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Principal component modeling of isokinetic moment curves for discriminating between the injured and healthy knees of unilateral ACL deficient patients

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ABSTRACT

Bilateral knee strength evaluations of unilateral anterior cruciate ligament (ACL) deficient patients using isokinetic dynamometry are commonly performed in rehabilitation settings. The most frequently-used outcome measure is the peak moment value attained by the knee extensor and flexor muscle groups. However, other strength curve features may also be of clinical interest and utility. The purpose of this investigation was to identify, using Principal Component Analysis (PCA), strength curve features that explain the majority of variation between the injured and uninjured knee, and to assess the capabilities of these features to detect the presence of injury. A mixed gender cohort of 43 unilateral ACL deficient patients performed 6 continuous concentric knee extension and flexion repetitions bilaterally at $60^\circ\ s^{-1}$ and $180^\circ\ s^{-1}$ within a 90° range of motion. Moment waveforms were analyzed using PCA, and binary logistic regression was used to develop a discriminatory decision rule. For all directions and speeds, a statistically significant overall reduction in strength was noted for the involved knee in comparison to the uninvolved knee. The discriminatory decision rule yielded a specificity and sensitivity of 60.5% and 60.5%, respectively, corresponding to an accuracy of ~62%. As such, the curve features extracted using PCA enabled only limited clinical usefulness in discerning between the ACL deficient and contra lateral, healthy knee. Improvement in discrimination capabilities may perhaps be achieved by consideration of different testing speeds and contraction modes, as well as utilization of other data analysis techniques.

1. Introduction

Isokinetic dynamometry-based strength evaluations of unilateral anterior cruciate ligament (ACL) deficient patients allow establishment of baseline scores to which the post-operative status may be compared, and may also be used to assess progress of pre-surgical conditioning programs. In such evaluations, comparisons of scores of the injured knee to those obtained from the uninvolved counterpart are routine, with the most frequently used outcome measure being the peak moment (PM) value attained by the knee extensor and flexor muscle groups (Eitzen et al., 2010). The widespread use of the PM value may be related to the intuitive understanding regarding its meaning, as well as the likelihood of a high association between the PM and other curve magnitude measures, such as average moment, work, and power (Dvir, 2004). That is, reporting of multiple outcomes may be redundant since they may provide the same information regarding muscle strength production capabilities.

Nonetheless, several investigations have pointed out that, in the bilateral isokinetic-based comparison of the injured and healthy knees of unilateral ACL deficient patients, there are other strength curve features that may be of clinical interest. Specifically, Eitzen et al. (2010) found in an angle-specific analysis of concentric knee extension moment curves that inter-limb strength deficiencies

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were most pronounced when considering strength values attained at knee flexion angles of less than 40° (i.e. approaching full knee extension). In an earlier study, Shirakura et al. (1992) found that while no bilateral deficiencies were detected when using PM values, these emerged when considering strength values obtained at less than 54° of knee extension. In addition, Stratford et al. (1987) and Ikeda et al. (2002) point out that, in some ACL deficient patients, the shape of the concentric knee extension moment curve of the injured limb assumes a rapid downward slope following the angle at which PM is reached, whilst in other patients the moment curve assumes a double hump shape (Kegerreis and Malone, 1982; Stratford et al., 1987). Lastly, frequency content analysis of isokinetic knee moment curves of ACL deficient patients revealed unsteadiness (i.e. higher frequency content) in strength production in comparison to the counterpart healthy knee or healthy controls (Bryant et al., 2011; Tsepis et al., 2004). Thus, based on previous findings, it seems that in the isokinetic-based assessment of knee musculature strength of unilateral ACL deficient patients, moment curve features other than the PM may reveal the presence of, or accentuate, bilateral deficiencies.

However, given the large number of potential measures that may be obtained from isokinetic-based strength curves, a question arises as to which of these variables are most suitable for extraction? One method by which this problem may be resolved is via analyses of moment waveforms using Principal Component Analysis (PCA) (see reviews by Astephen and Deluzio, 2009; Chau, 2001a; Daffertshofer et al., 2004; Wang et al., 2013). PCA, which to our knowledge has never been used for analyses of isokinetic moment waveforms, seems well-suited for the problem at hand since the exploratory nature of the method does not require *a priori* decisions regarding the selection of outcomes. Rather, PCA objectively identifies curve features that are uncorrelated, hence eliminating potential outcome redundancy. That is, the features identified using PCA provide different information regarding the sources of variation between compared scores (Astephen and Deluzio, 2009; Wang et al., 2013).

In addition, the extracted PCA features may be interpreted in a manner that is clinically relevant (Astephen and Deluzio, 2009; Brandon et al., 2013). In particular, it has been demonstrated that by utilizing visual interpretation methods (Brandon et al., 2013; O'Connor and Bottom, 2009; Ramsay and Silverman, 2002), differences in overall magnitude, phase shifting, and relative variations in the magnitude of local peaks can be discerned between two sets of curves (such as those obtained during isokinetic testing of the ACL deficient and healthy knee). Thus, PCA could allow a researcher to assess, for example, whether bilateral strength deficiencies are evident throughout the entire tested range of motion (ROM) or manifested only in a specific portion of the ROM, or whether there is a shift in the location of peaks (and since moment values can be expressed in relationship to an angular position vector, also allow stating the degree of this phase shift). From a clinical perspective, the identification of such features may assist in developing patient-specific pre-surgical conditioning programs. For example, if a bilateral strength deficiency was detected in only a portion of the ROM, it could be possible to construct an exercise program that, at least for a period of time, targets the strength-deficient portion of the ROM in order to achieve bilateral symmetry.

Furthermore, since by definition PCA identifies curve features that are uncorrelated, the use of these features is beneficial, from a statistical point of view (Hosmer et al., 2013), for development of a discriminatory model concerned with diagnosing the presence of injury. This issue is of interest since the accuracy of the most common clinical tests performed for diagnosis of ACL rupture (i.e. the Lachman; anterior drawer; and the pivot shift tests) is compromised due to dependence on the level of orthopaedic expertise (Benjaminse et al., 2006; Peeler et al., 2010). For example, the percentage of times the clinical tests concurred with the gold standard, surgical-based diagnosis of a ruptured ACL was found to be 46% for board certified therapists; 60% for family medicine physicians, and; 87% for orthopaedic surgeons (Peeler et al., 2010). Since those with lesser orthopaedic training or experience (e.g. physical therapists and athletic trainers) may be more skilled with performance of isokinetic dynamometry testing, exploring the possibility of improving the diagnostic accuracy of these professionals based on isokinetic strength outputs may facilitate effective referral to orthopaedic specialists, which in turn may result in lessening of health care costs. It should be noted that, to our knowledge, all of the previous research concerned with isokinetic-based strength of unilateral ACL deficient patients have not attempted to use outputs for purposes of objective diagnosis, but rather report upon comparative group differences between the injured and non-injured knee, or use qualitative examination of the moment curves to gain indications of the presence of injury. Thus, attempting to establish a quantitative prediction rule for diagnosis purposes is a novel endeavor in this particular subject area.

Accordingly, this investigation had two aims: Firstly, to exploit the underlying basis of PCA to identify orthogonal knee isokinetic strength curve features that are most prominent in explaining the variations between the involved and uninvolved knee of unilateral ACL deficient patients. Secondly, this investigation aimed at assessing whether these curve features may be used to discriminate between the involved and uninvolved knees for development of an objective prediction rule that may assist in determination of the presence of injury.

2. Methods

2.1. Participants

Injured participants were recruited through direct contact from a patient list awaiting surgical reconstruction of their ACL. Study exclusion criteria were identified using a self-report medical questionnaire and by physician consultation. These criteria included: current or previous musculoskeletal injury to the contralateral knee; being diagnosed with or being at risk of developing high blood pressure levels; carotid and coronary artery disease; and current use of medication (excluding contraceptives). ACL rupture was diagnosed by a single orthopaedic surgeon using standard clinical methods, and occasionally accompanied with signs observed utilizing magnetic resonance imaging. In all cases, final confirmation of a complete ACL rupture was achieved during the arthroscopic surgical procedure.

The patient cohort consisted of 44 participants. However, results of a single participant were excluded from the study, since it was confirmed during the surgical procedure that the injury sustained was not an ACL rupture. As such, data used were from 43 participants: 22 men (mean and standard deviation age: 31.2 ± 11 years, height: 176 ± 5 cm, mass: 84 ± 11 kg) and 21 women (age: 35.9 ± 13.8 years, height: 171 ± 11 cm, mass: 78 ± 21 kg). None of the participants had injury to the posterior or lateral collateral ligaments. However, 27 participants had at least one meniscal lesion of various severity and location, and 13 also had chondral lesions of various grades. Testing was performed between 2 and 12 months following the injurious event. The participants were engaged on average in 2.9 ± 2.2 h of physical activity primarily consisting of walking, running, and weight-lifting. None of the participants had previous experience with isokinetic-based strength testing. The study procedures were reviewed for ethical compliance and received approval by the Queen's University

Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

2.2. Procedures

Upon arrival to the laboratory, the participants were informed about the study's aims and procedures and thereafter provided written informed consent. Testing was performed on both the injured and non-injured knees. Participants performed a general warm-up consisting of cycling for 3 min on a stationary bicycle at a submaximal level, followed by examiner-guided stretches of the knee extensor and flexor muscle groups (Almosnino et al., 2011). Thigh musculature strength was assessed using a Biodex Multi-Joint System 4 isokinetic dynamometer (Biodex Medical Systems Inc., Shirley, NY, USA). Testing was performed in a seated position, with the chair's back rest set at 85°. The participant was secured to the chair using two straps across the chest, and single straps at the abdomen and distal thigh of the tested limb. The dynamometers' axis of rotation was aligned with lateral femoral condyle, and the lever arm pad was secured to the participant's distal shank at the level of the medial malleolus in a manner that did not restrict ankle joint motion. Testing was performed through a 90° range of motion (ROM), with 0° signifying full knee extension (Eitzen et al., 2010). For familiarization, the participants performed 5 continuous sets of 4 repetitions throughout the entire ROM at descending testing velocities from 180°/s to 60°/s in 30°/s increments. Thereafter, to facilitate production of maximal efforts, the participants performed 2 sets at the first testing velocity of 60°/s; each consisting of 2–3 repetitions at a self perceived 80% and 90% of maximal effort level, respectively. This was followed by 1–2 sets of 2 repetitions performed at maximal effort (Almosnino et al., 2011). Following 2–3 min of rest, the dynamometers setting was adjusted to the higher testing velocity of 180°/s and the maximal effort facilitation procedure was repeated.

Following 3–5 min of rest, the participants performed 1 set of 6 repetitions at each testing velocity. The uninvolved knee was always tested first (Dvir, 2004; Eitzen et al., 2010), and performance at the slower angular velocity always preceding the higher one. A rest period of 2–3 min was administered between sets (Celes et al., 2010), whilst a rest period of approximately 10 min separated testing of the two limbs. Throughout testing, the participants were encouraged to utilize the concurrent moment–time display, as well to grip the side handle bars as hard as they could; to brace their abdominal muscles in a manner such that their abdomen was pushing against the abdominal restraint; to maintain constant contact of the back of their head with the chair's headrest; and not to decelerate the lever arm at end ranges of motion (Almosnino et al., 2011).

Testing was performed by 2 different examiners with graduate degrees in health related fields who each possessed 2 years of experience in isokinetic testing of the knee, as well as other joints. To reduce potential inter-examiner induced variability, standardized instructions were given by both examiners to the participants regarding: the operation of the dynamometer; any risks related to participation; performance of the movement task; and use of the real-time graphical moment time-series for visual feedback purposes. The wording and tone of voice of the audible feedback given throughout testing was carefully controlled. Angular position, velocity, and moment data were sampled at 100 Hz using the manufacture's proprietary software and stored for offline analyses.

2.3. Data analyses

Gravity-corrected moment data were segmented into individual extension or flexion repetitions based on the angular position data vector. All repetitions were used in subsequent analyses, since for several participants the highest peak moment value was attained during performance of the first repetition, whilst for the majority of participants the last repetition was not the weakest one; this indicates that the subjects did not experience fatigue. To eliminate possible contributions of erroneous moment values at the initial and end ROM due to acceleration and deceleration of the lever arm (Bryant et al., 2009; Eitzen et al., 2010; Iossifidou and Baltzopoulos, 1998; Schwartz et al., 2010), only strength data obtained between 6°–84°, and 20°–70° was retained for efforts performed at 60°/s and 180°/s, respectively. The aforementioned ROM values corresponded to the largest ROM attained by any study participant without a noticeable moment artefact. These ROM were verified by the lead investigator who visually inspected (Tsepis et al., 2004) overlaid moment, lever arm velocity and angular position plots of each individual set. A moment artefact was defined as any noticeable spike that is close to or exceeds PM value during the initial acceleration phase of the lever arm or apparent during change of direction from extension to flexion, and vice versa. On occasion, due to data resolution limits the number of data points composing individual repetitions differed by 1 discrete point within a given set. As PCA procedures require that data are of equal length, all repetitions at 60°/s and 180°/s were interpolated using a piecewise cubic hermite interpolating polynomial to 130 and 42 data points corresponding to 78° and 50° of ROM in 0.61° and 1.19° increments, respectively. Note that the differences in the number of data points comprising the strength curves at each testing velocity are primarily due to the fixed sampling rate and the equivalent range of motion used in both testing velocities. This results in strength curves from the slow velocity trials having roughly three times as many data points as those obtained from the faster velocity trials. In addition, note that a larger portion of the ROM was eliminated from the faster trials.

PCA calculation procedures resemble those previously described for analysis of gait-derived waveforms (Brandon and Deluzio, 2011; Deluzio and Astephen, 2007; Deluzio et al., 1999, 1997; Reid et al., 2010): Extension and flexion data obtained at a testing velocity of 60°/s were arranged into two separate 516×130 matrices, where the number of rows corresponds to 43 participants $\times$ 6 individual repetitions $\times$ 2 legs (injured and non-injured), and the number of columns corresponds to discrete moment values of each repetition within the ROM. Similarly, data per direction obtained at 180°/s were arranged into two separate 516×42 matrices.

Each data matrix was mean centered, and the associated covariance matrix was subsequently calculated. The next step in computation involved the eigenvalue decomposition of the covariance matrix; this was achieved according to the principal component model $Z = [U^t X]$, where U is the transformation matrix that rotates the original data observations into a new coordinate system. The columns of U are the eigenvectors of the covariance matrix of the original data set, and are termed principal component loading vectors (Deluzio and Astephen, 2007; Deluzio et al., 1999, 1997). The PCs were extracted in a hierarchical fashion based on the amount of variation they explained; this was calculated by dividing the specific eigenvalue for each corresponding PC by the trace of the covariance matrix.

The next step involved a decision as to the number of PCs to retain for further analysis. Several methods have been used for such purposes (Fischer et al., 2012; Wang et al., 2013), including a decision to keep all PCs explaining a cumulative percentage of variation (e.g. 90% trace criterion, Reid et al., 2010); retaining all PCs whose eigenvalue is greater than 1 (e.g. Bockemühl et al., 2010); identification of a 'break'/'elbow' in a plot of the eigenvalues against the PCs (e.g. Muniz and Nadal, 2009), and retaining those PCs that ex-

Table 1
Description of the principal component (PC) models for isokinetic knee extension and flexion moment curves. Data presented as mean ± SD where appropriate.

Direction and testing velocity	PC #	Explained variance[a] (%)	PC Scores healthy knee	PC Scores injured knee	p Value
Extension 60°/s	1	83.5	−0.68 ± 2.96	0.68 ± 3.3	<0.001[b]
	2	13.6	−0.08 + 1.72	0.08 ± 1.38	0.36
	3	1.4	0.00 ± 0.45	0.00 ± 0.45	0.98
	4	0.8	−0.02 ± 0.33	0.02 ± 0.31	0.36
Flexion 60°/s	1	91.9	−0.33 ± 1.92	0.33 ± 1.87	0.001[b]
	2	4.6	−0.01 ± 0.43	0.01 ± 0.44	0.80
	3	1.7	0.00 ± 0.29	0.00 ± 0.29	0.98
	4	0.7	−0.01 ± 0.19	0.01 ± 0.14	0.41
Extension 180°/s	1	84.2	−0.22 ± 1.16	0.22 ± 1.29	<0.001[b]
	2	10.3	0.00 ± 0.01	0.00 ± 0.00	0.96
	3	1.8	−0.01 ± 0.15	0.01 ± 0.16	0.41
	4	1.2	−0.01 ± 0.14	0.01 ± 0.12	0.43
Flexion 180°/s	1	85.6	−0.88 ± 5.74	0.88 ± 5.81	0.002[b]
	2	6.5	0.04 ± 1.49	−0.04 ± 1.53	0.70
	3	2.8	0.04 ± 1.07	−0.04 ± 0.91	0.51
	4	1.7	0.10 ± 0.75	−0.10 ± 0.65	0.03

[a] Sum of explained variance: Extension 60°/s = 99.3%, Flexion 60°/s = 98.9%, Extension 180°/s = 97.5%, Flexion 180°/s = 96.6%.
[b] Denotes statistical difference between scores of the injured and contra lateral, healthy knee.

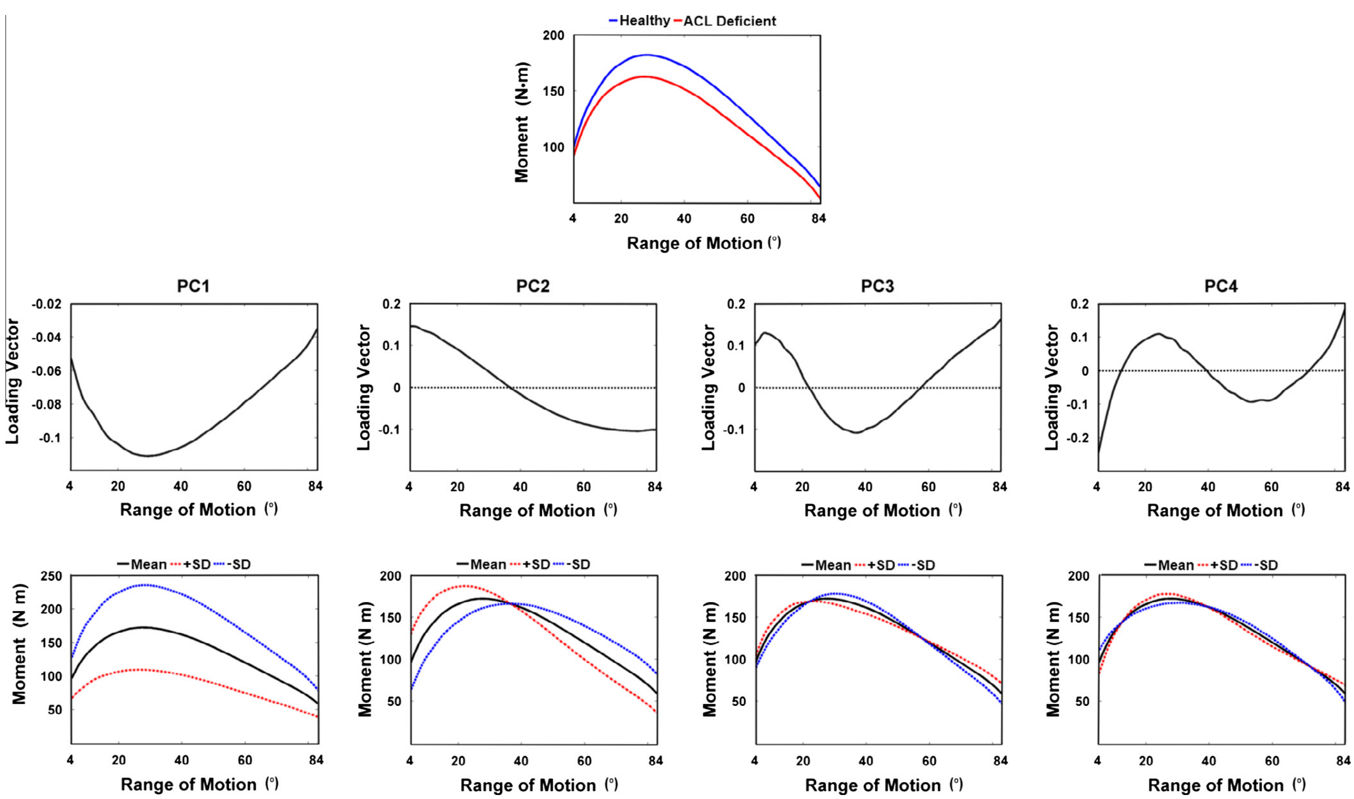

Fig. 1. Principal Component Analysis (PCA) results of isokinetic knee extension moment waveforms obtained at a testing velocity of 60°/s. 1st row: group mean moment waveform for the healthy (blue) and ACL deficient (red) knee. 2nd row: Loading vector plots of the PC of interest. 3rd row: Ensemble moment curve across all conditions ± 1 SD of the variation due to the PC loading vector shown in the 2nd row. Blue and Red SD curves correspond with Healthy and ACL deficient knees, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

plain more variance than can be expected by chance alone (e.g. Wrigley et al., 2006). In the current investigation, however, these methods were not used as there was a need to balance the following factors: (1) To avoid over-fitting of the developed discriminatory model, the number of PCs to be used was constrained *a priori* by a minimum 10 to 1 ratio of the number of cases (subjects) per independent variable (Steyerberg et al., 2000); (2) Despite capturing the majority of the variance, the first 1–2 PCs may not necessarily possess optimal discriminatory capabilities (Astephen and Deluzio, 2004), which is a primary aim of this investigation, and; (3) Conversely, higher order PCs may differ between groups, but are inherently less stable and more difficult to interpret in a clinically relevant manner (Brandon et al., 2013; Fischer et al., 2012). Therefore, we extracted the maximum of 4 PCs for each direction and testing velocity, for a total of 16 PC scores. Note that in all cases, these PCs were subsequently found to explain more than 96% of the variation between the involved and uninvolved knees.

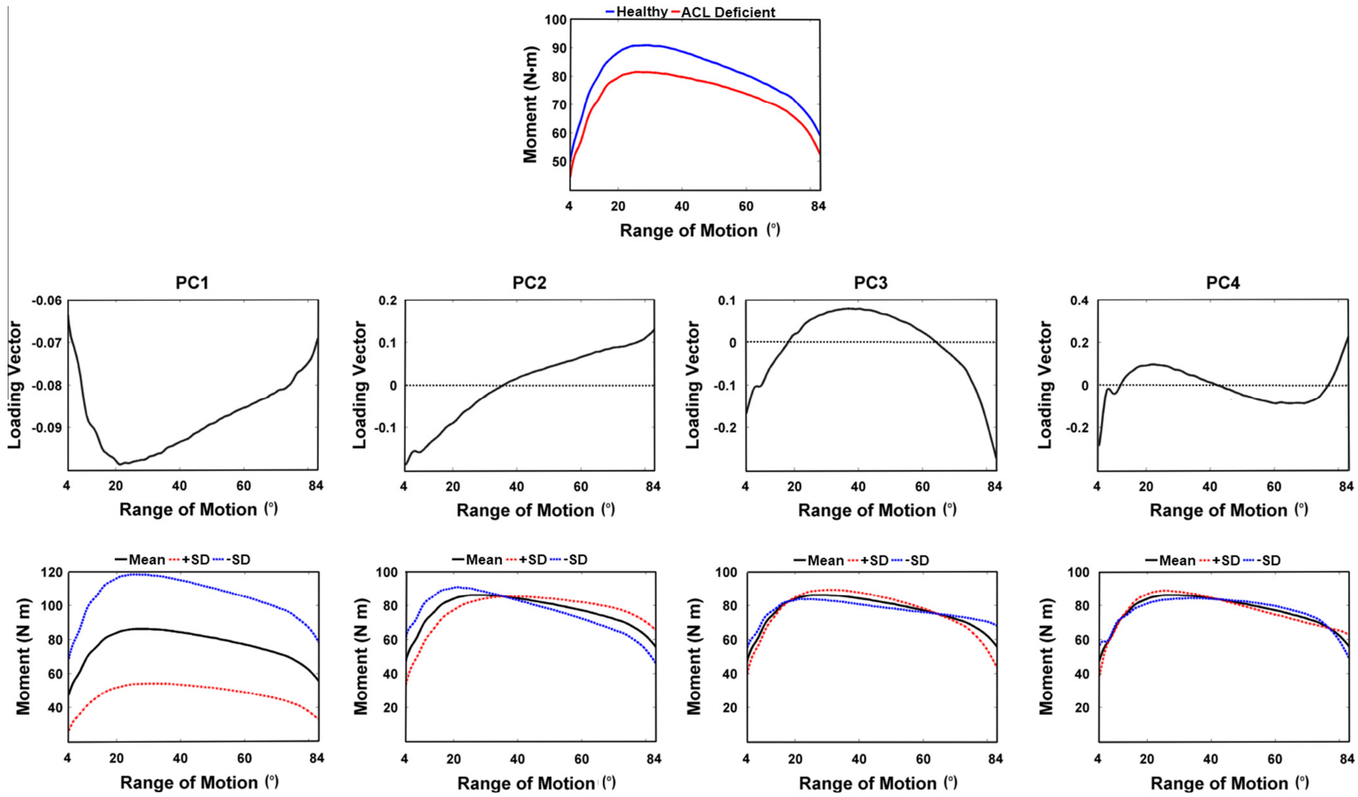

Fig. 2. Principal Component Analysis (PCA) results of isokinetic knee flexion moment waveforms obtained at a testing velocity of 60°/s. 1st row: group mean moment waveform for the healthy (blue) and ACL deficient (red) knee. 2nd row: Loading vector plots of the PC of interest. 3rd row: Ensemble moment curve across all conditions ± 1 SD of the variation due to the PC loading vector shown in the 2nd row. Blue and Red SD curves correspond with Healthy and ACL deficient knees, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.4. Statistical analyses

Prior to analyses, PC scores attained for each direction and testing velocity were assessed for normality of distribution by evaluation of normalized skewness and kurtosis scores, inspection of normal Q–Q plots, as well as Shapiro–Wilk test results. Data were judged to adhere to normality assumptions, and differences between PC scores attained by the ACL deficient and healthy leg were subsequently assessed using paired, two tailed *t*-tests. For all statistical comparisons, alpha level was preset at 0.05 and adjusted for multiple comparisons using a Bonferonni procedure. The 16 PCs retained for analysis were interpreted via inspection of loading vector plots, and plots of the ensemble mean temporal waveform across both injured and noninjured legs bounded by the contribution of a single PC pattern of variance, which in turn, was scaled by one standard deviation of the group PC-scores (Brandon et al., 2013; O'Connor and Bottom, 2009).

Development of a decision rule for differentiating between the ACL deficient and healthy knee was achieved by construction of a binary logistic regression-based model. A best subset selection method was utilized to examine all possible combinations of 4 PCs from flexion and extension trials at each speed as independent variables (65535 total possible models). The significance of these models was subsequently evaluated using critical values of the chi square score statistic. A receiver operating characteristic (ROC) curve was then constructed to assess the performance of the retained model. In specifics, performance of the decision rule is reported in terms of the area under the ROC curve and associated 95% confidence intervals, as well as the cut-off point that optimizes both the sensitivity (the number out of the total number of ACL deficient knees who were correctly classified as having an ACL rupture) and specificity (the number out of the total number of ACL intact knees correctly classified as being healthy). Both sensitivity and specificity values are expressed as percentages (Fritz and Wainner, 2001).

3. Results

Descriptive statistics of those PCs retained for analysis are presented in Table 1, and graphical depictions for each direction and speed are presented in Figs. 1–4. For all directions and speeds, only the first PCs exhibited statistically significant differences ($p < 0.002$ in all cases) between the involved and uninvolved knees. Based on the examination of the loading vectors and single PC reconstruction plots, the first PC for each direction and speed were interpreted as measures of overall magnitude. That is, the involved knee exhibited significantly less strength throughout the entire tested ROM in comparison to the uninvolved knee for both directions and testing velocities.

The only estimated logistic model found to exceed chi square score test significance criteria was composed of only one predictor: PC1 of extension efforts performed at 60°/s. The model takes the form:

$$\mathrm{Prob(Injured)} = \frac{\exp(0.001 + 0.141(\mathrm{PC1Ext60})}{(1 + \exp(0.001 + 0.141(\mathrm{PC1Ext60})} \quad (1)$$

The performance of this model can be assessed using the associated ROC curve presented in Fig. 5. The area under the ROC curve expressed as a percentage equaled 62.2 (95% CI 50.5% – 74.0%). The

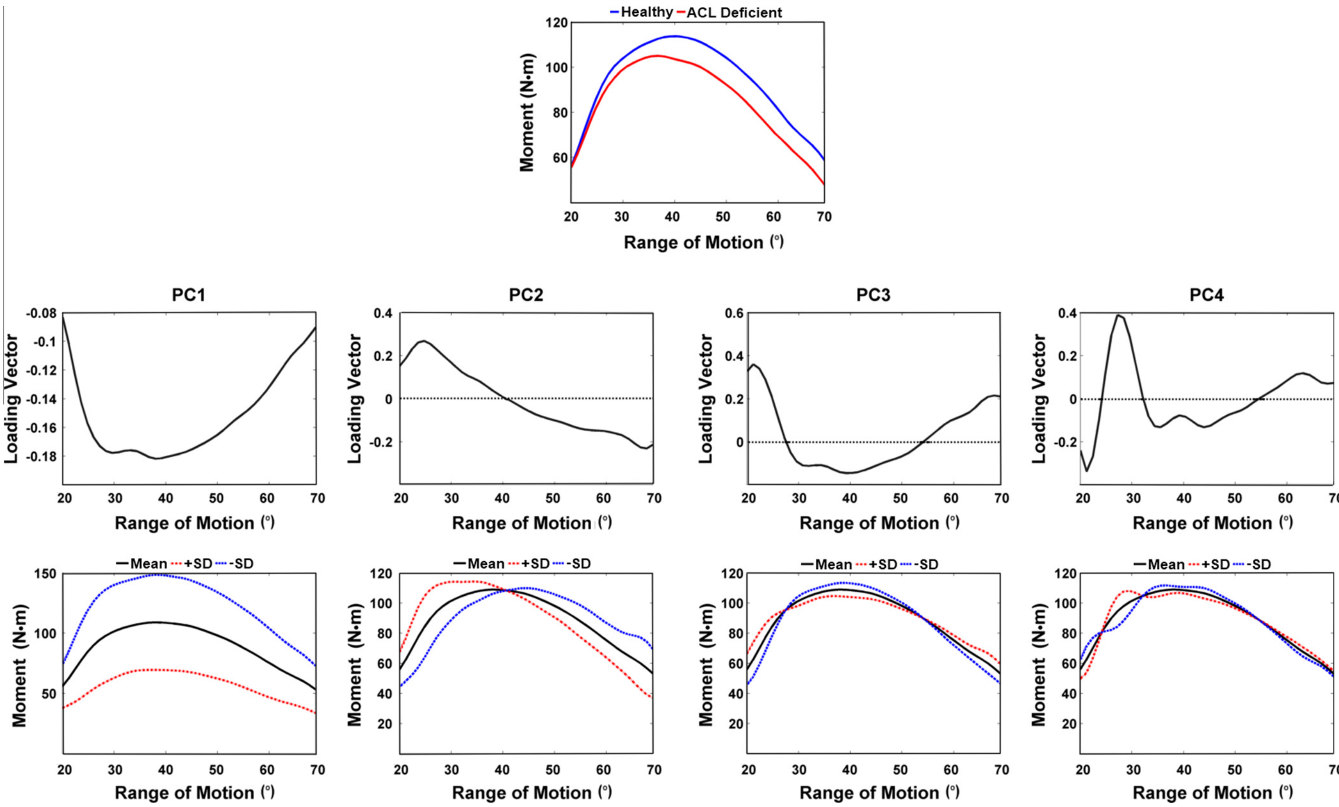

Fig. 3. Principal Component Analysis results of isokinetic knee extension moment waveforms obtained at a testing velocity of 180°/s. 1st row: group mean moment waveform for the healthy (blue) and ACL deficient (red) knee. 2nd row: Loading vector plots of the PC of interest. 3rd row: Ensemble moment curve across all conditions ± 1 SD of the variation due to the PC loading vector shown in the 2nd row. Blue and Red SD curves correspond with Healthy and ACL deficient knees, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

optimal cut-off point for differentiating between the injured and healthy knee yielded a sensitivity of 60.5% and a specificity of 60.5%.

4. Discussion

This investigation is the first to utilize PCA for the analysis of isokinetic-based strength curves, and the first to attempt to establish a quantitative prediction rule for detection of the presence of ACL deficiency using these outputs. It has been previously suggested that isokinetic moment curves obtained from participants with ACL deficiency deviate shape-wise from common observed patterns (Bryant et al., 2011, 2009; Ikeda et al., 2002; Kegerreis and Malone, 1982; Stratford et al., 1987; Tsepis et al., 2004), and exhibit more pronounced bilateral deficiencies if considering portions of the extension curve other than the PM (Eitzen et al., 2010; Shirakura et al., 1992). Thus, it seemed that the potential existed to utilize isokinetic moment output for detection of injury. However, the decision rule presented in the current investigation meant for such a purpose did not improve upon the accuracy of common clinical diagnostic tests when performed by experienced orthopaedic surgeons (Peeler et al., 2010). As such, several factors are in need of consideration for improvement of the current isokinetic-based diagnostic accuracy.

The first point relates to the appropriateness of using PCA for analysis of isokinetic moment curves. One of the underlying assumptions of PCA is that data is derived from a multivariate normal distribution, and given the lackluster results of the current investigation, we conducted a post hoc assessment of multivariate normality using a number of tests to assess whether this assumption was violated (Wang, 2013). In all cases, extension and flexion moment data were not normally distributed. However, we also performed these normality assessments on other data available to our disposal, and to which application of PCA proved to be successful (squat knee moment data, Almosnino et al., 2013; knee joint adduction moment gait waveforms; Brandon and Deluzio, 2011; lumbar spine kinematic waveforms during lifting, Sadler et al., 2011). These data did not adhere to normality assumptions either. Several notes with regards to the results of this post hoc analysis: Firstly, it should be noted that PCA is considered to be a statistically robust technique, which in essence means that analysis of data with non-Gaussian distribution characteristics does not seem to alter the interpretation of results (Reid and Spencer, 2009). In addition, it has been shown that PCA enables identification of curve features that differed between compared conditions, and these features were undetected when using standard outcome measures (e.g. Almosnino et al., 2013). Secondly, statistical significance is a function of sample size, and it could very well be that significant test results in the post hoc normality assessment we conducted were obtained simply due to the sheer number of variables comprising each set of curves. Thirdly, current proposed methods for the evaluation of multivariate normality possess inherent limitations that make the assessment a challenging exercise (Mecklin and Munfrom, 2004). In any case, the issue of non-normal raw data distribution has not, to our knowledge, been mentioned in previous investigations utilizing PCA for analysis of biomechanical waveforms, nor have investigations been conducted to assess the effects of this violation of this assumption on subsequent results. As such, further exploration of this particular issue is warranted in the general use of PCA on biomechanical-derived waveforms.

On a related point, it should be noted that other data reduction techniques have been found to offer superior discriminatory capa-

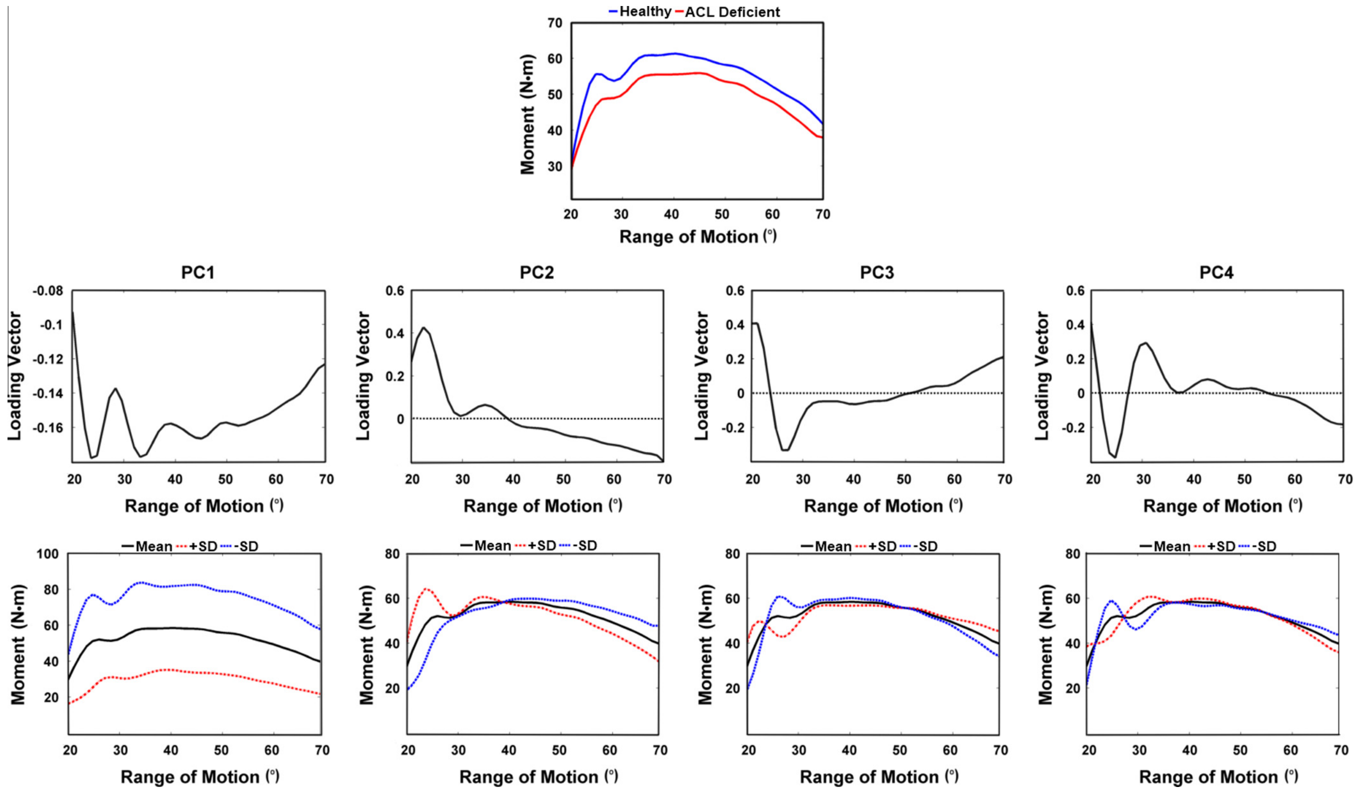

Fig. 4. Principal Component Analysis results of isokinetic knee flexion moment waveforms obtained at a testing velocity of 180°/s. 1st row: group mean moment waveform for the healthy (blue) and ACL deficient (red) knee. 2nd row: Loading vector plots of the PC of interest. 3rd row: Ensemble moment curve across all conditions ± 1 SD of the variation due to the PC loading vector shown in the 2nd row. Blue and Red SD curves correspond with Healthy and ACL deficient knees, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

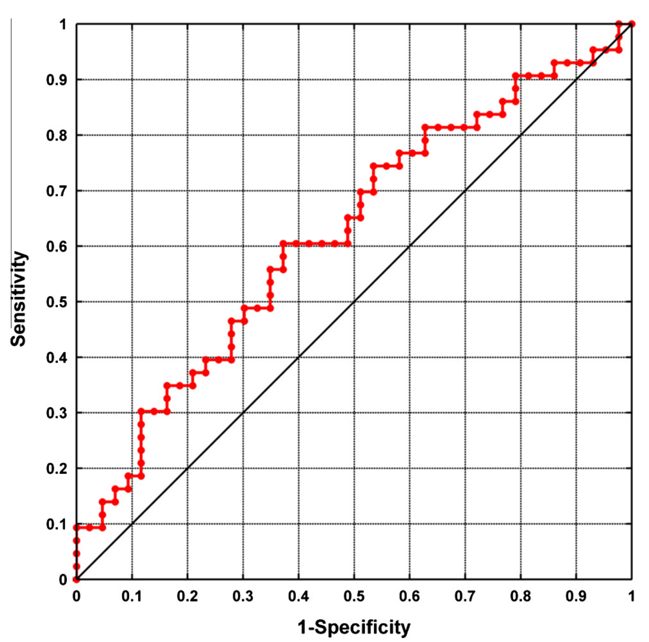

Fig. 5. Receiver operating characteristics curves for model designed to identify the injured knee. The optimal cut-off point for differentiating between the injured and healthy knee yielded a sensitivity of 60.5% and a specificity of 60.5%.

bilities in comparison with linear PCA in the analysis of biomechanical waveforms. For example, Wu et al. (2007) showed that application of kernel-based PCA (KPCA, a nonlinear feature extraction method) combined with support vector machines (SVM) learning algorithm improved classification accuracy of young and elderly gait patterns in comparison to application of linear PCA-based SVM. Thus, utilization of these and other methods (see review by Chau, 2001b) may be warranted in future investigations. However, note that unlike linear PCA, interpretations of biomechanical waveform features obtained from other dimensionality reduction methods (such as KPCA) are, to our knowledge, not as developed. Therefore, while discriminatory performance between the injured and non-injured knees may be improved, it may be difficult to associate clinical meaning with the discriminatory features.

In addition, several modifications may be warranted to the experimental protocol: Firstly, the bilateral comparison in unilateral ACL deficient patients, whilst common and easy to perform, may be disadvantageous since reductions in muscular strength capabilities may also be present in the healthy knee due to bilateral neural inhibition (Chmielewski et al., 2004; Konishi et al., 2003), or simply because of deteriorated muscular conditioning due to lack of participation in physical activity following the injurious incident. It may be that a discriminatory model developed using data obtained from ACL deficient patients and matched asymptomatic controls (which were not available to us at the time of publication) would be more sensitive to detection of strength curve abnormalities. This point is worthy of consideration since concentric knee moment waveforms obtained from healthy participants have been described to possess a distinct pattern with very little variation between participants, and also exhibit a high level of set-internal consistency (Ayalon et al., 2001; Almosnino et al., 2011). Thus, we contemplate that a family of curves obtained from healthy participants may form a multivariate distribution of scores which are clustered in very close proximity; thus potentially allowing for better discriminatory capabilities.

Secondly, isokinetic testing was performed utilizing only concentric contraction types, and arguably at the most common preset angular velocities reported for this patient population (Yüksel et al., 2011; Tsepis et al., 2004). The choice of this particular contraction mode these angular velocities is based on the following: First, there is an abundance of published data using these, hence allowing comparison of results across studies. Furthermore, it has been suggested that testing at 180°/s resembles knee angular velocities of several daily functional activities, and is recommended for performance earlier in the rehabilitative process (Wilk et al., 1994). In addition, it has been suggested that deficiencies in muscular strength capabilities seem to be more apparent at lower angular testing velocities in comparison to higher ones (Kellis, 2001), hence the performance of testing at 60°/s. However, a study by Zemach et al. (2009) revealed that in patients suffering from knee compromise (the majority involving the ACL), bilateral quadriceps muscular strength deficiencies as quantified by the PM were most apparent when examined eccentrically, and that these deficiencies were not dependent on the angular velocity prescribed. In so far as future considerations, it thus may be of value to try to differentiate between the involved and uninvolved knees utilizing data collected during performance of eccentric contractions. With regards to the choice of angular velocity, it should be noted that an increase in the testing velocity will inherently result in a decreased number of data points comprising each curve for a given ROM and sampling frequency. The effect of this may be a loss of potentially useful information. Given this, as well as the aforementioned indications in Zemach et al. (2009), it may be that testing at lower velocities than those employed in the current investigation may be advantageous for discriminatory purposes.

Thirdly, notwithstanding the possibility of PC comparisons not reaching statistical significance level due to a small sample size, another potentially impeding factor in our study is that our sample may be considered heterogeneous in terms of: sex, age, time since injury, physical activity status, and the presence of other concurrent pathologies. This heterogeneous sample may have contributed to large between-participant variation in waveform shapes obtained from both legs, which ultimately resulted in score distribution overlap that limited our model's sensitivity and specificity values. It is arguable that the ability to construct a decision rule that accounts for these possibly confounding variables is advantageous in the sense that the decision rule would be more practically applicable to the patient populations seen in some hospitals. However, given the lack of success in the current study, perhaps there is a need to construct decision rules for specific populations (e.g. female college athletes; military trainees; recreational adult male athletes, and perhaps sub samples of these, such as those with chondral lesions or meniscal tears of varying severity and location). Admittedly, this would require a considerable investment of time and resources, and therefore addressing the previous comments related to testing and data analysis procedures may perhaps be favorable prior to implementation of such future studies.

Lastly, the validity of strength outputs is based on the assumption that the participants exerted maximal voluntary contractions (MVC) during testing. This issue may be of concern in ACL deficient participants since, in our experience, not only are the majority of patients unaccustomed to isokinetic task demands, but also may be apprehensive to exert MVCs due to fear of injury or pain aggravation. Although we made efforts to address this point by providing participants with specific instructions regarding the dynamometers operation, and both a general and specific warm-up (including performance of maximal efforts), it is possible that altering the testing protocol to enhance the participants' motivation, confidence, or familiarity with the isokinetic testing on an individual basis might result in muscle contractions that are closer to a "true" MVC.

In conclusion, the discriminatory model constructed in this study enabled only limited clinical usefulness in discerning between the ACL deficient and contralateral, healthy knee. Improvement in discrimination capabilities may perhaps be achieved by consideration of additional control groups, different testing speeds and contraction modes, as well utilization of other data analysis techniques. At the current stage, clinical judgement regarding the level of effort exerted during testing is largely reliant on subjective observations of participant behavior as well as qualitative analysis of the isokinetic moment–time series. Thus, providing clinicians with more objective criteria regarding the level of effort is also an issue that is need of exploration.

Conflict of interest

Sivan Almosnino's current affiliation is with Research Environmental Associates Ltd. (REA), a private health and safety company based out of Markham, ON. The research was done as part of Dr. Almosnino's graduate studies at Queen's University, and this manuscript is not and was not funded by the company. As such, the authors declare that they do not have any financial or personal relationships with other people or organizations that could inappropriately influence the manuscript.

Disclosure

Excerpts of this investigation have been presented at the 9th Annual Ontario Biomechanics Conference, March, 16–18, 2012, Barrie, ON, Canada and at the 17th biannual Canadian Society of Biomechanics Conference, June 6–9, 2012, Vancouver, BC, Canada.

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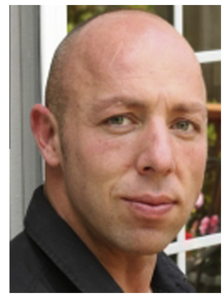

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