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Phase-dependent changes in local dynamic stability during walking in elderly with and without knee osteoarthritis

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ABSTRACT

Previously, we reported reduced time-averaged knee local stability, in the unaffected, but not the affected leg of elderly with knee osteoarthritis OA compared to controls. Since stability may show phase-related changes, we reanalyzed the dataset reported previously using time-dependent local stability, $\lambda(t)$, and also calculated time-averaged local stability, λ_s, for comparison.

We studied treadmill walking at increasing speeds, focusing on sagittal plane knee movements. 16 patients, 12 healthy peers and 15 young subjects were measured. We found a clear maximum in $\lambda(t)$ (i.e. minimum in stability) at around 60% of the stride cycle (StanceMax $\lambda(t)$), a second clear maximum (SwingMax $\lambda(t)$) at around 95% followed by a minimum between 70% and 100% (SwingMin $\lambda(t)$).

StanceMax $\lambda(t)$ of both legs was significantly higher in the OA than the young control group. Values for healthy elderly fell between those of the other groups, were significantly higher than in young adults, but there was only a trend towards a significant difference with the StanceMax $\lambda(t)$ of the OA group's affected side. Time-averaged and time-dependent stability measures within one leg were uncorrelated, while time-dependent stability measures at the affected side were inversely correlated with λ_s at the unaffected side.

The results indicate that time-dependent local dynamic stability might provide a more detailed insight into the problems of gait stability in OA than conventional averaged local dynamic stability measures and support the notion that the paradoxical decline in unaffected side time-averaged local stability may be caused by a trade-off between affected and unaffected side stability.

1. Introduction

One of the most pervasive threats to mobility in elderly is knee osteoarthritis (OA). With the aging of the population and the increasing incidence of obesity (Lawrence et al., 2008; Murphy et al., 2008), the prevalence of knee OA, and consequently burden on the society is rising. Among adults in western populations, knee OA is one of the most frequent causes of pain, loss of function and disability (Carmona et al., 2001; Van Saase et al., 1989).

Self-reported instability of the knee is one of the symptoms in knee OA, especially in the advanced stages of the disease (Knoop et al., 2012) and has negative functional implications (Felson et al., 2007; Fitzgerald et al., 2004; Schmitt and Rudolph, 2007). Buckling, giving way (Felson et al., 2007), and varus thrust are common signs that bother patients with knee OA (Chang et al., 2004). While the importance of self-reported instability is well accepted by researchers and clinicians, there is still no consensus about objective, accurate and reliable ways to measure "true" dynamic stability of the knee. One approach is to evaluate knee function by means of dynamic tests (hop tests, jump tasks, side-cutting maneuvers, etc.) (Fitzgerald et al., 2001; Reid et al., 2007). Such dynamic tests however have the problem that they reflect "knee stability" indirectly, and are influenced by other factors such as muscle strength, jump capacity, and familiarity with the task. Moreover, it is difficult and often impossible to perform these tests in older people or in subjects just after surgery (e.g., ACL reconstruction).

Another approach is through passive knee joint laxity measures (Hertling and Kessler, 1983). In spite of ample clinical application,

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it has been reported that self-reported knee instability is not directly associated with medial laxity (Schmitt et al., 2008). However, the direct effects of static laxity on functional abilities and perception of stability during activities of daily life appear to be relatively limited (Engström et al., 1993; Harilainen et al., 1995; Van der Esch et al., 2006; Walla et al., 1985). Similar results were reported in populations other than knee OA. For instance studies on individuals with anteriar cruciate ligament (ACL) deficiency revealed that in some patients, no symptoms of self-reported knee instability were reported, in spite of increased anterior knee laxity (Ciccotti et al., 1994; Fitzgerald et al., 2000; Lephart et al., 1989; Rudolph et al., 2001).

Given the limitations of the above methods to capture knee stability, researchers continue to look for variables that capture dynamic stability during tasks such as walking. One of the most accepted ones is the local divergence exponent (λ_s). The local divergence exponent measures the rate of divergence after small perturbations, and thus assesses the stability of a movement pattern (Bruijn et al., 2013; Dingwell and Cusumano, 2000). Positive values of λ_s indicate instability, with higher values indicating higher instability. Usually, λ_s is estimated as an average across the gait cycle, which limits the assessment of possible variations in the instantaneous state space divergence (Ihlen et al., 2012a). However, according recent studies, local stability changes within a stride cycle, especially during the transitions between single and double support phases (Ali and Menzinger, 1999; Ihlen et al., 2012b; Norris et al., 2008).

In a previous study of our group, a significantly higher λ_s of knee kinematics (i.e. decreased stability) was reported in a group of knee OA patients at their unaffected side compared to their healthy peers, while no difference was present at the affected side (Fallah Yakhdani et al., 2010). Fallah Yakhdani et al. explained their findings as a compensatory strategy that patients used in order to reduce the kinetic demands on the affected leg, which consequently led to a higher unaffected λ_s. This hypothesis may be tested by looking into changes of λ_s over the gait cycle. More to the point, the new method of time-dependent local dynamic stability $\lambda(t)$, which is sensitive to state space divergence changes within a stride cycle, may be a better tool to look into the phase-related variation than the conventional λ_s (Ihlen et al., 2012a).

Thus the current study aimed to reanalyze the dataset reported previously by Fallah-Yakhdani et al. (2010) using phase-dependent stability measures. We hypothesized that knee stability would be different for different phases during the stride cycle, and that these differences might explain why previously we found instability only in the unaffected leg in knee OA. Since we previously calculated time averaged λ_s based on a state-space built from time delayed copies, which cannot be used when calculating time-dependent $\lambda(t)$, we also recalculated time averaged $\lambda_{s.}$

2. Patients and methods

The data set reported by Fallah-Yakhdani et al. (2010) was reanalyzed for the current study. 16 subjects with unilateral knee osteoarthritis (age, 62.3 ± 10.7 years) waitlisted for unilateral total knee arthroplasty were recruited from 2 university hospitals. In addition, 12 healthy (62.0 ± 12.6 years), age and BMI matched elderly and 15 healthy young subjects (22.9 ± 3.9 years) were recruited. Each subject signed an informed consent and the protocol was approved by the medical ethical committee of the VUmc.

All three groups were asked to walk on a treadmill (Bonte Technology, Culemborg, The Netherlands) at 6 different walking speeds, from 1.4 to 5.4 km/h (increments of 0.8 km/h). At each speed, subjects walked for 4-minutes, of which the last 2 minutes were recorded. Gait kinematics were measured using an opto-electric system, OptoTrak™ (Bruijn et al., 2013) (Northern Digital, Waterloo, Ontario, Canada), with two 3-camera arrays. Clusters of 3 markers (Infrared Light Emitting Diodes), fixed on light metal plates, were attached to the thighs, shanks, and heels with neoprene bands. A range of walking speeds was applied as it has been reported that stability is speed dependent (Bruijn et al., 2009; Dingwell and Marin, 2006).

The subjects were informed about their right to stop the measurement whenever they wanted, in such a case the treadmill belt was stopped and the last speed was recorded as the highest speed for that subject.

To assess knee symptoms and function, subjects filled in the Western Ontario and McMaster Universities osteoarthritis index (WOMAC). A Dutch version of WOMAC was used, which is a reliable and valid instrument for avaluation of pain and physical functioning in OA patients (Roorda et al., 2004). By way of clinical characterization of the subjects, we included “pain”, “stiffness”, and “physical function” subscales of the WOMAC.

2.1. Data analysis

2.1.1. Pre-processing

Gait events (i.e. foot-strike and foot off) were calculated from the foot cluster marker trajectories. Heel strikes were inferred from the minimum vertical position of the heel markers; stride time was calculated as the average time difference between consecutive ipsilateral foot-strikes. Shank and thigh segment orientations were calculated and the sagittal plane angles of these segments were expressed as rotations around the transverse axis. Subsequently, angular velocities were calculated by taking the derivatives of the obtained angles. Next, to calculate phase dependent stability, the first 40 strides of each time series were selected, and normalized to $40 \times 100 = 4000$ data points, while maintaining temporal variability between strides (Bruijn et al., 2009). Four-dimensional state spaces of knee motion were then made using the sagittal plane angle and angular velocity time series of the thigh and shank segments (Note that in using phase dependent stability, one can not use delay-embedding, as this would cause “mixing” of the phases) (Ihlen et al., 2012a). Next, for each data point that was at heelstrike, the nearest neighbor was found (i.e. the point with minimal Euclidean distance to that point), and the distance between these points was calculated and tracked for 100 samples (i.e. one stride) over time. Next, the mean of the logarithm of these curves was taken, to create a curve of divergence over a stride. These curves were then filtered, with a 2nd order 5 Hz low pass dual pass butterworth filter, after which the derivative with respect to time was calculated, resulting in a time series of local divergence exponents. Positive values imply divergence, that is, instability, with higher positive values revealing more instability. After inspection of these curves, we found a clear maximum between 40% and 70% (StanceMax $\lambda(t)$), and a second clear maximum (SwingMax $\lambda(t)$) followed by a minimum between 70% and 100% (SwingMin $\lambda(t)$). These maximum and minimum values were extracted from the third stride in the divergence curve, since in the first stride(s), and used for statistical analysis (Fig. 1). We also calculated time-averaged λ_s from the same state-spaces using Rosensteins algorithm (Bruijn et al. 2013; Rosenstein et al., 1993; Stenum et al., 2014).

All analysis was done using Custom-made MATLAB 7.14.0 (The MathWorks, Natick, MA) programs.

As not all patients could walk at all speeds, we used General Estimating Equations (GEE) (Liang and Zeger, 1986), which is a technique capable of dealing with missing values. GEEs for time-averaged λ_s, StanceMax $\lambda(t)$, SwingMax $\lambda(t)$, and SwingMin $\lambda(t)$ were calculated with Speed as covariate and Group as factor. When there was a significant effect, or interaction with, Group, the

Least Significant Difference (LSD) post-hoc test was used to perform a pairwise comparison of the three groups. Non-significant interactions were left out. For the patient group, the analysis was done for their affected and unaffected leg separately (and later separate GEE's for the difference between the legs were performed), while for the controls, the average of the two sides was used.

Relations between time-averaged λ_s and time dependent measures of stability (StanceMax $\lambda(t)$, SwingMax $\lambda(t)$, SwingMin $\lambda(t)$), were assessed with partial correlation coefficients corrected for speed for the affected and unaffected legs of the patient group. A significance level of $P < 0.05$ was used for all tests.

3. Results

The two elderly groups were comparable in age, height, weight, and BMI (Table 1). The number of subjects included for analysis, in each group for each speed, is shown in Table 2. Subjects' data were excluded if there were not enough strides for that speed, or if the data quality was low.

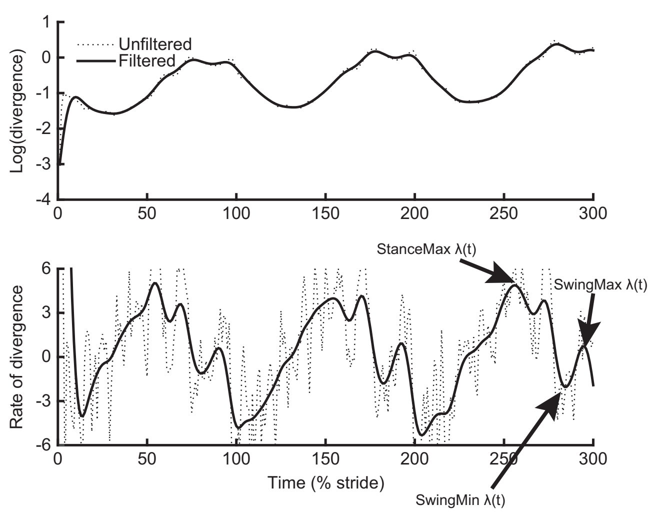

Fig. 1. (A) Example of a divergence curve with divergence starting from heelstrike. Dotted lines represent unfiltered data, solid filtered data. (B) $\lambda(t)$ calculated from the unfiltered (dotted) and filtered (solid) data presented in A. Area's were values for statistical analysis were extracted are indicated by arrows.

3.1. Time-averaged stability

While results on λ_s (see Fig. 2, compared to Fig. 2 in Fallah Yakhdani et al., 2010)), were qualitatively similar as reported previously, there were some quantitave differences, most likely due to the different state spaces used. In the current study, there was a significant Speed × Group interaction for analyses with affected and unaffected sides (Table 3), indicating that healthy elderly showed a steeper decrease in time-averaged λ_s with increasing speed, compared to young controls (Table 3). Time-averaged λ_s showed no significant difference between the three groups neither for the affected, nor for the unaffected side (Table 3). Comparing the two sides of the patients group, there was a trend towards significantly higher value of time-averaged λ_s at the unaffected side compared to the affected side ($p=0.066$).

4. Time dependent stability

On the affected side, patients, had a higher (indicating lower stability) StanceMax $\lambda(t)$ compared to young controls (Table 3) and a trend towards being significantly higher compared to their healthy peers (Table 3 and Fig. 3). StanceMax $\lambda(t)$ was also significantly higher for the unaffected side of the OA patients, when compared to the young controls ($p < 0.001$), but not when compared to healthy elderly. Healthy elderly had a significantly higher StanceMax $\lambda(t)$ than young controls ($p < 0.001$).

SwingMax $\lambda(t)$ at both affected and unaffected sides showed no significant difference between the three groups (no main effect of Group or Group × Speed interaction).

Regarding SwingMin $\lambda(t)$, there was a significant Speed × Group interaction (Table 3), indicating that healthy elderly showed a steeper decrease in the SwingMin $\lambda(t)$ with increasing speed, compared to young controls. There was also a significant effect of Group at both affected and unaffected sides for SwingMax $\lambda(t)$ and post-hoc analysis identified that SwingMax $\lambda(t)$ was significantly lower for the healthy elderly group compared to the young controls.

Separate GEE comparing the affected and unaffected sides in the OA group showed no significant differences between the two

Table 1
Subjects' characteristics.

Groups	Patients ($n=16$)	Healthy Elderly ($n=12$)	Young controls ($n=15$)	*P* value			
Basic characteristics							
Age (years)[a]	62.3 (10.7)	62.0 (12.6)	22.9 (3.9)	0.95			
Height (cm)[a]	169.7 (11.6)	171.7 (10.2)	173.5 (8.3)	0.64			
Weight (kg)[a]	85.9 (16.4)	86.9 (17.2)	66.7 (9.4)	0.88			
BMI (kg/m^2)[a]	29.7 (4.1)	29.4 (4.9)	22.1 (1.5)	0.85			
Gender (M/F)	5/11	4/8	5/10				
Clinical characteristics					**Post-hoc *P* value**		
					Patients vs. elderly	**Patients vs. young controls**	**Elderly vs. young controls**
WOMAC Pain Score[b]	2.35 (0.21)	0.09 (0.07)	0.01 (0.01)	< **0.001**	< **0.001**	< **0.001**	0.35
WOMAC Joint Stiffness Score[b]	2.56 (0.27)	0.23 (0.18)	0.03 (0.03)	< **0.001**	< **0.001**	< **0.001**	0.35
WOMAC Physical Activity Score[b]	2.3 (0.19)	0.07 (0.05)	0.00	< **0.001**	< **0.001**	< **0.001**	0.09

OA = osteoarthritis; BMI = Body mass index.

[a] Data are presented as mean (SD). The *P* value corresponds to an ANOVA comparing the two elderly groups.

[b] Data are presented as mean (SD). The *P* value corresponds to Kruskal–Wallis test (with post-hoc tests) comparing the three groups.

Table 2
Reasons for exclusion of trials and total number of subjects included in analysis per speed level.

	Speed (km/h)	Unable	**Unaffected leg**			**Affected leg**		
			< 40 strides	Data quality	**Total included**	< 40 strides	Data quality	**Total included**
Patients	1.4	0	2	2	**12**	2	1	**13**
	2.2	5	4	2	**5**	4	2	**5**
	3	7	1	1	**7**	1	2	**6**
	3.8	7	1	3	**5**	1	2	**6**
	4.6	9	2	1	**4**	1	2	**4**
	5.4	11	1	2	**2**	1	3	**1**
Control	1.4	0	0	1	**11**			
	2.2	0	1	1	**10**			
	3	0	1	1	**10**			
	3.8	0	0	2	**10**			
	4.6	0	0	2	**10**			
	5.4	1	0	3	**8**			
Young	1.4	0	0	0	**15**			
	2.2	0	0	0	**15**			
	3	0	0	0	**15**			
	3.8	0	0	0	**15**			
	4.6	0	0	0	**15**			
	5.4	0	0	1	**14**			

Unable = subject was unable to walk at given speed.

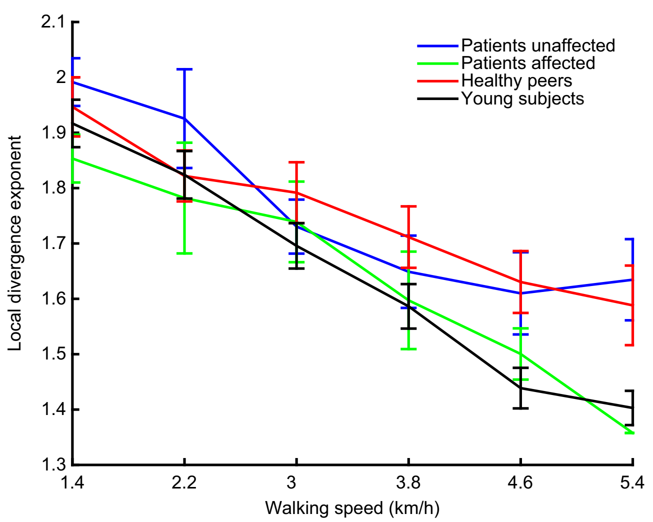

Fig. 2. Mean values of λ_s for the affected and unaffected leg of patients, healthy controls and young controls, at all speed levels. Error bars represent standard deviations.

sides regarding the four variables, but only revealed a significant interaction of Side × Speed for SwingMax $\lambda(t)$ (p=0.019), revealing that the SwingMax $\lambda(t)$ increased more on the Subjects' affected side with increasing speed, compared to the unaffected side.

5. Partial correlations

For the ipsilateral legs, the time-averaged λ_s values were not correlated to the time-dependent stability measures StanceMax $\lambda(t)$, SwingMax $\lambda(t)$, and SwingMin $\lambda(t)$ (Table 4). However, time-averaged λ_s of the unaffected leg was negatively correlated to StanceMax $\lambda(t)$ and SwingMax $\lambda(t)$ and positively correlated with SwingMin $\lambda(t)$.

StanceMax $\lambda(t)$ and SwingMax $\lambda(t)$ were significantly or tended to be negatively correlated to SwingMin $\lambda(t)$ within the same leg and finally StanceMax $\lambda(t)$ and SwingMax $\lambda(t)$ were positively correlated between legs (Table 4).

6. Discussion

The main aim of the present study was to assess whether differences in knee stability across the gait cycle could explain our earlier seemingly contradictory findings that subjects with knee OA had lower knee stability on their unaffected side. Our hypothesis was partially confirmed, that is, OA patients showed lower knee stability compared to the young control group on both sides and a tendency towards a lower knee stability compared to healthy elderly on the affected side, between 40% and 70% of the stride cycle (StanceMax $\lambda(t)$).

The results on λ_s that we reported here are quantitatively different from those of Fallah Yakhdani et al. (2010). Nonetheless, qualitatively, results appear similar, and correlations between the previous estimates of λ_s and our current estimates are high. Most importantly, as previously, λ_s tended to be higher for the unaffected leg than for the affected leg in OA patients, a finding that is rather surprising, and that we sought to better understand in this study. Fallah-Yakhdani et al. argued that the findings for the unaffected side, might be the result of an adaptation that these patients make in order to ease the kinetic demands on the affected side (Mandeville et al., 2008). The negative correlations between time-averaged λ_s and StanceMax $\lambda(t)$ found here suggest that the patients may be compromising the unaffected side's stability for the stability of the affected side. Interestingly, time dependent measures were not correlated to time averaged values within the same leg, suggesting that these measures really contain different information. In addition, the time dependent stability measures showed patterns that were more logical from a clinical point of view (i.e. higher instability in the affected leg, albeit non-significant). These findings suggest that time dependent measures of stability may provide more sensitive information about stability.

We found negative correlations between SwingMin and StanceMax within the same leg (amplitude of the time-dependent lamba increases), which suggests that fast divergence in stance phase is compensated by fast convergence in swing phase.

The Maximum value of $\lambda(t)$ was observed around 60% of the stride cycle, which is known to be the transition from the stance phase to the swing phase of the same side (also known as the weight transfer phase). Similar intra-cyclical changes during weight transfer were reported by Ihlen et al. (2012a, 2012b) with a higher maximum for healthy older adults compared to youngs

Table 3
Regression coefficients (B) from GEEs on λ(t) with Speed as covariate (from 0.39 through 1.50 m/s), and Group as factor (young controls, knee OA patients, and healthy elderly), separately for the patients' affected and unaffected leg.

	Group	*post-hoc*			Speed	Speed × group	P
	P	***OA* vs. *HE***	***OA* vs. *Y***	***Y* vs. *HE***	**P**	**P**	
Affected leg							
Time-averaged λ_s	0.741				< **0.001**	**0.002**	**OA vs. Y**: 0.514 **OA vs. HE**: 0.079 **HE vs. Y**: **0.001**
StanceMax $\lambda(t)$[a]	< **0.001**	0.072	< **0.001**	< **0.001**	< **0.001**		
SwingMax $\lambda(t)$[b]	0.597				< **0.001**		
SwingMin $\lambda(t)$[c]	**0.002**	0.676	0.208	**0.039**	< **0.001**	**0.045**	**OA vs. Y:** 0.884 **OA vs. HE:** 0.174 **HE vs. Y: 0.013**
Unaffected leg							
Time-averaged λ_s	0.583				< **0.001**	**0.003**	**OA vs. Y**: 0.273 **OA vs. HE**: 0.238 **HE vs. Y**: **0.001**
StanceMax $\lambda(t)$	< **0.001**	0.245	< **0.001**	< **0.001**	< **0.001**		
SwingMax $\lambda(t)$	0.838				< **0.001**		
SwingMin $\lambda(t)$	< **0.001**	0.241	0.399	**0.038**	< **0.001**	**0.029**	**OA vs. Y:** 0.129 **OA vs. HE:** 0.626 **HE vs. Y: 0.014**

The bold *p*-values are significant according to the least significant difference.
OA = Osteoarthritic patients; HE = Healthy elderly; Y = young controls.

[a] Maximum value of $\lambda(t)$during the late stance.
[b] Maximum value of $\lambda(t)$during the swing phase.
[c] Minimum value of $\lambda(t)$ during the swing phase.

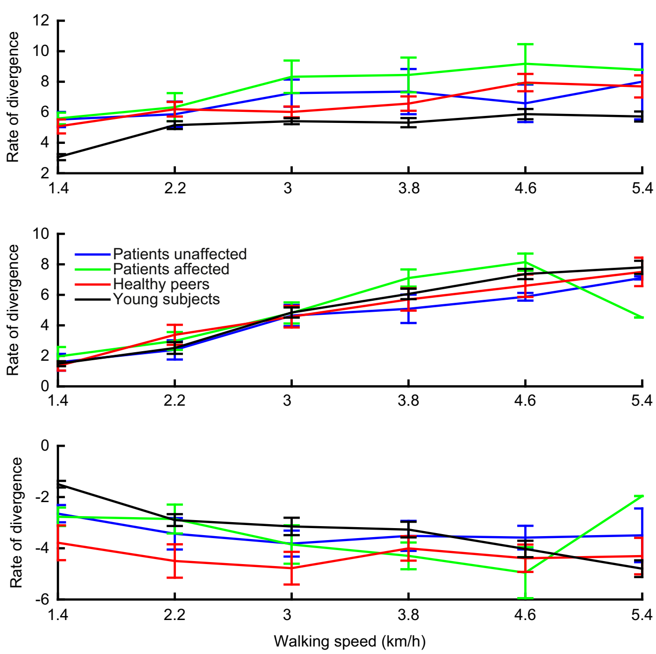

Fig. 3. Mean values of (A) StanceMax $\lambda(t)$, (B) SwingMax $\lambda(t)$, and (C) SwingMin $\lambda(t)$ for the affected and uaffected leg of the patients, healthy controls and young controls, at all speed levels. Error bars represent standard deviations.

controls. Hubley-Kozey et al. (2009) reported a reduced push-off burst of gastrocnemius activity during gait in severe OA patients. Considering that the OA patients who participated in the current study were suffering from severe knee OA, the absence of proper gastrocnemius activity prior to toe-off might be an explanation for the observed higher instability during weight transfer in this study. Interestingly, a recent paper (Kim and Collin, in press) showed that by manipulating push off, stability could be either increased or decresed, thereby suggesting and important role for push-off in maintaining a stable gait. In addition, a recent modeling study (Fu et al., 2014) showed that an otherwise unstable limit cycle model could be stabilized by including intermittent control in the form of a push-off burst. Altogether, these findings highlight the importance of transition from the stance phase to the swing phase in gait stability. However, why this would show up as an unstable phase remains somewhat unclear.

The current study was able to objectively quantify and more specifically pinpoint the local dynamic instability within a stride during walking. These findings lead us to conclude that a decreased stability of knee movement in the sagittal plane was found in OA, but the fact that the instability was also increased at the unaffected side, puts into question whether this is a specific impairment of gait in the knee OA group or a more generic effect also present to some extent in the healthy elderly (Fallah Yakhdani et al., 2010; Sharma et al., 2003).

7. Limitations

This study has several limitations. First, it has been reported that the statistical precision of estimates of λ_s depends on the number of strides projected into the state space (Bruijn et al., 2009) and this likely true also for $\lambda(t)$. But in the current study, to avoid excessive effort for patients, we used only 40 strides per speed level. Including six speed levels however, increases statistical precision, if effects are consistent across speeds.

Second, our methods differed in several aspects from the studies of Ihlen et al. First, we time normalized data before calculating divergence curves, to be able to calculate the mean rate of divergence as it is normally calculated. An analysis in which the divergence curves were normalized to the gait cycle did not yield different results. Second, our choice of state space is different from Ihlen's, as we choose to specifically investigate knee kinematics, and to remain as close to the Fallah Yakhdani paper as possible. This may have lead to somewhat different results, but checks on the location of the initial nearest neighbors indicated that our 4 Dimensions were sufficient.

Table 4
Partial orrelations, corrected for speed, between time-averaged λ_s and time dependent measures (StanceMax $\lambda(t)$, SwingMax $\lambda(t)$, and SwingMin $\lambda(t)$). Of the unaffected and affected legs of the patients.

	Unaffected				Affected		
	StanceMax $\lambda(t)$	SwingMax $\lambda(t)$	SwingMin $\lambda(t)$	λ_s	StanceMax $\lambda(t)$	SwingMax $\lambda(t)$	SwingMin $\lambda(t)$
Unaffected							
StanceMax $\lambda(t)$							
SwingMax $\lambda(t)$	0.197						
SwingMin $\lambda(t)$	**−0.631**	−0.266					
λ_s	−0.217	−0.202	0.232				
Affected							
StanceMax $\lambda(t)$	**0.485**	0.071	**−0.385**	**−0.344**			
SwingMax $\lambda(t)$	0.050	**0.580**	0.038	**−0.438**	0.117		
SwingMin $\lambda(t)$	**−0.332**	−0.055	0.202	**0.459**	**−0.378**	**−0.429**	
λ_s	−0.144	−0.004	0.296	**0.379**	−0.153	−0.229	**0.372**

Values printed in bold are significant at 0.05 level.

Finally, although the group size is comparable to other biomechanical OA papers, it is still relatively small, and final conclusions should be made with caution. However, findings are inspiring for further research in this area.

8. Conclusion

In conclusion, the present study used a new method to indentify the changes of local dynamic stability within a stride in a group of patients with knee OA and compared the results to healthy peers and a group of healthy young adults. The results indicate that time-dependent local dynamic stability might provide a more detailed insight into the problems of gait stability in OA than conventional averaged local dynamic stability measures. Its potential clinical relevance needs to be established in studies with larger samples.

Conflict of interest statement

None of the authors of this paper have any financial and personal relationships with other people or organizations that could inappropriately influence (bias) the presented work.

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