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 extrasynovial 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. The subjects kept taping their knees until their symptoms were significantly reduced for everyday activities. 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 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 whenever they had to stand for prolonged periods.

Table 1: Subject characteristics.

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

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 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 stay 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.

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 2: Weight bearing gluteal exercise.

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 marginated 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 marginated 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.

**Immediate effect of taping the knee**

The patella was rolled $1.5^\circ$ 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 decent 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.

**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).

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.

**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 $2^\circ$ 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 margined 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).

<table>
<thead>
<tr>
<th>MRI measures</th>
<th>Paired Differences</th>
<th>Sig (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95% Confidence Interval of the Difference</td>
</tr>
<tr>
<td>I IPFP area</td>
<td>-3.91</td>
<td>-5.01</td>
</tr>
<tr>
<td>IPFP perimeter</td>
<td>-0.73</td>
<td>-1.5</td>
</tr>
<tr>
<td>IPFP depth</td>
<td>-0.81</td>
<td>-2.35</td>
</tr>
<tr>
<td>PT-T angle</td>
<td>0.88</td>
<td>-4.31</td>
</tr>
<tr>
<td>Patella height</td>
<td>1.69</td>
<td>0.66</td>
</tr>
<tr>
<td>Patella pitch</td>
<td>-0.55</td>
<td>-2.11</td>
</tr>
<tr>
<td>Patella drift</td>
<td>1.16</td>
<td>0.66</td>
</tr>
<tr>
<td>Patella tilt</td>
<td>0.04</td>
<td>-2.52</td>
</tr>
</tbody>
</table>

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].
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 marginalized the synovial surfaces.

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.

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

<table>
<thead>
<tr>
<th>Subject</th>
<th>Subspinous BMLs</th>
<th>Subchondral BMLs</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change in number</td>
<td>Change in size</td>
<td>Change in intensity</td>
</tr>
<tr>
<td>1</td>
<td>No lesion</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>3</td>
<td>No change</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>4</td>
<td>↑</td>
<td>No change</td>
<td>↓</td>
</tr>
<tr>
<td>5</td>
<td>No change</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>6</td>
<td>No change</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>7</td>
<td>No change</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>8</td>
<td>No change</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>9</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>10</td>
<td>No change</td>
<td>Mixed↑↓</td>
<td>↑</td>
</tr>
<tr>
<td>11</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>12</td>
<td>No change</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

P=Patella; T=Trochlea; LFC=Lateral Femoral Condyle; LTC=Lateral Tibial Condyle; MFC=Medial Femoral Condyle, MTC=Medial Tibial Condyle.
Unlike Javaid et al. [13], who suggested the presence of BMLs in the subspinous tibial region predicted knee pain development, we did not find a significant relationship between a reduction in subspinous 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.

Acknowledgement

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References


