



Reduction in knee adduction moment via non-invasive biomechanical training: A longitudinal gait analysis study

Amir Haim^{a,b,*}, Guy Rubin^c, Nimrod Rozen^c, Yulya Goryachev^a, Alon Wolf^a

^a Biorobotics and Biomechanics Lab (BRML), Faculty of Mechanical Engineering, Technion-Israel Institute of Technology, Haifa, Israel

^b Department of Orthopedic Surgery, Sourasky Medical Center, Tel Aviv, Israel

^c Department of Orthopaedic Surgery, Ha'Emek Medical Center, Afula, Israel

ARTICLE INFO

Article history:

Accepted 5 October 2011

Keywords:

AposTherapy
Footwear-generated biomechanical training
Gait analysis
Knee adduction moment
Knee osteoarthritis
Plasticity of gait patterns

ABSTRACT

Biomechanical non-invasive interventions have been previously reported to reduce pain and facilitate superior levels of function in patients with medial knee osteoarthritis [OA]. One such treatment is the AposTherapy, a customized program utilizing a foot-worn biomechanical device allowing center of pressure modification and continuous perturbation during gait. The influence of this intervention on objective gait metrics has yet to be determined. The aim of the current study was to prospectively examine changes in kinetic and kinematic parameters in patients enrolled in this treatment program. Twenty-five females with symptomatic bilateral medial compartment knee OA were enrolled in the customized daily treatment program. All patients underwent barefoot gait analysis testing and completed subjective questionnaires prior to treatment initiation and on two follow-up visits. Significantly reduced knee adduction moment (KAM) magnitude was noted during barefoot walking after three and nine months of treatment. On average, the knee adduction impulse and the 1st and 2nd KAM peaks were reduced by 13%, 8.4%, and 12.7%, respectively. Furthermore, moment reduction was accompanied by elevated walking velocity, significant pain reduction, and increased functional activity. In addition to symptomatic improvement, our results suggest that this treatment program can alter kinetic gait parameters in this population. We speculate that these adaptations account for the symptomatic and functional improvement reported for this intervention.

© 2011 Elsevier Ltd. All rights reserved.

1. Introduction

Osteoarthritis (OA) is a complex disorder of the hyaline joints, characterized by wear, softening, and thinning of the articular cartilage and diminished compliance of the sub-chondral bone (Bijlsma et al., 2011; Felson and Zhang, 1998; Iannone and Lapadula, 2003). The knee is the most prevalent weight-bearing joint prone to the development of this destructive process, with the medial compartment affected nearly 10 times more often than the lateral compartment (Oliveria et al., 1995). Vast evidence supports the role of biomechanical factors in the pathophysiology of this disease (Radin et al., 1991). Abnormal joint loads have been related to the development and progression of the arthritic process (Radin et al., 1991; Roemhildt et al., 2010).

Abnormally high knee adduction moments (KAM) have been described in association with medial knee OA (Andriacchi, 1994; Sharma et al., 1998). Elevated KAM has been linked with the

progression of knee OA (Miyazaki et al., 2002), and has been recognized as a marker of disease severity (Hurwitz et al., 2002; Sharma et al., 1998).

Gait deviations have been reported in individuals suffering from knee OA (Baliunas et al., 2002; Debi et al., 2009; Elbaz et al., 2010; Gok et al., 2002; Hurwitz et al., 2000) and are thought to represent a compensatory protective mechanism intended to reduce stress and range of motion about the injured joint (Debi et al., 2009). With disease progression, altered morphological joint properties diminish the effectiveness of these mechanisms. Moreover, substantial evidence suggests that impairment of the neuromuscular control system and proprioceptive deficits are present in subjects suffering from knee OA and contribute to the load burden by altering joint biomechanics (Hortobagyi et al., 2005; Hurley, 2003; Johansson et al., 2000; Lewek et al., 2005). Several authors stressed the role of these contributions to the pathogenesis of the disease, suggesting that they convey elevated joint stress with higher impact loads and facilitate the development of cartilage degeneration (Sharma et al., 2003; Slemenda et al., 1998).

Biomechanical interventions focusing on foot center of pressure (COP) manipulation, agility, and perturbation training have been suggested for the treatment of knee OA (Bar-Ziv et al., 2010;

* Corresponding author at: Biorobotics and Biomechanics Lab (BRML), Faculty of Mechanical Engineering, Technion-Israel Institute of Technology, Haifa 32000, Israel. Tel.: +972 52 4262129.

E-mail address: amirhaim@gmail.com (A. Haim).

Elbaz et al., 2010; Fitzgerald et al., 2002; Hurley and Scott, 1998; Thorstensson et al., 2007). Such interventions were reported to facilitate superior levels of functional activity, to reduce pain, and to influence spatiotemporal parameters during gait (Bar-Ziv et al., 2010; Elbaz et al., 2010; Erhart et al., 2010; Fitzgerald et al., 2002; Roddy et al., 2005; Thorstensson et al., 2007). One such treatment modality is the AposTherapy, a customized program utilizing daily treatment with a novel foot-worn biomechanical device capable of modifying the foot's COP and thus altering the KAM. In addition, the device is designed to generate perturbations as the patient walks, challenging the neuromuscular control system. In the recent studies (Bar-Ziv et al., 2010; Elbaz et al., 2010) knee OA patients who completed treatment, reported reduction in pain and improvement in functioning levels. However, a longitudinal gait evaluation of this treatment approach has yet to be performed.

The current study was devised to examine the outcome of a cohort of medial knee OA patients who were enrolled in a customized biomechanical training program. Our aim was to evaluate alterations of gait metrics in a prospective longitudinal study, in order to determine whether the favorable subjective self-reported data previously reported are accompanied by a modification in gait patterns. We hypothesized that patients undergoing this biomechanical treatment program would demonstrate alteration of kinetic and kinematic parameters, in particular the magnitude of the KAM, and that their subjective self-reported evaluation would demonstrate a favorable outcome.

2. Methods

Participants. The study group was comprised of 25 female patients with symptomatic bilateral medial compartment knee OA. Patients were allocated to the study by a senior orthopedic surgeon. Inclusion criteria: symptomatic physician-diagnosed medial knee OA for at least six months, fulfillment of the ACR (American College of Rheumatology) criteria for OA of the knee. Participants' mean age was 62 ± 7 years; height was 1590 ± 56.54 mm; weight was

77.2 ± 9.99 kg; KL grade was 3 ± 0.9 ; WOMAC score was 4.09 ± 2.29 cm; and coronal knee alignment was $1.52 \pm 5.28^\circ$ (positive values corresponded to varus knee alignment).

Radiographs were taken at the beginning of the study to confirm the presence of definite radiographic signs of OA in the medial compartment of the knee according to the KL scale, with no signs of notable lateral compartment joint space narrowing or KL grade 2, or greater involvement in the lateral tibiofemoral and patellofemoral compartments.

Patients were assigned to moderate (KL 2) and severe (KL 3–4) knee OA subgroups based on the KL grade of the more symptomatic knee. Pain was assessed by means of the self-reported Western Ontario and McMaster Osteoarthritis Index (WOMAC). In addition, participants completed the SF-36 health survey. Exclusion criteria included any other orthopedic musculoskeletal or neurological pathology, prior knee surgery (excluding arthroscopy), significant co-morbidities affecting back, hip or foot, other major systemic diseases, and inability to ambulate without the use of a walking aid.

All subjects enrolled in the study were asked to refrain from using any analgesic medication for a 5-day washout period prior to gait analysis testing and clinical evaluations. Moreover, patients were prohibited from participating in any other treatment programs throughout the study period. Approval of the Ethics Sub-Committee was obtained and informed consent was given by all participants. The study was registered in the NIH clinical trial registration system (no. NCT00724139). The purpose and methods of the study were explained to the subjects.

Lower limb alignment. The knee alignment was measured on double-limb anteroposterior radiographs, with subjects standing barefoot with knees in full extension. The mechanical axis was formulated by the angle formed between an axis from the center of the femoral head to the center of the knee femoral intercondylar notch and an axis from the center of the tip of the tibial spine to the ankle talus (Moreland et al., 1987). Mean and SD coronal knee alignment were $1.52 \pm 5.28^\circ$ (positive values corresponded to varus knee alignment). Thirteen patients had varus alignment of the knee and 12 had neutral or mild valgus alignment. All radiographs were assessed by a single trained investigator.

Biomechanical intervention. The biomechanical device (Apos System, Apos Medical and Sports Technologies Ltd., Herzliya, Israel) utilized in the study has been described previously by our group (Haim et al., 2008). In brief, the device consists of two convex-shaped biomechanical elements attached to each foot using a platform in the form of a shoe, allowing customized calibration of the apparatus (Fig. 1). By shifting the biomechanical elements in the coronal and the sagittal planes, the device can be individually calibrated to shift the trajectory of the foot's center of pressure (COP) during gait, thereby altering the orientation of the ground reaction force (GRF) vector. This enables decreasing the pressure load from the affected area in the joint during gait (Haim et al., 2008). The convex form

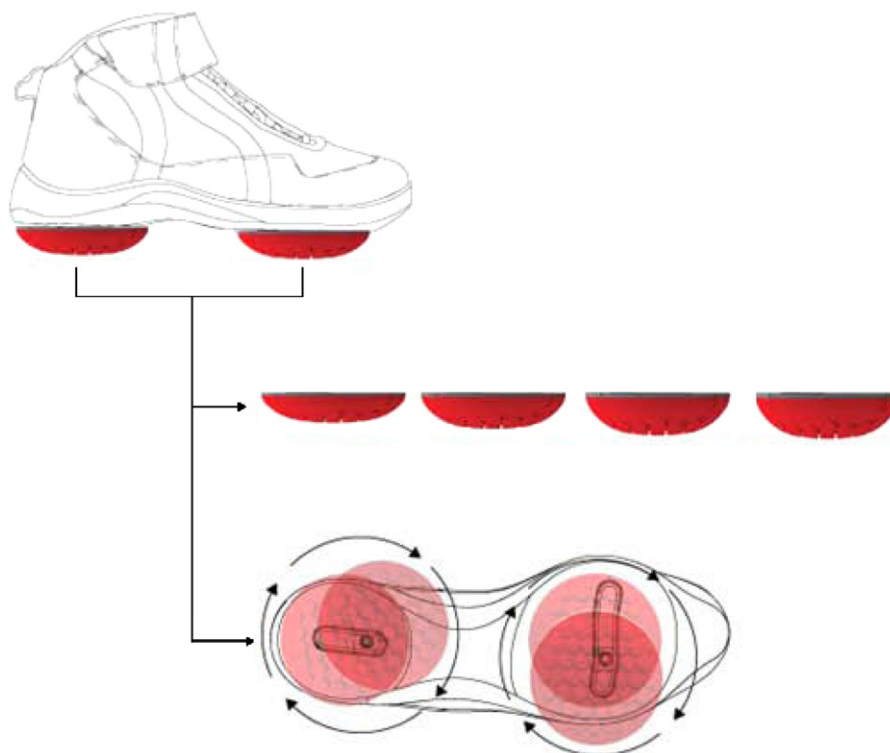


Fig. 1. Biomechanical platform and mobile elements.

of the biomechanical elements generates perturbations applied throughout the stance phase of the gait cycle, enabling dynamic, functional, and repetitive training intended to improve neuromuscular control.

Experimental protocol. Baseline evaluation performed prior to treatment initiation included functional assessment and physical examination, barefoot three-dimensional gait analysis, and subjective evaluation by means of the self-reported questionnaire. The device was calibrated for each patient after baseline assessment by a single certified physiotherapist. Calibration was carried out in accordance with our previous findings (Haim et al., 2008). These findings showed that shifting the hindfoot element of the Apos device laterally from the neutral position and shifting the forefoot element medially from the neutral position will reduce knee adduction forces. The first position of the elements for the “functional neutral sagittal axis” was determined and documented. The functional neutral axis was defined as the position in which the apparatus caused the least valgus or varus torque at the ankle of the individual being examined. Next, the biomechanical elements were shifted (posterior laterally, anterior medially) from the neutral sagittal axis. The magnitude of the parasagittal offset was determined by the patient feedback regarding pain reduction and stability. Re-calibration was performed as necessary at the follow-up visit. Patients were instructed to follow a treatment protocol based on walking during activities of daily living, starting with 10 min of indoor walking each day during the first week and gradually increasing to 30 min of daily outdoor walking at the fourth week and for the rest of the treatment period. Consecutive gait analysis testing and subjective evaluation was carried out twice more during the study period: at the 3-month and the 9-month endpoints.

Data acquisition and processing. Three-dimensional motion analysis was performed using an 8-camera Vicon motion analysis system (Oxford Metrics Ltd., Oxford, UK) for kinematic data capture. The GRF were recorded by two AMTI OR6-7-1000 force plates. Kinematic and kinetic data were collected simultaneously while the subjects were asked to walk barefoot at a self-selected velocity over a 10 m walkway. Passive reflective markers were fixed with adhesive tape to anatomical landmarks identified by an experienced physician. A standard marker set was used to define joint centers and axes of rotation (Kadaba et al., 1990). A knee alignment device (KAD; Motion Lab Systems Inc., Baton Rouge LA) was utilized to estimate the three-dimensional alignment of the knee flexion axis during the static trial. Knee joint moments in the coronal plane were calculated using inverse dynamic analyses from the kinematic data and force platform measures using ‘PlugInGait’ (Oxford Metrics, Oxford, UK). All the analyses were performed for the more symptomatic knee, as selected by the patient. Joint moments were normalized for body mass and reported in SI units (N-m/kg). A program purposely written in the MATLAB software was used to examine the outcome measures. Six trials were collected per subject, values were calculated from each trial, and the average was determined across the trials for each subject.

Outcome measures. Outcome measures included KAM magnitude (knee adduction impulse, loading response (1st) peak and terminal stance (2nd) peak), knee and hip sagittal kinematics, spatiotemporal parameters (cadence, stride time, stride length, step length, walking speed, and step width), self-reported pain via the WOMAC index, and the SF-36 health survey.

Statistical analysis. All statistical analysis was carried out by an independent biostatistician. Mean values and standard deviation were present for all continuous measurements. Non-parametric Friedman tests were used for the comparison of self-reported pain and functional subjective data, spatiotemporal (cadence, step length, step width, gait velocity), kinetic (1st and 2nd acceleration peaks and the knee adduction impulse values), and kinematic (knee and hip range of motion) parameters in the baseline and the two follow-up evaluations. A probability of less than 0.05 was considered as statistically significant. All analyses were performed using SPSS (version 17.0).

3. Results

All 25 patients enrolled in the study completed the treatment program with satisfactory compliance (i.e. adherence of > 75% to the proposed treatment protocol). Two patients had brief (3–4 weeks) treatment intermissions, one due to plantar fasciitis and the other due to trochanteric bursitis, both of which resolved spontaneously.

At mid-treatment evaluation (3 months post treatment initiation), a significant albeit small increase in walking velocity was found. On average, walking velocity increased by 0.07 m/s relative to pretreatment testing (from 1.00 ± 0.13 to 1.07 ± 0.14 m/s, $p=0.017$). The cadence increased by 5 steps/min (from 105.54 ± 9.54 to 110.08 ± 7.59 steps/min); however this change did not reach statistical significance ($p=0.058$). End-point evaluation did not significantly differ from that of mid-treatment. Mean values of the additional spatiotemporal parameters tested did not significantly differ during the testing period.

Post-treatment testing demonstrated a reduction of the KAM magnitude during the stance phase. At the 3-month post-treatment evaluation, group values for the magnitude of the 1st and the 2nd peaks of the KAM and the magnitude of the knee adduction impulse were significantly lower relative to pre-treatment testing ($p=0.002$, <0.001 , <0.001 , respectively). An additional decline of the KAM magnitude values was noted at the end-point evaluation. On average at the end point testing, the knee adduction impulse and the 1st and the 2nd KAM peaks were reduced by 0.54 N-m/kg*sec, 0.06 N-m/kg, and 0.07 N-m/kg, respectively, a reduction of 13%, 8.4%, and 12.7%, respectively, from the pre-training values (Table 1).

Reduction of the knee impulse was similar for both the subgroups. Reduction of the 1st peak was more profound for the moderate OA subgroup while reduction of the 2nd peak was more profound for the severe subgroup (Table 2); however, this trend was not significant.

Group averaged sagittal knee and hip joint kinetics during stance phase did not differ significantly post-treatment from that of baseline testing (Table 3).

Patient self-reported WOMAC pain scores and function scores revealed a significantly favorable outcome at the 3-month follow-up and the 9-month end-point ($p < 0.001$). Subjects reported significant pain relief after three months of treatment with a mean difference of 2.36 cm and an additional minor relief at the 9-month end point (Table 4). On the WOMAC function scale, the subjects reported significant improvement with a mean decrease of 2.5 cm after three months and 2.9 cm after nine months. The SF-36 health survey showed significant favorable changes after three months and after nine months of treatment (Table 4).

Table 1
Comparison of KAM values (N=25).

	Loading response (1st) peak [N-m/kg]	Terminal stance (2nd) peak [N-m/kg]	Knee adduction impulse [N-m/kg*sec]
Group values			
Pretraining	0.71 ± 0.18	0.55 ± 0.15	3.92 ± 1.16
Post training (3 months)	0.65 ± 0.15	0.48 ± 0.15	3.38 ± 1.23
Post training (9 months)	0.60 ± 0.16	0.45 ± 0.15	3.25 ± 1.20
P	0.002	< 0.001	< 0.001

Note: Values represent mean values and standard deviation.

Table 2
Comparison of KAM values—subgroup analysis.

	Loading response (1st) peak [N-m/kg]	Terminal stance (2nd) peak [N-m/kg]	Knee adduction impulse [N-m/kg*sec]
KL 3–4 subgroups			
Pretraining	0.72 ± 0.18	0.59 ± 0.15	4.04 ± 1.06
Post training (3 months)	0.63 ± 0.14	0.48 ± 0.14	3.34 ± 1.11
Post training (9 months)	0.59 ± 0.15	0.46 ± 0.15	3.33 ± 1.18
P	0.005	0.001	0.002
KL 2 subgroup			
Pretraining	0.71 ± 0.20	0.48 ± 0.13	3.74 ± 1.34
Post training (3 months)	0.67 ± 0.17	0.47 ± 0.16	3.44 ± 1.46
Post training (9 months)	0.60 ± 0.19	0.44 ± 0.15	3.14 ± 1.27
P	0.150	0.020	0.045

Note: Values represent mean values and standard deviation.

Table 3
Comparison of mean knee and hip sagittal kinematics values ($n=25$).

Knee flexion angle	Initial contact	Peak knee extension (terminal stance)	Total range of motion
Pretraining	9.13 ± 4.99	7.85 ± 3.54	52.59 ± 7.03
Post training (3 months)	10.25 ± 4.16	6.13 ± 2.57	53.11 ± 6.69
Post training (9 months)	9.38 ± 4.82	6.31 ± 2.08	55.39 ± 6.43
P	0.61	0.2	0.06
Hip flexion angle	Peak hip flexion (loading response)	Peak hip extension (terminal stance)	Total range of motion
Pretraining	1.78 ± 7.62	48.52 ± 9.07	46.73 ± 7.47
Post training (3 months)	0.13 ± 5.89	46.09 ± 7.10	45.97 ± 5.20
Post training (9 months)	0.79 ± 7.41	47.5 ± 8.82	46.71 ± 6.34
P	0.33	0.53	0.88

Note: All values represent degree of knee flexion angle; values represent the mean values and standard deviation.

Table 4
Clinical outcome via self-reported subjective questionnaires.

	Baseline	Follow-up (3 months)	Final (9 months)	P value
WOMAC				
Pain	4.1 ± 2.3	1.7 ± 1.3	1.6 ± 1.5	< 0.001
Stiffness	5.2 ± 3.2	2.5 ± 2.1	1.6 ± 1.5	< 0.001
Function	4.6 ± 2.2	2.1 ± 1.6	1.7 ± 1.2	< 0.001
SF-36				
Physical functioning	48.1 ± 22.2	67.9 ± 18.8	68.1 ± 15	< 0.001
Limitation due to physical health	41.7 ± 42.1	72.9 ± 31.2	70.8 ± 35.9	0.005
Limitation due to emotional problem	55.6 ± 45.7	69.4 ± 36.7	80.6 ± 30.9	0.09
Energy/fatigue	54.4 ± 17.9	62.9 ± 17.4	68.3 ± 15	0.004
Emotional well-being	67.2 ± 13.5	76.5 ± 8.5	74.5 ± 8.3	0.25
Social functioning	64.1 ± 28.6	87 ± 17.1	93.2 ± 11.6	< 0.001
Pain	39.7 ± 17.2	67.4 ± 20.9	63.65 ± 18.3	< 0.001
General health	62.5 ± 15.2	66.7 ± 13.5	72.6 ± 12	0.001

Notes: Outcome measures: The WOMAC questionnaire includes 24 questions in a VAS format (0–10 cm scale), where each value represents the average score for the pain/stiffness/function sub-categories.

SF-36 Health survey (0–100 scale).

Mean values are presented as mean ± SD.

The p-value represents the group differences in the three examination points.

4. Discussion

The current longitudinal study examined the outcome of continuous biomechanical treatment (AposTherapy) incorporating load reduction and repetitive perturbation stimuli for medial knee OA patients. Similar to the previous studies (Bar-Ziv et al., 2010; Elbaz et al., 2010), functional and subjective self-reported measurements were significantly influenced by this biomechanical intervention. The data presented in this report indicate that significant alterations in the kinetic gait parameters are accompanied by these changes.

Motion gait analyses demonstrated a significant reduction in the magnitude of the knee adduction impulse and of the 1st and the 2nd peaks of KAM after three and nine months of treatment. The KAM has been acknowledged as a marker for disease severity, and is increasingly utilized as an outcome measure in intervention studies. Several authors have reported KAM reduction with biomechanical training; Thorstenson et al. (2007) reported that, following an 8-week supervised exercise program for knee OA patients, peak adduction moment during one-leg rise was reduced, yet KAM during gait did not significantly differ. Erhart et al. (2010) reported a 6.6% reduction of KAM for subjects with knee OA wearing variable-stiffness shoes for six months. In the previous studies (Haim et al., 2008; Haim et al., 2010), we demonstrated that the tested apparatus can alter the foot center of pressure in the sagittal and the coronal planes, thereby conveying modulation of joint loads, reducing pain, and enabling exposure to repetitive perturbation stimuli during gait. We speculate that this vigorous intervention (AposTherapy) and the

longer follow-up in the current study led to enhanced proprioceptive capabilities and muscle activation patterns, thereby decreasing KAM values during gait.

Pre-training gait analysis testing revealed that the 2nd peak of the KAM was higher for the KL 3–4 subgroup than for the KL 2 subgroup. This finding is in agreement with the report by Mundermann et al. (2005) that examined KAM in patients with knee OA and matched healthy controls. In patients with severe knee OA, Mundermann et al. (2005) reported that both the 1st and the 2nd peaks of the KAM were elevated, while the 2nd peak was lower in patients early in the course of the disease.

The data presented here offers significant clinical implications for subjects with medial compartment knee OA. Elevated KAM has been identified as a key component responsible for excessive medial compartment loads in this population, contributing to disease progression. Previous studies have described inadequate neuromuscular control and elevated co-contractions in this population and have suggested that they convey elevated KAM magnitude (Fisher and Pendergast, 1997; Sharma et al., 1999). The present study concurs with the paradigm that sub-optimal muscle activation contributes to abnormal KAM magnitude in this population. Furthermore, the results presented here demonstrate that the KAM can be effectively influenced by continuous biomechanical perturbation training coupled with load redistribution via modification in COP, in various stages of the disease. Reduction of KAM could account for the improved function and pain reduction seen here. Moreover, since elevated KAM is a dominant factor in continued joint destruction, these findings may alter the

natural history of this pathology and suggest that such training could possibly halt disease progression.

Several limitations arising from the current study should be noted. Firstly, the study cohort was relatively small, although statistical significance was reached for all primary outcome measurements. Another limitation of this study was the lack of a control group. Ideally, this control group would be comprised of knee OA patients instructed to carry out the same treatment procedure without using the biomechanical device. Nevertheless, the primary outcome measurements of this study were objective gait parameters that are not frequently used in longitudinal knee OA studies. Moreover, a prospective controlled study implementing the same interventional methodology reported similar functional outcomes, supporting the validity of the current study (Bar-Ziv et al., 2010). Finally, the current study focused on a unique group (i.e., females with medial compartment knee OA). These results are therefore applicable only for subjects with characteristics similar to those of the study cohort.

In conclusion, these results demonstrate that the KAM, a key component of the pathomechanic process of medial compartment knee OA, can be successfully altered via non-invasive biomechanical intervention. In addition to functional and symptomatic improvement, such an outcome may lead to delay in disease development and progression.

Conflict of interest statement

No author has any conflict of interest to declare.

Acknowledgment

The authors thank Apos Medical and Sports Technologies Ltd. for their generosity in contributing the devices used in the study.

References

- Andriacchi, T.P., 1994. Dynamics of knee malalignment. *Orthopedic Clinics of North America* 25, 395–403.
- Baliunas, A.J., Hurwitz, D.E., Ryals, A.B., et al., 2002. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis and Cartilage* 10, 573–579.
- Bar-Ziv, Y., Beer, Y., Ran, Y., et al., 2010. A treatment applying a biomechanical device to the feet of patients with knee osteoarthritis results in reduced pain and improved function: a prospective controlled study. *BMC Musculoskeletal Disorders* 11, 179.
- Bijlsma, J.W., Berenbaum, F., Lefeber, F.P., 2011. Osteoarthritis: an update with relevance for clinical practice. *Lancet* 377, 2115–2126.
- Debi, R., Mor, A., Segal, O., et al., 2009. Differences in gait patterns, pain, function and quality of life between males and females with knee osteoarthritis: a clinical trial. *BMC Musculoskeletal Disorders* 10, 127.
- Elbaz, A., Mor, A., Segal, G., et al., 2010. APOS therapy improves clinical measurements and gait in patients with knee osteoarthritis. *Clinical Biomechanics* (Bristol, Avon) 25, 920–925.
- Erhart, J.C., Mündermann, A., Elspas, B., et al., 2010. Changes in knee adduction moment, pain, and functionality with a variable-stiffness walking shoe after 6 months. *Journal of Orthopaedic Research* 28, 873–879.
- Felson, D.T., Zhang, Y., 1998. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. *Arthritis and Rheumatism* 41, 1343–1355.
- Fisher, N.M., Pendergast, D.R., 1997. Reduced muscle function in patients with osteoarthritis. *Scandinavian Journal of Rehabilitation Medicine* 29, 213–221.
- Fitzgerald, G.K., Childs, J.D., Ridge, T.M., Irrgang, J.J., 2002. Agility and perturbation training for a physically active individual with knee osteoarthritis. *Physical Therapy* 82, 372–382.
- Gok, H., Ergin, S., Yavuzer, G., 2002. Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. *Acta Orthopaedica Scandinavica* 73, 647–652.
- Haim, A., Rozen, N., Dekel, S., et al., 2008. Control of knee coronal plane moment via modulation of center of pressure: a prospective gait analysis study. *Journal of Biomechanics* 41, 3010–3016.
- Haim, A., Rozen, N., Wolf, A., 2010. The influence of sagittal center of pressure offset on gait kinematics and kinetics. *Journal of Biomechanics* 43, 969–977.
- Hortobagyi, T., Westerkamp, L., Beam, S., et al., 2005. Altered hamstring-quadriciceps muscle balance in patients with knee osteoarthritis. *Clinical Biomechanics* (Bristol, Avon) 20, 97–104.
- Hurley, M.V., 2003. Muscle dysfunction and effective rehabilitation of knee osteoarthritis: what we know and what we need to find out. *Arthritis and Rheumatism* 49, 444–452.
- Hurley, M.V., Scott, D.L., 1998. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. *British Journal of Rheumatology* 37, 1181–1187.
- Hurwitz, D.E., Ryals, A.R., Block, J.A., et al., 2000. Knee pain and joint loading in subjects with osteoarthritis of the knee. *Journal of Orthopaedic Research* 18, 572–579.
- Hurwitz, D.E., Ryals, A.R., Case, J.P., et al., 2002. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. *Journal of Orthopaedic Research* 20, 101–107.
- Iannone, F., Lapidula, G., 2003. The pathophysiology of osteoarthritis. *Aging Clinical and Experimental Research* 15, 364–372.
- Johansson, H., Pedersen, J., Bergenheim, M., Djupsjobacka, M., 2000. Peripheral afferents of the knee: their effects on central mechanisms regulating muscle stiffness, joint stability, and proprioception and coordination. In: Lephart, S.M., Fu, F.H. (Eds.), *Proprioception and Neuromuscular Control in Joint Stability*, Human Kinetics, Champaign, pp. 5–23.
- Kadaba, M.P., Ramakrishnan, H.K., Wootten, M.E., 1990. Measurement of lower extremity kinematics during level walking. *Journal of Orthopaedic Research* 8, 383–392.
- Lewek, M.D., Ramsey, D.K., Snyder-Mackler, L., Rudolph, K.S., 2005. Knee stabilization in patients with medial compartment knee osteoarthritis. *Arthritis and Rheumatism* 52, 2845–2853.
- Miyazaki, T., Wada, M., Kawahara, H., et al., 2002. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Annals of the Rheumatic Diseases* 61, 617–622.
- Moreland, J.R., Bassett, L.W., Hanker, G.J., 1987. Radiographic analysis of the axial alignment of the lower extremity. *Journal of Bone and Joint Surgery (American)* 69, 745–749.
- Mundermann, A., Dyrby, C., Andriacchi, T., 2005. Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis and Rheumatism* 52, 2835–2844.
- Oliveria, S.A., Felson, D.T., Reed, J.L., Cirillo, P.A., Walker, A.M., 1995. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis and Rheumatism* 38, 1134–1141.
- Radin, E.L., Burr, D.B., Caterson, B., et al., 1991. Mechanical determinants of osteoarthrosis. *Seminars in Arthritis and Rheumatism* 21 (3 Suppl 2), 12–21.
- Roddy, E., Zhang, W., Doherty, M., et al., 2005. Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee—the MOVE consensus. *Rheumatology (Oxford)* 44, 67–73.
- Roemhildt, M.L., Coughlin, K.M., Peura, G.D., et al., 2010. Effects of increased chronic loading on articular cartilage material properties in the lapine tibiofemoral joint. *Journal of Biomechanics* 43, 2301–2308.
- Sharma, L., Dunlop, D.D., Cahue, S., et al., 2003. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. *Annals of Internal Medicine* 138, 613–619.
- Sharma, L., Hurwitz, D.E., Thonar, E.J., et al., 1998. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis and Rheumatism* 41, 1233–1240.
- Sharma, L., Lou, C., Felson, D.T., et al., 1999. Laxity in healthy and osteoarthritic knees. *Arthritis and Rheumatism* 42, 861–870.
- Slemenda, C., Heilman, D.K., Brandt, K.D., et al., 1998. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? *Arthritis and Rheumatism* 41, 1951–1959.
- Thorstensson, C.A., Henriksson, M., von Porat, A., et al., 2007. The effect of eight weeks of exercise on knee adduction moment in early knee osteoarthritis—a pilot study. *Osteoarthritis and Cartilage* 15, 1163–1170.