose tissue, has also been proposed as a potential significant source of OA-related knee pain [20-22]. The posterior surface of the IPFP is covered with synovium and extends posteriorly through the intercondylar notch of femur contiguous with the anterior cruciate ligament [23]. The IPFP is a highly vascular and pain sensitive structure which influences knee biomechanics [24]. Nerves within the IPFP contain substance P fibres as well as type IVa free nerve endings, making this one of the most pain sensitive structures in the knee [25-27]. Knee pain has been experimentally induced, by injecting hypertonic saline into the fat pad of asymptomatic individuals [28]. Pro-inflammatory cytokines have been found in the infrapatellar fat pads of patients with knee OA [22]. Using an established OA model in rodents, Clements et al. [21] injected monoiodoacetate into the knee joint and found marked IPFP inflammatory changes on day 1, suggesting the fat pad as an early source of OA pain. After 21 days of marked weight-bearing asymmetry, the rodents exhibited IPFP fibrosis. IPFP fibrosis has been shown to cause chronic knee pain and stiffness in humans [20].

Non-operative management of knee OA is relatively successful in improving OA symptoms [29,30]. There is good evidence that improved quadriceps strength and perhaps even gluteal strength may decrease knee symptoms sufficiently, reducing the need for TKR [31-34]. There have been no studies however, evaluating MRI scans,

pre and post successful physiotherapy intervention for patients with knee OA, to give some insight into the potential causes of the episodic acute, disabling pain experienced by patients with knee OA. Thus, the aim of this pilot study was to determine whether any changes in patellar alignment, indirectly implying improved quadriceps muscle tone, IPFP volume, IPFP appearance or BMLs could be observed on MRI in patients with OA-related knee pain pre and post a specific physiotherapy intervention.

Methods

Subject selection

Twelve consecutive patients (7 males, 5 females, mean age 61 years, range 40-80 years) with radiological evidence of tibio-femoral, patello-femoral or tri-compartmental OA, who presented to a physiotherapy clinic for treatment of OA related knee pain, participated in the study.

All individuals provided informed written consent and institutional ethics approval was obtained. All subjects documented the distribution of pain and completed a functional OA knee pain questionnaire (KOOS) pre and 6 months post physiotherapy treatment. Pain of >5/10 on a visual analogue scale (VAS) was reproduced by stepping up and/or down onto a box which was 23 cm high; as well as during supine testing of the knee by either a static quadriceps contraction or a passive extension and/or passive flexion manoeuvre. See Table 1 for more detail about subject characteristics. Prior to commencing physiotherapy, subjects received MRI scans pre and post knee tape intervention, as well as follow up MRI scans 4 months (range 2 to 6 months from baseline scan) following 6 sessions of specific physiotherapy treatment. Subjects received physiotherapy once a week for a month, then a further two treatments, which were 2 weeks apart. All subjects were reviewed at 6 and 12 months following cessation of formal physiotherapy treatment to determine if there had been any symptom recurrences.

Subject	Age	Comorbidities	Pain Medication	VAS
1 (M)	57	No	Nil	5/10 stairs, 7/10 flexion OP
2 (M)	66	occasional pain other knee,	Nil	6/10 stairs, 8/10 flexion OP
3 (F)	80	Severe OA changes CS, LS, opposite hip, hands, peripheral neuropathy, ventricular fibrillation	6 Panadol osteo/day, Lyrica 75mg/day for neuropathy, can't take NSAIDs	8/10 extension OP, 6/10 stairs, 10/10 flexion OP
4 (F)	43	4 knee surgeries both knees for patellar instability, opposite hip gluteal tendinopathy	No medication effective	10/10 walking, 10/10 quads contraction, unable to do stairs
5 (F)	40	No	Nil	5/10 downstairs, 3/10 extension OP
6 (M)	69	Some pain in other knee-not scanned	Nil	7/10 Flexion OP, 4/10 down stairs
7 (F)	54	Bilateral knee OA, LS OA	Occasional Voltaren	6/10 down stairs, 8/10 flexion OP, 6/10 quads set
8 (M)	68	Other knee mild OA	Nil	5/10 down stairs, 4/10 extension OP, 8/10 flexion OP
9 (M)	75	ACL graft 15 years previously	Nil	6/10 Flexion OP
10 (F)	61	Bilateral PF OA	1 course of Mobic	8/10 walking, 10/10 quads contraction
11 (M)	76	OA LS, degenerative bilateral rotator cuff tears	Occasional Neurofen	FOP 7/10; walking 5/10
12 (M)	58	ipsilateral hip replacement, contralateral tibial osteotomy, LS OA, bilateral wrist and shoulder tendinopathies	Occasional Panadol Osteo	Quads set 8/10, Stairs up 5/10

Table 1: Subject characteristics.

As the premise was that the IPFP was inflamed and a major source of the symptoms, physiotherapy treatment was designed to initially decrease pain by taping to unload the fat pad by lifting the tissue from the tibial tuberosity towards the patella and by pulling the tibia forward (Figure 1). The tape needed to provide an immediate >50% decrease in symptoms on stairs and passive extension and/or flexion manoeuvres. The subjects wore the tape continuously for a week, after which time it was removed and they were instructed how to apply the tape themselves. The subjects kept taping their knees until their symptoms were significantly reduced for everyday activities. The subjects were given a specific exercise regime that was to be done in a pain free manner, so their symptoms were not increased. The exercise regime consisted of instruction of how to get in and out of a chair without using their hands; improving stair climbing; weight bearing

gluteal exercises simulating the stance phase of gait, which were tailored to the individual, so those with more pain started with more bilateral support in the exercise and those with less pain placed more weight through their symptomatic leg (Figures 2 and 3); prone figure four hip stretches; and small knee bends with gluteal squeeze. Subjects were asked to do the exercise program at least twice daily and were expected to continue as a maintenance strategy as a daily routine. If the tibial varum deformity was not too large, subjects were also asked to adopt a modified ballet 3rd position, involving slight femoral external rotation and the legs touching with soft, not locked knees, whenever they had to stand for prolonged periods.

Patient stands 45° to the wall, the knee of the leg closest to wall is bent up against wall for balance, the heel of that leg is raised off the floor, toes stand on the floor (simulating push off). The patient stands

tall with their weight back through the heel of the outside leg, the pelvis is slightly tilted posteriorly and the knee of the outside leg is slightly bent (just off lock). The patient then externally rotates the top part of the thigh slightly, without moving the hip or the foot. This contraction is held for 15 seconds and repeated 3 times and performed at least 3 times per day. This exercise should always be pain free.

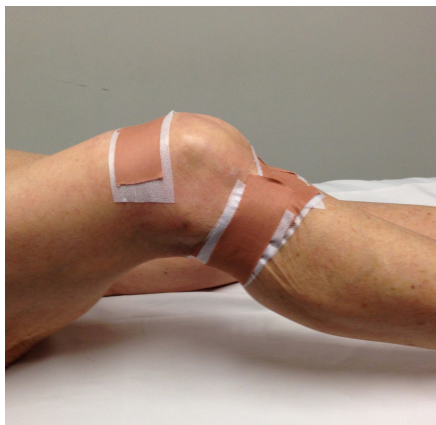


Figure 1: Taping patella and the fat pad for OA knee.



Figure 2: Weight bearing gluteal exercise.

MRI data acquisition

MR images were acquired with a 1.5 T scanner using a dedicated 8-channel phased-array knee coil. The MRI protocol consisted of (a) contiguous 4 mm thick proton density weighted images (TR 3000, TE 35) in standard axial/coronal/sagittal planes, and (b) fat-suppressed axial and sagittal images of equivalent thickness using either fat-saturation proton density weighted or STIR technique. The scan parameters provided sub-millimetre in-plane spatial resolution (pixel size 0.4-0.5 mm).

Fat pad volume could not be directly estimated due to the lack of any available automated MRI segmentation tool, so indirect measures of fat pad volume were therefore utilized, with images of identical or

near-identical location and plane on the pre and post-treatment MRI examinations carefully compared for changes in (a) IPFP depth, area and perimeter at a single chosen level; (b) the angle between distal patellar tendon & adjacent anterior tibial cortex; and (c) patellar alignment relative to femur.

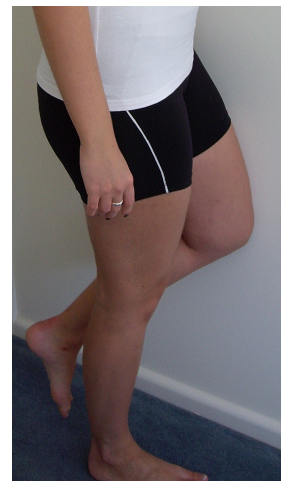


Figure 3: Weight bearing gluteal exercise progression.

The exercise is the same as Figure 2 except that the foot of the leg closest to the wall is lifted off the ground with the knee of that leg on the wall for balance. The leg closest to the wall does not push against the wall.

The IPFP, subspinous tibial bone marrow and subchondral bone marrow were also assessed for changes in oedema signal and cystic changes on fat-suppressed MRI sequences after subjectively 'equalising' the overall displayed tissue brightness and contrast on the pre and post-treatment examinations. A "patellofemoral" pattern of IPFP oedema was recorded if the affected portion of fat pad margined the inferior rim of patella. A "tibiofemoral" pattern of IPFP oedema was recorded if the affected portion of fat pad involved the lingular segment or margined the anterior tibiofemoral joint line. Slight differences in patient positioning between baseline and post-treatment MRI examinations were minimized or eliminated by using the multiplanar image reformatting (MPR) capability of an open-source medical software tool [35]. Any measurements taken from baseline pre-treatment axial, sagittal or coronal sequences were compared with identically matched MPR-generated sections from the corresponding progress post-treatment axial, sagittal or coronal sequences. Changes in patellar position were similarly measured from identical or near-identical planes of reference obtained through the femur (Figure 4): (a) patellar 'height' relative to the axial plane; (b) patellar 'tilt' and 'pitch' relative to the coronal plane; and (c) patellar 'roll' and 'drift' relative to the sagittal plane. Patellar height, pitch and drift were measured in millimeters. Patellar roll and tilt were measured in degrees.

Statistical analysis

Paired t tests were used to evaluate i) changes in KOOS scale pre and post physiotherapy intervention ii) MRI changes pre and post tape and iii) MRI changes pre and post physiotherapy intervention. Confidence intervals (CI) at 95% for differences between conditions

were calculated and an alpha of $p < 0.05$ was used to determine statistical significance. Statistical analyses were performed using IBM SPSS v21.0.

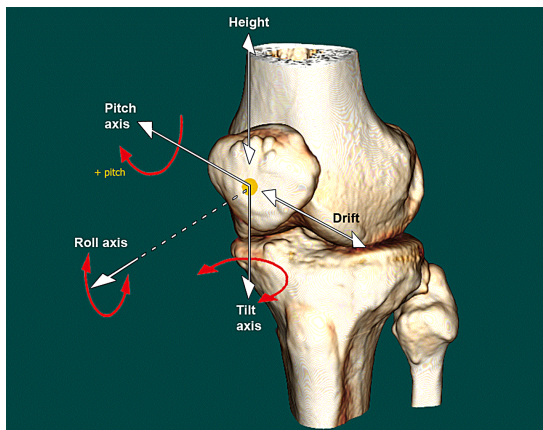


Figure 4: Parameters of change in patellar alignment.

Two independent musculoskeletal radiologists, one of whom was blinded to whether the scan was pre or post treatment, reviewed the MRIs.

Results

KOOS scales

Physiotherapy treatment improved the KOOS subscales, particularly with regard to sport and quality of life changes ($p = 0.001$). Before commencing the physiotherapy program most patients were unable to participate in sport and the quality of life measures were low. After physiotherapy there were improvements in all the KOOS measurements (Figure 5).

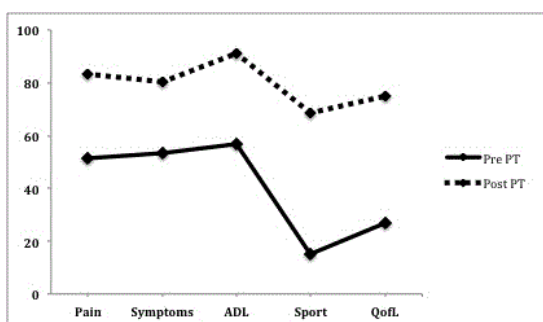


Figure 5: KOOS pre and 6 months post physiotherapy treatment.

All patients were participating in activities of their choice, which included walking, golf, tennis, skiing, sailing and zumba dancing, with minimal or no discomfort, although some were still taping their knees for more vigorous pursuits.

Immediate effect of taping the knee

The patella was rolled 1.5° more varus after tape was applied to the knee ($p = 0.0002$), but there was no difference in the other patellar parameters. The VAS score for stair ascent or descent decreased from 5/10 to 1/10 after taping and for supine testing of quadriceps contraction, extension or flexion overpressure from 7/10 to 1/10 after taping. Figure 6 gives an example of one subject (80 years of age) pre taping, post taping and 3 months after treatment.

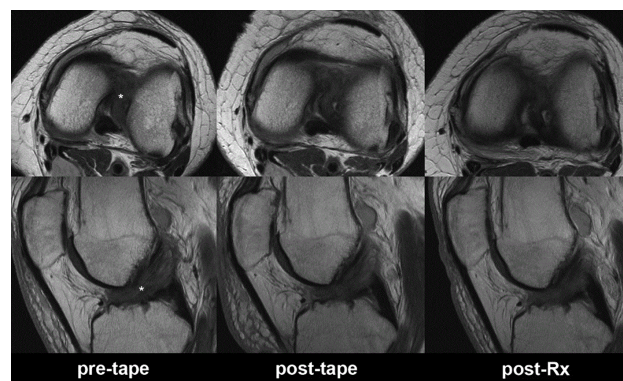


Figure 6: Effect of taping and physiotherapy.

Axial (top row) and sagittal (bottom row) proton density weighted MR images are shown immediately before taping, immediately after taping and subsequent to a course of successful physical therapy. A degenerate ACL (asterisk) shows diffuse myxoid thickening with associated bulge at the anterior intercondylar notch. Immediately following the application of tape, there is (a) slight inferior shift and increased pitch of the patella with a consequent increase in overall anteroposterior diameter of the infra-patellar fat pad, and (b) an apparent decrease in ACL thickness due to the medial tibial condyle being pulled slightly anterior (relative to the femur) by the tape, with consequent lengthening of the ligament. Three months after the completion of physical therapy, with pain now resolved and tape no longer required, MRI shows maintenance of improved alignment at both the patello-femoral and tibia-femoral articulations, with (i) patellar height now significantly increased from the pre-treatment baseline due to improved resting quadriceps tone, and (ii) persistent lengthening and apparent thinning of the myxoid ACL that shows the lateral tibial condyle has maintained its corrected position.

MRI changes after treatment

There was substantial agreement (percent agreement 83.3%; kappa coefficient 0.73) between the two radiologists reviewing the pre and post treatment scans for fat pad signal and BMLs.

Patellar position and fat pad size measurements: The patella was 1.7 mm higher ($p = 0.004$), more medial by 1.2 mm ($p = 0.0001$), and rolled 2° more varus ($p = 0.001$) following treatment. There was no difference in fat pad size measurements following treatment (Table 2).

Fat pad signal: Fat pad signal decreased in all subjects. There were two distinct patterns of resolving fat pad oedema, occurring either alone or more commonly together: 1) a patellofemoral pattern in which fat pad oedema marginated the inferior rim of patella, mostly on the lateral side (Figure 7); and 2) a tibiofemoral pattern, in which

fat pad oedema margined the anterior synovial fringe of the medial or lateral joint compartments, usually including the lingular projection of the fat pad at the anterior intercondylar notch (Figure 8).

MRI measures	Paired Differences			Sig tailed) (2-
	Mean	95% Confidence Interval of the Difference		
		Lower	Upper	
I IPFP area	-3.91	-5.01	2.85	0.554
IPFP perimeter	-0.73	-1.5	0.05	0.063
IPFP depth	-0.81	-2.35	0.73	0.268
PT-T angle	0.88	-4.31	6.07	0.713
Patella height	1.69	0.66	2.61	0.004
Patella pitch	-0.55	-2.11	0.99	0.445
Patella drift	1.16	0.66	1.67	0.0001
Patella tilt	0.04	-2.52	2.59	0.975

Patella roll	2.05	1.12	2.97	0.001
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Table 2: Differences in MRI of fat pad and patellar measurements after physical therapy treatment.

Bone marrow lesions: BMLs, which comprised cystic changes and/or marrow oedema, showed a mixed response in number, size or signal intensity at subchondral and subspinous locations (Table 3). Subspinous BMLs increased in size/intensity in >50% subjects (7/12) and increased in number in one third of subjects (4/12).

Subchondral BMLs, which were variable and scattered about all compartments of the knee, changed in number at separate locations, decreasing in overall number in 25% of subjects (3/12). Subchondral BMLs showed a mixed increase/decrease in size/intensity at separate locations within the knee joint in the majority (9/12), with a decrease in size/intensity in only 25% of subjects (3/12).

Discussion

All patients in our pilot study experienced significant improvement in symptoms and increased functional outcomes, in contrast to more intensive exercise programs which have been found to have little or no effect on pain and/or function in middle-aged patients with moderate to severe radiographic knee OA [36].

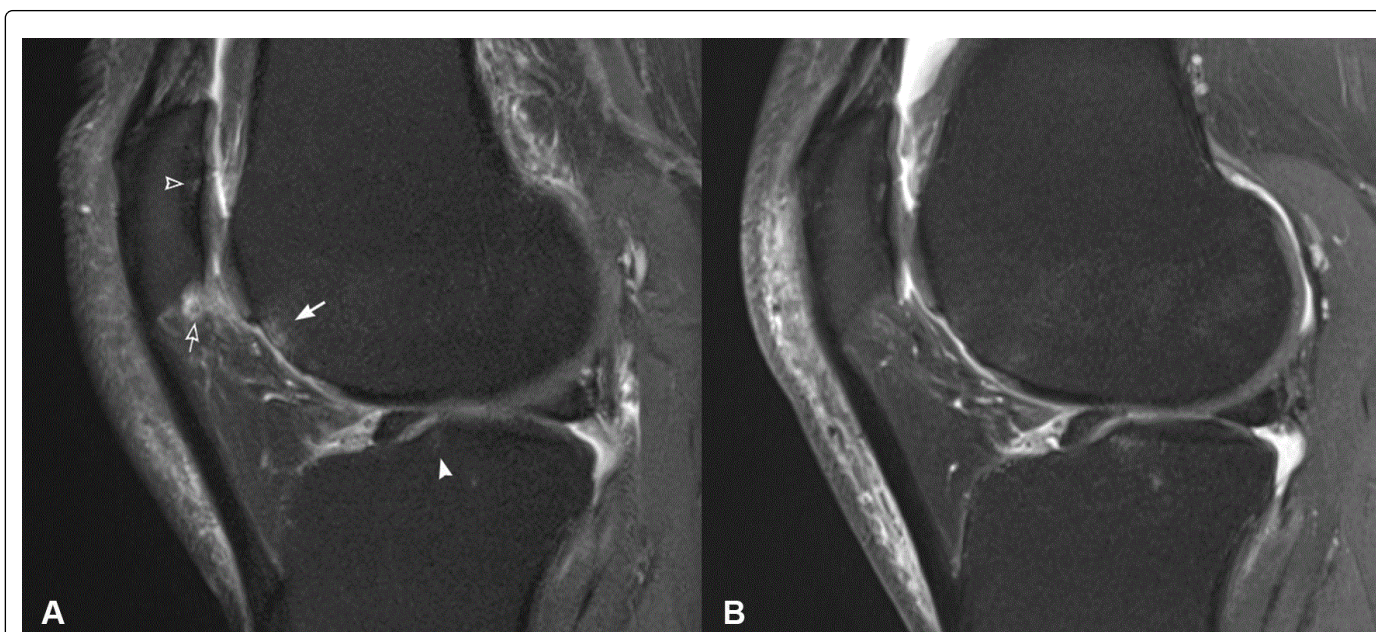


Figure 7: Patellofemoral pattern of fat pad oedema and BMLs: A) Before treatment there is localized fat pad oedema at the inferior rim of the patella (open arrow), subchondral BMLs at both patella (open arrowhead) and trochlea (solid arrow), and a subtle subspinous BML at the tibia (solid arrowhead). (B) Progress scan obtained after physiotherapy 3 months later shows resolution of fat pad oedema, no change in patellar BML, resolution of trochlear BML and increase in subspinous tibial BML.

Our rehabilitation program consisted of neuromuscular, weight bearing training for the whole lower limb, which aimed to subtly change the way the patients moved. The program had to be easy for the patient to do, requiring no equipment, so it could be at any time, in any place, taking no more than five minutes to complete, to ensure compliance of the exercise program. The pattern of MRI change after the physiotherapy program, demonstrated a reduction in fat pad

oedema, as well as an improvement in resting quadriceps tone with an increase in patellar height, and more specifically, vastus medialis (VM) tone, with a shift of the patella into a more medial position and varus orientation. We found that decreased knee pain after treatment seemed to correlate with reduced fat pad oedema on MRI, suggesting a decrease in fat pad inflammation, reflecting a reduction of the pro-inflammatory cytokines which have been shown to originate from the

IPFP, as well as synovial cells and articular chondrocytes [22]. As pro-inflammatory cytokines contribute to cartilage breakdown, any treatment that reduces IPFP inflammation can only be advantageous in minimizing the further progression of knee OA and improving knee joint loading [22]. The exact cause for IPFP oedema remains speculative. Although the localized, rather than generalized, distribution of this change is thought to suggest mechanical impingement as the most likely mechanism, the possibility of an underlying or concomitant localized synovitis is raised by the observation that IPFP oedema also marginated the synovial surfaces.

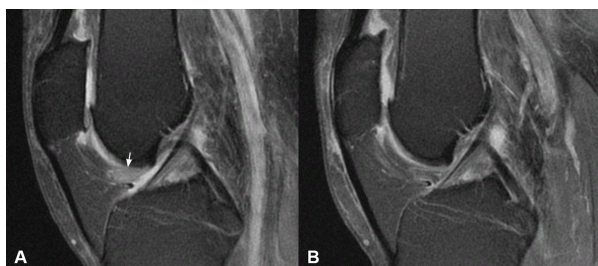


Figure 8: Tibiofemoral pattern of fat pad oedema after fall onto knee: (A) Localised oedema (arrow) involves the lingula of the infra-patellar fat pad before treatment. (B) Progress scan obtained after physiotherapy 2 months later shows resolution of oedema.

The IPFP is highly nociceptive, so a decrease in IPFP inflammation could account for the decrease in the OA related knee pain, supporting the work of Clements et al. [21], who suggested the IPFP was a source of OA related knee pain, after they found marked IPFP inflammatory changes caused rapid weight-bearing asymmetry in rodents. Irritation of the IPFP inhibits quadriceps activity, which may partially explain

the quadriceps atrophy in symptomatic OA knees [37,38]. For treatment success in our study, the patients' pain needed to be reduced by at least 50%. Pain has an inhibitory effect on quadriceps muscle activity [36-39]. Taping the knee has been found to reduce pain, improve VM timing, increase the tolerance to knee joint loading and alter patellar position [40-43]. With the symptoms reduced immediately by tape, the patients in our study were able to perform their training program with minimal or no symptoms.

The altered patellar position on MRI after treatment indicates an increase in quadriceps strength and consequently greater dynamic knee stability, which is further evidenced by the enhanced physical function of the subjects in our study. The quadriceps muscle functions eccentrically during the early stance phase of gait to decelerate the limb prior to heel strike, reducing impulse loading and thus minimising stress on the articular cartilage, thereby, protecting the knee joint [44]. In middle-aged individuals with decreased quadriceps strength, there are not only reports of increased knee pain [45], but MRI scans have demonstrated increased patellofemoral cartilage loss and tibiofemoral joint space narrowing [46]. In a recent MRI study involving 117 OA knee patients, Wang et al. [47] found increased VM size was associated with reduced knee pain at 2 years and reduced medial tibial condyle cartilage loss at 4.5 years from baseline. These authors concluded that optimising VM size was critical to reducing OA progression and decreasing the need for TKR [47].

We found a mixed pattern of BML changes in the pre and post-treatment scans, supporting the findings of Felson et al. [12], who found that BMLs could fluctuate in volume over 6-12 weeks. As there was no consistent pattern to the changes in BMLs in distribution, size or intensity, we could not conclude that decreases in BMLs in any region of the knee were the reason for the reduction in OA related knee pain in the patients in our study.

Subject	Subspinous BMLs			Subchondral BMLs			
	Change in number	Change in size	Change in intensity	Location	Change in number	Change in size	Change in intensity
1	No lesion	NA	NA	P, LFC	↓	↓	↓
2	↑	↑	↑	P, T, LFC	Mixed↑↓	Mixed↑↓	Mixed↑↓
3	No change	↓	↓	P, T, LFC, LTC	No change	Mixed↑↓	Mixed↑↓
4	↑	No change	↓	P, T, MFC	↓	Mixed↑↓	Mixed↑↓
5	No change	↓	↓	MFC	No change	↓	↓
6	No change	↓	↓	P, T, LFC, LTC	↑	Mixed↑↓	Mixed↑↓
7	No change	↑	↑	P, T, LFC, LTC	Mixed↑↓	Mixed↑↓	Mixed↑↓
8	No change	↑	↑	P, T, LFC	↑	Mixed↑↓	Mixed↑↓
9	↑	↑	↑	P, T	No change	Mixed↑↓	Mixed↑↓
10	No change	Mixed↑↓	↑	P, T	No change	Mixed↑↓	↓
11	↓	↑	↑	All except LTC	Mixed↑↓	Mixed↑↓	Mixed↑↓
12	No change	↑	↑	All except MTC	Mixed↑↓	↓	↓

P=Patella; T=Trochlea; LFC=Lateral Femoral Condyle; LTC=Lateral Tibial Condyle; MFC=Medial Femoral Condyle, MTC=Medial Tibial Condyle.

Table 3: Pre to post treatment MRI changes in bone marrow lesions.

Unlike Javaid et al. [13], who suggested the presence of BMLs in the subspino-tibial region predicted knee pain development, we did not find a significant relationship between a reduction in subspino-tibial BMLs and pain reduction, as the majority of our subjects showed an increase of both size and intensity in BMLs in this region on their post treatment scan.

We postulate that, whenever the knee joint repeatedly fails to move in optimal alignment, there are several mechanical consequences that, either alone or together, might contribute to pain: (1) impingement of the synovium and/or IPFP at the joint margins resulting in synovitis and/or panniculitis; (2) excessive loading of the articular surfaces and menisci resulting in focally increased subchondral bone or meniscal stress [12,48], and (3) overloading of the joint capsule and/or ligamentous structures. Any successful treatment strategy must therefore decrease pain, and endeavour to improve joint stability and alignment. The use of externally applied tape may serve to not only unload the irritated IPFP, but also assist joint stability until the dynamic stabilisers are sufficiently strong to control alignment and avoid both excessive soft tissue loading and subchondral bone stress. Kinetic and kinematic studies are required to determine whether specific physical therapy intervention does change the alignment and improve the joint loading in OA related knee pain patients.

Limitations of the Study

As this was a pilot study, we only had 12 subjects who were scanned pre and post physiotherapy intervention. Nevertheless, our results are statistically significant and are very promising for an extremely cost-effective approach to managing OA-related knee pain. A larger, longitudinal, multicenter trial is now required to determine if the MRI changes can be consistently obtained, as well as, maintained over the long term. We used a 1.5 T MR scanner utilizing standard clinical sequences with good in-plane spatial resolution but 4mm slice thickness, whereas isotropic 3D sequences now available on 3T scanners would likely provide better-matched tissue cross-sections and more reliable measurements. We were unable to directly measure IPFP volume and instead used only indirect measures such as IPFP perimeter at a single level. We relied on subjective visual inspection to assess change in IPFP and BML signal, but we had good agreement between the two radiologists reviewing the pre and post treatment scans.

Conclusion

A specific physiotherapy program for OA related knee pain, consisting of unloading painful structures, training the gluteal and quadriceps muscles in functional positions was effective, in not only decreasing pain and improving functional outcome, but also effective in changing patellar position, and fat pad oedema as measured on MRI. The symptom abatement seemed to correlate with both 1) decreased IPFP fat pad oedema, which suggests that fat pad inflammation may be an important contributor to the severe disabling pain experienced by many OA knee patients; and 2) increased quadriceps resting tone, as inferred by subtle but consistent changes in resting patellar alignment, which appears to be related to the subjects' improved functional performance. As the cost of arthritis treatment soars, specific physiotherapy intervention should be considered as an initial, minimally invasive, cost effective option for improving treatment outcomes and promoting patient self-management.

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References

1. Brooks PM (2006) The burden of musculoskeletal disease--a global perspective. *Clin Rheumatol* 25: 778-781.
2. Carmona L, Ballina J, Gabriel R, Laffon A; EPISER Study Group (2001) The burden of musculoskeletal diseases in the general population of Spain: results from a national survey. *Ann Rheum Dis* 60: 1040-1045.
3. Dawson J, Linsell L, Zondervan K, Rose P, Randall T, et al. (2004) Epidemiology of hip and knee pain and its impact on overall health status in older adults. *Rheumatology (Oxford)* 43: 497-504.
4. McErlain DD, Milner JS, Ivanov TG, Jencikova-Celerin L, Pollmann SI, et al. (2007) Painful Realities: The economic impact of Arthritis in Australia in 2007. *Access Economics*.
5. Nguyen US, Zhang Y, Zhu Y, Niu J, Zhang B, et al. (2011) Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. *Ann Intern Med* 155: 725-732.
6. Piscitelli P, Iolascon G, Di Tanna G, Bizzi E, Chitano G, et al. (2012) Socioeconomic burden of total joint arthroplasty for symptomatic hip and knee osteoarthritis in the Italian population: a 5-year analysis based on hospitalization records. *Arthritis Care Res* 64: 1320-1327.
7. Cubukcu D, Sarsan A, Alkan H (2012) Relationships between Pain, Function and Radiographic Findings in Osteoarthritis of the Knee: A Cross-Sectional Study. *Arthritis* 2012: 984060.
8. Bedson J, Croft PR (2008) The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord* 9: 116.
9. Chang CB, Han I, Kim SJ, Seong SC, Kim TK (2007) Association between radiological findings and symptoms at the patellofemoral joint in advanced knee osteoarthritis. *J Bone Joint Surg Br* 89: 1324-1328.
10. Schiphof D, Kerkhof HJ, Damen J, de Klerk BM, Hofman A, et al. (2013) Factors for pain in patients with different grades of knee osteoarthritis. *Arthritis Care Res (Hoboken)* 65: 695-702.
11. Sengupta M, Zhang YQ, Niu JB, Guermazi A, Grigorian M, et al. (2006) High signal in knee osteophytes is not associated with knee pain. *Osteoarthritis Cartilage* 14: 413-417.
12. Felson DT, Parkes MJ, Marjanovic EJ, Callaghan M, Gait A, et al. (2012) Bone marrow lesions in knee osteoarthritis change in 6-12 weeks. *Osteoarthritis Cartilage* 20: 1514-1518.
13. Javaid MK, Lynch JA, Tolstykh I, Guermazi A, Roemer F, et al. (2010) Pre-radiographic MRI findings are associated with onset of knee symptoms: the most study. *Osteoarthritis Cartilage* 18: 323-328.
14. Knoop J, Dekker J, Klein JP, van der Leeden M, van der Esch M, et al. (2012) Biomechanical factors and physical examination findings in osteoarthritis of the knee: associations with tissue abnormalities assessed by conventional radiography and high-resolution 3.0 Tesla magnetic resonance imaging. *Arthritis Res Ther* 14: R212.
15. Roemer FW, Neogi T, Nevitt MC, Felson DT, Zhu Y, et al. (2010) Subchondral bone marrow lesions are highly associated with, and predict subchondral bone attrition longitudinally: the MOST study. *Osteoarthritis Cartilage* 18: 47-53.
16. Stahl R, Jain SK, Lutz J, Wyman BT, Le Graverand-Gastineau MP, et al. (2011) Osteoarthritis of the knee at 3.0 T: comparison of a quantitative and a semi-quantitative score for the assessment of the extent of cartilage lesion and bone marrow edema pattern in a 24-month longitudinal study. *Skeletal Radiol* 40: 1315-1327.
17. Torres L, Dunlop DD, Peterfy C, Guermazi A, Prasad P, et al. (2006) The relationship between specific tissue lesions and pain severity in persons with knee osteoarthritis. *Osteoarthritis Cartilage* 14: 1033-40.

18. Zhang Y, Nevitt M, Niu J, Lewis C, Torner J, et al. (2011) Fluctuation of knee pain and changes in bone marrow lesions, effusions, and synovitis on magnetic resonance imaging. *Arthritis Rheum* 63: 691-699.
19. Guermazi A, Niu J, Hayashi D, Roemer FW, Englund M, et al. (2012) Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: population based observational study (Framingham Osteoarthritis Study). *BMJ* 345:e5339.
20. Bastiaansen-Jenniskens YM, Wei W, Feijt C, Waarsing JH, Verhaar JA, et al. (2013) Infrapatellar fat pad of OA patients stimulates fibrotic processes in cultured synovial cells; a possible role for Prostaglandin F2a *Arthritis Rheum*.
21. Clements KM1, Ball AD, Jones HB, Brinckmann S, Read SJ, et al. (2009) Cellular and histopathological changes in the infrapatellar fat pad in the monoiodoacetate model of osteoarthritis pain. *Osteoarthritis Cartilage* 17: 805-812.
22. Ushiyama T, Chano T, Inoue K, Matsusue Y (2003) Cytokine production in the infrapatellar fat pad: another source of cytokines in knee synovial fluids. *Ann Rheum Dis* 62: 108-112.
23. Dragoo JL, Johnson C, McConnell J (2012) Evaluation and treatment of disorders of the infrapatellar fat pad. *Sports Med* 42: 51-67.
24. Bohnsack M, Wilharm A, Hurschler C, Rühmann O, Stukenborg-Colsman C, et al. (2004) Biomechanical and kinematic influences of a total infrapatellar fat pad resection on the knee. *Am J Sports Med* 32: 1873-80.
25. Bohnsack M, Meier F, Walter GF, Hurschler C, Schmolke S, et al. (2005) Distribution of substance-P nerves inside the infrapatellar fat pad and the adjacent synovial tissue: a neurohistological approach to anterior knee pain syndrome. *Arch Orthop Trauma Surg* 125: 592-597.
26. WitoÅski D, Wagrowska-Danielewicz M (1999) Distribution of substance-P nerve fibers in the knee joint in patients with anterior knee pain syndrome. A preliminary report. *Knee Surg Sports Traumatol Arthrosc* 7: 177-183.
27. Wojtys EM, Beaman DN, Glover RA, Janda D (1990) Innervation of the human knee joint by substance-P fibers. *Arthroscopy* 6: 254-263.
28. Bennell K, Hodges P, Mellor R, Bexander C, Souvlis T (2004) The nature of anterior knee pain following injection of hypertonic saline into the infrapatellar fat pad. *J Orthop Res* 22: 116-121.
29. Devos-Comby L, Cronan T, Roesch SC (2006) Do exercise and self-management interventions benefit patients with osteoarthritis of the knee? A meta-analytic review. *J Rheumatol* 33: 744-756.
30. Katz JN, Brophy RH, Chaisson CE, de Chaves L, Cole BJ, et al. (2013) Surgery versus physical therapy for a meniscal tear and osteoarthritis. *N Engl J Med* 368: 1675-1684.
31. Henriksen M, Aaboe J, Simonsen EB, Alkjaer T, Bliddal H (2009) Experimentally reduced hip abductor function during walking: Implications for knee joint loads. *J Biomech* 42: 1236-1240.
32. Lange AK, Vanwanseele B, Fiatarone Singh MA (2008) Strength training for treatment of osteoarthritis of the knee: a systematic review. *Arthritis Rheum* 59: 1488-1494.
33. Segal NA, Glass NA, Felson DT, Hurley M, Yang M, et al. (2010) Effect of quadriceps strength and proprioception on risk for knee osteoarthritis. *Med Sci Sports Exerc* 42: 2081-2088.
34. Thorp LE, Wimmer MA, Foucher KC, Sumner DR, Shakoor N, et al. (2010) The biomechanical effects of focused muscle training on medial knee loads in OA of the knee: a pilot, proof of concept study. *J Musculoskelet Neuronal Interact* 10: 166-173.
35. Rosset A, Spadola L, Ratib O (2004) OsiriX: an open-source software for navigating in multidimensional DICOM images. *J Digit Imaging* 17: 205-216.
36. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C (2005) Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. *BMC Musculoskelet Disord* 6: 27.
37. Henriksen M, Rosager S, Aaboe J, Graven-Nielsen T, Bliddal H (2011) Experimental knee pain reduces muscle strength. *J Pain* 12: 460-467.
38. Hodges PW, Mellor R, Crossley K, Bennell K (2009) Pain induced by injection of hypertonic saline into the infrapatellar fat pad and effect on coordination of the quadriceps muscles. *Arthritis Rheum* 61: 70-77.
39. Henriksen M, Alkjaer T, Lund H, Simonsen EB, Graven-Nielsen T, et al. (2007) Experimental quadriceps muscle pain impairs knee joint control during walking. *J Appl Physiol* (1985) 103: 132-139.
40. Cowan SM, Bennell KL, Hodges PW (2002) Therapeutic patellar taping changes the timing of vasti muscle activation in people with patellofemoral pain syndrome. *Clin J Sport Med* 12: 339-347.
41. Crossley KM, Marino GP, Macilquham MD, Schache AG, Hinman RS (2009) Can patellar tape reduce the patellar malalignment and pain associated with patellofemoral osteoarthritis? *Arthritis Rheum* 61: 1719-1725.
42. Gilleard W, McConnell J, Parsons D (1998) The effect of patellar taping on the onset of vastus medialis obliquus and vastus lateralis muscle activity in persons with patellofemoral pain. *Phys Ther* 78: 25-32.
43. Derasari A, Brindle TJ, Alter KE, Sheehan FT (2010) McConnell taping shifts the patella inferiorly in patients with patellofemoral pain: a dynamic magnetic resonance imaging study. *Phys Ther* 90: 411-419.
44. Rice DA, McNair PJ, Lewis GN (2011) Mechanisms of quadriceps muscle weakness in knee joint osteoarthritis: the effects of prolonged vibration on torque and muscle activation in osteoarthritic and healthy control subjects. *Arthritis Res Ther* 13: R151.
45. Amin S, Baker K, Niu J, Clancy M, Goggins J, et al. (2009) Quadriceps strength and the risk of cartilage loss and symptom progression in knee osteoarthritis. *Arthritis Rheum* 60: 189-198.
46. Segal NA, Glass NA, Torner J, Yang M, Felson DT, et al. (2010) Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. *Osteoarthritis Cartilage* 18: 769-775.
47. Wang Y, Wluka AE, Berry PA, Siew T, Teichtahl AJ, et al. (2012) Increase in vastus medialis cross-sectional area is associated with reduced pain, cartilage loss, and joint replacement risk in knee osteoarthritis. *Arthritis Rheum* 64: 3917-3925.
48. Hayashi D, Englund M, Roemer FW, Niu J, Sharma L, et al. (2012) Knee malalignment is associated with an increased risk for incident and enlarging bone marrow lesions in the more loaded compartments: the MOST study. *Osteoarthritis Cartilage* 20: 1227-1233.

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